Health Information and Quality Authority

An tÚdarás Um Fhaisnéis agus Cáilíocht Sláinte

# Health technology assessment of chronic disease self-management support interventions

**16 December 2015**

*Safer Better Care*

# About the Health Information and Quality Authority

The Health Information and Quality Authority (HIQA) is an independent Authority established to drive high quality and safe care for people using our health and social care and support services in Ireland. HIQA's role is to develop standards, inspect and review health and social care and support services, and support informed decisions on how services are delivered. HIQA's ultimate aim is to safeguard people using services and improve the quality and safety of services across its full range of functions.

HIQA's mandate to date extends across a specified range of public, private and voluntary sector services. Reporting to the Minister for Health and the Minister for Children and Youth Affairs, the Health Information and Quality Authority has statutory responsibility for:

- **Setting Standards for Health and Social Services** – Developing person-centred standards, based on evidence and best international practice, for health and social care and support services in Ireland.
- **Regulation** – Registering and inspecting designated centres.
- **Monitoring Children's Services** – Monitoring and inspecting children's social services.
- **Monitoring Healthcare Quality and Safety** – Monitoring the quality and safety of health services and investigating as necessary serious concerns about the health and welfare of people who use these services.
- **Health Technology Assessment** – Providing advice that enables the best outcome for people who use our health service and the best use of resources by evaluating the clinical effectiveness and cost-effectiveness of drugs, equipment, diagnostic techniques and health promotion and protection activities.
- **Health Information** – Advising on the efficient and secure collection and sharing of health information, setting standards, evaluating information resources and publishing information about the delivery and performance of Ireland's health and social care and support services.

# Foreword

An estimated 30% of adults living in Ireland are affected by chronic diseases. These are long-term conditions that are managed rather than cured, and which are responsible for a significant proportion of premature deaths and healthcare utilisation. The burden of chronic disease is increasing in part due to an aging population, with estimates that the number of adults with chronic diseases will increase to 40% by 2020. Many of these chronic conditions can be prevented or delayed by reducing key risk factors such as smoking, obesity, excessive alcohol consumption, physical inactivity, hypertension and high cholesterol.

Self-management support interventions are any interventions that help patients to manage portions of their chronic disease or diseases through education, training and support. These include disease-specific interventions that are tailored to the condition, such as for example diabetes, and generic interventions that are not tailored for any specific disease or diseases and could in theory be used in populations with range of chronic conditions. Formal chronic disease self-management support is currently available in Ireland through a number of routes including through individual hospitals and clinical programmes in the HSE, and from organisations such as Arthritis Ireland and Diabetes Ireland. The optimal programme(s) that should be implemented and to whom they should be made available has not previously been assessed.

The purpose of this report was to examine the clinical and cost-effectiveness of both non-disease-specific and disease-specific self-management support interventions. Disease-specific interventions were evaluated for asthma, chronic obstructive pulmonary disease, diabetes and a number of cardiovascular diseases (stroke, hypertension, ischaemic heart disease and heart failure).

The health technology assessment (HTA) was requested by the Health Service Executive (HSE) to inform the development of a chronic disease self management support framework for the Irish health service. The assessment was carried out by an Evaluation Team from the HTA Directorate in HIQA. A multidisciplinary Expert Advisory Group was established to provide advice on the assessment.

HIQA would like to thank the Evaluation Team, the members of the Expert Advisory Group, and all those who contributed to the preparation of this report.

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Health Information and Quality Authority

# Advice to the Health Service Executive (HSE)

This health technology assessment (HTA) examined the clinical and cost-effectiveness of non disease specific (or generic) self-management support interventions for chronic diseases and disease-specific interventions for asthma, chronic obstructive pulmonary disease (COPD), diabetes (Type 1 and Type 2) and cardiovascular disease (stroke, hypertension, coronary artery disease and heart failure).

Broadly, self-management support interventions are any interventions that help patients to manage portions of their chronic disease, or diseases, through education, training and support.

The review of clinical effectiveness was restricted to self-management support interventions evaluated through randomised controlled trials in adult populations. Given the volume of literature available, the clinical effectiveness of self-management support interventions was evaluated using an 'overview of reviews' approach where systematic reviews were reviewed rather than the primary evidence. Systematic reviews were undertaken for each disease area. In the case of asthma, COPD, Type 1 and Type 2 diabetes, stroke and hypertension, these were undertaken as updates to a recent high quality review (PRISMS report) commissioned by the UK National Institute for Health Research that was published in 2014.

The cost-effectiveness of generic and disease-specific self-management support interventions was evaluated by undertaking systematic reviews of the available literature for each area.

General findings common across all the sections of this report are presented below. Specific advice in relation to the various generic and disease-specific interventions is outlined in the dedicated advice sections.

The general findings of this HTA, which precede and inform HIQA's advice, are as follows:

- A broad range of self-management and self-management support interventions exist which impacts on the clarity of what constitutes effective self-management support. The interventions described by the included studies were heterogeneous and frequently complex, comprising numerous components.
- This HTA considered evidence from over 2,000 randomised controlled trials as presented across 160 systematic reviews of clinical effectiveness. Evidence on

the likely cost implications and cost-effectiveness of self-management support interventions was considered from 181 costing and cost-effectiveness studies.

- Evidence of the clinical-effectiveness of chronic disease self-management support interventions provides a complex picture. An overview of reviews makes use of pooled clinical effectiveness data, sometimes across a large number of primary studies, and in many cases of heterogeneous data. While the pooled estimate may show limited effect, individual studies may show more or less effect. As with any intervention, there may be subgroups of patients that experienced greater treatment effect than others.
- Randomised controlled trials typically had small sample sizes and a short duration of follow-up, limiting the applicability and validity of the findings, and potentially failing to capture long-term benefits or to demonstrate if observed benefits could be sustained.
- Most economic analyses were conducted alongside these randomised controlled trials, limiting their ability to determine if observed savings could be sustained. The costing methodology and perspective adopted differed greatly between studies making it difficult to summarise and aggregate findings. Evidence of cost-effectiveness for a wide range of self-management support interventions in patients with chronic disease was generally of limited applicability to the Irish healthcare setting.
- International evidence suggests that most self-management support interventions are relatively inexpensive to implement. Reported costs vary according to the intensity of the intervention, but are typically low relative to the overall cost of care for the chronic disease in question. In some instances, the interventions resulted in modest cost savings through reduced healthcare utilisation. However, it is unclear if costs would be similar if programmes are rolled out to a larger population or if economies of scale might apply. Longer-term evidence is required to determine if benefits are sustained and if costs change over time. Although generally inexpensive on a per patient basis, the budget impact of these interventions could be substantial due to the large number of eligible patients.
- The individuals eligible for self-management support interventions are likely to experience high levels of multimorbidity whereby they have multiple chronic conditions, a number of which may be amenable to self-management. For people with multimorbidity, a coherent evidence-based approach that acknowledges their various conditions and how they interact is essential.
- Where chronic disease self-management support interventions are provided, it is critical that the implementation and delivery of the interventions are subject to

routine and ongoing evaluation. This would help to ensure that they are delivering benefits to patients, and allow the content and format of the interventions to be refined.

Based on these findings HIQA's advice to the Health Service Executive (HSE) is as follows:

Good evidence of effectiveness was found for certain chronic disease self-management support interventions, while limited or no evidence of effectiveness was found for others. The evidence for generic and the disease-specific interventions is presented in the following advice sections.

The HSE should prioritise investment in those interventions for which there is good evidence of clinical effectiveness. Where chronic disease self-management support interventions are provided, it is critical that an agreed definition of self-management support interventions is developed and the implementation and delivery of the interventions are standardised at a national level and subject to routine and ongoing evaluation.

Most interventions are relatively inexpensive to implement relative to the costs of treating chronic disease and, in some instances, can result in modest cost savings through reductions or shifts in healthcare utilisation. However, due to the numbers of eligible patients, the budget impact of these interventions may be substantial.

# Advice – Generic self-management support interventions

Generic self-management support interventions are those that can be used by any individual with one or more chronic diseases and are not tailored to support management of a specific chronic disease.

The key findings of this HTA in relation to generic self-management support interventions, which precede and inform HIQA's advice, are as follows:

- Based on 25 systematic reviews (362 randomised controlled trials), a wide variety of generic self-management support interventions was identified. These were broadly grouped as chronic disease self-management programmes (mainly the Stanford model), telemedicine, web-based interventions, complex interventions focussed on a single health outcome, and 'other' self-management support interventions.
- The majority of the literature retrieved for the chronic disease self-management programmes assessed the Stanford model. The evidence was of low to very low quality and was without long-term follow-up. No evidence was found of improvements in health care utilisation. Some evidence of short-term improvements in the patient-reported outcomes of self-efficacy, health behaviour (exercise) and health outcomes (pain, disability, fatigue and depression) were found for the chronic disease self-management programmes, primarily for the Stanford programme.
- Some evidence of improvements in healthcare utilisation, diet adherence, patient engagement, and self-reported health status was found in literature that assessed the impact of a range of self-management support interventions on a single health outcome; however, it is not possible to determine which types of intervention or components contributed to the positive results.
- Some evidence of improvements in outcomes was also found for other generic interventions, specifically for telephone-delivered cognitive behavioural therapy (health status), personalised care planning (depression), motivational interviewing (physical activity), and nurse-led interventions using the information-motivation-behavioural skills model (medication adherence).
- Limited evidence was found that web-based cognitive behaviour therapy can have a positive impact on psychosocial outcomes.
- Insufficient evidence was found to determine if:

  - computer-based chronic disease self-management programmes are superior to usual care or standard 'face to face' versions of the Stanford chronic disease self-management programme.
  - short-term improvements in activities of daily living and mobility observed with in-home care are sustained in the longer term.

- The optimal format of generic self-management support, the diseases in which it is likely to provide benefit, and the duration of effectiveness, if any, is still unclear.
- Based on 25 costing and cost-effectiveness studies, the economic literature was grouped into four main intervention types: chronic disease self-management programmes, telemedicine, web-based interventions and 'other' interventions. Evidence of cost-effectiveness was generally of limited applicability to the Irish healthcare setting.
- There is limited evidence of cost-effectiveness for generic chronic disease self-management support interventions. The most consistent evidence is for chronic disease self-management programmes, but potential benefits are dependent on how efficiently the programme is run, and there is no evidence regarding longer term cost savings.
- Chronic disease self-management and telephone-based telemedicine programmes are relatively cheap to implement, but the magnitude of any cost saving in terms of reduced healthcare utilisation is unclear. The short follow-up periods used in the included studies means that it is not possible to determine if any savings are sustained.
- Where reported, the cost of the generic self-management support interventions was low. Although generally inexpensive on a per patient basis, the budget impact will be sizeable if implemented for all eligible patients with chronic disease(s).

Based on these findings HIQA's advice to the Health Service Executive (HSE) is as follows:

Based on the available evidence, it is still unclear what the optimal format of generic self-management support interventions is, the diseases in which they are likely to provide benefit, and their duration of effectiveness, if any.

The reported cost of generic self-management support interventions is generally low on a per-patient basis. However, given the high prevalence of chronic diseases in Ireland, the budget impact could be very substantial if implemented for all eligible patients.

# Advice – Asthma

The key findings of this HTA in relation to asthma-specific self-management support interventions, which precede and inform HIQA's advice, are as follows:

- Based on 12 systematic reviews (90 randomised controlled trials), a range of self-management support interventions for asthma were identified. These focused primarily on patient education and use of written action plans with evidence also for behavioural interventions, complex interventions comprising a range of mainly education-based supports, and use of text messaging and the Chronic Care Model to improve treatment and medication adherence.
- Good evidence was found that self-management support interventions can improve quality of life, reduce hospital admissions and use of urgent and unscheduled healthcare.
- The optimal intervention format of self-management support is not clear, but should include education supported by a written asthma action plan as well as improved skills training including the use of inhalers and peak flow meters.
- Behavioural change techniques are associated with improved medication adherence and a reduction in symptoms.
- Based on 12 costing and cost-effectiveness studies, the economic literature was grouped into four main intervention types: education programmes, internet-based self-management support, telemedicine, and 'other' self-management support interventions.
- Limited evidence was found to suggest that:
    - self-management support education programmes, using a combination of individual and group sessions, may be at least cost-neutral in patients with mild to moderate disease.
    - nurse-led telephone review for patients with high-risk asthma is a relatively low cost intervention that may reduce costs by reducing healthcare utilisation, although evidence of effect in the included studies was mixed.

Based on these findings HIQA's advice to the Health Service Executive (HSE) is as follows:

Self-management support interventions for patients with asthma can improve quality of life, reduce hospital admissions and use of urgent and unscheduled healthcare. The optimal intervention format is not clear, but should include education supported by a written asthma action plan as well as improved skills training including the use of inhalers and peak flow meters.

Behavioural change techniques are associated with improved medication adherence and a reduction in symptoms.

Economic studies suggest that that education programmes, using a combination of individual and group sessions, may be at least cost-neutral in patients with mild to moderate disease. Limited evidence was found to suggest that nurse-led telephone review for patients with high-risk asthma is a relatively low cost intervention that may reduce costs by reducing healthcare utilisation, although evidence of effect in the included studies was mixed. Evidence to support the cost-effectiveness of other self-management support interventions is more limited or conflicting.

# Advice – Chronic obstructive pulmonary disease

The key findings of this HTA in relation to self-management support interventions for patients with chronic obstructive pulmonary disease (COPD), which precede and inform HIQA's advice, are as follows:

- Based on 16 systematic reviews (185 randomised controlled trials), a range of self-management support interventions for patients with COPD were identified. These included patient education and use of written action plans, pulmonary rehabilitation, telemedicine, complex self-management support interventions and outreach nursing programmes. Standard pulmonary rehabilitation comprises many aspects of chronic disease self-management support and hence is included here; however, interventions such as education, exercise and behavioural changes are also core components of pulmonary rehabilitation, so the boundary between the intervention types is ill-defined.
- Very good evidence was found that education is associated with a reduction in COPD-related hospital admissions with limited evidence found that it is associated with improvements in health-related quality of life. There is no evidence that action plans when used alone and in absence of other self-management supports reduce healthcare utilisation or lead to improvements in quality of life.
- Very good evidence was found that pulmonary rehabilitation, which includes exercise training, is associated with moderately large, clinically significant improvements in health-related quality of life and functional exercise capacity in people with COPD. Large variation in the design of pulmonary rehabilitation programmes makes it difficult to identify their optimal format.
- Good evidence was found that complex self-management support interventions (involving multiple components and, or multiple professionals with the intervention delivered by a variety of means) are associated with improvements in health-related quality of life. No evidence was found of a statistically significant benefit regarding mortality while there was limited evidence of reductions in health care utilisation. Although it is not clear which components of self-management support relate to these improvements, education and exercise seem to be effective.
- Some evidence was found that:
    - telemedicine as part of a complex intervention decreases healthcare utilisation, with no evidence found of an impact on mortality.
    - outreach nursing programmes improve health-related quality of life.

- Based on 27 costing and cost-effectiveness studies, the economic literature was grouped into five main intervention types: self-management support programmes, pulmonary rehabilitation, telemedicine, case management, and 'other' self-management support interventions.
- Evidence was found that:
    - self-management support education programmes could result in potential cost savings due to reduced healthcare utilisation in patients with moderate to severe disease, depending on the efficiency with which the programmes are run.
    - case management may be cost saving for selected groups of patients with severe disease.
- Limited evidence was found that pulmonary rehabilitation is cost-effective in patients with moderate to severe COPD disease.
- Evidence for the cost-effectiveness of telemedicine interventions is mixed, with more applicable evidence suggesting that telehealth monitoring is not cost-effective.
- The reported per-patient cost of self-management interventions varied according to the intensity of the intervention, but was typically low relative to the overall cost of care of these patients. Ireland has a high prevalence of COPD so the budget impact of implementing self-management support interventions for these patients is likely to be sizeable.

Based on these findings HIQA's advice to the Health Service Executive (HSE) is as follows:

Education is associated with a reduction in COPD-related hospital admissions with limited evidence of improvements in health-related quality of life.

Pulmonary rehabilitation, which includes exercise training, is associated with moderately large, clinically significant improvements in health-related quality of life and functional exercise capacity in people with COPD. Large variation in the design of pulmonary rehabilitation programmes makes it difficult to identify their optimal format.

Complex self-management support interventions (involving multiple components and, or multiple professionals with the intervention delivered by a variety of means) are associated with improvements in health-related quality of life with limited evidence of reductions in health care utilisation. It is unclear which components lead to these improvements, but education and exercise seem to be effective.

There is some evidence that telemedicine may result in reductions in healthcare utilisation and that outreach nursing programmes can lead to improvements in health-related quality of life.

Economic studies suggest that education programmes and case management may be cost saving for selected patients, depending on the efficiency with which the programmes are run. There is limited evidence that pulmonary rehabilitation may be cost-effective in patients with moderate to severe COPD disease.

The reported per-patient cost of self-management interventions varied according to the intensity of the intervention, but was typically low relative to the overall cost of care of these patients. The overall budget impact of self-management support interventions may be considerable due to the high prevalence of COPD in Ireland.

# Advice – Diabetes

The key findings of this HTA on self-management support interventions for adults with Type 1 and Type 2 diabetes, which precede and inform HIQA's advice, are as follows:

- For Type 1 diabetes, two systematic reviews were identified. These related to psychological self-management support interventions (11 randomised controlled trials) and structured diabetes education (15 randomised controlled trials).
- For adults with Type 1 diabetes:
    - Based on a single systematic review, there is no evidence of effectiveness of psychological treatments in improving glycaemic control and reducing psychological distress.
    - Based on a single systematic review of structured education programmes, there is very limited evidence that these interventions lead to improved outcomes of quality of life and episodes of severe hypoglycaemia.
- For Type 2 diabetes, based on 27 systematic reviews (347 randomised controlled trials), identified self-management support interventions were broadly grouped into education interventions, chronic disease self-management programmes, telemedicine and 'other' self-management support interventions.
- For adults with Type 2 diabetes, there is:
    - Very good evidence that education, including culturally-appropriate education, improves blood glucose control in the short term (less than 12 months).
    - Good evidence that behavioural interventions (specifically patient activation interventions which actively engage patients by promoting increased knowledge, confidence and, or skills for disease self-management) are associated with modest improvements in blood glucose control (HbA1C).
    - Good evidence that various forms of telemedicine are associated with improvements in blood glucose control in the short term. Some evidence that chronic disease self-management programmes are associated with small improvements in blood glucose control in the short term.
    - Evidence of improvements in blood glucose control for a diverse range of self-management support interventions and in particular educational

interventions which differ also in their frequency, intensity and mode of delivery.

- Based on the available evidence, it is not possible to provide clear recommendations on the optimal content and format of self management support for adults with Type 2 diabetes. Evidence suggests that various models of delivery may be equally effective. Impact on resource utilisation was not assessed in any of the reviews. Quality of life remained unaltered.
- Based on 38 costing and cost-effectiveness studies, the economic literature for Type 1 and Type 2 diabetes was grouped into three main intervention types: education programmes, telemedicine, and pharmacist-led programmes. The better quality studies used data from randomised controlled trials and then extrapolated lifetime benefits using one of a number of simulation models that predict outcomes based on risk-factors.
- The best economic evidence was found in support of self-management support education programmes with modelled results suggesting that the interventions are cost-effective relative to usual care.
- Based on limited evidence it is not possible to say if telemedicine interventions are cost-effective relative to usual care while there was insufficient evidence of adequate quality to consider the cost-effectiveness of pharmacist-led interventions.

Based on these findings, HIQA's advice to the Health Service Executive (HSE) is as follows:

There is very limited evidence that structured education programmes lead to improvements in quality of life and episodes of severe hypoglycaemia for adults with Type 1 diabetes.

There is very good evidence that education, including culturally-appropriate education improves blood glucose control in patients with Type 2 diabetes in the short term (less than 12 months).

There is good evidence that behavioural interventions are associated with modest improvements in blood glucose control (HbA1C).

There is good evidence that various forms of telemedicine are associated with improvements in blood glucose control in the short term.

There is some evidence of short term improvements in blood glucose control with chronic disease self-management programmes and for a diverse range of self-

management support interventions and in particular educational interventions which differ also in their frequency, intensity and mode of delivery.

Based on the available evidence, it is not possible to provide clear recommendations on the optimal content and format of self management support for adults with Type 2 diabetes. Evidence suggests that various models of delivery may be equally effective.

Economic studies suggest that education programmes may be cost-effective relative to usual care.

# Advice – Stroke

The key findings of this HTA in relation to self-management support interventions in post-stroke patients, which precede and inform HIQA's advice, are as follows:

- Based on 27 systematic reviews (228 randomised controlled trials), four broad types of self-management support intervention were identified. These focused on rehabilitation therapy (including general rehabilitation, virtual reality-based rehabilitation and telerehabilitation), self-management programmes, information provision and 'other' self-management support interventions.
- Good evidence was found that general rehabilitation therapy delivered in early stroke recovery has a positive impact on activities of daily living and extended activities of daily living. Virtual reality-based rehabilitation was found to improve upper limb function and activities of daily living when used as an add-on to usual care.
- Some evidence was found that:
    - information provision improves patient and carer knowledge of stroke, aspects of patient satisfaction, with small reductions (which may not be clinically significant) in patient depression scores.
    - stroke liaison emphasising education and information can have a positive impact on quality of life.
- Based on the available evidence, it is not possible to draw conclusions in relation to the effectiveness of:
    - self-management programmes delivered to post-stroke patients.
    - psychosocial interventions, motivational interviewing, lifestyle interventions, multidisciplinary care or family-orientated models of care.
- The identified economic literature was limited to four costing and cost-effectiveness studies relating to exercise-based programmes and computer-based rehabilitation therapy. The four included studies provided very limited evidence regarding the costs or cost-effectiveness of self-management programmes for post-stroke patients.

Based on these findings HIQA's advice to the Health Service Executive (HSE) is as follows:

The best evidence was found for general rehabilitation therapy which if delivered in early stroke recovery has a positive impact on activities of daily living and extended activities of daily living. Virtual reality-based rehabilitation improves upper limb function and activities of daily living when used as an add-on to usual care.

Some evidence was found that information provision can improve patient and carer knowledge of stroke and some aspects of patient satisfaction with some evidence that stroke liaison emphasising education and information can have a positive impact on quality of life.

Evidence regarding the clinical and cost-effectiveness of other self-management support interventions for post-stroke patients is more limited, or conflicting.

# Advice – Ischaemic heart disease

The key findings of this HTA in relation to self-management support interventions for adults with ischaemic heart disease, which precede and inform HIQA's advice, are as follows:

- Based on 14 systematic reviews (244 randomised controlled trials), five broad types of self-management support intervention were identified for patients with ischaemic heart disease. These focused on patient education, exercise, psychosocial or behavioural changes, home-based services or telehealth. Interventions such as education, exercise and behavioural changes are core components of cardiac rehabilitation, so the boundary between standard cardiac rehabilitation services and chronic disease self-management support is ill-defined.
- Good evidence of a statistically significant reduction in mortality was found for exercise programmes (including exercise-based cardiac rehabilitation) in suitable patient cohorts from studies with follow-up periods greater than 12 months. Exercise –based interventions are also associated with fewer rehospitalisations but inconsistent results have been reported for myocardial infarction rates.
- Some evidence was found that patient education programmes are associated with an improvement in interim outcomes such as smoking cessation and reduced blood pressure, but there is uncertainty about how long any such effect persists.
- Limited evidence was found:
    - to demonstrate the effectiveness of behavioural modification interventions, although some have reported positive effects on smoking cessation and symptom management.
    - that comparable home- and telehealth-based cardiac rehabilitation interventions achieve similar outcomes to centre-based interventions.
- Based on 15 costing and cost-effectiveness studies, the economic literature was broadly grouped into four main intervention types: cardiac rehabilitation, case management, telemedicine, and 'other interventions'.
- Compared with no rehabilitation, there is evidence that cardiac rehabilitation can create cost savings as a result of reductions in health care utilisation.
- It is not possible to draw conclusions in relation to the cost-effectiveness of telemedicine-delivered self-management support interventions and nurse-led case management programmes due to the heterogeneity of the interventions assessed and equivocal findings.

- The reported per-patient cost of self-management interventions varied according to the intensity of the intervention, but was typically low relative to the overall cost of care of these patients.

Based on these findings, HIQA's advice to the Health Service Executive (HSE) is as follows:

Exercise-based interventions (including exercise-based cardiac rehabilitation) can reduce mortality and rehospitalisations in selected patients with ischaemic heart disease. The optimal format of these interventions and the duration of effectiveness are still unclear. These interventions can result in modest cost savings through reductions or shifts in healthcare utilisation.

Some evidence was also found that patient education programmes are associated with an improvement in interim outcomes such as smoking cessation and reduced blood pressure. Evidence regarding the clinical and cost-effectiveness of other self-management support interventions for patients with ischaemic heart disease is more limited, or conflicting.

# Advice – Hypertension

The key findings of this HTA in relation to self-management support interventions for adults with hypertension, which precede and inform HIQA's advice, are as follows:

- Sixteen systematic reviews (240 randomised controlled trials) of the clinical-effectiveness of self-management support interventions were identified for inclusion in this overview of reviews. A diverse range of interventions was identified with the largest volume of evidence obtained for reviews where self-monitoring of blood pressure was the main intervention. The remaining reviews assessed a range of self-management support interventions.
- Good evidence was found that self-monitoring of blood pressure alone or using a range of additional support, including telemedicine, is beneficial in lowering systolic and diastolic blood pressure. However, the clinical significance and durability of the effect are unclear. Additional support seems to enhance the blood pressure lowering effect.
- There is limited evidence of effectiveness of patient education interventions when used alone in improving medication adherence or blood pressure control, but these may form an important part of more complex interventions.
- There is some evidence that a range of complex self-management support interventions (that is involving multiple components, multiple providers and modes of delivery) lead to improvements in blood pressure control. A patient-specific approach may be the most beneficial, involving components tailored to the individual patient with hypertension.
- Some evidence was found that:
    - community pharmacist interventions which include patient education can lead to reductions in systolic and diastolic blood pressure.
    - simplification of medication regimens improves adherence although the clinical significance of this effect may be small.
- Based on 14 costing and cost-effectiveness studies, the economic literature assessed a diverse range of interventions with the largest volume of evidence obtained for reviews where self-monitoring of blood pressure was the main intervention. The remaining reviews assessed a range of self-management support interventions. The available evidence was largely for patients with uncontrolled hypertension.
- The cost-effectiveness results were inconsistent across outcomes of ambulatory blood pressure, costs, and healthcare utilisation. In some studies, the

intervention had a positive effect; in others it was negative, relative to usual care. The cost per patient of delivering the interventions was generally low.

- The context of high levels of undetected hypertension and poor blood pressure control in Ireland must be considered when evaluating the applicability of the findings of this overview. There are substantial levels of unmet need for routine care in Ireland, which may impact the estimated incremental benefits of self-management support interventions for hypertension.

Based on these findings HIQA's advice to the Health Service Executive (HSE) is as follows:

Good evidence was found that self-monitoring of blood pressure alone or using a range of additional support, including telemedicine, is beneficial in lowering systolic and diastolic blood pressure, although the clinical significance and durability of the effect is unclear.

There is some evidence that a range of complex self-management support interventions (that is involving multiple components, multiple providers and modes of delivery) lead to improvements in blood pressure control. A patient-specific approach may be the most beneficial, involving components tailored to the individual patient with hypertension.

There is some evidence that community pharmacy interventions, which include patient education, may lead to improvements in blood pressure control.

Evidence regarding the clinical and cost-effectiveness of other self-management support interventions for patients with hypertension is more limited, or conflicting.

There are substantial levels of unmet need for routine care in Ireland that may impact the applicability of these findings and the potential incremental benefits of self-management support.

# Advice – Heart failure

The key findings of this HTA in relation to self-management support interventions for adults with heart failure, which precede and inform HIQA's advice, are as follows:

- Based on 20 systematic reviews (248 randomised controlled trials), five broad types of self-management support intervention were identified. These focused on patient education, psychosocial and behavioural interventions, exercise interventions, home visits, and telehealth (including telemedicine and structured telephone support). Interventions such as education, prescribed exercise and behavioural changes are core components of cardiac rehabilitation, so the boundary between standard cardiac rehabilitation services and chronic disease self-management support is ill-defined.
- Statistically significant reductions were reported for:
    - mortality for both telehealth interventions and home visit programmes in selected patients. However, there was a lack of consistency across reviews that examined these types of interventions, with some studies reporting no effect.
    - the rate of hospital readmissions for exercise interventions, home visit programmes and telehealth interventions.
- Limited evidence was found to support the effectiveness of patient education programmes or behavioural modification interventions.
- Despite the positive results that have been reported for telemedicine and structured telephone support interventions, concerns have been raised about these being considered the standard of care for the management of heart failure patients due to inconsistent findings across studies and a lack of understanding about which specific elements of the interventions contribute to the improved outcomes.
- Based on 46 costing and cost-effectiveness studies, the economic literature was grouped into five main intervention types: education, telemedicine, multidisciplinary care, disease management and 'other' self-management support interventions. The quality of the studies was generally poor, with only four identified as high-quality studies.
- Based on randomised controlled trials that showed improvements in health-related quality of life and reductions in healthcare utilisation, the majority of telemedicine interventions reported cost savings relative to usual care, although the interventions assessed were heterogeneous.

- Based on randomised controlled trials that showed reductions in healthcare utilisation, certain disease management and education programmes were found to be cost-effective or cost saving relative to usual care.
- The reported per-patient cost of self-management interventions varied according to the intensity of the intervention, but was typically low relative to the overall cost of care of heart failure patients.

Based on these findings, HIQA's advice to the Health Service Executive (HSE) is as follows:

Telehealth and home visit interventions are associated with reductions in mortality in selected patients with heart failure although the reductions in mortality were not consistently seen across all studies.

Exercise-based interventions (including exercise-based cardiac rehabilitation), telehealth and home visit interventions can reduce rehospitalisations in selected patients with heart failure over periods of six to 12 months.

Despite the positive results reported for telehealth interventions in some studies, concern has been raised about these being considered standard of care for the management of heart failure patients due to inconsistent findings across studies and insufficient information to identify which specific elements of the interventions contribute to improving outcomes.

Economic studies suggest that telemedicine, disease management and education interventions may be cost-effective or cost saving where they achieve reductions in healthcare utilisation or improvements in health-related quality of life.

Evidence to support the clinical and cost-effectiveness of other self-management support interventions is more limited.

# Executive summary

## I. Background

In December 2014, the Health Information and Quality Authority (HIQA) received a request from the Health Service Executive (HSE) to examine the clinical and cost-effectiveness of generic self-management support (SMS) interventions for chronic diseases and disease-specific interventions for chronic obstructive pulmonary disease (COPD), asthma, cardiovascular disease and diabetes.

## II. Terms of Reference

Following an initial scoping of the technology, the terms of reference for this assessment were agreed between the Authority and the HSE:

- To review the clinical and cost-effectiveness of generic chronic disease self-management support interventions.
- To review the clinical and cost-effectiveness of disease-specific chronic disease self-management support interventions, including:
    - asthma
    - chronic obstructive pulmonary disease (COPD)
    - diabetes (Type 1 and Type 2)
    - stroke
    - ischaemic heart disease
    - hypertension
    - heart failure.
- Based on this assessment, to advise on the optimal chronic disease self-management support interventions to be implemented by the HSE.

This HTA was conducted using the general principles of HTA and employing the processes and practices used by the Authority in such projects.

An Expert Advisory Group was established comprising representation from the HSE (Health and Wellbeing division and Integrated Care Programme for chronic disease, Nursing and Midwifery Planning and Development unit), patient organisations, national and international experts in chronic disease management, and clinical specialists. An evaluation team was appointed comprising internal Authority staff. A Public Health Specialist Registrar in the HSE and two additional external staff assisted with the systematic review and data extraction.

## III. Self-management support description

A broad range of self-management and self-management support definitions exist which may reflect the lack of clarity on what constitutes effective self-management support.

For the purpose of this review, the 2003 definitions of self-management and self-management support agreed by the US Institute of Medicine were used. Self-management was defined as 'the tasks that individuals must undertake to live with one or more chronic diseases. These tasks include having the confidence to deal with the medical management, role management and emotional management of their conditions'. Self-management support was thus defined as 'the systematic provision of education and supportive interventions by health care staff to increase patients' skills and confidence in managing their health problems, including regular assessment of progress and problems, goal setting, and problem-solving support'. Self-efficacy focuses on increasing an individual's confidence in their ability to carry out a certain task or behaviour, thereby empowering the individual to self-manage. Many self-management support interventions target self-efficacy to improve outcomes.

Self-management support interventions to enhance core self-management skills and improve self-efficacy can include different components (education, training, provision of information or equipment) delivered in a variety of formats such as, education programmes, telemedicine, health coaching and motivational interviewing. A range of delivery methods also exist such as group or individual, face-to-face or remote, professional or peer-led. These interventions can be generic or disease-specific. Generic self-management support interventions are not tailored for any specific disease and could, in theory, be used in populations with a range of chronic conditions, including those with more than one chronic disease.

Generic self-management supports and disease-specific self-management supports are currently provided in Ireland through a range of programmes. However, the efficacy of many of these programmes has not been evaluated at a national level, nor an assessment made as to the optimal programme(s) that should be implemented and to whom they should be made available. It is thought that self-management support interventions may be a worthwhile adjunct to best medical care to allow patients to take control of and manage portions of their own care. The cost of the intervention is predicted to be low relative to, for example, the potential resource savings associated with a reduction in the number of general practitioner (GP) visits, emergency department visits or hospitalisations. However, at present there is uncertainty regarding the benefits of self-management support interventions in the short and long term.

This uncertainty regarding the format of optimal self-management support presents an obstacle to informed decision making about the provision of this intervention in the Irish public healthcare system.

## IV. Methodology

This HTA examined the clinical-effectiveness of generic self-management support interventions for chronic diseases and disease-specific interventions for asthma, chronic obstructive pulmonary disease (COPD), diabetes (Type 1 and Type 2) and cardiovascular disease (stroke, hypertension, ischaemic heart disease and heart failure). The review of clinical effectiveness was restricted to self-management support interventions evaluated through randomised controlled trials in adult populations. Given the volume of literature available, the clinical effectiveness of self-management support interventions was evaluated using an 'overview of reviews' approach, where systematic reviews were reviewed rather than the primary evidence. Where existing high quality reviews were identified, these were updated rather than undertaking a new overview of reviews.

A search for systematic reviews evaluating generic chronic disease self-management support interventions was conducted in Pubmed, Embase and the Cochrane library up to February 2015. The PRISMS review commissioned by the UK National Institute for Health Research published in 2014 was used as a starting point for the systematic reviews for asthma, COPD, Type 1 and Type 2 diabetes, stroke and hypertension. For these diseases, this assessment includes an update to the PRISMS report with additional searches run in Pubmed, Embase and the Cochrane library from 2012 to 1 April 2015. The results of the updated search as well as the original PRISMS findings are reported.

A search for systematic reviews were run in Pubmed, Embase and the Cochrane library from 2009 to 1 April 2015 for the remaining diseases included in the Terms of Reference for this project (heart failure and ischaemic heart disease), but which were not assessed in the PRISMS report.

Data extraction and quality appraisal were conducted using the general principles of HTA and in accordance with national guidelines. The cost-effectiveness of generic and disease-specific self-management support interventions was evaluated by undertaking systematic reviews of the available literature for each of the disease categories. In tandem with the systematic review of clinical effectiveness, the search for economic evaluations was carried out in Pubmed, EMBASE and the Cochrane Library. The same search terms were used with the exception of terms for systematic review and meta-analysis. In place of these, search terms and filters for economic evaluations were applied. In addition, systematic reviews of self-management support interventions identified through the clinical effectiveness

search that included cost or economic outcomes were used to identify additional studies. The search was carried out up until 4 March 2015.

Data extraction and quality appraisal were conducted using the general principles of HTA and employing the processes and practices used by the Authority in such projects.

## V. Generic (non-disease specific) self-management support interventions

As noted, generic self-management support interventions are those that can be used by any individual with one or more chronic diseases and are not tailored to support management of a specific chronic disease. These interventions aim to enhance core self-management skills and improve self-efficacy. Generic interventions include the behavioural change chronic disease self-management programmes that focus mainly on improving self-efficacy such as the UK Expert Patients Programme (peer-led), the Flinders model™ (physician-led), and the generic version of the Stanford programme (peer-led).

Based on 25 systematic reviews (362 randomised controlled trials), a wide variety of generic self-management support interventions was identified. These were broadly grouped as chronic disease self-management programmes (mainly the Stanford model), telemedicine, web-based interventions, a range of self-management support interventions focussed on a single health outcome, and 'other' self-management support interventions.

The majority of the literature retrieved for the chronic disease self-management programmes assessed the Stanford model. The evidence was of low to very low quality and was without long-term follow-up. No evidence was found of improvements in health care utilisation. Some evidence was found of short-term improvements in the patient-reported outcome of self-efficacy and for short-term improvements in health behaviour (exercise) and health outcomes (pain, disability, fatigue and depression), primarily for the Stanford chronic disease self-management programme. Also compared were different modes of delivery for the intervention. Insufficient evidence was found to determine if computer-based chronic disease self-management programmes are superior to usual care or standard 'face to face' versions of the Stanford chronic disease self-management programme.

Based on systematic reviews and underpinning primary randomised controlled trials that were of limited quantity and quality, limited evidence was found that web-based cognitive behaviour therapy can have a positive impact on psychosocial outcomes.

Literature was found that assessed the impact of a diverse range of self-management support interventions targeting a single outcome (for example,

healthcare utilisation, quality of life, or diet adherence). Some evidence of improvements in healthcare utilisation, diet adherence, patient engagement, and self-reported health status was found, however it was not possible to determine which types of intervention or components of self-management support contributed to the positive results.

The category of 'other' self-management support interventions comprised a diverse range of other generic interventions. Some evidence of improvements in outcomes for telephone-delivered cognitive behavioural therapy (improvements in health status); nurse-led interventions using the information-motivation-behavioural skills model (improved medication adherence); with some evidence also that personalised care planning and motivational interviewing can have a positive impact on depression and physical activity, respectively. Short-term improvements in activities of daily living, instrumental activities of daily living and mobility were also observed with in-home care (defined as care predominantly in the patient's home that was curative, preventive or supportive in nature and aimed to enable clients to live at home). However, due to limited study follow-up it is not known if the effects are sustained in the longer term.

In summary, based on the available evidence for the clinical effectiveness of generic self-effectiveness interventions, the optimal format of generic self-management support, the diseases in which they are likely to provide benefit, and the duration of effectiveness, if any, is still unclear. Tailoring self-management support to a specific disease may be more beneficial as a patients' knowledge of their own disease is believed to be an essential component of self-management.

Based on 25 costing and cost-effectiveness studies, the economic literature for generic self-management support interventions was grouped into four main intervention types: chronic disease self-management programmes, telemedicine, web-based interventions and 'other' interventions. Limited evidence of cost-effectiveness for generic chronic disease self-management support interventions was found. The most consistent evidence was for chronic disease self-management programmes, but potential benefits were dependent on how efficiently the programme was run with no evidence found of longer term cost savings. Evidence of cost-effectiveness was generally of limited applicability to the Irish healthcare setting. The international literature suggests that chronic disease self-management and telephone-based telemedicine programmes are relatively cheap to implement, but the magnitude of any cost saving in terms of reduced healthcare utilisation is unclear. The short follow-up periods used in the included studies meant that it was not possible to determine if any savings were sustained. Where reported, the cost of the generic self-management support interventions was low. However, although generally inexpensive on a per patient basis, the budget impact would be sizeable if

access to generic self-management support interventions was implemented for all eligible patients with chronic disease(s).

## VI. Asthma

Asthma is a chronic inflammatory condition of the airways characterised by recurrent episodes of wheezing, breathlessness, chest tightness and coughing. Ireland has the fourth highest prevalence of asthma worldwide, affecting an estimated 450,000 people. At least one person dies from asthma every week in Ireland. Rates of hospitalisation and attendance at emergency departments in Ireland, as well as frequent use of unscheduled (out-of-hours) care indicate the suboptimal asthma control in the majority of patients.

Based on 12 systematic reviews (90 randomised controlled trials), a range of self-management support interventions for asthma were identified. The interventions were typically complex, that is involving multiple components and or modes of delivery of self-management support, but were typically based on patient education, skills training, and use of written action plans, with evidence also for behavioural interventions, text messaging and the Chronic Care Model to improve treatment and medication adherence.

Good evidence was found that self-management support interventions for patients with asthma can improve quality of life, reduce hospital admissions and use of urgent (emergency department visits) and unscheduled healthcare. The findings did not take consideration of the underlying risk of hospitalisations and urgent healthcare use as these were not reported in the systematic reviews, so it is not possible to quantify the absolute benefit of the interventions. Good evidence was also found that behavioural change techniques are associated with improved medication adherence and a reduction in symptoms. There was substantial heterogeneity in the format and intensity of the self-management support interventions, the study populations, study follow-up duration and assessed outcomes, which makes it difficult to formulate clear recommendations on the optimal intervention format of this self-management support. However, the evidence suggests that it should include education supported by a written asthma action plan as well as improved skills training including the use of inhalers and peak flow meters.

The economic literature for asthma-specific self-management support interventions was broadly grouped into four main intervention types: education programmes, internet-based self-management support, telemedicine, and 'other' self-management support interventions with a total of 12 costing and cost-effectiveness studies identified. Limited evidence was found to suggest that self-management support education programmes, using a combination of individual and group sessions, may

be at least cost-neutral in patients with mild to moderate disease. Similarly, limited evidence was found that nurse-led telephone review for patients with high-risk asthma (that is, with a history of frequent hospitalisations or emergency department visits) is a relatively low cost intervention that may reduce costs by reducing healthcare utilisation, although evidence of effect in the included studies was mixed.

The 2013 Irish Asthma Control in General Practice guidelines state that essential features to achieve guided self-management in asthma include: education and motivation, self-monitoring to assess control with educated interpretation of key symptoms, regular review of asthma control and a written action plan. Work by the HSE's National Clinical Programme for Asthma is underway to improve asthma management in Ireland. A national model of care for asthma is being finalised which includes self-management components and details a collaborative approach between primary and secondary healthcare professionals and patients to provide a safe, seamless patient experience within the heath system. The findings from this review support the inclusion of evidence-based asthma self-management support interventions in Ireland.

## VII. Chronic obstructive pulmonary disease

Chronic obstructive pulmonary disease (COPD) is a common preventable and manageable disease, characterised by persistent airflow limitation. The clinical course of COPD is one of gradual impairment with episodes of acute exacerbations that contribute to the deterioration of a person's health status. Ireland has one of the highest standardised death rates for COPD in the European Union, and also has one of the highest rates of hospital admissions for exacerbations of COPD in the OECD. Pulmonary rehabilitation is acknowledged by all international guidelines as a key component of the management of COPD.

Based on 16 systematic reviews (185 randomised controlled trials), a range of self-management support interventions for patients with COPD were identified. These included patient education and use of written action plans, pulmonary rehabilitation, telemedicine, complex self-management support interventions and outreach nursing programmes. Standard pulmonary rehabilitation comprises many aspects of chronic disease self-management support and hence is included here; however, interventions such as education, exercise and behavioural changes are also core components of pulmonary rehabilitation, so the boundary between the intervention types is ill-defined.

Very good evidence was found that education is associated with a reduction in COPD-related hospital admissions with limited evidence found that education is associated with improvements in health-related quality of life. Action plans when used alone and in the absence of other self-management supports were not found to reduce healthcare utilisation or lead to improvements in quality of life.

Very good evidence was found that pulmonary rehabilitation, which includes exercise training, is associated with clinically significant improvements in health-related quality of life. Clinically significant improvements were also reported for functional exercise capacity. Substantial variation was noted in the design, duration and intensity of the pulmonary rehabilitation programmes, making it difficult to identify their optimal format.

Good evidence was found that complex self-management support interventions (involving multiple components and, or multiple professionals with the intervention delivered by a variety of means) are associated with improvements in health-related quality of life. No evidence was found of a statistically significant benefit regarding mortality while there was limited evidence of reductions in health care utilisation. The interventions and patient populations assessed varied widely making it difficult to provide clear recommendations on the most effective components of these self-management support packages, however interventions containing education and exercise seem to be effective.

Some evidence was found that telemedicine as part of a complex health intervention decreases healthcare utilisation, with no evidence of an impact on mortality. The telemedicine interventions assessed were heterogeneous in nature, but typically were defined as healthcare at a distance that involved the communication of data (using telephones, video cameras and the internet) from the patient to the health carer, who then provides feedback regarding the management of the condition. Some evidence was also found that outreach nursing programmes improve health-related quality of life in patients with COPD.

The economic literature for COPD-specific self-management support interventions was grouped into five main intervention types: self-management support programmes, pulmonary rehabilitation, telemedicine, case management, and 'other' self-management support interventions. A total of 27 costing and cost-effectiveness studies were identified for inclusion.

Evidence from the international literature was found that self-management support education programmes could result in potential cost savings due to reduced healthcare utilisation in patients with moderate to severe disease, depending on the efficiency with which the programmes are run. Evidence was also found that case management may be cost saving for selected groups of patients with severe disease. Limited evidence was found that pulmonary rehabilitation is cost-effective in patients with moderate to severe COPD disease, with evidence from one Irish study (which was limited to 22 weeks follow-up) indicating that pulmonary rehabilitation may not be cost-effective in patients with mild to moderate disease.

Evidence for the cost-effectiveness of telemedicine interventions was mixed, with more applicable evidence suggesting that telehealth monitoring is not cost-effective. The reported per-patient cost of self-management interventions in the international literature varied according to the intensity of the intervention, but was typically low relative to the overall cost of care of these patients. Ireland has a high prevalence of COPD so the budget impact of implementing self-management support interventions for these patients is likely to be sizeable.

The applicability of the international evidence depends on the extent to which the comparator (usual care in these RCTs) is representative of usual care in Ireland. Differences may exist in how care is provided, impacting the adherence to recommended standard of care. Particular difficulties have included delays in the diagnosis of COPD due to limited access to spirometry testing in primary care. Targets have been set by the HSE's Clinical Care Programme for COPD to address this issue. Access to pulmonary rehabilitation is variable, although again improving access is a stated focus of the Clinical Care Programme.

## VIII. Diabetes

Diabetes is a progressive disease with disabling long-term complications if not properly managed. Tight control of blood sugar levels and blood pressure can reduce or delay disease progression. Type 1 diabetes is characterised by deficient insulin production and requires daily administration of insulin. Type 2 diabetes results from the body's ineffective use of insulin. Type 2 diabetes comprises 90% of people with diabetes around the world, and is largely the result of excess body weight and physical inactivity.

For adults with Type 1 diabetes, two systematic reviews of self-management support interventions were identified for inclusion. Based on a single systematic review (11 randomised controlled trials), no evidence was found that psychological treatments improve glycaemic control or reduce psychological distress. Meanwhile, based on a single systematic review (15 randomised controlled trials) of structured education programmes, very limited evidence was found that these interventions lead to improved outcomes of quality of life and episodes of severe hypoglycaemia in adults with Type 1 diabetes.

For adults with Type 2 diabetes, 27 systematic reviews (347 randomised controlled trials) of self-management support interventions were identified for inclusion. The interventions were broadly grouped into education interventions, chronic disease self-management programmes, telemedicine and 'other' self-management support interventions.

Very good evidence was found that education, including culturally-appropriate education, improves blood glucose control in the short term (less than 12 months).

Good evidence was found that behavioural interventions (specifically patient activation interventions which actively engage patients by promoting increased knowledge, confidence and, or skills for disease self-management) are associated with modest improvements in blood glucose control (glycosolated haemoglobin, HbA1C). Good evidence was also found for improvements in blood glucose control in the short term with various forms of telemedicine. The interventions were heterogeneous and included computer-based software applications, telephone support, and electronically transmitted recommendations from clinicians in response to transmission of self-monitored glucometer data. Meanwhile some evidence was found that diabetes-specific chronic disease self-management programmes are associated with small improvements in blood glucose control in the short term. Evidence of improvements in blood glucose control was also found for a diverse range of SMS interventions and in particular educational interventions which differed also in their frequency, intensity and mode of delivery.

Based on the available clinical evidence, it is not possible to provide clear recommendations on the optimal content and format of self management support for adults with Type 2 diabetes. The evidence suggests that various models of delivery may be equally effective. Of note, impact on resource utilisation was not assessed in any of the reviews. Quality of life remained unaltered.

Based on 38 costing and cost-effectiveness studies, the economic literature for Type 1 and Type 2 diabetes was grouped into three main intervention types: education programmes, telemedicine, and pharmacist-led programmes. The better quality studies used data from randomised controlled trials and then extrapolated lifetime benefits using one of a number of simulation models that predict outcomes based on risk-factors.

The best economic evidence was found in support of self-management support education programmes with modelled results suggesting that the interventions are cost-effective relative to usual care. Based on limited evidence, it is not possible to say if telemedicine interventions are cost-effective relative to usual care while there was insufficient evidence of adequate quality to consider the cost-effectiveness of pharmacist-led interventions.

Structured education programmes are currently available in Ireland for adults with Type 1 and Type 2 diabetes based on a range of models. A 2009 Health Service Executive (HSE) review of diabetes structured education noted that these programmes should be integrated into standard diabetes care. The HSE's National Clinical Care Programme is currently developing a model of care through which it is proposed all patients should have access to a structured integrated care package covering all aspects of their diabetes care. The choice of a standard programme or set of programmes should be supported by the available evidence.

## IX. Stroke

Stroke is the neurological condition that results from brain damage caused by either blockage or rupture of a blood vessel in the brain. Each year in Ireland, approximately 7,000 people are hospitalised following stroke. Due to an aging population, the burden of stroke-related disease is expected to increase, with predicted increases of 11% to 15% in the proportion of the population aged 65 or older by 2021. It is estimated that between 30% and 40% of stroke survivors develop some degree of functional dependence requiring assistance in performing basic activities of daily living (ADLs).

Based on 27 included systematic reviews (228 randomised controlled trials), four broad types of self-management intervention were identified for adult post-stroke patients. These focused on rehabilitation therapy (including general rehabilitation, virtual reality-based rehabilitation and telerehabilitation), self-management programmes, information provision and 'other' self-management support interventions.

Good evidence was found that general rehabilitation therapy delivered in early stroke recovery has a positive impact on activities of daily living and extended activities of daily living. Virtual reality-based rehabilitation (that is, using commercial gaming consoles or specifically developed consoles adopted in clinical settings) ) was found to improve upper limb function and activities of daily living when used as an add-on to usual care, although it is still unclear which characteristics of virtual reality are most important and if the effects are sustained in the longer term. Meanwhile, based on limited evidence, telerehabilitation (using telephone or internet to facilitate communication between the patient and provider) does not appear to improve ADL or upper limb function for post-stroke patients compared with usual care.

Some evidence was found that information provision improves patient and carer knowledge of stroke, aspects of patient satisfaction, with small reductions (which may not be clinically significant) in patient depression scores. Similarly, some evidence was found that stroke liaison emphasising education and information can have a positive impact on quality of life. However, based on the available evidence, it is not possible to draw conclusions in relation to the effectiveness of self-management programmes delivered to post-stroke patients or for psychosocial interventions, motivational interviewing, lifestyle interventions, multidisciplinary care or family-orientated models of care.

The identified economic literature was limited to four costing and cost-effectiveness studies relating to exercise-based programmes and computer-based rehabilitation therapy. The four included studies provided very limited evidence regarding the costs or cost-effectiveness of self-management programmes for post-stroke patients.

As a chronic disease, stroke is very different to other long-term illnesses in that it is a sudden onset disease with varying levels of sudden, potentially permanent impairments. This is reflected in the stroke self-management support clinical-effectiveness literature retrieved, which is largely focused on rehabilitation therapy. A review of stroke services in Ireland noted gaps in care, particularly in relation to rehabilitation services. A model of care has been developed by the HSE's National Clinical Programme for Rehabilitation Medicine to address these deficits. This advocates a framework where patients are managed by specialist rehabilitation clinicians working as part of a managed clinical rehabilitation network with a view to extending access to specialist rehabilitation services for people with acquired disability.

## XII. Ischaemic heart disease

Ischaemic heart disease (IHD) is a chronic condition characterised by narrowing and hardening of the arteries that supply blood to the heart muscle. IHD claims around 5,000 lives annually in Ireland, which represents approximately half of all cardiovascular deaths. As well as being associated with significant mortality, it can also weaken the heart muscle over time, which can lead to the development of heart failure and cardiac arrhythmias.

Based on 14 systematic reviews (244 randomised controlled trials), five broad types of self-management support intervention were identified for patients with ischaemic heart disease in this overview of reviews. These focused on patient education, exercise, psychosocial or behavioural changes, home-based services or telehealth. Interventions such as education, exercise and behavioural changes are noted to be core components of cardiac rehabilitation, so the boundary between standard cardiac rehabilitation services and chronic disease self-management support is ill-defined.

Good evidence of a statistically significant reduction in mortality was found for exercise programmes (including exercise-based cardiac rehabilitation) in suitable patient cohorts from studies with follow-up periods greater than 12 months. Exercise –based interventions were also found to be associated with fewer rehospitalisations, but inconsistent results have been reported for myocardial infarction rates. Limited evidence was found that comparable home- and telehealth-based cardiac rehabilitation interventions achieve similar outcomes to centre-based interventions.

Some evidence was found that patient education programmes are associated with an improvement in interim outcomes such as smoking cessation and reduced blood pressure, but there is uncertainty about how long any such effect persists. Meanwhile limited evidence was found to demonstrate the effectiveness of

behavioural modification interventions, although some studies have reported positive effects on smoking cessation and symptom management.

Based on 15 costing and cost-effectiveness studies, the economic literature was broadly grouped into four main intervention types: cardiac rehabilitation, case management, telemedicine, and 'other interventions'.

When compared with no rehabilitation, international evidence was found that cardiac rehabilitation can create cost savings as a result of reductions in health care utilisation. However, it it is not possible to draw conclusions in relation to the cost-effectiveness of telemedicine-delivered self-management support interventions and nurse-led case management programmes due to the heterogeneity of the interventions assessed and equivocal findings. The reported per-patient cost of the various self-management interventions varied according to the intensity of the intervention, but was typically low relative to the overall cost of care of these patients.

The model of care developed by the national clinical programme in Ireland for acute coronary syndromes recommends that cardiac rehabilitation programmes are established within the acute setting to treat hospitalised patients prior to discharge, with follow-up secondary prevention programmes in the primary care setting. It is a stated (as of 2013) goal that 90% of eligible patients are referred to early cardiac rehabilitation services (Phase 3), within four weeks of hospital discharge. A 2013 survey identified found significantly different staffing levels and resources between cardiac rehabilitation services, lengthy waiting times for some individual services and wide variation in availability of multidisciplinary teams, which meant that not all patients received the best possible cardiac rehabilitation.

## X. Hypertension

The World Health Organization's Health 2020 policy identifies high blood pressure or hypertension as the world's most prevalent, but preventable disease. An estimated 64% of the population over 50 years of age in Ireland has high blood pressure. Hypertension is a serious medical condition that often has no symptoms, but significantly increases the risks of heart, brain, kidney and vascular disease. The risk associated with increasing blood pressure is continuous, with each 2 mmHg rise in systolic blood pressure associated with a 7% increased risk of mortality from ischaemic heart disease and a 10% increased risk of mortality from stroke.

Sixteen systematic reviews (240 randomised controlled trials) of the clinical-effectiveness of self-management support interventions for adults with hypertension were identified for inclusion in this overview of reviews. A diverse range of interventions was identified with the largest volume of evidence obtained for reviews

where self-monitoring of blood pressure was the main intervention. The remaining reviews assessed a range of self-management support interventions.

Good evidence was found that self-monitoring of blood pressure alone or using a range of additional support, including telemedicine, is beneficial in lowering systolic and diastolic blood pressure. However, the clinical significance and durability of the effect are unclear. Additional support seems to enhance the blood pressure lowering effect.

Limited evidence of effectiveness was found for patient education interventions when used alone in improving medication adherence or blood pressure control, although it is noted that these may form an important part of more complex interventions. Some evidence was found that a range of complex SMS interventions (that is involving multiple components, multiple providers and modes of delivery) lead to improvements in blood pressure control. There was substantial heterogeneity in the format and intensity of the self-management support interventions, the study populations and study follow-up duration, making it difficult to formulate clear recommendations on the optimal intervention format of self-management support for patients with hypertension. A patient-specific approach may be the most beneficial, involving components tailored to the individual patient with hypertension.

Some evidence was found that community pharmacist interventions which include patient education can lead to reductions in systolic and diastolic blood pressure. Similarly, some evidence was found that simplification of medication regimens improves adherence although the clinical significance of this effect may be small.

Based on 14 costing and cost-effectiveness studies, the economic literature assessed a diverse range of interventions with the largest volume of evidence obtained for reviews where self-monitoring of blood pressure was the main intervention. The remaining reviews assessed a range of self-management support interventions. The available international evidence was largely for patients with uncontrolled hypertension. The results were inconsistent across outcomes of ambulatory blood pressure, costs, and healthcare utilisation. In some studies, the intervention had a positive effect; in others it was negative, relative to usual care. This evidence from the international literature indicated that the cost per patient of delivering self-management support interventions was generally low.

The applicability of the findings to Ireland is affected by a number of factors including the definition of routine care. For example, usual care for hypertension in Ireland may differ to that in the UK's NHS system where adherence to quality standards is incentivised by the quality-of-outcomes framework. Data indicate high levels of undetected hypertension and poor levels of blood pressure in Ireland. This context must be considered when evaluating the applicability of the findings of this

overview. There are substantial levels of unmet need for routine care in Ireland, which may impact on whether the estimated incremental benefits of self-management support interventions for hypertension apply in the Irish setting.

## XI. Heart failure

Heart failure is a chronic condition characterised by an inability of the heart to pump blood effectively, due to systolic and or diastolic dysfunction. The average age at diagnosis is 76 years and the overall prevalence of heart failure in Ireland is approximately 1.1%, with a five-year mortality rate of 36%. Prevalence is increasing due to better management of the disease and the ageing population, which has resulted in congestive heart failure becoming one of the most common reasons for emergency admission to hospitals in Ireland.

Based on 20 systematic reviews (248 randomised controlled trials), five broad types of self-management support intervention were identified. These focused on patient education, psychosocial and behavioural interventions, exercise interventions, home visits, and telehealth (including telemedicine and structured telephone support). Interventions such as education, prescribed exercise and behavioural changes are core components of cardiac rehabilitation, so the boundary between standard cardiac rehabilitation services and chronic disease self-management support is ill-defined.

Statistically significant reductions in mortality were reported for both telehealth interventions and home visit programmes in selected patients. There was however a lack of consistency across reviews that examined these types of interventions, with some studies reporting no effect. Statistically significant reductions in the rate of hospital readmissions were also noted for exercise interventions, home visit programmes and telehealth interventions for selected heart failure patients. Meanwhile, limited evidence was found to support the effectiveness of patient education programmes or behavioural modification interventions. Despite the positive results that have been reported for telemedicine and structured telephone support interventions, concerns have been raised about these being considered the standard of care for the management of heart failure patients due to inconsistent findings across studies and a lack of understanding about which specific elements of the interventions contribute to the improved outcomes.

The included economic literature was grouped into five main intervention types: education, telemedicine, multidisciplinary care, disease management and 'other' self-management support interventions. A total of 46 costing and cost-effectiveness studies were identified. The quality of the studies was generally poor, with only four identified as high-quality studies.

Based on individual randomised controlled trials that showed improvements in health-related quality of life and reductions in healthcare utilisation, the majority of telemedicine interventions reported cost savings relative to usual care, although the interventions assessed were heterogeneous. Similarly, based on individual randomised controlled trials that showed reductions in healthcare utilisation, certain disease management and education programmes were found to be cost-effective or cost saving relative to usual care.

The reported per-patient cost of self-management interventions in the international literature varied according to the intensity of the intervention, but was typically low relative to the overall cost of care of heart failure patients.

The applicability of the clinical and cost-effectiveness evidence for heart failure-specific self-management support interventions is affected by the variability in routine care including the current provision of cardiac rehabilitation services in Ireland. The HSE's clinical programme for heart failure has developed a model of care for the public health service, which describes two main models for rehabilitation programmes for heart failure patients. The extent to which this is in place was examined in a 2013 survey which found significantly different staffing levels and resources between cardiac rehabilitation services, lengthy waiting times for some individual services and wide variation in availability of multidisciplinary teams. This means that not all patients receive optimal cardiac rehabilitation. There is also considerable uncertainty about access to primary prevention services for patients with heart failure who have not been hospitalised following an acute cardiovascular event.

## XIII. Discussion

In total, this HTA considered a large volume of evidence including over 2,000 randomised controlled trials as presented across 1 systematic reviews.

The overview of reviews approach used for the clinical-effectiveness review enabled an assessment of a large quantity of evidence for a range of intervention types across a number of disease areas in a relatively short period of time. However, an overview of reviews places one at a remove from the primary evidence and reliant on the quality of the available reviews. However, given their typical sample sizes, it is not possible to draw strong conclusions about effectiveness based on a single, or a number of small randomised controlled trials. Therefore it is unlikely that more recent randomised controlled trials not captured in an overview of reviews would be sufficient to substantially alter recommendations informing major policy decisions.

The majority of the trials underpinning the clinical effectiveness data had relatively short-term follow-up of participants. The majority of systematic reviews were based on randomised controlled trials with no more than 12 months of follow-up. It is

unclear whether effects observed at six or 12 months might be sustained over longer time horizons.

Evidence of the clinical-effectiveness of chronic disease self-management support interventions provides a complex picture. Certain forms of disease-specific interventions, as discussed above, have been shown to improve outcomes over periods of six to 12 months. Longer term outcome data are generally not collected. Based on the available evidence, the optimal format of generic self-management support, the diseases in which it is likely to provide benefit, and the duration of effectiveness, if any, is still unclear.

Most economic analyses were conducted alongside these randomised controlled trials, limiting their ability to determine if observed savings could be sustained. The costing methodology and perspective adopted differed greatly between studies making it difficult to summarise and aggregate findings. To be cost-effective, an intervention must first be clinically effective; given the heterogeneity of interventions assessed in the clinical effectiveness review and the variability in the format, intensity and mode of delivery of the interventions assessed, it is difficult to generalise the evidence. However, evidence of cost-effectiveness for a wide range of self-management support interventions in patients with chronic disease was generally of limited applicability to the Irish healthcare setting.

International evidence suggests that most self-management support interventions are relatively inexpensive to implement. Reported costs vary according to the intensity of the intervention, but are typically low relative to the overall cost of care for the chronic disease in question. In some instances, the interventions resulted in modest cost savings through reduced healthcare utilisation. However, it is unclear if costs would be similar if programmes are rolled out to a larger population or if economies of scale might apply. Longer-term evidence is required to determine if benefits are sustained and if costs change over time. Although generally inexpensive on a per patient basis, the budget impact of these interventions could be substantial due to the large number of eligible patients.

With the exception of generic self-management support interventions, the identified reviews related to disease-specific interventions. The included populations are likely to experience high levels of multimorbidity whereby patients have multiple chronic conditions, a number of which may be amenable to self-management. Providing a single disease-specific intervention may not be suitable for enabling successful self-management. Equally, exposure to numerous interventions may be counter-productive, placing an unsustainable burden on the individual. For people with multimorbidity, a coherent evidence-based approach that acknowledges their various conditions and how they interact is essential.

## XIV. Conclusion

Evidence of the clinical-effectiveness of chronic disease self-management support interventions provides a complex picture. There was a large quantity of evidence of variable quality. Although for many intervention types there was limited evidence of effect, some interventions were shown to lead to improved health and, or reduced healthcare utilisation over short-term time horizons. The best evidence of benefit is associated with disease-specific interventions.

The HSE should prioritise investment in those interventions for which there is good evidence of clinical effectiveness. Where chronic disease self-management support interventions are provided, it is critical that an agreed definition of self-management support interventions is developed and the implementation and delivery of the interventions are subject to routine and ongoing evaluation. This would help to ensure that they are delivering benefits to patients, and allow the content and format of the interventions to be refined. Evaluation will also provide a longer-term perspective not currently available in the literature, and will support decisions about the optimal delivery of such interventions.

Most interventions are relatively inexpensive to implement relative to the costs of treating chronic disease and, in some instances, can result in modest cost savings through reductions or shifts in healthcare utilisation. However, due to the numbers of eligible patients, the budget impact of these interventions may be substantial.

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# List of abbreviations used in this report

| | |
|---|---|
| **BRUCIE** | Better Regulation Using Carbohydrate and Insulin Education (Diabetes programme) |
| **CBT** | cognitive-behavioural therapy |
| **CDSMP** | chronic disease self-management programme – Stanford programme |
| **CODE** | Community Orientated Diabetes Education (Diabetes programme developed by Diabetes Ireland) |
| **DAFNE** | Dose Adjustment For Normal Eating |
| **DESMOND** | Diabetes Education and Self-Management for Ongoing and Newly Diagnosed (Diabetes Programme) |
| **ES** | effect size |
| **EPP** | Expert Patient Programme (UK programme based on Stanford model) |
| **HC** | health coaching |
| **HTA** | health technology assessment |
| **I(C)T** | information (and communication) technology |
| **MI** | motivational interviewing |
| **NIHR** | National Institute of Health Research |
| **PICO** | population - intervention - comparator – outcomes |
| **PRISMS** | Practical Systematic Review of Self-Management Support |
| **QoL** | quality of life |
| **RCT** | randomised controlled trial |
| **R-AMSTAR** | Revised Assessment of Multiple Systematic Reviews |
| **SD** | standard deviation |
| **SMBP** | self-monitoring of blood pressure |
| **SMD** | standard mean difference |
| **SMS** | self-management support |

# Acknowledgements

The Authority would like to thank all of the individuals and organisations who provided their time, advice and information in support of this health technology assessment (HTA).

### The membership of the Expert Advisory Group was as follows:

| | |
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## Members of the Evaluation Team:

Members of the Authority's Evaluation Team were Dr Fiona Cianci, Dr Mark Gouldson, Dr Patricia Harrington, Patrick Moran, Dr Linda Murphy, Michelle O'Neill, Dr Máirín Ryan, Dr Conor Teljeur and Shaun Walsh.

# 1 Introduction

## 1.1 Background to request

In December 2014, the Health Information and Quality Authority (HIQA) received a request from the Health Service Executive (HSE) to examine the clinical and cost-effectiveness of generic self-management support (SMS) interventions for chronic diseases and disease-specific interventions for chronic obstructive pulmonary disease (COPD), asthma, cardiovascular disease and diabetes.

## 1.2 Terms of Reference

Following an initial scoping of the technology, the terms of reference for this assessment were agreed between the Authority and the HSE:

- **Phase I:** To review the clinical and cost-effectiveness of generic chronic disease self-management support interventions.
- **Phase II:** To review the clinical and cost-effectiveness of disease-specific chronic disease self-management support interventions.
    - **Phase IIa:** The diseases include chronic obstructive pulmonary disease (COPD), asthma, and diabetes.
    - **Phase IIb:** The diseases include cardiovascular disease – stroke, hypertension, heart failure and ischaemic heart disease.
- Based on this assessment, to advise on the optimal chronic disease self-management support interventions to be implemented by the HSE.

## 1.3 Overall approach

This health technology assessment (HTA) was conducted using the general principles of HTA and employing the processes and practices used by HIQA in such projects. In summary:

- The Terms of Reference of the HTA were agreed between HIQA and the Health Service Executive.
- An Expert Advisory Group was established. The role of the Expert Advisory Group was to inform and guide the process, provide expert advice and information and to provide access to data where appropriate. The terms of reference of the Expert Advisory Group are included below. A full list of the

membership of the Expert Advisory Group is available in the acknowledgements section of this report.

- An evaluation team was appointed comprising internal HIQA staff. Additionally, Dr Fiona Cianci, a Public Health Specialist Registrar in the Health Service Executive (HSE), Shaun Walsh and Dr Mark Gouldson assisted with the systematic review and data extraction.
- Following review by the Expert Advisory Group with amendments made, as appropriate, the final draft report was submitted to the Board of the Authority for approval. The completed report was submitted to the Minister for Health and the HSE as advice and published on the Authority's website.

The Terms of Reference of the Expert Advisory Group were to:

- Contribute to the provision of high quality and considered advice by HIQA to the HSE.
- Contribute fully to the work, debate and decision-making processes of the group by providing expert guidance, as appropriate.
- Be prepared to provide expert advice on relevant issues outside of group meetings, as requested.
- Provide advice to HIQA regarding the scope of the analysis.
- Support the Evaluation Team led by HIQA during the assessment process by providing expert opinion and access to pertinent data, as appropriate.
- Review the project plan outline and advise on priorities, as required.
- Review the draft report from the Evaluation Team and recommend amendments, as appropriate.
- Contribute to HIQA's development of its approach to HTA by participating in an evaluation of the process on the conclusion of the assessment.

# 2 Chronic disease self-management

This chapter describes the general purpose of self-management support (SMS) interventions. It provides a description of the different types of SMS interventions evaluated in the following chapters and the theories that underpin them.

## 2.1 Description of self-management

A broad range of self-management and self-management support (SMS) definitions exist which may reflect the lack of clarity on what constitutes effective SMS.

For the purpose of this review, the 2003 definitions of self-management and SMS agreed by the US Institute of Medicine are used. Self-management is defined as 'the tasks that individuals must undertake to live with one or more chronic diseases. These tasks include having the confidence to deal with the medical management, role management and emotional management of their conditions'. SMS is thus defined as 'the systematic provision of education and supportive interventions by health care staff to increase patients' skills and confidence in managing their health problems, including regular assessment of progress and problems, goal setting, and problem-solving support.'[1;2]

Figure 2.1 (on page 6) by Taylor et al. shows the process by which SMS enables individuals to improve their medical, emotional and risk management behaviours.[2;3] This illustrates that to effect change, individuals need to acquire or develop five core self-management skills: problem-solving; decision-making; appropriate resource utilisation; forming a partnership with a health-care provider; and taking necessary actions.[2;4;5] The final step is mediated by the patient's self-efficacy which is required to enact these skills and deliver behaviour change. Self-efficacy, one of the core concepts of social cognitive theory, focuses on increasing an individual's confidence in their ability to carry out a certain task or behaviour, thereby empowering the individual to self-manage.[2] SMS interventions to enhance these five core self-management skills and to improve self-efficacy can include different components (education, training, provision of information or equipment) delivered in a variety of formats such as, education programmes, telemedicine, health coaching and motivational interviewing. A range of delivery methods also exist such as group or individual, face-to-face or remote, professional or peer-led. These interventions can be generic, that is, they can be used across a range of chronic diseases or disease-specific, that is, designed for a specific disease type.

Generic SMS is currently provided in Ireland through programmes such as those run by Arthritis Ireland, Beaumont hospital and the HSE's ('Quality of Life') SMS programme. These programmes are all based on a model developed in Stanford University (Stanford model). Disease-specific programmes are also available. For

example, there are a range of diabetes-specific programmes for both Type 1 (DAFNE and Berger programmes) and Type 2 diabetes (DESMOND, X-PERT, and the CODE programme developed by Diabetes Ireland). A wide range of education programmes and peer-support groups are also available, including those provided by voluntary organisations, such as the Asthma Society, COPD Ireland, Croí, Diabetes Ireland, and the Irish Heart Foundation. However, the efficacy of many of these programmes has not been evaluated at a national level nor an assessment made as to the optimal programme or programmes that should be implemented and to whom they should be made available.

SMS interventions may be a worthwhile adjunct to best medical care to allow patients to take control of and manage portions of their own care. The cost of the intervention is predicted to be low relative to, for example, the potential resource savings associated with a reduction in the number of general practitioner (GP) visits, emergency department visits or hospitalisations. However, at present there is uncertainty regarding the benefits of SMS interventions in the short and long term. Also there is uncertainty about the optimal format that SMS should take. Should it be programme-based and if so, what type of programme is best? Should remote solutions be implemented? What is the evidence of cost-effectiveness? While some initiatives are already available in Ireland, their implementation is not consistent and may not be adequate to meet the growing burden of chronic diseases. With co-morbidity being common in the ageing population and the rise in the number of patients with multi-morbidity, is there a need for generic SMS interventions that can be applied across a range of chronic diseases? Are generic skills sufficient to manage chronic diseases? Evidence on the general care of patients with multiple morbidities is limited, but it has been reported that interventions that focus on particular risk factors may be more effective.[6] Alternatively, is there a need for disease-specific SMS interventions to manage certain aspects of selected chronic diseases? Or can a combination of generic tools combined with disease-specific components be used to optimise care?

The uncertainty regarding the format of optimal SMS presents an obstacle to informed decision making about the provision of this intervention in the Irish public healthcare system.

**Summary statement**

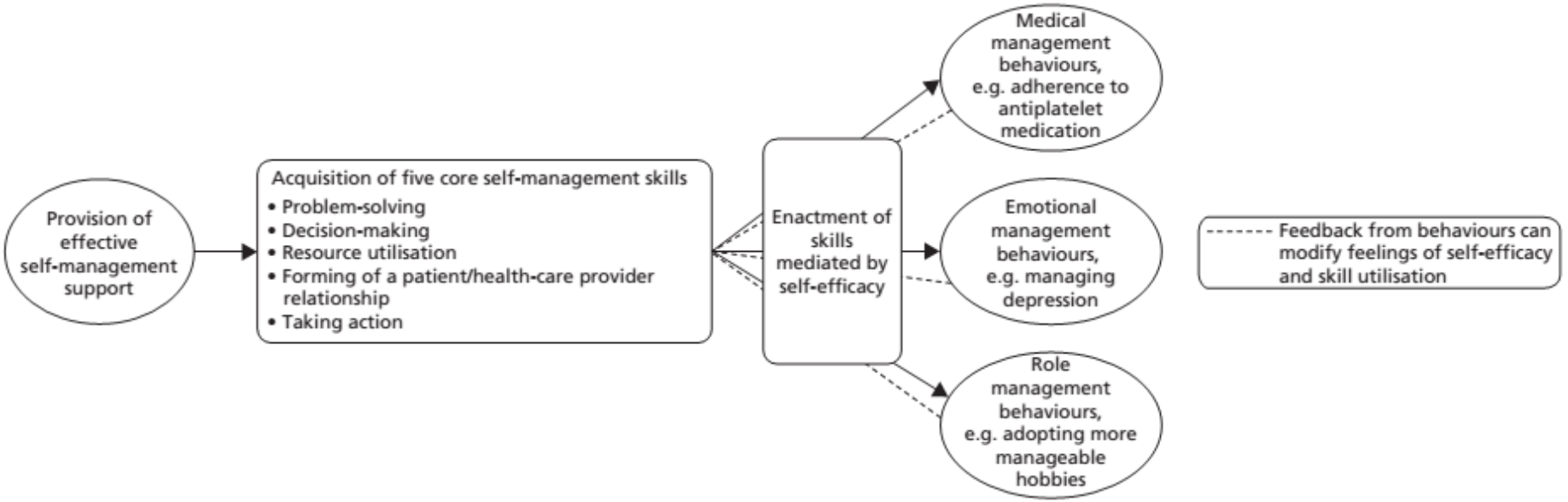
A broad range of self-management and self-management support definitions exist. For this review, the 2003 definitions agreed by the US Institute of Medicine are used:

Self-management is defined as 'the tasks that individuals must undertake to live with one or more chronic diseases. These tasks include having the confidence to deal with medical management, role management and emotional management of their conditions. '

Self-management support is defined as 'the systematic provision of education and supportive interventions by health care staff to increase patients' skills and confidence in managing their health problems, including regular assessment of progress and problems, goal setting, and problem-solving support.'

Self-management support interventions are any interventions that help patients to manage portions of their chronic disease or diseases through education, training and support.

**Figure 2.1 The process of adoption of self-management behaviours taken from Taylor et al. (adapted from Corbin and Strauss and Lorig and Holman).[2;3;5]**



## 2.2 Description of the interventions

Phase I and Phase II of this assessment include appraisal of generic and disease-specific SMS interventions that help patients manage portions of their chronic disease through education, training and support, respectively. Included were:

- All formats and delivery methods (group or individual, face-to-face or remote, professional or peer-led).
- All studies that include a large component of SMS.

The following sections include some descriptions of well known SMS interventions. Further disease-specific interventions are discussed in the chapters on individual diseases.

### 2.2.1 Chronic disease self-management models/programmes

The following section includes a brief description of the most well-known and widely-used health behaviour change theories and health behaviour change interventions and programmes. A recent review by the New Zealand Guidelines Group included a detailed description of some of these interventions, and as such portions of these descriptions are summarised and referenced below.[7] Disease-specific programmes, where relevant, are discussed in the individual disease-specific sections of this report.

#### Health behaviour change theories

**Trans-Theoretical Theory[7]**

This model is based on the theory that behaviours can be modified. It is related to a person's readiness to change, the stages that they progress through to change and doing the right thing (processes) at the right time (stages). As such, tailoring interventions to match a person's readiness or stage of change is said to be essential. The model comprises emotions, cognitions and behaviours, and includes measures of self-efficacy and temptation. It has been used to modify target behaviour such as smoking cessation and stress management.

**Social Learning/Social Cognitive Theory[7]**

This theory proposes that behaviour change is affected by environmental influences, personal factors, and attributes of the behaviour itself. A central component of this theory is also self-efficacy. As well as belief in the behavioural change, the individual must value the outcomes they believe will occur as a result.

### Theory of Reasoned Action and Theory of Planned Behaviour[7]

This social cognitive theory of reasoned action states that individual performance of a target behaviour is determined by the person's intention to perform that behaviour based on their attitude toward the behaviour and the influence of their social environment or subjective norm. The shared components are behavioural beliefs and attitudes, normative beliefs, subjective norms and behavioural intentions. The Theory of Planned Behaviour adds to the Theory of Reasoned Action, the concept of perceived control over the opportunities, resources, and skills necessary to perform a behaviour. These are considered to be critical in behavioural change. This is congruent with the concept of self-efficacy.

### Cognitive Behavioural Theory and Cognitive Behavioural Therapy (CBT)[7]

This is a highly-structured psychotherapeutic method used to alter distorted attitudes and problem behaviours by identifying and replacing negative inaccurate thoughts and changing the rewards for behaviours. CBT attempts to help an individual make sense of overwhelming problems by breaking them down into smaller parts. CBT can take place on a one-to-one basis or with a group of people. It can be conducted from a self-help book or computer programme. The duration of the intervention can range from six weeks to six months depending on the problem and the individual; sessions usually last 30 to 60 minutes with a trained therapist.

## Behaviour change programmes or models based on a single health behaviour change theory (including adaptations or modifications)

### The Chronic Care Model

This model was developed by Wagner in the MacColl Institute in the 1990s in response to the increasing burden of chronic disease and the varying approaches of management and care (social learning/cognitive theory).[8;9] It is focused on changing a reactive system – responding mainly when a person is sick – to a more proactive system which focuses on supporting patients to self-manage. A principle part of the model is that the patient has a central role in managing their health and in particular self-efficacy. It is a high-level organisational or system level of health service provision and identifies the essential elements of a health care system that encourage high-quality care including the community, the health system, SMS, delivery system design, decision support and clinical information systems. As such, this is a higher level model than for example, the Stanford model and UK Expert Patient Programme which are discussed below, as SMS is only one component of the chronic care model.

### Personalised care planning or 'building the house of care'

The management and care of long-term conditions tends to be seen as the clinician's responsibility rather than a collaborative endeavour with active patient involvement and effective SMS. In the UK, the King's Fund describe the 'house of care' in 2013, a metaphor which was devised to help those working in primary care adapt the chronic care model to their own situation. It encompasses all people with long-term conditions; and assumes an active role for patients, with collaborative personalised care planning at its heart.[(10)] Personalised care planning is described as a collaborative process in which patients and clinicians identify and discuss problems caused by, or related to the patient's condition, and develop a plan for tackling these. It has been described as a conversation, or series of conversations, in which they agree goals and actions for managing the patient's condition.[(11)]

### Stanford Programme

This is based on the concept of self-efficacy within social learning theory. It was originally developed by Stanford University in the US. It uses peer educators to build self-efficacy in a group setting. The Stanford chronic disease self-management programme (CDSMP) is a generic programme, that is, it can be used for patients with a range of chronic diseases. It is based on the fact that people with chronic disease have similar concerns and, with specific skills and training, can effectively manage aspects of their own conditions.[(12)] The programme consists of two and a half hour workshops once a week for six weeks and while generally administered in community settings, is also available online.

### UK Expert Patient Programme (EPP)

This is a modification of the Stanford model above and was introduced into the UK in 2002 and branded the EPP.[(13)] Similar to Stanford's CDSMP, it uses peer educators and consists of six weekly workshops conducted in community settings; it is also available as an on-line tool. The topics discussed during the workshops are also similar to those presented in the Stanford workshops. It covers topics such as: healthy eating, exercise, pain management, relaxation, action planning and problem solving.[(13)] It promotes patient knowledge by teaching the skills necessary for people to effectively manage their own chronic conditions, with support from physician team members.

## Behaviour change programmes or models based on multiple health behaviour change theories

### Flinders Programme™

The Flinders programme™ is a clinician-driven, behavioural change programme (based on multiple health behaviour change theories) that emphasises the role physicians have in building patient self-efficacy and the need to actively engage patients using the principles of cognitive behavioural therapy (CBT) during patient-physician interactions (one-on-one). The programme has seven principles of self-management which allow individuals to:[14]

1. Have knowledge of their condition.
2. Follow a treatment plan (care plan) agreed with their health professionals.
3. Actively share in decision making with health professionals.
4. Monitor and manage signs and symptoms of their condition.
5. Manage the impact of the condition on their physical, emotional and social life.
6. Adopt lifestyles that promote health.
7. Have confidence, access and the ability to use support services.

### Other programmes or models

Other SMS interventions are based on behavioural theories such as the health belief model, the theory of reasoned action, the trans-theoretical model, the information-motivation-behavioural skills model and the theory of planned behaviour. They all specify determinants of behaviour that could potentially be changed to improve health and quality of life. The other SMS interventions that were identified as part of the systematic review of efficacy were motivational interviewing and health coaching which are similar, but distinct approaches.[15] The differences between these interventions are described briefly below.

- Motivational interviewing – based on the trans-theoretical model of behavioural change and 'readiness to change'. It uses a brief approach such as 60 minutes of counselling and education to increase motivation and commitment to change. Once that is achieved, other approaches are pursued.
- Health coaching – based on the trans-theoretical model of behavioural change and 'readiness to change'. It is a standalone, comprehensive intervention with a minimum of six sessions.
- Information-motivation-behavioural skills model – This is a behavioural theory which identifies constructs (including information, motivation and behaviour skills) that are needed for successful self-management or adherence.

### 2.2.2 Chronic disease self-management – Telemedicine including internet support

Telemedicine, a term coined in the 1970s, literally means 'healing at a distance' and signifies the use of information and communication technology (ICT) to improve patient outcomes by increasing access to care and medical information.[16] However, there is no one universally accepted definition of telemedicine, so that the literature in this area describes a myriad of interventions delivered through different mechanisms for different purposes. A 2007 publication found 104 definitions of telemedicine in the peer-reviewed literature. Despite this, telemedicine was found to typically comprise four major elements: supply of medical care, use of technology, mitigation of issues of distance, and provision of benefits.[17] The World Health Organisation (WHO) has adopted the following broad description:

> 'The delivery of health care services, where distance is a critical factor, by all health care professionals using information and communication technologies for the exchange of valid information for diagnosis, treatment and prevention of disease and injuries, research and evaluation, and for the continuing education of health care providers, all in the interests of advancing the health of individuals and their communities.'[16;18]

Telemedicine is constantly evolving to incorporate new advancements in technology and to respond and adapt to changing health needs. Telemedicine applications typically have two formats; synchronous which involves real-time interaction (that is, via the telephone or videoconferencing) or asynchronous communication (not real-time, for example via text messages, email or devices that permit store-and-forward transmission of data [for example, a home glucose metre]). Asynchronous methods that use store-and-forward transmission typically forward the data to a health professional who reviews the data and uses their clinical judgement to make recommendations to the individual. Telemedicine also includes internet- or web-based support (sometimes referred to as e-health). This can include internet versions of, for example, the online version of the Stanford CDSMP described above. Internet-based support offers an alternative to face-to-face interventions which could be beneficial if resources are limited.

## 2.3 Key messages

- Self-management is defined as the tasks that individuals must undertake to live with one or more chronic diseases.
- Self-management support interventions are any interventions that help patients to manage portions of their chronic disease or diseases through education, training and support.
- Self-efficacy, one of the core concepts of social cognitive theory, focuses on increasing an individual's confidence in their ability to carry out a certain task or behaviour, thereby empowering the individual to self-manage.
- Self-management support interventions can include a variety of formats such as, education programmes, telemedicine (text messages, email, internet-based support), health coaching and motivational interviewing. A range of delivery methods also exist such as group or individual, face-to-face or remote, professional or peer-led.
- There are several behaviour change programmes which focus mainly on improving self-efficacy. These include generic programmes such as the UK Expert Patients Programme (peer-led) and the Flinders model™ (physician-led), and the generic and disease-specific Stanford programme (peer-led).

# 3 Methodology

## 3.1 Clinical-Effectiveness

This health technology assessment (HTA) of self-management support (SMS) interventions was undertaken as a series of rapid HTAs. As per the terms of reference, individual disease-specific assessments were prepared for asthma, chronic obstructive pulmonary disease, diabetes, cardiovasculuar disease (hypertension, stroke, ischaemic heart disease, and heart failure) as well as an assessment of generic SMS interventions not tailored to any one specific disease. The term 'rapid HTA' is analogous to that of a 'mini-HTA'; both terms are widely used in the international HTA setting to refer to a HTA with restricted research questions whose purpose is to inform decision making in a particular service setting or for a specific group of patients. Based on the approach used in a full HTA assessment, a rapid HTA uses a truncated research strategy with the review of published literature often restricted to a review of the secondary literature (including systematic reviews, meta-analysis, guidelines etc.) and does not include development of an independent economic model. This approach is useful when undertaking assessments that are proportionate to the needs of the decision maker.

A systematic review of chronic disease self-management support (SMS) interventions was undertaken for generic interventions and disease-specific interventions for each of the identified chronic diseases to identify, appraise and synthesise the best available evidence on their clinical effectiveness and safety.

This review included:

- development of a systematic review protocol
- appraisal and synthesis of all available evidence in line with international best practice in systematic reviews of interventions.

### 3.1.1 Literature review

A scoping review of the literature was carried out in preparation for this project and a large body of clinical effectiveness literature was identified. This included multiple systematic reviews of varying quality and scope that evaluated a range of SMS interventions. Based on the volume of literature available and the project timelines, an overview of reviews was considered to be the most efficient method to assess the clinical effectiveness of SMS interventions.

'Overviews of reviews' also known as, 'meta-reviews' or 'reviews of reviews' are an efficient way to gather a large body of the best available evidence in a single source to provide broad, cumulative statements that summarise the current evidence on the effectiveness of interventions. The term 'overview of reviews' is used by the

Cochrane Library and will be used in this report from this point on. An overview of reviews allows the findings of separate reviews to be compared and contrasted, thereby providing clinical decision makers with the evidence they need. The overview of reviews is limited to a summary of systematic reviews, that is reviews that are prepared using a systematic approach, and is itself done according to the principles of systematic reviewing. The disadvantage of this approach is the inability of an overview of reviews to reflect the most recent literature: following publication of a randomised controlled trial (RCT), it must first be captured in a systematic review, before subsequently being captured in an overview of reviews. This approach would therefore be less suitable for a fast-moving area where there are rapid advances in the technology. However, given their sample sizes, it is not appropriate to draw conclusions on the effect of an intervention based on a single, or a number of small RCTs. Therefore, it is unlikely that more recent RCTs not captured in an overview of reviews would be sufficient to substantially alter recommendations informing major policy decisions. As noted the scoping review identified a large body of clinical effectiveness literature. For efficiency, it was agreed that if a recent high quality review that met our inclusion criteria was retrieved, then it would be used as a starting point for this report.

**Phase I:**

A de novo search for systematic reviews evaluating generic chronic disease SMS interventions was conducted in PubMed, Embase and the Cochrane Library (Database of Abstracts of Reviews of Effects [DARE], Cochrane Database of Systematic Reviews [CDSR] and Health Technology Assessment Database [HTA]). No language restrictions were applied. The search was limited to reviews of randomised controlled trials (RCTs) and systematic reviews of RCTs. Initially a start date of 1993 (the year in which the Cochrane Collaboration was established) was used as it marked the widespread initiation of high-quality systematic reviews. However, this was subsequently amended to 2009 due to the volume of systematic reviews retrieved. This was deemed appropriate given that the retrieved high quality reviews published after 2009 included the earlier RCT data. All searches were carried out up to 10 February 2015. A search of reference lists of relevant studies and previous review articles was also performed. The criteria used for including studies are shown in Table 3.1. Full details of the search strings used and the retrieved results are provided in Appendix A3.1.

**Phase II:**

During scoping, the following recent high quality overview of reviews was retrieved: "A rapid synthesis of the evidence on interventions supporting self-management for people with long-term conditions: PRISMS – Practical systematic Review of Self-Management Support for long-term conditions",[(2)] hereafter referred to as the PRISMS report. This review was commissioned by the UK National Institute for

Health Research (NIHR) in 2012 and published in 2014. Based on a systematic search of the literature up to 1 June 2012, it summarised the best available evidence for SMS for a range of diseases including asthma, chronic obstructive pulmonary disease (COPD), Type 1 and Type 2 diabetes, stroke and hypertension.1 For these diseases, this assessment therefore was limited to an update to the PRISMS report and was completed by running additional searches in PubMed, Embase and the Cochrane Library from 2012 to 1 April 2015, see Appendix A3.1. The results of the updated search as well as the original PRISMS findings are reported in the relevant chapters of this assessment with any changes to the PRISMS findings clearly documented. PRISMS also included a qualitative meta-review and implementation systematic review which assessed SMS at an organisational and professional level.[(2)] These sections of the PRISMS review were not updated and the results are not included here as it was beyond the immediate scope of this HTA. PRISMS did not include telehealth reviews as they deemed them to be typically about mode of delivery rather than content of what was delivered. Telehealth interventions were included in the updated review. De novo systematic reviews were undertaken for the remaining diseases included in the Terms of Reference for this project (heart failure and ischaemic heart disease) as these were not assessed in the PRISMS report. Systematic searches were run in PubMed, Embase and the Cochrane Library from 2009 to 1 April 2015, see Appendix A3.1.

### Table 3.1. PICOS criteria for study eligibility

| | |
|---|---|
| **Population** | **Phase I:** Adults ≥ 18 years old with at least one chronic disease. This includes common physical conditions such as asthma, COPD, arthritis, diabetes and cardiovascular diseases.<br><br>**Phase II:** Adults ≥ 18 years old with the specified disease (Type I or Type II diabetes mellitus, asthma, COPD, ischaemic heart disease, heart failure, hypertension or stroke). |
| **Intervention** | **Phase I:** Any generic self-management support intervention which helps patients manage aspects of their chronic disease through education, training and support.<br><br>All formats and delivery methods (group or individual, face-to-face or remote, professional or peer-led). All studies that include a large component of self-management support. The intervention is assessed in more than one chronic disease.<br><br>**Phase II:** Any disease-specific self-management support intervention which helps patients manage aspects of their chronic disease through education, training and support. |

[1] The dates for the searches varied for the different diseases, however, June 2012 was the earliest review.

| | |
|---|---|
| | All formats and delivery methods (group or individual, face-to-face or remote, professional or peer-led). All studies that include a large component of self-management support. The intervention is assessed in diabetes mellitus (Type I and Type II), asthma, COPD, ischaemic heart disease, heart failure, hypertension, or stroke. |
| **Comparator** | Studies where self-management support plus best medical care is compared with best medical care. |
| **Outcomes** | ▪ Health care utilisation (including unscheduled use of healthcare services – for example, GP visits, emergency department visits, hospital (re)admissions, hospital length of stay)<br>▪ Patient-centered outcomes relating to patient quality of life, patient satisfaction, self-efficacy<br>▪ Health outcomes (including biological markers of disease) |
| **Study design** | Systematic reviews of randomised controlled trials or systematic reviews (overview of reviews). |

**Key**: **COPD** – chronic obstructive pulmonary disease; **GP** – general practitioner.

As noted in Section 2.1, there is no universally accepted definition for self-management or SMS. This creates problems when attempting to identify, analyse and assess the available literature. Interventions may target different recipients (for example, patients, carers, health care professionals), include different components (for example, education, information, practical support, provision of equipment, social support, lifestyle advice, prompts, financial incentives), be delivered in different formats (for example, face-to-face, remote, web-based), be provided or facilitated by different individuals including healthcare personnel and trained or untrained lay persons, as well as differing in their intensity and duration. However, a consistent theme is that SMS interventions are typically complex interventions that include more than one component of SMS. For this reason, and consistent with the PRISMS report, with the exception of education interventions, this review did not assess single component SMS (for example, simple text message appointment reminders and drug reminder packaging). Other disease-specific inclusion or exclusion criteria are included in the individual disease chapters.

Given the wide range of SMS interventions identified, where possible the SMS interventions were classified by intervention type. Categorising the interventions into groups facilitated reporting and allowed study cross-over (overlap) to be assessed per intervention type.

### 3.1.3 Data extraction and quality assurance

Preliminary screening of all returned results was carried out by a single person to eliminate studies that were clearly not relevant. Assessment of eligibility of studies and identification of multiple reports from single studies was carried out independently by two people. Any disagreements were resolved by discussion.

Data extraction was performed independently by two people, with disagreements resolved by discussion. To adequately inform decisions in relation to the quantity and quality of evidence underpinning the findings of this assessment, quality assurance of the systematic reviews and meta-analyses was undertaken. The approach adopted and the tools used are discussed below. The quality of the primary studies underpinning the systematic reviews were not directly evaluated, instead information was extracted from the systematic reviews on the quality of the primary evidence, where reported.

**Phase I and Phase II**

Assessment of the quality of included systematic reviews was performed by two people independently using the Revised Assessment of Multiple Systematic Reviews (R-AMSTAR) quality appraisal tool.[19;20] This is an 11-item tool with item scores ranging from 1 to 4, providing therefore a possible range of up to 44 for the R-AMSTAR total scores. The methodology used by the PRISMS group was adopted given the validity of their approach and to facilitate interpretation and reporting of systematic reviews. The evidence was weighted by the quality of the systematic reviews retrieved (as indicted by the R-AMSTAR score) and the size of the studies they included (total number of participants included within the systematic review) to give an overall value (range * to ***) for each review (Table 3.2).

**Table 3.2. PRISMS quality ratings for systematic reviews[2]**

| Quality of studies | | |
|---|---|---|
| **Overall Value** | **Quality of systematic review using R-AMSTAR** | **Systematic review sample size** |
| * | Lower quality (R-AMSTAR score <31) | Smaller sample size (<1,000 participants). |
| ** | Lower quality (R-AMSTAR score <31) | Larger sample size (≥1,000 participants) |
| ** | Higher quality (R-AMSTAR ≥31) | Smaller sample size (<1,000 participants). |
| *** | Higher quality (R-AMSTAR ≥31) | Larger sample size (≥1,000 participants) |

**Note**: This table is taken from the PRISMS study by Taylor et al..[2]

If an included systematic review performed a quality of evidence assessment, this information was also collected during the data extraction process. Tools used included the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) system criteria[21] and the Jadad Scale.[22] GRADE identifies five key elements that can be used to rate confidence in the estimates of intervention effects. The criteria are: risk of bias; inconsistency of results; indirectness of evidence; imprecision; and publication bias. Assessing and combining these components determines the quality of evidence for each outcome of interest as 'high' (further research is very unlikely to change our confidence in this estimate of effect); 'moderate' (further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate); 'low (further research is likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate); and 'very low (any estimate of effect is very uncertain). The Jadad scale is a validated seven-item scale that assesses the quality of RCT methods relevant to random assignment, double blinding and the accountability of all patients including withdrawals; scores range from 0 (very poor) to 5 (rigorous). An 11-item scale with a range of 0 to 13 points has also been described; scores of nine or less are considered poor quality, while scores greater than nine are considered to be of good quality.

If a meta-analysis was undertaken, the quality and strength of evidence were evaluated in order to facilitate interpretation of the findings. Each meta-analysis was reviewed using a 43-item questionnaire that evaluated the data sources used, the analysis of individual studies by meta-analysts, the conduct of the meta-analysis, and its reporting and interpretation.[23] Based on this, each meta-analysis was graded as being of low, moderate or high quality. A grading of 'low quality' referred to studies where the conclusions were at high risk of bias due to poor data collection or methods of data synthesis. The conclusions in studies identified as 'moderate quality' were at risk of bias, but were likely to be broadly accurate, while studies graded as 'high quality' were very likely to have conclusions that accurately reflected the available evidence.

Where available, data on the validity of the RCTs included in each meta-analysis were extracted to determine their risk of bias, that is, the risk that they overestimated or underestimated the true intervention effect. Biases are broadly categorised as selection bias, performance bias, detection bias, attrition bias, reporting bias and other potential sources of bias. Bias is typically assessed using a specific tool, such as the Cochrane Risk of Bias Tool. For each element the risk of bias is assessed as low, high or unclear. For each meta-analysis, the number of primary studies that were rated as being at low risk of bias (or rated as high quality) was reported relative to the total number of primary studies.

Finally, as done by the PRISMS group, a value ranging from 0 (no evidence of effect) to *** / --- very strong evidence of effect in favour of the intervention/control was assigned to each finding based on the probability of the event (Table 3.3). Effect sizes reported in the individual reviews are not just based on probabilities but include ranges of effects and confidence intervals.

### Table 3.3 PRISMS evidence of effect[2]

| Evidence of effect | | |
|---|---|---|
| **Value** | **Probability** | **Evidence of effect** |
| 0 | p>0.05 | No evidence of effect. |
| +/– | 0.05≥p>0.01 | Some evidence of effect in favour of intervention/control. |
| ++/– – | 0.01≥p>0.001 | Strong evidence of effect in favour of intervention/control. |
| +++/– – – | p≤0.001 | Very strong evidence of effect in favour of intervention/control. |

**Note**: This table is taken from the PRISMS study by Taylor et al..[2]

## 3.2 Costs and Cost-Effectiveness

### 3.2.1 Literature review

A review of cost-effectiveness studies was undertaken to assess the available evidence for self-management support (SMS) interventions. Studies were included if they compared the costs and consequences of a SMS intervention to routine care.

A search was carried out to identify economic analyses of SMS interventions. In tandem with the systematic review of clinical effectiveness, the search for economic evaluations was carried out in PubMed, EMBASE and the Cochrane Library. The same search terms were used with the exception of terms for systematic review and meta-analysis. In place of these, search terms and filters for economic evaluations were applied. In addition, systematic reviews of SMS interventions identified through the clinical effectiveness search that included cost or economic outcomes were used to identify additional studies. The search was carried out up until 4 March 2015.

The PICOS (Population, Intervention, Comparator, Outcomes, Study design) analysis used to formulate the search is presented in Table 3.4 below.

**Table 3.4. PICOS analysis for identification of relevant studies**

| | |
|---|---|
| **Population** | **Phase I:** Adults ≥ 18 years old with at least one chronic condition.<br><br>**Phase II:** Adults ≥ 18 years old with the specified disease (Diabetes Type I or Type II, asthma, COPD, ischaemic heart disease, heart failure, hypertension or stroke). |
| **Intervention** | **Phase I:** Any generic self-management support intervention that helps patients to manage aspects of their chronic disease care through education, training or support.<br><br>**Phase II:** Any disease-specific self-management support intervention that helps patients to manage aspects of their chronic disease care through education, training or support. |
| **Comparator** | Routine care. |
| **Outcomes** | Cost or cost-effectiveness of intervention. |
| **Study design** | Randomised controlled trials, case-control studies, observational studies, economic modelling studies. |

**Key**: **COPD** – chronic obstructive pulmonary disease.

Studies were excluded if:

- application of the SMS was limited to a population with a single specified chronic disease (Phase I only),
- a nursing home or non-community dwelling population was included,
- they included a paediatric population,
- cost data were not clearly reported,
- published prior to 2000 (limited relevance).

### 3.2.2 Data extraction and quality assurance

Preliminary screening of all returned results was carried out by a single person to eliminate studies that were clearly not relevant. Assessment of eligibility of studies and identification of multiple reports from single studies was carried out independently by two people. Any disagreements were resolved by discussion.

Studies were classified into intervention types, where applicable, corresponding to the categories used for the assessment of clinical effectiveness.

In accordance with national HTA guidelines, assessment of the quality of the studies identified was performed independently by two people with the studies subsequently assessed for their transferability to the Irish healthcare setting. Any disagreements were resolved by discussion. The Consensus on Health Economic Criteria (CHEC)-list was used to assess the quality of the studies.[24] This tool is useful to evaluate economic evaluations that are being considered for inclusion in a systematic review with a view to increasing the transparency and comparability of the reviews. For studies that included an assessment of cost-utility or an economic modelling approach, assessment of the relevance of the studies to the Irish healthcare setting and their credibility was considered using a questionnaire from the International Society of Pharmacoeconomic Outcomes Research (ISPOR).[25] This tool is used and tailored towards appraising conventional economic evaluations which typically assess a set number of interventions in a specific population.

Costs reported in each of the studies were inflated to 2014 using the local consumer price index and expressed in Irish Euro using the purchasing power parity exchange rate.[26]

# 4 Generic self-management support for a range of chronic diseases

This health technology assessment (HTA) of generic self-management support (SMS) for a range of chronic diseases is one of a series of rapid HTAs assessing SMS interventions for chronic diseases. Section 4.1 provides a brief description of the chronic diseases assessed followed by separate reviews of the clinical (Section 4.2) and cost-effectiveness (Section 4.3) literature for generic SMS interventions. Brief descriptions of the background and methods used are included with full details provided in Chapter 3. Section 4.4 includes a discussion of both the clinical and cost-effectiveness findings. The report concludes with a list of key points in relation to generic SMS support (Section 4.5).

## 4.1 Description of the disease

This review assesses the clinical-effectiveness of generic self-management support (SMS) interventions which help patients manage aspects of their chronic disease through education, training and support. Reviews which assess interventions in more than one chronic disease are included per the PICOS criteria, Chapter 3 Table 3.1.

## 4.2 Review of clinical effectiveness of generic self-management support interventions

### 4.2.1 Background and Methods

Details of the background and methods for this assessment are included in Chapters 1 to 3 of this report. Briefly, an aim of this health technology assessment (HTA) is to review the clinical effectiveness of self-management support (SMS) interventions for a number of chronic conditions. Given the large volume of literature available, it was noted that an update of an existing high quality systematic review of SMS interventions could be considered sufficient to inform decision making.

In December 2014 a high-quality overview of reviews was published by the National Institute for Health Research in the UK. The Practical Systematic Review of Self-Management Support for long-term conditions (PRISMS) study comprised an overview of systematic reviews of randomised controlled trials (RCTs) up to 1 June 2012, and was itself undertaken according to the principles of systematic reviewing. Generic SMS interventions were not specifically addressed in the PRISMS report. This assessment therefore presents a de novo review of systematic reviews for these interventions. A search of PubMed, Embase and the Cochrane Library was undertaken to February 2015, see Appendix A3.1 for details. In accordance with the PICOS agreed with the key stakeholder, this assessment was limited to SMS interventions for adults aged 18 and over, with Phase I specifically addressing

generic interventions that could be used in a range of chronic diseases. As noted in Chapter 2, there is no universally accepted definition for self-management or SMS. This creates problems when attempting to identify, analyse and assess the available literature. However, a consistent theme is that SMS interventions are typically complex interventions that include more than one component (for example, education, information, practical support, provision of equipment, social support, lifestyle advice, prompts, financial incentives) of SMS. For this reason, with the exception of education interventions, this review did not assess single component SMS (for example, simple text message appointment reminders and drug reminder packaging). Further, to differentiate between SMS interventions that can be used in a range of chronic conditions and disease-specific interventions, studies that limited their inclusion criteria to a single chronic disease were excluded from the assessment of generic interventions.

Data extraction and quality assurance of the systematic reviews, meta-analyses and the risk of bias associated with the primary literature was undertaken as described in Chapter 3.1.3. In summary, in order to determine the quantity, quality, strength and credibility of evidence underpinning the various SMS interventions, quality assurance of both the systematic review methodology (R-AMSTAR) and the meta-analyses (Higgins et al.'s quality assessment tool)[23] was undertaken. While the R-AMSTAR score was used to determine the quality of the systematic reviews, the scores were then weighted by patient or participant trial size, with the quality of evidence being downgraded if the review was based on fewer than 1,000 participants. The quality of the primary evidence was not evaluated directly; however, where reported, information on the risk of bias of the primary studies was extracted from the systematic reviews.

### 4.2.2 Description of the interventions

Generic SMS interventions are interventions that can be used by any individual with a chronic disease and are not specifically tailored to support management of one chronic disease. A general description of self-management and typical generic SMS interventions is included in Chapter 2.

### 4.2.3 Results – Clinical-effectiveness

The search identified 25 completed studies that met the inclusion criteria, see Table 4.1. Details of the total numbers of citations retrieved by the searches, numbers of duplicates, numbers of studies and reasons for excluding studies are included in Appendix A4.1.

Based on the range of SMS interventions identified, the studies were broadly categorised into one of four intervention types: chronic disease self-management

programmes, telemedicine, web-based telemedicine, 'complex SMS interventions, effect on a specific outcome' and 'other SMS interventions'. Study overlap was assessed to identify studies that added little or no additional evidence. When substantial overlap was observed between two or more systematic reviews, we based our analyses on the higher quality or more comprehensive review. While many of the systematic reviews identified also included evidence for disease-specific interventions, the summary provided here is limited to the evidence for generic interventions compared with usual care.

The following sections summarise the literature retrieved for each of the four categories and include an assessment of the efficacy of the generic SMS interventions in that category and the quality of the evidence underpinning the assessment. In order to emphasise the relevance of the findings, results are grouped by the quality of the systematic review (using the R-AMSTAR score and size of the patient population). If a meta-analysis was completed, its quality was assessed as per Chapter 3 and graded as being of low, moderate or high-quality. A grading of 'low quality' referred to studies where the conclusions were at high-risk of bias due to poor data collection or methods of data synthesis. The conclusions in studies identified as 'moderate quality' were at risk of bias, but were likely to be broadly accurate, while studies graded as 'high-quality' were very likely to have conclusions that accurately reflected the available evidence (Chapter 3, Table 3.1).

### Table 4.1. Generic: Summary of systematic reviews retrieved, classified by intervention type

| Author (year) | Intervention |
|---|---|
| **Chronic disease self-management programmes** | |
| Boult (2009)[27] | Self-management focusing on the Stanford CDSMP |
| Franek (2013)[28] | SMS interventions – mainly Stanford CDSMP |
| Inouye (2011)[29] | Comprehensive care model – a component of which is chronic disease self-management which includes analysis of the Stanford CDSMP |
| Jonker (2009)[30] | Health behaviour change for chronic care – multiple conditions section focuses on generic models, mainly Stanford CDSMP |
| NZGG (2011)[7] | Self-management: cognitive behavioural therapies, health education, alternative therapies |
| Quinones (2014)[31] | Educational group visits for the management of chronic health conditions, mainly Stanford CDSMP |

| Author (year) | Intervention |
|---|---|
| **Telemedicine** | |
| Beratarrechea (2014)[32] | Mobile health interventions (cell phone voice communication, text messaging) |
| Muller (2011)[33] | Telephone-delivered CBT of varying intensities |
| Wootton (2012)[34] | Telemedicine (20 years) |
| **Web-based telemedicine** | |
| Bossen (2014)[35] | Self-guided web-based physical activity interventions |
| De Jong (2014)[36] | Internet-based asynchronous communication between health providers and patients |
| Eland de Kok (2011)[37] | E-health interventions (interactive websites, internet) (monitoring, treatment instructions, self-management training (coaching) and general information and web-based messaging) |
| Kuijpers (2013)[38] | Web-based interventions for patient empowerment and physical activity |
| McDermott (2013)[39] | Computers to deliver chronic disease self-management programmes |
| Paul (2013)[40] | Web-based approaches (CBT or information websites or access to expert advice ) impact on psychosocial health |
| Samoocha (2010)[41] | Web-based interventions effectiveness on patient empowerment |
| **Complex SMS interventions** | |
| Desroches (2013)[42] | Interventions to enhance adherence to dietary advice |
| Panagioti (2014)[43] | SMS interventions – 'Mixed problems' section includes the Stanford CDSMP. Remaining RCTs are not programmes or are disease-specific |
| Simmons (2014)[44] | Personalised health care (effect of patient engagement) |
| **Other SMS** | |
| Kivela (2014)[45] | Health coaching by health care professional |
| Ontario (2013)[46] | In-home care (care in the home, community, supportive housing, or long-term care facilities.) |
| O'Halloran (2014)[47] | Motivational interviewing |
| van Camp (2013)[48] | Nurse-led interventions to enhance medical adherence |
| Chang (2014)[49] | Information motivation behavioural skills |
| Coulter (2015)[11] | Personalised care planning - support behaviour change |

**Key**: **CBT**: Cognitive behavioural therapy; **CDSMP**: Chronic disease self-management programme; **RCTs**: Randomised controlled trials; **SMS**: Self-management support

#### 4.2.3.1 Summary of findings

Detailed summaries of the systematic reviews including the intervention, outcomes assessed, duration of follow-up, sample size (number of RCTs and total number of participants, and the evidence of effect) are included in Appendix A4.2. Table 4.2 below details the results of the quality assurance assessment of the systematic reviews and provides a summary of findings for selected outcomes from the various meta-analyses assessing the impact of generic SMS interventions in a range of chronic diseases.

## Table 4.2. Summary characteristics and findings for selected outcomes for included studies

| Study | Quality of Systematic Review | | | Primary Studies | | Quality of Meta-analysis | Health care utilisation (SMD) | QoL (SMD) |
|---|---|---|---|---|---|---|---|---|
| | R-AMSTAR score | Partici-pants | Quality | n | low-risk[a] | | | |
| Chronic disease self-management programmes | | | | | | | | |
| **Franek** 2013[28] | 28 | 6,074 | ** | 10 | 0 | Moderate | -0.03 (-0.09 to 0.04) GP visits<br>-0.05 (-0.18 to 0.09) ED visits<br>-0.06 (-0.13 to 0.02) H.Days<br>-0.09 (-0.24 to 0.05) Hosp. | 0.25 (0.12 to 0.39) Self-efficacy<br>-0.24 (-0.40 to -0.07) SR health<br>-0.20 (-0.29 to -0.12) health distress |
| **NZGG** 2011[7] | 28 | >1,000 | ** | 10 | [b] | N/A | | |
| Telemedicine | | | | | | | | |
| **Beratarrechea 2014**[32] | 30 | 4,604 | ** | 9 | 0 | N/A | | |
| **Muller** 2011[33] | 28 | 1,093 | ** | 8 | 1 | Low | | ES: 0.225 (0.105 to 0.344) Health status |
| **Wootton** 2012[34] | 22 | 37,695 | ** | 141 | [c] | N/A | | |
| Telemedicine web-based | | | | | | | | |
| **Bossen** 2014[35] | 28 | > 1,000 | ** | 7 | 5 | N/A | | |
| **De Jong** 2014[36] | 29 | 6,067 | ** | 15 | [d] | N/A | | |
| **Eland de Kok** 2011[37] | 24 | 11,203 | ** | 12 | 3 | N/A | | |
| **Kuijpers** 2013[38] | 26 | 5,204 | ** | 19 | 4 | N/A | | |
| **McDermott** 2013[39] | 26 | 1,506 | ** | 11 | 3 | N/A | | |
| **Paul** 2013[40] | 28 | 9,814 | ** | 11 | [c] | N/A | | |
| **Samoocha** 2010[41] | 33 | 3,417 | *** | 14 | 2 | Moderate | | 0.05 (-0.25 to 0.35) Self-efficacy |

**Abbreviations**: **ES** – effect size; **H.Days** – hospital days; Hosp. – hospitalisations; **N/A** = not applicable; **SMD** = standard mean difference; **SR health** – self-rated health

**Note**: [a] Number of the total primary studies identified as being at low risk of bias. [b] One of the 24 studies was included in this review and was rated as unclear risk of bias. [c] Risk of bias of primary studies not assessed. [d] Risk of bias not reported for individual studies.

## Table 4.2. (continued) Summary characteristics and findings for selected outcomes for included studies

| Study | Quality of Systematic Review | | | Primary Studies | | Quality of Meta-analysis | Health care utilisation (SMD) | QoL (SMD) |
|---|---|---|---|---|---|---|---|---|
| | R-AMSTAR score | Partici-pants | Quality | n | low-risk[a] | | | |
| Complex SMS interventions | | | | | | | | |
| **Desroches** 2013[42] | 37 | 9,445 | *** | 38 | 6 | N/A | | |
| **Panagioti** 2012[43] | 36 | 4,695 | *** | 11 | 3 | Moderate | ES: -0.12 (-0.20 to -0.03) | 0.13 (0.02 to 0.24) |
| **Simmons** 2014[44] | 31 | 3,023 | *** | 10 | 4 | N/A | | |
| Other SMS | | | | | | | | |
| **Chang** 2014[49] | 29 | 2,605 | ** | 12 | 4 | N/A | | |
| **Coulter** 2015[11] | 38 | 10,856 | *** | 19 | 6 | High | | -0.36 (-0.52 to -0.20) depression<br>NS HRQoL |
| **Kivela** 2014[45] | 30 | >1,000 | ** | 13 | [c] | N/A | | |
| **O'Halloran** 2014[47] | 33 | 1,176 | *** | 10 | 1 | Moderate | | |
| **Ontario** 2013[46] | 30 | >1,000 | ** | 12 | 4 | Moderate | | |
| **van Camp** 2013[48] | 29 | 2,587 | ** | 10 | 9 | Low | | |

**Abbreviations**: **ES** – effect size; **HRQoL** – health-related quality of life; **N/A** = not applicable; **NS** = non significant; **SMD** = standard mean difference.

Note: [a] Number of the total primary studies identified as being at low risk of bias. [b] Risk of bias of primary studies not reported. [c] Risk of bias not reported for individual studies.

## Table 4.2. (continued) Summary characteristics and findings for selected outcomes for included studies

| Study | Quality of Systematic Review | | | Primary Studies | | Quality of Meta-analysis | Health behaviours (SMD) | Health outcomes (SMD) |
|---|---|---|---|---|---|---|---|---|
| | R-AMSTAR score | Partici-pants | Quality | n | low-risk[a] | | | |
| Chronic disease self-management programmes | | | | | | | | |
| **Franek** 2013[28] | 28 | 6,074 | ** | 10 | 0 | Moderate | 0.16 (0.09 to 0.23) Aerobic exercise | -0.11 (-0.17 to -0.04) pain<br>-0.14 (-0.24 to -0.05) disability<br>-0.15 (-0.22 to -0.08) fatigue<br>-0.15 (-0.28 to -0.03) depression |
| **NZGG** 2011[7] | 28 | >1,000 | ** | 10 | [b] | N/A | | |
| Telemedicine | | | | | | | | |
| **Beratarrechea** 2014[32] | 30 | 4,604 | ** | 9 | 0 | N/A | | |
| **Muller** 2011[33] | 28 | 1,093 | ** | 8 | 1 | Low | | |
| **Wootton** 2012[34] | 22 | 37,695 | ** | 141 | [c] | N/A | | |
| Telemedicine web-based | | | | | | | | |
| **Bossen** 2014[35] | 28 | > 1,000 | ** | 7 | 5 | N/A | | |
| **De Jong** 2014[36] | 29 | 6,067 | ** | 15 | [d] | N/A | | |
| **Eland de Kok** 2011[37] | 24 | 11,203 | ** | 12 | 3 | N/A | | |
| **Kuijpers** 2013[38] | 26 | 5,204 | ** | 19 | 4 | N/A | | |
| **McDermott** 2013[39] | 26 | 1,506 | ** | 11 | 3 | N/A | | |
| **Paul** 2013[40] | 28 | 9,814 | ** | 36 | [c] | N/A | | |
| **Samoocha** 2010[41] | 33 | 3,417 | *** | 14 | 2 | Moderate | | |

**Abbreviations**: **N/A** = not applicable; **SMD** = standard mean difference.

**Note**: [a] Number of the total primary studies identified as being at low risk of bias. [b] One of the 24 studies was included in this review and was rated as unclear risk of bias. [c] Risk of bias of primary studies not assessed. [d] Risk of bias not reported for individual studies.

## Table 4.2. (continued) Summary characteristics and findings for selected outcomes for included studies

| Study | Quality of Systematic Review | | | Primary Studies | | Quality of Meta-analysis | Health behaviours (SMD) | Health outcomes (SMD) |
|---|---|---|---|---|---|---|---|---|
| | R-AMSTAR score | Partici-pants | Quality | n | low-risk[a] | | | |
| Complex SMS interventions | | | | | | | | |
| **Desroches** 2013[42] | 37 | 9,445 | *** | 38 | 6 | N/A | | |
| **Panagioti** 2012[43] | 36 | 4,695 | *** | 9 | 3 | Moderate | | |
| **Simmons** 2014[44] | 31 | 3,023 | *** | 10 | 4 | N/A | | |
| Other SMS | | | | | | | | |
| **Chang** 2014[49] | 29 | 2,605 | ** | 12 | 4 | N/A | | |
| **Coulter** 2015[11] | 38 | 10,856 | *** | 19 | 6 | High | | MD: -0.24% (-0.35 to -0.14) HbA1c<br>MD: -0.264 mmHg (-4.47 to -0.82) SBP<br>NS SBP<br>NS Cholesterol<br>NS BMI |
| **Kivela** 2014[45] | 30 | >1,000 | ** | 13 | [c] | N/A | | |
| **O'Halloran** 2014[47] | 33 | 1,176 | *** | 10 | 1 | Moderate | 0.19 (0.06 to 0.32) physical activity | |
| **Ontario** 2013[46] | 30 | >1,000 | ** | 12 | 4 | Moderate | MD: -0.14 (-0.27 to -0.01) ADL<br>MD: -0.12 (-0.29 to 0.05) Mobility<br>MD: -0.13 (-0.29 to 0.03) IADL | MD: 0.80 (0.54 to 1.19) Mortality |
| **van Camp** 2013[48] | 29 | 2,587 | ** | 10 | 9 | Low | 5.39 (1.70 to 9.07) Medication adherence (short term)<br>9.46 (4.68 to 14.30) Medication adherence (long term) | |

**Abbreviations**: **ADL**= activities of daily living; **BMI** = body mass index; **IADL** = Instrumental activities of daily living – e.g. accessing health care; **N/A** = not applicable; **NS** = non significant; **SBP** = systolic blood pressure; **SMD** = standard mean difference.

**Note**: [a] Number of the total primary studies identified as being at low risk of bias. [b] Risk of bias of primary studies not reported. [c] Risk of bias not reported for individual studies.

#### 4.2.3.2 Chronic disease self-management programmes

Six systematic reviews of chronic disease self-management programmes were identified for inclusion (one meta-analysis, five narrative reviews), see Appendices A4.2.1 and A4.2.2 for details.[7;27-31] The reviews were published between 2009 and 2014, and covered a range of chronic diseases such as osteoarthritis, chronic obstructive pulmonary disease (COPD), hypertension, stroke, and patients with multiple chronic diseases. Some reviews included specific populations such as 'vulnerable older people', Asian/Pacific islanders, Bangladeshi, and UK populations.

The six retrieved reviews included 25 unique randomised controlled trials (RCTs) of which there were 11 unique RCTs on the Stanford chronic disease self-management programme (CDSMP) or a variant thereof (for example, the Stanford CDSMP in varying populations and two RCTs on the UK's Expert Patient Programme [EPP]). There was considerable study overlap between the reviews as shown in Table 4.3. Other programmes that were assessed included the Flinders programme™ as described in Section 2.2.1 (n=1), 'Making the most of your healthcare' programme (n=1 RCT), 'Women Take PRIDE' programme (n=1 RCT), a fit and strong programme (n=1 RCT), a cognitive behavioural group programme (n=1 RCT) and a seven-week individual self-management and coping skills training programme (n=1 RCT).

**Table 4.3. Chronic disease self-management programmes: Study overlap between the included reviews**

| Review (year) | Quinones (2014) | Franek (2013) | Jonker (2009) | Boult (2009) | Inouye (2011) | NZGG (2011) |
|---|---|---|---|---|---|---|
| Quinones (2014) | **4** (4 CDSMP) | | | | | |
| Franek (2013) | 4 | **10** (9 CDSMP) | | | | |
| Jonker (2009) | 4 | 7 | **8** (8 CDSMP) | | | |
| Boult (2009) | 2 | 3 | 3 | **10** (3 CDSMP) | | |
| Inouye (2011) | 1 | 3 | 3 | 2 | **3** (3 CDSMP) | |
| NZGG (2011) | 4 | 8 | 7 | 3 | 3 | **2 SR + 8 RCTs*** (10 CDSMP) |

**Abbreviations: CDSMP =** Stanford chronic disease self-management programme or variant thereof, e.g. UK's Expert Patient Programme (**EPP**). ***Note**: The NZGG included two systematic reviews and 8 additional RCTs.

A systematic review retrieved by the New Zealand Guideline Group (NZGG) included a 2007 Cochrane review and meta-analysis by Foster et al.[50] that assessed self-management education programmes by lay leaders and which they had rated as 'good quality'. This Cochrane review included seven RCTS on the Stanford CDSMP, but their meta-analysis also included five RCTs on the arthritis version of the

Stanford self-management programme and five disease-specific RCTs.[50] Two further RCTs were included in the New Zealand Guideline Group review for motivational interviewing and for a primary-care-based diet and physical activity intervention. As this section is limited to a review of the generic CDSM programmes, these results are not discussed here.

Two reviews (Franek et al. and Jonker et al.) focused on the Stanford CDSMP, while Franek et al. included one additional RCT on the 'Making the most of your healthcare' programme. The reviews summarised the evidence for 10 and eight RCTs, respectively with an overlap of seven RCTs between them.[28;30]

Substantial overlap was also found with the other published systematic reviews. To minimise duplication, only results from Franek et al. and the New Zealand Guideline Group reviews are discussed, and is limited to the relevant, non-disease-specific findings. The R-AMSTAR scores of methodological quality of the two included systematic reviews were 28 out of 44, see Table 4.2, with both rated as '*two-star*' reviews based on their quality and size. The most common methodological limitations identified in the quality assessment of systematic reviews were failure to provide explicit statements that the scientific quality of the included RCTs had been assessed and evaluated; and failure to consider the quality of the scientific evidence in formulating the conclusions, see Appendix A4.2.2.

**Two star (**) reviews**

Health care utilisation outcomes:

A review and meta-analysis by Franek et al. which mainly assessed the Stanford CDSMP (nine out of 10 RCTs) reported no significant difference in health care utilisation (GP visits, emergency department visits, days in hospital, hospitalisation) between the Stanford CDSMP intervention and usual care.[28] This was based on a RCT follow-up of four to 12 months (with a median of six months). Using the GRADE criteria, the authors rated the included evidence as very low quality on the basis that there was a lack of concealment allocation and blinding in the trials, a lack of appropriate intention-to-treat analysis, and because the utilisation data came from patient recall rather than administrative data, meaning that there was a high degree of uncertainty around the results. A narrative review by the New Zealand Guideline Group concurred with this finding; it reported no significant difference in outcomes in terms of health care utilisation (based on five RCTs, only n=1 additional RCT compared to Franek et al. for the UK EPP).[7]

Patient reported outcomes (Quality of Life, patient satisfaction, self efficacy):

Franek et al. reported a small, statistically significant difference in patient-reported outcomes in favour of the Stanford CDSMP compared with usual care. More

specifically, it reported small, statistically significant improvements in self-efficacy, self-rated health, health distress, cognitive symptom management and communication with a health professional.[28] The authors rated this evidence as low quality based on the GRADE criteria.

The New Zealand Guideline Group reported no evidence of a difference in terms of quality of life for the Stanford CDSMP (n=1 RCT for the UK EPP) compared with usual care, although they noted that results from the UK's Expert Patient Programme (EPP) suggest more positive outcomes for patients with lower self-efficacy or health-related quality of life at baseline.[7]

Health behaviour outcomes (exercise, diet adherence):

Four reviews reported on health behaviour outcomes.[7;28-30] The meta-analysis by Franek et al. reported a small, statistically significant difference in favour of the CDSMP compared with usual care in terms of aerobic exercise. The authors assessed the evidence as being of 'low quality' using the GRADE criteria.[28]

Health outcomes (including biological markers of disease):

Three reviews reported on health outcomes.[28-30] The review and meta-analysis by Franek et al. reported a small, statistically significant difference in favour of the CDSMP compared with usual care in terms of pain, disability, fatigue and depression.[28] This was based on evidence rated as low quality using the GRADE criteria.[28]

**Summary statement for chronic disease self-management programmes**

The majority of the literature retrieved assessed the Stanford chronic disease self-management programme (CDSMP). Based on evidence assessed as being of very low quality and without long-term follow-up, there is no evidence of improvements in health care utilisation. Based on RCT evidence assessed as being of low quality, there is some evidence of short-term improvements in the patient-reported outcome of self-efficacy. There is some short-term evidence of improvement in health behaviour outcomes (exercise) and health outcomes (pain, disability, fatigue and depression) for the Stanford CDSMP.

### 4.2.3.3 Telemedicine

This section summarises the evidence retrieved for a range of telemedicine solutions. Not included are systematic reviews that specifically assessed web-based support (that is to say, web-based versions of the Stanford CDSMP and other web-based interventions) - these are reported separately in Section 4.2.3.4.

Three systematic reviews of telemedicine applications for chronic disease self-management were identified for inclusion (one meta-analysis, two narrative reviews).[32-34] Detailed summaries of the systematic reviews including the intervention, outcomes assessed, duration of follow-up, sample size (number of RCTs and total number of participants, and the evidence of effect) are included in Appendices A4.2.3 and A4.2.4. The reviews were published between 2011 and 2014, and covered a range of chronic diseases including osteoarthritis, diabetes, asthma, and cancer. The review by Wootton et al. reported on 20 years of telemedicine and retrieved a total of 141 RCTs and 22 systematic reviews.[34] The remaining two reviews reported on the impact of mobile health interventions on chronic diseases in developing countries (Beratarrechea et al.) and telephone-based cognitive based therapy (Muller et al.). A total of 156 unique RCTs were identified, with little cross-over between reviews (Table 4.4).

**Table 4.4. Telemedicine: Study overlap within the included reviews**

| Review (year) | Muller (2011) | Beratarrecha (2014) | Wootton (2011) |
|---|---|---|---|
| Muller (2011) | **8** | | |
| Beratarrechea (2014) | 0 | **9** | |
| Wootton (2012) | 0 | 2 | **141** |

The R-AMSTAR scores of methodological quality of systematic reviews ranged from 22 to 30 out of 44, see Table 4.2, with all rated as '*two star*' in this section. Common methodological limitations were failure to provide explicit statements that the scientific quality of the included RCTs had been assessed and evaluated; and failure to consider the quality of the scientific evidence in formulating the conclusions.

**Two star (**) reviews**

Patient reported outcomes (Quality of Life, patient satisfaction, self efficacy):

Two reviews presented patient-reported outcomes.[32;33] A low quality meta-analysis by Muller et al. (eight RCTs) reviewed varying intensities of telephone-delivered cognitive behavioural therapy (CBT) in people with chronic illness. It reported a significant improvement in health status following telephone-delivered CBT.[33] A

narrative review by Beratarrechea et al. reported improvements in health-related quality of life (two out of two RCTs) using mobile health interventions.[32]

Sub-group analyses were reported in the review by Muller et al. which examined the effects of amount of therapist contact, CBT focus and degree to which illness was immediately life-threatening.[33] It was noted that trials including fewer than five hours of therapist contact had a greater impact on health outcomes than trials in which participants had five or more hours of contact. Moderator analysis revealed little difference between interventions where the CBT focused mainly on emotions, compared with interventions where the CBT principles were mainly focused on the physical illness. The review also reported that telephone-delivered CBT was more effective in patients with non-life threatening illnesses.[33]

Health outcomes (including biological markers of disease):

A narrative review by Beratarrechea et al. reported health outcomes for telephone-delivered CBT.[32] It reported an improvement in a range of clinical outcomes using mobile health interventions in four out of five RCTs.[32]

One review reported on 20 years of telemedicine retrieving a total of 141 RCTs and 22 systematic reviews.[34] However, this review did not assess telemedicine specifically for self-management, but stated that its main roles have been in providing education (to improve self-management), in enabling information transfer (for example, telemonitoring), in facilitating contact with health professionals (for example, telephone support and follow-up) and in improving electronic records. It concluded that 73% of studies were favourable to telemedicine in chronic disease management, 26% were neutral and 1% were unfavourable. This was based on synthesising different outcomes for a range of diseases without any weighting of studies.

**Summary statement for telemedicine**

Based on the systematic reviews and the underpinning primary RCTs which were of limited quantity and quality, there is limited evidence that telephone-delivered cognitive behavioural therapy has a positive impact on health status.

#### 4.2.3.4 Web-based interventions

Seven systematic reviews of web-based chronic disease self-management interventions were identified for inclusion (one meta-analysis, six narrative reviews), see Appendices A4.2.5 and A4.2.6 for details.[35-41] The reviews were published between 2010 and 2014 and cover a range of chronic diseases such as diabetes, mental health, asthma, cancer, back pain and heart failure. The reviews assessed the web-based version of the Stanford CDSMP (n=1);[39] the effects of e-health on the chronically ill (n=1);[37] the effect of web-based interventions on physical activity

(n=2);[35;38] patient empowerment (n=2);[38;41] and psychosocial health (n=1);[40] respectively in patients with chronic diseases. A final review by de Jong et al. assessed web-based asynchronous communication[2] between health providers and patients with chronic conditions.[36] While this review could alternatively have been included in the telemedicine section, it was included here as it was mainly focused on web-based interventions. The seven systematic reviews comprised 78 unique RCTs with limited overlap between reviews (see Table 4.5).

**Table 4.5. Web-based: Study overlap between the included reviews**

| Review (year) | McDermott (2013) | Bossen (2014) | Kuijpers (2013) | de Jong (2014) | Paul (2013) | Samoocha (2010) | Eland de Kok (2011) |
|---|---|---|---|---|---|---|---|
| McDermott (2013) | **11** | | | | | | |
| Bossen (2014) | 0 | **7** | | | | | |
| Kuijpers (2013) | 0 | 3 | **19** | | | | |
| De Jong (2014) | 0 | 0 | 3 | **15** | | | |
| Paul (2013) | 0 | 0 | 0 | 0 | **11** | | |
| Samoocha (2010) | 0 | 0 | 3 | 3 | 0 | **14** | |
| Elan de Kok (2011) | 0 | 0 | 0 | 0 | 0 | 0 | **12** |

The R-AMSTAR scores of methodological quality of systematic reviews ranged from 24 to 33 out of 44, see Table 4.2. Broadly, the evidence assessed was of variable quality (with the quality of evidence underpinning individual conclusions generally low or not stated) and lacked long-term follow-up. The review by Samoocha et al. (2010) rated as the highest quality in this section as '*three stars',* (the remaining were rated '*two star*'). A common methodological limitation was failure to consider the quality of the scientific evidence in formulating the conclusions.

### Three star (***) reviews

Patient reported outcomes (Quality of Life, patient satisfaction, self efficacy):

A moderate quality meta-analysis by Samoocha et al. (three RCTs) reported no difference between web-based interventions and usual care in increasing general self-efficacy.[41]

### Two star (**) reviews

Health care utilisation outcomes:

[2] Non-concurrent communication by, for example, email.

Three narrative reviews reported health care utilisation outcomes.[36;37;39] The review by de Jong et al. reported a non-significant decrease in health care utilisation based on two RCTs.[36] In contrast, the review by McDermott et al., which compared the web-based Stanford CDSMP with no self-management, reported no difference in healthcare utilisation based on one RCT.[39] Eland-de Kok et al. reported only small effects for e-health on healthcare use based on one study and no significant differences in resource use in two studies.[37]

Patient-reported outcomes (Quality of Life, patient satisfaction, self efficacy):

Patient-reported outcomes were assessed in three *'two-star'* reviews.[36;38;40] The narrative review by de Jong et al. reported an increase in self-efficacy (one RCT), self-care (one RCT) and dyspnoea management (based on one RCT).[36] In terms of psychosocial outcomes, Paul et al. reported significant improvements in favour of the intervention in 20 out of 36 studies and no effect reported in 11 out of 36 studies.[40] Compared with usual care, Kuijpers et al. reported a significant increase in patient empowerment in four out of 13 RCTs; increases for both the intervention and the control in three out of 13 RCTs, and no difference in four out of 13 RCTs. They reported that patient satisfaction was generally high (10 RCTs).[38] Some studies noted potential usability issues when using web-based self-management.

Health behaviour outcomes (exercise, diet adherence):

Four narrative reviews reported health behaviour outcomes.[35;36;38;39] McDermott et al. compared the web-based Stanford CDSMP with no self-management and reported that the web-based Stanford CDSMP was more effective (11 studies), but that there was no evidence that the web-based version was better that the 'face to face' version of the Standard programme.[39] De Jong et al. reported improvements in general health behaviours in seven studies.[36] Bossen et al. reported a statistically significant improvement in physical activity in three out of seven studies, and no difference in four out of seven studies.[35] Kuijpers et al. reported improvements in physical activity in two out of 14 studies, but that physical activity increased for both the intervention and control groups in six out of 14 studies.[38] Eland-de Kok et al. reported mixed effects (improvements and no improvements) in terms of health outcomes when the intervention was used in addition to, or instead of, usual care.[37]

**Summary statement for web-based telemedicine**

There is insufficient evidence to determine if computer-based chronic disease self-management programmes are superior to usual care or standard 'face to face' versions of the Stanford programme. There is limited evidence that web-based cognitive behaviour therapy can have a positive impact on psychosocial outcomes.

#### 4.2.3.5 A range of self-management support interventions – effect on a specific outcome

The following section includes systematic reviews that assessed the impact of a range of SMS interventions on a specific outcome. Three systematic reviews were identified for inclusion: one meta-analysis; two narrative reviews, one of which was a Cochrane review. The reviews were published between 2013 and 2014 and covered chronic diseases such as cardiovascular diseases or hypertension, respiratory diseases and diabetes. The reviews assessed a range of SMS interventions to reduce health care utilisation,[(43)] improve dietary advice adherence[(42)] and to improve patient engagement[(44)] see Appendices A.4.2.7 and A4.2.8 for details.

There was no study cross-over between reviews with 57 unique RCTs identified. The review and meta-analysis by Panagioti et al. assessed the impact of several SMS interventions in populations with a range of chronic diseases to reduce health care utilisation. The meta-analysis synthesised evidence from 13 RCTs; of note four have already been commented on in the chronic disease self-management programmes section, so there is some duplication of evidence here.[(43)] Simmons et al. also assessed a range of SMS interventions, including chronic disease self-management programmes, internet-based programmes, self-help groups, and health coaching in one disease, with one RCT assessing the chronic disease self-management programme in several diseases. While the reviews by Panagioti et al. and Simmons et al. could alternatively have been included in section 3.2.1 on CDSMP, they are included here as Panagioti et al. combined the results of chronic disease self-management programmes and other SMS interventions in their meta-analysis and Simmons et al. based their conclusions on combining results of SMS interventions.

The R-AMSTAR scores of methodological quality of systematic reviews ranged from 26 to 37 out of 44, see Table 4.2, with all three reviews rated *'three-star'* (Desroches et al. Panagioti et al and Simmons et al.). A common methodological limitation was failure to consider the quality of the scientific evidence in formulating the conclusions.

**Three star (***) reviews**

Health care utilisation outcomes:

A moderate quality meta-analysis by Panagioti et al. of nine RCTs (four RCTs for the Stanford CDSMP) reported a small, but statistically significant reduction in hospital use.[(43)] However, it also reported that RCTs rated as having a high risk of bias reported greater reductions in health care utilisation. It was noted that a minority of SMS studies reported reductions in health-care utilisation in association with

decrements in health; the details of the intervention and exact numbers are not clear. The review also reported a small, but positive impact on health outcomes.[43]

Patient reported outcomes (Quality of Life, patient satisfaction, self efficacy):

A narrative review by Simmons et al. specifically assessed patient engagement for a range of SMS interventions.[44] It reported improvements in patient engagement (nine out of 10 studies, four of which rated as high quality) and self-reported health status (10 out of 10 studies, four of which rated as high quality).[44] It also reported improvements favouring the intervention in clinical markers of disease in five out of ten studies (four of which rated as high quality).[44]

Health behaviour outcomes (exercise, diet adherence):

A Cochrane review by Desroches et al. assessed a range of interventions to improve diet adherence.[42] A meta-analysis was not undertaken due to the broad range of interventions assessed. Compared with usual care, 32 of 98 dietary adherence outcomes favoured the intervention group, four favoured the control group and 62 had no significant difference between groups. Statistically significant improvements in diet adherence were found in RCTs assessing telephone follow-up, video, contract, feedback, nutritional tools and multiple tools. No statistically significant improvements in diet adherence was found in RCTs assessing the benefit of group sessions, individual sessions, reminders, restriction, and behaviour change technique interventions compared with usual care.

**Summary statement for a range of self-management support interventions**

There is some evidence that a range of self-management support interventions can lead to small, but significant reductions in health care utilisation. However, it is not possible to identify which types of SMS interventions or components of SMS contribute to the positive results. Based on one high quality narrative review, there is some evidence of improvements in diet adherence with a range of self-management support interventions (telephone follow-up, video, contract, feedback, nutritional tools and multiple tools). There is some evidence of improvements in patient engagement and self-reported health status for a range of SMS interventions (such as chronic disease self-management programmes, internet based programmes, self-help groups, health coaching) based on one narrative review.

### 4.2.3.6 Other SMS interventions

The following section includes six systematic reviews of other interventions for chronic disease self-management (four meta-analyses and two narrative reviews), see Appendices A4.2.9 and A4.2.10 for details.[45-49;51] The reviews were published between 2013 and 2015, and covered a range of chronic diseases, including HIV,

obesity and heart failure. Interventions included health coaching (narrative review, n=1),[45] nurse-led interventions for medication adherence (meta-analysis, n=1),[48] motivational interviewing to increase physical activity (meta-analysis, n=1),[47] the Health Quality Ontario group on in-home care (narrative review and meta-analysis, n=1),[46] personalised care planning (meta-analysis, n=1)[51] and information-motivation-behavioural skills model (narrative review, n=1).[49] There was minimal study cross-over between reviews with 73 unique RCTs. The review by Health Quality Ontario assessed in-home care for a range of diseases with a section on 'chronic disease multimorbid patients'; it included a total of two RCTs.[46]

The R-AMSTAR scores of methodological quality of systematic reviews ranged from 29 to 38 out of 44, see Table 4.2, with two reviews rated *'three stars'* (Coulter et al., O'Halloran et al.) and the remaining rated '*two stars'*(Chang et al., Kivela et al., Ontario, van Camp et al.). A common methodological limitation was failure to consider the quality of the scientific evidence in formulating the conclusions.

**Three star (***) reviews**

Patient reported outcomes (Quality of Life, patient satisfaction, self efficacy):

A high quality meta-analysis (n=19 RCT) by Coulter et al. reported a small effect in favour of personalised care for depression based on moderate quality evidence.[51]

Health behaviour outcomes (exercise, diet adherence):

Based on a moderate quality meta-analysis of eight RCTs, O'Halloran et al. reported that motivational interviewing led to improvements in physical activity and, based on a further narrative review) improvements in weight loss (significantly improved results in three out of three RCTs).[47]

**Two star (**) reviews**

Patient reported outcomes (Quality of Life, patient satisfaction, self efficacy):

A narrative review by Kivela et al. on health coaching reported significant improvements in terms of physical health status (three out of four studies), self-efficacy (two out of three studies), satisfaction of treatment (two out of two studies) and mental health (two out of three studies) in the short term (<8 months) with non-significant improvements in the longer-term (12 to 24 months).[45]

Health behaviour outcomes (exercise, diet adherence):

Two narrative reviews (Kivela et al. on health coaching[45] and Chang et al. on information-motivation-behavioural skills model [49]) and a meta-analysis (van Camp et al. on nurse-led interventions[48]) reported on health behaviour outcomes. Kivela

et al. reported significant improvements in weight loss (three out of three RCTs) and physical activity (six out of 10 studies). The meta-analysis by van-Camp et al. reported improved medication adherence using nurse-led interventions (quality rated acceptable to high)[48] while the narrative review by Chang et al. reported improved medication adherence using the information-motivation-behavioural skills model (five out of six studies).[49] The latter review also reported significant behavioural changes at the first post intervention assessment (10 out of 12 studies) and a likely reduction in high-risk sexual behaviour for HIV patients only.[49]

Health outcomes (including biological markers of disease):

Three reviews on health coaching,[45] in-home care[46] and information-motivation-behavioural skills model[49] reported on a range of health outcomes. In-home care was defined as care predominantly in the patient's home that was curative, preventive or supportive in nature and aimed to enable clients to live at home. The meta-analysis by Health Quality Ontario group reported no difference between in-home care and usual care for all-cause mortality, but noted improvements in activities of daily living, instrumental activities of daily living and mobility with in-home care.[46] The narrative reviews by Kivela et al. and Chang et al. reported improvements in health outcomes in the short term (diabetes only, statistically significant in two out of four studies less than six months and not significant in a further two at six to 12 months),[45] improvements in two out of five studies[49]).

**Summary statement for other SMS interventions**

There is some evidence that personalised care planning and motivational interviewing can have a positive impact on depression and physical activity, respectively. There is some evidence that nurse-led interventions or using the information-motivation-behavioural skills model lead to improvements in medication adherence. There is some evidence that in-home care leads to improvements in activities of daily living, instrumental activities of daily living and mobility. Due to limited study follow-up, it is not known if the effects observed are sustained in the longer term.

## 4.3 Review of cost-effectiveness of generic self-management support interventions

A review of cost-effectiveness studies was carried out to assess the available evidence for generic self-management support (SMS) interventions for varying chronic diseases. Studies were included if they compared the costs and consequences of a generic SMS intervention with routine care.

### 4.3.1 Search strategy

A search was carried out to identify economic analyses of SMS interventions. In tandem with the systematic review of clinical effectiveness, the search for economic evaluations was carried out in MEDLINE, EMBASE and the Cochrane Library. The same search terms were used with the exception of terms for systematic review and meta-analysis. In place of these, search terms and filters for economic evaluations were applied. In addition, fourteen systematic reviews of SMS interventions were identified through the results of the clinical effectiveness search that included cost or economic outcomes; these were used to identify additional studies.[32;34;37;52-62] The search was carried out up until 4 March 2015.

The PICOS (Population, Intervention, Comparator, Outcomes, Study design) analysis used to formulate the search is presented in Table 4.6 below.

**Table 4.6. PICOS analysis for identification of relevant studies**

| | |
|---|---|
| **Population** | Adults ≥ 18 years old with at least one chronic condition. |
| **Intervention** | Any generic self-management support intervention that helps patients to manage aspects of their chronic disease care through education, training or support. |
| **Comparator** | Routine care. |
| **Outcomes** | Cost or cost-effectiveness of intervention. |
| **Study design** | Randomised controlled trials (RCTs), case-control studies, observational studies, economic modelling studies. |

Studies were excluded if:

- application of the SMS was limited to a population with a single specified chronic disease
- a nursing home or non-community dwelling population was included
- it included a paediatric population
- cost data were not clearly reported
- published prior to 2000 (due to limited relevance).

As outlined in Chapter 3.2.2 and in accordance with national HTA guidelines, assessment of the quality of the studies using the Consensus on Health Economic Criteria (CHEC)-list was performed independently by two people. For studies that included an assessment of cost-utility or an economic modelling approach, assessment of the relevance to the Irish healthcare setting and their credibility was considered using a questionnaire from the International Society of Pharmacoeconomics and Outcomes Research (ISPOR).

### 4.3.2 Results

The bibliographic search returned 525 studies from across the three databases, which equated to 491 unique studies after removal of duplicates (see Appendix A4.1. A further 70 studies were identified from hand searching references in previously published systematic reviews. Preliminary screening of all returned results was carried out by a single person to eliminate studies that were clearly not relevant. Assessment of eligibility of studies and identification of multiple reports from single studies was carried out independently by two people. Any disagreements were resolved by discussion. After removing irrelevant studies based on the titles and abstracts, 37 studies were identified for a full-text review. A further 12 studies were excluded based on various exclusion criteria, leaving 25 included studies.

This review retrieved few conventional economic evaluations; many of the retrieved studies gathered cost data as part of an RCT or case-control type study or completed costing studies. Results of the assessment indicate that the data available are limited in quality, see Appendix A4.3 for details.

Studies were predominantly conducted in the US (15), with five studies from the UK, two from Canada, two from Australia and one from Norway. The included studies were all published between 2000 and 2014. The characteristics of the included studies are given in Table 4.7. Costs reported in each of the studies were inflated to 2014 pricing levels using the local consumer price index and expressed in Irish Euro using the purchasing power parity index.

## Table 4.7 Included studies

| Study | Country | Intervention |
|---|---|---|
| **Aanesen (2011)**[63] | Norway | Smart house technology and video visits |
| **Ahn (2013)**[64] | US | Chronic Disease Self-Management Programme |
| **Battersby(2007)**[65] | Australia | Behavioural and care planning (CDSMP)* |
| **Bendixen (2009)**[66] | US | Telerehabilitation |
| **Dimmick (2000)**[67] | US | Rural telemedicine programme |
| **Doolittle (2000)**[68] | US | A telehospice service providing hospice care in the home |
| **Elliott (2008)**[69] | UK | Telephone-based pharmacy advisory service |
| **Finkelstein(2006)**[70] | US | Telemedicine delivered home healthcare using videoconferencing and physiologic monitoring |
| **Graves (2009)**[71] | Australia | Telephone counselling for physical activity and diet |
| **Griffiths (2005)**[72] | UK | Culturally adapted self-management programme |
| **Henderson(2013)**[73] | UK | Community-based telehealth intervention |
| **Jerant (2009)**[74] | US | Home- or telephone-based peer-led chronic illness self-management support |
| **Johnston (2000)**[75] | US | Remote video technology for home health care |
| **Katon (2012)**[76] | US | Multi-condition collaborative treatment programme. Physician-supervised nurses collaborated with primary care physicians to provide treatment of multiple disease risk factors. |
| **Lorig (2001)**[77] | US | Chronic Disease Self-Management Programme |
| **Moczygemba(2012)**[78] | US | Pharmacist-provided telephone medication therapy management |
| **Noel (2000)**[79] | US | Telemedicine integrated with nurse case management for the homebound elderly. |
| **Noel (2004)**[80] | US | Home telehealth programme |
| **Page (2014)**[81] | US | Six-week group education and support programme |
| **Pare (2013)**[82] | Canada | Tele-homecare programme for elderly patients with chronic health problems |
| **Richardson (2008)**[83] | UK | Lay-led self-care support group ("Expert Patients Programme") |
| **Schwartz (2010)**[84] | US | Online chronic disease self-management programme |
| **Scott (2004)**[85] | US | Group outpatient model for chronically ill, older patients |
| **Steventon (2013)**[86] | UK | Telephone health coaching service (Birmingham OwnHealth) |
| **Tousignant (2006)**[87] | Canada | Rehabilitation through teletreatment |

*An output of this research was the Flinders model of self-management support programme.

The studies were classified into four intervention types corresponding to those used for the assessment of clinical effectiveness: chronic disease self-management (CDSM) programmes; telemedicine; internet-based telemedicine; other SMS interventions. The following sections consider the evidence by intervention type.

#### 4.3.2.1 Chronic disease self-management programmes

Six studies were retrieved that assessed chronic disease self-management programmes: two US studies evaluated the Stanford CDSMP,[64;77] one UK study assessed the Expert Patients Programme (a UK version of the Stanford CDSMP),[83] one UK study was based on a culturally-adapted version of the Expert Patients Programme, and one US costing study evaluated a group education and support programme.[81] The sixth study was a costing study that ran alongside four RCTS in four areas in Australia. This research subsequently led to the development of the Flinders model of SMS.[65] Five of the studies used a comparator of routine care, while the sixth was a costing study with no comparator (see Table A4.3.2). With the exception of the Lorig study,[77] which was restricted to four disease groups (heart disease, lung disease, stroke or arthritis), patient populations included those with any chronic conditions. The size of the study population was between 476 and 4,603 patients. For studies that included treatment costs, follow-up varied between four and 24 months.

Estimated costs per participant for the chronic disease self-management programmes were reported in the five studies. The most recent assessment of the Stanford CDSMP was in 2013 by Ahn et al. [64] which estimated a cost of €335 per participant (ranging between €168 and €690, depending on the number of participants per workshop and the cost of running a workshop). Based on 2005 data, Richardson et al. estimated a cost of €380 per participant for the UK version of the CSDMP, the Expert Patients Programme.[83] The culturally-adapted version of the Expert Patients Programme cost €192 per participant to deliver.[72] Finally, the education and support programme evaluated by Page et al. had an estimated cost of €172 per participant.[81]

In terms of incorporating the costs associated with treatment, four of the studies included healthcare utilisation costs.[64;65;77;83] Three studies calculated costs as part of an RCT while the fourth study used observational data. Three studies reported cost savings associated with the intervention. The two US studies reported savings of €364 over 12 months and between €511 and €682 over 24 months. The UK study estimated savings of €41 per participant over six months. The US studies therefore estimated greater savings, although these differences may relate to greater hospitalisation costs rather than improved clinical effectiveness. The authors of the Australian study noted that the trials demonstrated individual health and well-being

can be improved through patient-centred care, but was not able to demonstrate a sufficient reduction in hospital admissions to pay for the costs of coordinated care.[65]

The UK study also estimated the effect of the intervention on quality of life.[83] The study collected information on participant quality of life at baseline and six months using the EQ5D instrument (a standardised instrument for use as a measure of health outcome). The intervention was associated with an estimated quality adjusted life year (QALY) gain of 0.02 per person over six months, resulting in an incremental cost effectiveness ratio of -€2,052 per QALY.

#### 4.3.2.2 Telemedicine

Fifteen studies were identified that assessed a variety of telemedicine interventions (see Table A4.3.3). Interventions typically involved video or telephone interaction between the patient and healthcare professional in place of physical visits by the clinician or provider. The intention in most of the interventions was to increase efficiency by reducing the amount of time spent by healthcare professionals in transit to and from patients. The time saving and associated opportunity cost had to be contrasted with the cost of setting up the service, which often required capital expenditure on equipment for patients to enable telemedicine, particularly in the case of video visits.

Fourteen of the studies were based on patient data gathered either as part of an RCT, case-control study or observational study. Study sizes ranged from four to 9,977 patients; one study modelled costs based on published data.[63] Where reported, the mean age of patients was generally over 70 years, although one study had a mean age of 58 years.[71] The comparator was routine care for the particular patient population. Seven of the studies included patient populations with any of several chronic conditions.[63;66-68;70;79;86] Six studies included patients with one of a number of specified chronic conditions.[69;71;73;75;80;82] Two studies included patients eligible for medication therapy management and a prescription for physiotherapy follow-up. Patient follow-up ranged from two to 24 months.

Of the three studies that evaluated videoconference visits, two found modest cost savings per patient visit;[70;75] one of these was restricted to the costs of nurse visits, and hence it is unclear if there were any benefits in terms of other healthcare utilisation costs.[70] A modelling study of video visits found that the technology could be cost-effective if there were substantial efficiency gains for healthcare professionals (for example, through less time spend travelling to patients' homes).[63]

Two studies investigated telephone-based medicine management services.[69;78] Elliott et al. found that adherence improved in the intervention group, and estimated

a cost saving of €3,296 per additional adherent patient; however, study follow-up was limited to two months, rendering the sustainability of these effects unclear. Moczygemba et al. reported reductions in drug costs for the intervention group and increases in the same 12 month follow-up for the control group.[78] It should be noted in the latter study that the intervention participants were self-selected.

Two studies reported increased healthcare utilisation in the intervention group.[66;86] In the study by Bendixen et al. the increased utilisation was explained by increases in the areas of preventive medicine, including laboratory and radiology, and primary and geriatric patient care.[66] Meanwhile, Steventon et al. found increased emergency admissions and secondary care costs in the intervention group that could not be explained.[86]

Studies of telemedicine in a rural setting, for home hospice care and for physiotherapy follow-up all found reduced visit costs, but it was unclear how many face-to-face visits could be replaced by telephone visits.[67;68;87] Per visit savings were estimated to be €70, €41 and €74, respectively. Savings of €70 were estimated in a study that focussed on a rural population where the average distance travelled per visit was 61 miles.[67]

Two US studies of home telehealth by Noel et al. found either no difference in costs between control and intervention, or a slightly greater reduction for control than intervention.[79;80] The sample sizes were small (19 and 104 patients, respectively) and the latter study had a follow-up of no more than 12 months.

Graves et al. evaluated a telephone counselling service for patients with Type 2 diabetes or hypertension in a disadvantaged community in Australia.[71] The intervention was compared with usual care, although for ethical reasons usual care had to include the provision of literature and feedback to participants. It was also compared to the baseline data which was described as a real control. Utilities were estimated based on SF-36 responses by study participants. Compared with usual care, the intervention had an incremental cost-effectiveness ratio (ICER) of €115,352 per quality-adjusted life year (QALY), which in turn had an ICER of €17,861 per QALY relative to the real control (baseline) data. The willingness-to-pay threshold was reported as €94,000 per QALY. Although not cost-effective relative to usual care, the authors reported an ICER of €42,603 for the intervention relative to baseline data. The usual care comparator acted as a brief intervention, but there was no evidence to support it as an ongoing intervention and they concluded that the baseline data represented the true comparator.

A telehomecare programme was assessed in a Canadian study.[82] The technology was a tactile screen and an integrated modem that came programmed with a personalised monitoring protocol that monitored various health parameters, costing

an average €323 to provide per patient. Some measures of healthcare utilisation, such as nurse home visits, increased during and after the intervention. The average cost per patient was €1,058 less with the intervention compared to baseline. Patient satisfaction data were collected after four months using the system, and showed a generally high degree of satisfaction. A UK telehealth study had intervention costs of €214 for equipment and €368 for monitoring services.[73] The intervention resulted in an increased cost per patient of €268 over 12 months. The incremental cost-effectiveness ratio was estimated at €119,337 per QALY, suggesting that the intervention is unlikely to be considered cost-effective.

#### 4.3.2.3 Internet-based telemedicine

A single study evaluating an internet-based disease management programme was found (Table A4.3.4).[84] The study used a retrospective, quasi-experimental, cohort design to compare participants and matched non-participants in the programme. Participants had a mean age of 47 and were members of a health insurance programme. The intervention was an online generic chronic disease management tool. Healthcare expenditure in participants was compared to predicted expenditure using data on non-participants. It was estimated that annual healthcare expenditure decreased by €743 per participant. It was also estimated that there was a return on investment of €10 for every Euro spent after one year using the online self-management programme. Use of a modelling approach to determine predicted expenditure introduced uncertainty into the interpretation of the results that was not clearly accounted for in the study report. The authors were employees of the company that produced and marketed the online tool being evaluated for the providing health insurer.

#### 4.3.2.4 Other SMS models

Three studies were identified that assessed other models of self-management, both with 24 months of follow-up data (Table A4.3.5).[74;76;85]

Jerant et al. compared costs for a one-to-one home-based peer-led chronic illness self-management training programme that was delivered in home or by telephone with usual care in an RCT with 12 months follow-up involving patients aged 40 years and older with one or more of six common chronic illnesses (arthritis, asthma, COPD, heart failure, depression, diabetes). Although the in-home intervention had a limited effect on self efficacy (observed at six weeks and six months only), no effect was observed for other outcomes or for healthcare expenditures. When delivered by telephone, no significant effect was observed on any outcome.[74]

Katon et al. compared a multi-condition collaborative treatment programme with usual primary care in outpatients with depression and poorly controlled diabetes or

coronary heart disease.[76] The mean patient age was 57 years. A generic tool combining elements of interventions for depression, diabetes and chronic disease self-management was applied across the three diseases. A nurse manager was involved to enhance self-management. QALYs were estimated with improvements in biomarkers such as HbA1C and systolic blood pressure. The intervention was associated with an increase in depression-free days and increased QALYs. There was an estimated mean cost saving of €1,741 per QALY and €5 per depression-free day.

A group outpatient visit model was assessed by Scott et al.[85] Groups met with their primary care physician and a nurse every month for 90 minutes; allied health professionals would attend if necessary. Meetings included a nurse review of patient charts and blood pressure readings. Patients in the intervention group had lower healthcare utilisation and the monthly cost was €60 less per patient than for the control group. There was no evidence of effect on functional outcomes.

## 4.4 Discussion

This section discusses the main findings from the review of the clinical-effectiveness and cost-effectiveness literature.

### 4.4.1 Clinical-effectiveness

A vast range of generic self-management support (SMS) interventions is available and this is evident in the large body of literature retrieved as part of this review. The retrieved reviews were generally assessed to be of low to medium quality, with Cochrane reviews and meta-analyses typically being rated as having the highest quality.

Broadly, the largest body of literature was retrieved for generic chronic disease self-management programmes, mainly the Stanford CDSMP. Clinically minimal, short-term improvements in patient-reported outcomes, health behaviour, and health outcomes in favour of the Stanford CDSMP compared with usual care were noted, but the results were based on evidence of low quality. Common methodological limitations were a lack of concealment allocation and blinding in the trials, and a lack of appropriate intention-to-treat analysis, meaning that there is a high degree of uncertainty around the results. Generally, some small reductions in healthcare utilisation were reported in individual RCTs for chronic disease self-management programmes and in a review of a range of generic SMS interventions, with no evidence of a negative impact on health outcomes.

The remaining generic SMS tools comprised a heterogeneous set of interventions that have been assessed for a diverse range of chronic diseases. While there is a large quantity of evidence, it is not clear that this evidence is of sufficient quality.

There is a trend to small, clinically minimal improvements in a range of chronic diseases; the evidence is typically of low quality with a short term follow-up. It is possible that there are subgroups of people with chronic diseases that may respond better to generic SMS interventions. For example, as highlighted in the systematic review by the New Zealand Guideline Group (Section 4.2.3.2) a post-hoc subgroup analysis of the UK's Expert Patient Programme (EPP) suggested that patients with lower self-efficacy and health-related quality of life at baseline experienced greater benefits participating in the CDSMP. However, based on the available evidence, it is not possible to determine if there are subgroups of people with chronic diseases that may respond better to generic SMS interventions and which of these interventions is more effective.

As such, the optimal format of generic SMS, the diseases in which it is likely to provide benefit, and the duration of effectiveness, if any, is still unclear. Some reviews suggest that SMS should be tailored to a specific disease as patients knowledge of their own disease is believed to be an essential component of self-management. Consideration may also need to be given to patient age when tailoring generic programmes as the average age may differ considerably depending on the chronic condition under consideration. While the increasing prevalence of multimorbidity (commonly defined as the co-occurrence of two or more chronic medical conditions within an individual) has been noted as a potential limitation to the role of generic SMS interventions, it has also been highlighted that interventions that are targeted at either specific combinations of common conditions, or at specific risk factors or functional difficulties for patients with multiple conditions, may be more effective.[88] This is particularly important given the evidence that the presence of multimorbidity is predictive of future functional decline and leads to worse health outcomes with the effect being more pronounced in patients with increasing numbers of chronic disease and is linked to disease severity.[88] The need for tailored interventions is also emphasised by the fact that some multimorbid patients may be too ill to participate in some forms of SMS or may have substantial existing treatment burden, attending multiple providers for a range of complex treatments.

More research is needed to explore the long-term, 12 months and greater, effect of generic self-management interventions across all outcomes and to explore the impact of self-management on clinical outcomes.

### 4.4.2 Cost-effectiveness

The 25 included studies evaluated a wide range of interventions; while the six studies evaluating chronic disease self-management programmes were relatively homogeneous, the telemedicine interventions comprised a heterogeneous group.

Many of the studies gathered cost data as part of an RCT or case-control type study with relatively small sample sizes. While this approach may address questions of efficacy, it may not be readily applicable when the intervention is rolled out to a larger population. The cost per patient of delivering some of the interventions, such as the CDSM programmes, is dependent on the number of participants in each group. Economy of scale issues mean that the average cost may be higher if implemented in rural or sparsely populated areas where there may be fewer participants per group. The results for telemedicine were the converse, where the greatest savings could be achieved in areas with the longest travel times for care providers to reach patients' homes.

Follow-up tended to be short, with all but one study recording between two and 24 months of data. It is unclear whether the costs of providing the interventions or any observed changes in healthcare utilisation will be sustained beyond the study period, or even if there is a trend within the recorded data. For telemedicine interventions that replace face-to-face visits with video or telephone interaction, patient satisfaction may be high initially, but could reduce over time; however, follow-up of included studies was too short to evaluate this issue.

Few of the studies were structured as conventional economic evaluations, and hence there was frequently a lack of clarity regarding methodology. The wide variety of study settings mean that it is difficult to determine if the costs used are similar to what might accrue in an Irish context.

Two studies showed increased healthcare utilisation in the intervention group,[66;86] with one of those studies reporting that it was due to increased preventive care.[66] Most of the included studies appeared to use a payer perspective, although generally this was not clearly reported. For patients with chronic conditions in Ireland there may be substantial out-of-pocket expenses due to primary care utilisation.

In summary, there is limited evidence on the cost-effectiveness of generic chronic disease SMS interventions. The available evidence is for a heterogeneous set of interventions and comprised results from a number of RCTs with typically small sample sizes and short follow-up periods. This is in contrast to the review of the clinical effectiveness literature, which included 25 systematic reviews of 362 unique RCTs. The general finding is that chronic disease self-management programmes and telephone-based telemedicine programmes are relatively cheap to deliver per patient, but the magnitude of any cost saving in terms of reduced healthcare utilisation is unclear. Although generally inexpensive on a per-patient basis, the budget impact could be very substantial if implemented for all eligible patients.

Based on the available evidence, it is not possible to state whether implementing a generic chronic disease SMS intervention would be likely to result in cost savings, or

if such savings would be sustainable. The most consistent evidence is in regard to chronic disease self-management programmes, but the potential benefit is dependent on how efficiently the programme is run and there is no evidence of longer term cost savings.

## 4.5 Key messages

- Generic chronic disease self-management support (SMS) interventions comprise a heterogeneous group for which there is limited evidence of clinical effectiveness. Generally low or unreported quality of included studies that typically had only short term follow-up means that there is a high degree of uncertainty around the results.
- The majority of the literature retrieved assessed the Stanford chronic disease self-management programme (CDSMP). Based on RCT evidence assessed as being of low quality, there is some evidence of short-term improvements in the patient-reported outcome of self-efficacy. There is some short-term evidence of improvement in health behaviour outcomes (exercise) and health outcomes (pain, disability, fatigue and depression) for CDSMPs.
- Based on the systematic reviews and the underpinning primary RCTs which were of limited quantity and quality, there is some evidence that telephone-delivered cognitive behavioural therapy has a positive impact on health status.
- There is insufficient evidence to determine if computer-based chronic disease self-management programmes are superior to usual care or standard 'face to face' versions of the Stanford CDSMP. There is limited evidence that web-based cognitive behaviour therapy can have a positive impact on psychosocial outcomes.
- There is some evidence that a range of self-management support interventions can lead to a small, but significant reduction in health care utilisation; however, it is not possible to identify which types of SMS interventions or components of SMS contribute to the positive results. Based on one high quality narrative review, there is some evidence of improvements in diet adherence with a range of SMS interventions (telephone follow-up, video, contract, feedback, nutritional tools and multiple tools). There is some evidence of improvements in patient engagement and self-reported health status for a range of SMS interventions (such as chronic disease self-management programmes, internet based programmes, self-help groups, health coaching).
- There is some evidence that personalised care planning and motivational interviewing can have a positive impact on depression and physical activity, respectively. There is some evidence that nurse-led interventions using the information-motivation-behavioural skills model leads to improvements in

medication adherence. There is some evidence that in-home care leads to improvements in activities of daily living, instrumental activities of daily living and mobility. Due to limited study follow-up, it is not known if the effects observed are sustained in the longer term.

- The optimal format of generic self-management support, the diseases in which it is likely to provide benefit, and the duration of effectiveness, if any, is still unclear.
- There is limited evidence of cost-effectiveness for generic chronic disease self-management support interventions. Studies were typically based on cost data collected alongside RCTs that used small sample sizes and short follow-up periods. The most consistent evidence is for chronic disease self-management programmes, but potential benefits are dependent on how efficiently the programme is run, with no evidence regarding longer term cost savings.
- Chronic disease self-management and telephone-based telemedicine programmes are relatively cheap to implement, but the magnitude of any cost saving in terms of reduced healthcare utilisation is unclear and it is not possible to determine if any savings are sustained.
- Where reported, the cost of the generic SMS interventions was generally low on a per-patient basis. However it is unclear if costs would be similar when programmes are rolled out to a larger population or if economies of scale might apply. Longer-term evidence would be required to determine if benefits in intervention groups are sustained, and whether costs change over time. Given the high prevalence of chronic diseases in Ireland, the budget impact would be substantial if implemented for all eligible patients.
- Based on the description of the healthcare systems, the epidemiology, and the patient populations in the included studies, and assuming that what constitutes 'usual care' is similar in Western countries, the majority of findings of this overview of clinical effectiveness are expected to be applicable to the Irish healthcare setting.

# 5 Asthma

This health technology assessment (HTA) of asthma self-management support (SMS) is one of a series of rapid HTAs assessing SMS interventions for chronic diseases. Section 5.1 provides a brief description of asthma followed by separate reviews of the clinical (Section 5.2) and cost-effectiveness (Section 5.3) literature for SMS interventions in asthma. Brief descriptions of the background and methods used are included with full details provided in a separate document (Chapter 3). Section 5.4 includes a discussion of both the clinical and cost-effectiveness findings. The report concludes with a list of key points in relation to asthma SMS support (Section 5.5).

## 5.1 Description of the disease

Asthma is a chronic inflammatory condition of the airways characterised by recurrent episodes of wheezing, breathlessness, chest tightness and coughing.[89] Ireland has the fourth highest prevalence of asthma worldwide, affecting an estimated 450,000 people. At least one person dies from asthma every week in Ireland.[89] The strongest risk factors for developing asthma are inhaled substances and particles that may provoke allergic reactions or irritate the airways.[90] Medication can control symptoms of asthma and avoidance of asthma triggers can also reduce its severity.[90] Appropriate management of asthma can enable people to enjoy a good quality of life.[90]

The Irish Asthma Control in General Practice guidelines (2013), adapted from the GINA Global Strategy for Asthma Management and Prevention, state that essential features to achieve guided self-management in asthma include: education and motivation, self-monitoring to assess control with educated interpretation of key symptoms, regular review of asthma control and a written action plan.[89] This is based on evidence rated as 'Evidence A' (rich body of randomised controlled trial [RCT] data) by GINA. The 2013 guidelines highlight rates of hospitalisation and attendance at emergency departments in Ireland, as well as frequent use of unscheduled (out-of-hours) care which indicate the suboptimal asthma control in the majority of patients. Care issues identified include low uptake of objective lung function tests for diagnosis and management, infrequent use of asthma action plans and poor patient education. Current aims of the Health Service Executive's (HSE) National Clinical Programme for asthma include that all patients diagnosed with asthma are enrolled in a structured asthma programme, to include issues such as: education about asthma, personal trigger factors and medication, assessment of control, inhaler device and technique and information about smoking cessation and exposure to second hand smoke.[91] However, the optimal format and delivery of such programmes has not been determined.

## 5.2 Review of clinical-effectiveness of SMS interventions

### 5.2.1 Background and methods

Details of the background and methods for this assessment are included in Chapters 1 to 3 of this report. Briefly, an aim of this health technology assessment (HTA) is to review the clinical effectiveness of disease-specific self-management support (SMS) interventions for a number of chronic conditions including asthma. Given the large volume of literature available, it was noted that an update of an existing high-quality systematic review of SMS interventions could be considered sufficient to inform decision making.

In December 2014 a high-quality overview of reviews was published by the National Institute for Health Research in the UK. The Practical systematic Review of Self-Management Support for long-term conditions (PRISMS) overview comprised an overview of systematic reviews of randomised controlled trials (RCTs) up to 1 June 2012. This overview was undertaken according to the principles of systematic reviewing. An update to the PRISMS report was completed by running additional searches in Pubmed, Embase and the Cochrane library from 2012 to 1 April 2015, see Appendix A3.1. As noted in Chapter 3.1.1, SMS interventions are typically complex interventions that include more than one component of SMS. For this reason, and consistent with the PRISMS report, with the exception of education interventions, this review did not assess single component SMS (for example, simple text message appointment reminders and drug reminder packaging). In accordance with the Population, Intervention, Comparator, Outcomes, Study design (PICOS) criteria agreed with the key stakeholder, this assessment is limited to SMS interventions for adults aged 18 and over. Results from the updated search are reported in addition to a summary of the findings of the PRISMS report. PRISMS did not include telehealth reviews as they were typically about mode of delivery rather than content of what was delivered, telehealth interventions that incorporated a significant component of self management support were however included in this updated review.

Data extraction and quality assurance of the systematic reviews, meta-analyses and the risk of bias associated with the primary literature was undertaken as described in Chapter 3.1.3. In summary, in order to determine the quantity, quality, strength and credibility of evidence underpinning the various SMS interventions, quality assurance of both the systematic review methodology (R-AMSTAR score weighting by patient or participant trial size) and meta-analyses (Higgins et al.'s quality assessment tool),[23] was undertaken. While the R-AMSTAR score was used to determine the quality of the systematic reviews, the scores were then weighted by patient or participant trial size, with the quality of evidence being downgraded if the review

was based on fewer than 1,000 participants. The quality of primary evidence was not evaluated directly; where reported, information on the risk of bias of the primary studies was extracted from the systematic reviews.

### 5.2.2 Description of the interventions

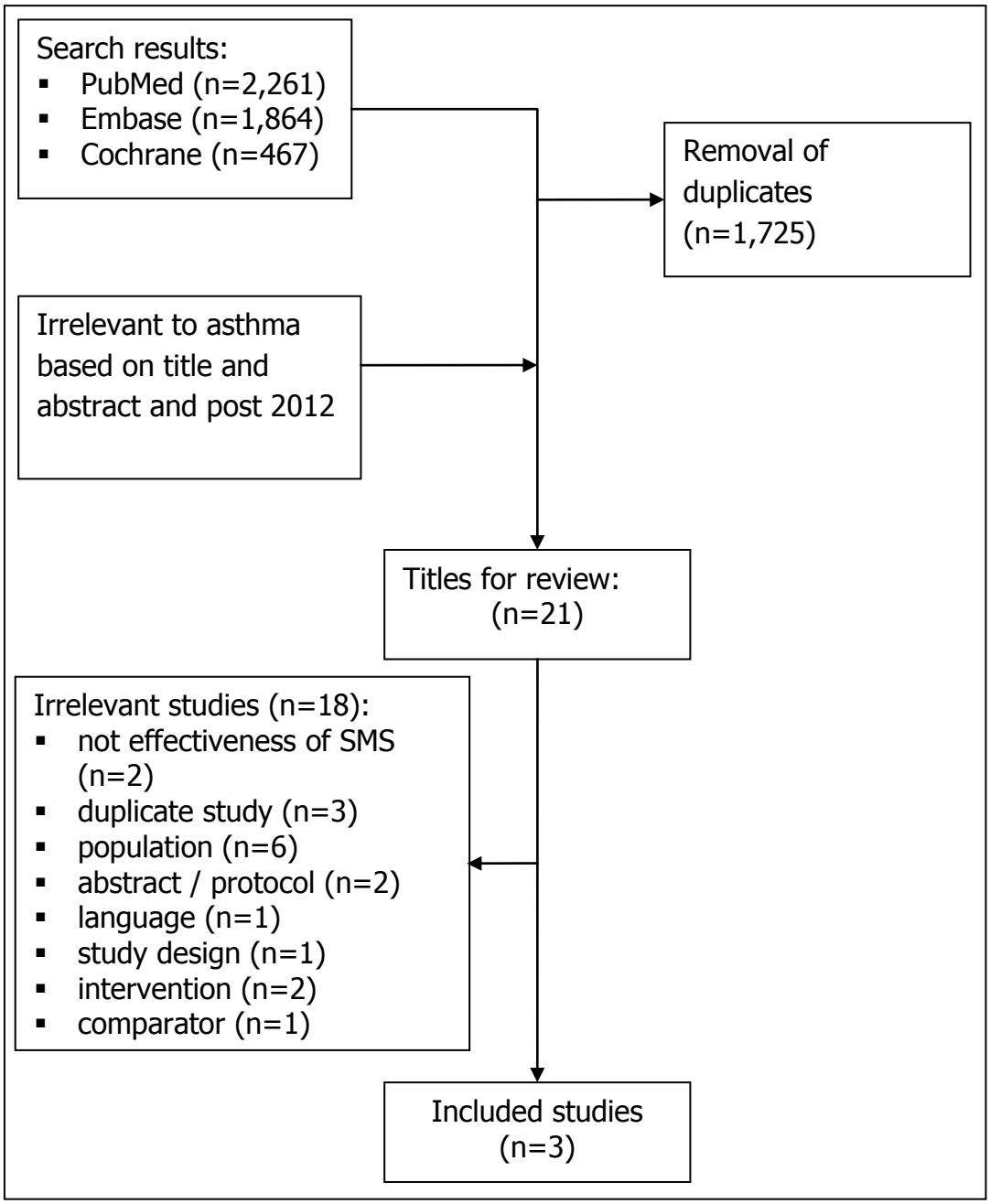
A general description of self-management and typical SMS interventions is included in the Background and Methods chapter. Asthma-specific interventions introduced in this Phase II report include written action (or management) plans (WAPs). These are written plans that a person with asthma develops with their doctor to help them control their condition. A written action plan typically shows their daily treatment, such as the type or types of medicine to take and when to take them. It describes how to control asthma in the long term and how to handle worsening symptoms, or attacks. The plan explains when to call the doctor or go to the emergency department.

### 5.2.3 Results – Clinical-effectiveness

The PRISMS review retrieved a total of 18 systematic reviews of asthma-specific self-management interventions and generic interventions used in patients with asthma. Of these, eight specifically focused on interventions in adults over 18 years of age. One additional systematic review that included both adults and children provided sufficient detail that adult-only results could be extracted.[2] The PRISMS report was updated to April 2015 using the search string in Appendix 1. A further three systematic reviews were retrieved (Figure 5.1) which assessed text messaging,[92] behaviour change techniques[93] and combinations of SMS interventions including education.[94] Summary details of the reviews are included in Table 5.1.

For the 12 reviews, the number of included RCTs per systematic review ranged from four[95] to 39[93;94] with the total number of participants ranging from 475[92] to 7,883.[96] The 12 systematic reviews contained 90 unique RCTs with study overlap between the reviews reported in Table 5.2. The publication date of the systematic reviews ranged from 2002 to 2015 while that of the included RCTs ranged from 1979[97] to 2011.[93] RCT study locations were typically in Europe or North America.

**Figure 5.1. Flowchart of included studies from updated search**



## Table 5.1. Summary of systematic reviews identified for inclusion

| Author (year) | Intervention |
|---|---|
| Reviews retrieved by PRISMS | |
| Bailey (2009)[95] | Education programmes -Culturally orientated |
| Tapp (2007)[97] | Education while attending emergency department |
| Gibson (2002)[98] | Educational programmes (including WAPs) |
| Powell (2002)[99] | Education (including WAPs) |
| Gibson (2004)[100] | Written Action Plans (WAPs) |
| Ring (2007)[101] | Action plans - Encourage use |
| Toelle (2004)[102] | WAPs |
| Moullec (2012)[103] | Medication adherence – components of Chronic Care Model |
| Newman (2004)[104] | Range of SMS interventions |
| Additional reviews retrieved in the updated search | |
| Blakemore (2015)[94] | Range of SMS interventions |
| Denford (2014)[93] | Range of behaviour change techniques |
| DiBello (2014)[92] | Text messaging – adherence to treatment and medication |

**Key**: **SMS** = self-management support; **WAP** = written action plans.

**Table 5.2 Study overlap between the included systematic reviews (PRISMS report plus the systematic reviews from the updated search).[3] Adapted from PRISMS review.[(2)]**

| | Review (year) | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | | 9 | 10 | 11 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| PRISMS retrieved reviews | | | | | | | | | | | | | |
| 1 | Bailey (2009) | **4** | | | | | | | | | | | |
| 2<br>3 | Gibson (2002)<br>Gibson (2004) | 2 | **38** | | | | | | | | | | |
| 4 | Moullec (2012) | 0 | 6 | **18** | | | | | | | | | |
| 5 | Newman (2004) | 1 | 8 | 6 | **18** | | | | | | | | |
| 6 | Powell (2002) | 0 | 6 | 2 | 4 | **15** | | | | | | | |
| 7 | Ring (2007) | 0 | 3 | 2 | 1 | 2 | **14** | | | | | | |
| 8 | Tapp (2007) | 0 | 2 | 2 | 2 | 0 | 2 | **13** | | | | | |
| 9 | Toelle (2004) | 0 | 3 | 1 | 2 | 6 | 0 | 0 | **7** | | | | |
| Reviews retrieved in updated search | | | | | | | | | | | | | |
| 10 | Denford (2014) | 1 | 9 | 7 | 6 | 2 | 3 | 5 | 0 | | **39** | | |
| 11 | DiBello (2014) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | 0 | **5** | |
| 12 | Blakemore (2015) | 0 | 11 | 5 | 6 | 3 | 4 | 9 | 1 | | 11 | 0 | **39** |

*The Cochrane review by Toelle et al. was withdrawn in 2011 based on the search being out of date. The author states that written action plans are now viewed as a component of asthma self-management rather than a standalone intervention.

[3]PRISMS review is based on a search from 1993 to June 2012. This search was updated to April 2015.

#### 5.2.3.1 Summary of findings

Detailed summaries of the systematic reviews including the intervention, outcomes assessed, duration of follow-up, sample size (number of RCTs and total number of participants), and the evidence of effect are included in Appendix A.5.1. The following are reported based on the findings from PRISMS and the additional systematic reviews retrieved in the updated search. As per Chapter 3, the quality of the systematic reviews was assessed and graded. The R-AMSTAR scores ranged from 23 to 39, with scores of 31 or more indicating a high-quality systematic review. When weighted according to the number of participants in the original RCTs (<1,000 or ≥ 1,000), six of the systematic reviews were assigned the highest quality rating (three-star ***),[93;94;97-99;101] while five reviews each were rated as two-star **[95;100;102-104] and one as one-star*[92] in terms of their quality and size.

If a meta-analysis was completed, its quality was assessed as per Chapter 3 and graded as being of low, moderate or high-quality. Eight of the systematic reviews included meta-analyses, of which six were assessed as high-quality and two were assessed as low quality. A grading of 'low quality' referred to studies where the conclusions were at high-risk of bias due to poor data collection or methods of data synthesis. Studies graded as 'high-quality' were likely to have conclusions that accurately reflected the available evidence (see also Chapter 3, Table 3.1). Table 5.3 below details the number of primary studies within the review, and the quality assessment of both the systematic reviews and meta-analyses and the evidence underpinning them and provides a summary of findings for selected outcomes from the various meta-analyses assessing the impact of SMS interventions in asthma.

## Table 5.3 Study details, quality assurance and summary of findings from meta-analysis of impact of self-management support interventions on health-related quality of life and resource utilisation

| Study | Quality of systematic review | | | Primary Studies | | Meta-analysis quality | QoL (MD) | Hospitalisation (RR)[b] | ED (RR) |
|---|---|---|---|---|---|---|---|---|---|
| | R-AMSTAR score | Participants | Quality rating | n | Low risk of bias[a] | | | | |
| **Bailey** 2009[(95)] | 36 | 617 | ** | 4 | 1 | High | 0.25 (0.09 to 0.41) | | |
| **Gibson** 2002[(98)] | 39 | 6,090 | *** | 38 | 8 | High | 0.29 (0.11 to 0.47) | 0.64 (0.50 to 0.82) | 0.82 (0.73 to 0.94) |
| **Gibson** 2004[(100)] | 39 | NR | ** | 38 | NR | Low | | 0.46 (0.26 to 0.81)<br>0.66 (0.48 to 0.91)<br>0.65 (0.48 to 0.88)<br>0.23 (0.07 to 0.71)<br>0.59 (0.44 to 0.78) | |
| **Moullec** 2012[(103)] | 27 | 3,006 | ** | 18 | NR | Low | | | |
| **Newman** 2004[(104)] | 23 | 2,004 | ** | 18 | NR | NA | | | |
| **Powell** 2002[(99)] | 34 | 2,460 | *** | 15 | 5 | NA | | | |
| **Ring** 2007[(101)] | 35 | 4,588 | *** | 14 | 1 | NA | | | |
| **Tapp** 2007[(97)] | 39 | 2,157 | *** | 13 | 5 | High | | 0.50 (0.27 to 0.91) | 0.66 (0.41 to 1.07) |
| **Toelle** 2004[(102)] | 38 | 967 | ** | 7 | 2 | High | | 1.17 (0.31 to 4.43) | 0.86 (0.44 to 1.67) |
| **Denford** 2014[(93)] | 33 | 7,883 | *** | 39 | NR | High | | | |
| **DiBello** 2014[(92)] | 30 | 475 | * | 5 | | NA | | | |
| **Blakemore** 2015[(94)] | 37 | 4,246 | *** | 39 | 8 | High | | | |

**Key**: **ED** = emergency department; **MD** = mean difference; **NA** = not applicable; **NR** = not reported; **QoL** = quality of life; **RR** = relative risk.

[a] Number of the total primary studies identified as being at low risk of bias. [b] Figures for Gibson 2004 relate to different action plan components

[c] It is assumed that the definitions used for unscheduled care and urgent care are similar.

## Table 5.3 (continued). Study details, quality assurance and summary of findings from meta-analysis of impact of SMS interventions on health-related quality of life and resource utilisation

| Study | Quality of systematic review | | | Primary Studies | | Meta-analysis quality | Unscheduled/ urgent healthcare use (RR)[c] | Unscheduled doctor visits (RR)[c] |
|---|---|---|---|---|---|---|---|---|
| | R-AMSTAR score | Participants | Quality rating | n | Low risk of bias | | | |
| **Bailey 2009**[95] | 36 | 617 | ** | 4 | 1 | High | | |
| **Gibson 2002**[98] | 39 | 6,090 | *** | 38 | 8 | High | | 0.68 (0.56 to 0.81) |
| **Gibson 2004**[100] | 39 | NR | ** | 38 | NR | Low | | |
| **Moullec 2012**[103] | 27 | 3,006 | ** | 18 | NR | Low | | |
| **Newman 2004**[104] | 23 | 2,004 | ** | 18 | NR | NA | | |
| **Powell 2002**[99] | 34 | 2,460 | *** | 15 | 5 | NA | | |
| **Ring 2007**[101] | 35 | 4,588 | *** | 14 | 1 | NA | | |
| **Tapp 2007**[97] | 39 | 2,157 | *** | 13 | 5 | High | | |
| **Toelle 2004**[102] | 38 | 967 | ** | 7 | 2 | High | | 1.34 (1.01 to 1.77) |
| **Denford 2014**[93] | 33 | 7,883 | *** | 39 | NR | High | 0.71 (0.56 to 0.90) | |
| **DiBello 2014**[92] | 30 | 475 | * | 5 | | NA | | |
| **Blakemore 2015**[94] | 37 | 4,246 | *** | 39 | 8 | High | 0.79 (0.67 to 0.94) | |

**Key**: **ED** = emergency department; **MD** = mean difference; **NA** = not applicable; **NR** = not reported; **QoI** = quality of life; **RR** = relative risk.

[a]Number of the total primary studies identified as being at low risk of bias
[b]Figures for Gibson 2004 relate to different action plan components
[c]It is assumed that the definitions used for unscheduled care and urgent care are similar.

### Three star (***) reviews

Based on two 'three-star'[97;98] and two 'two-star' reviews,[100;102] PRISMS reported that there is evidence that SMS interventions for patients with asthma reduce hospital admissions. Based on one three-star, they reported that SMS interventions (including asthma education, self-monitoring of peak expiratory flow or symptoms, regular medication review, and a written action plan) increase quality of life. They noted that optimal asthma self-management should include education supported by a written asthma action plan. They also noted that symptom-based plans are as good as peak flow-based plans.

In the updated search, additional good quality evidence was retrieved to support the use of a number of SMS interventions in patients with asthma. A 2015 meta-analysis by Blakemore et al. of 39 RCTs comprising 4,246 patients assessed a number of 'complex interventions' (that is, including multiple components or modes of delivery of SMS), mainly education and skills-related for asthma self management.[94] Based on a high-quality meta-analysis, they reported that the odds of urgent healthcare use were 21% lower in the intervention group, although only eight of the 39 studies included were considered at low risk of bias. Interventions that included education, skills training and relapse prevention were found to be effective; however, the only intervention to remain significant in the multivariate meta-regression was skills training. The authors suggested therefore that improved skills training including the use of inhalers and peak flow meters would help to ensure that patients receive the optimum preventative medication and could have a central role in the reduction of urgent healthcare use for adults with asthma.

A 2014 meta-analysis of 39 RCTs comprising 7,883 patients by Denford et al. assessed a range of behaviour change techniques in asthma SMS interventions.[93] Based on a high-quality meta-analysis, they reported very strong evidence that the interventions are effective in reducing symptoms, are associated with a significant increase in adherence to preventive medication, and that there is evidence that asthma-specific SMS interventions reduce unscheduled health care use. The quality of the primary studies was evaluated, but not reported. The authors concluded that it was not possible to determine the optimal content of asthma SMS interventions from the available evidence.[93]

### Two star (**) reviews

Based on one 'two-star' review (two RCTs) PRISMS reported that education should be culturally sensitive with evidence of improvements in asthma-related quality of life for culturally-orientated programmes in minority groups.[95]

Based on a further 'two-star' review, PRISMS reported that greater adherence to inhaled corticosteroids was seen when more components of the Chronic Care Model were included within interventions.[103] Components included self-management education, behavioural support, decision support, and delivery system design. However, it was noted that only a small number of component combinations were tested, limiting the ability to determine which components were most important for success.[103]

### One star (*) reviews

The narrative synthesis of five RCTs and one observational study by DiBello et al. reported that text messaging intervention programmes may have a positive impact on medication adherence rates as well as perceived control of asthma.[92] The text programmes varied from medication and appointment reminders, general education and management strategies, to customised treatment instructions based on peak flow results (transmitted also by SMS), with variability also in the duration of follow-up and outcome measures used. Other clinical outcomes that may also show a positive effect from a text messaging intervention were measures of lung function. However, these results were based on small sample sizes and short-term follow-up. They also reported that there is no statistical evidence clearly indicating if the number of emergency department visits will decrease or increase with the use of a text messaging intervention.

**Summary statement**

Based on the quantity and quality of the systematic reviews and the underpinning primary randomised controlled trials (RCTs) there is good evidence that asthma self-management support interventions improve quality of life and reduce hospital admissions and the use of urgent and unscheduled health care. Optimal asthma self-management should include education supported by a written asthma action plan as well as improved skills training focused on the skills such as the use of inhalers and peak flow meters. Behavioural change techniques are associated with improved medication adherence and a reduction in symptoms.

## 5.3 Review of cost-effectiveness of self-management support interventions

A review of cost-effectiveness studies was carried out to assess the available evidence for self-management support (SMS) interventions for asthma. Studies were included if they compared the costs and consequences of a SMS intervention to routine care.

### 5.3.1 Search strategy

A search was carried out to identify economic analyses of SMS interventions. In conjunction with the systematic review of clinical effectiveness, the search for economic evaluations was carried out in MEDLINE, EMBASE and the Cochrane Library. The same search terms were used with the exception of terms for systematic review and meta-analysis. In place of these, search terms and filters for economic evaluations were applied. In addition, any systematic reviews of SMS interventions identified through the results of the clinical effectiveness search that included cost or economic outcomes were used to identify additional studies. The search was carried out up until 4th March 2015.

The PICOS (Population, Intervention, Comparator, Outcomes, Study design) analysis used to formulate the search is presented in Table 5.4 below.

**Table 5.4 PICOS analysis for identification of relevant studies**

| | |
|---|---|
| **Population** | Adults ≥ 18 years old that had asthma. |
| **Intervention** | Any self-management support intervention that helps patients with asthma through education, training or support. |
| **Comparator** | Routine care. |
| **Outcomes** | Cost or cost-effectiveness of intervention. |
| **Study design** | Randomised controlled trials, case-control studies, observational studies, economic modelling studies. |

Studies were excluded if:

- a nursing home or non-community dwelling population was included,
- it included a paediatric population,
- cost data were not clearly reported,
- published prior to 2000 as it would have limited relevance.

As outlined in Chapter 3.2.2 and in accordance with national HTA guidelines, assessment of the quality of the studies using the Consensus on Health Economic Criteria (CHEC)-list was performed independently by two people. For studies that included an assessment of cost-utility or an economic modelling approach, assessment of the relevance to the Irish healthcare setting and their credibility was considered using a questionnaire from the International Society of Pharmacoeconomics and Outcomes Research. Studies that were considered poor quality are not discussed below, although data from these studies are included in the evidence tables.

### 5.3.2 Results – Cost-effectiveness

The initial screening retrieved 64 papers relating to asthma. Of these, 27 studies were identified for full text review, with the remaining 37 excluded as irrelevant or unsuitable based on screening of abstract or full text. A further 15 were excluded according to our various exclusion criteria, leaving 12 articles included in this review. Data extraction was carried out independently by two reviewers.

Two studies each were conducted in the United States (US), the Netherlands and the UK, with one each from Canada, Australia and Norway. Three Finnish studies were identified that examined the same cohort at one, three and five years follow-up. The included studies were all published between 1998 and 2011. The characteristics of the included studies are given in Table 5.5. Costs reported in each of the studies were inflated to 2014 pricing using the local consumer price index for health and expressed in Irish Euro using the purchasing power parity exchange rate.[105]

**Table 5.5 Characteristics of the studies included**

| Study | Country | Intervention |
|---|---|---|
| **Castro (2003)**[106] | US | Case management |
| **Corrigan (2004)**[107] | Canada | SMS education programme |
| **Donald (2008)**[108] | Australia | Nurse-led telephone review |
| **Gallefoss (2001)**[109] | Norway | SMS education programme |
| **Kauppinen (1998, 1999, 2001)**[110-112]* | Finland | SMS education programme |
| **Parry (2012)**[113] | UK | Cognitive Behavioural Therapy (CBT) for asthma-related anxiety |
| **Pinnock (2005)**[114] | UK | Nurse-led telephone review |
| **Shelledy (2009)**[115] | US | In-house case management including environmental assessment |
| **van der Meer (2011)**[116] | Netherlands | Internet SMS programme |
| **Willems (2007)**[117] | Netherlands | Nurse-led telephone review with remote peak flow monitoring |

* While studies published prior to 2000 were excluded based on limited relevance, the earlier studies by Kauppinen were included as they referred to follow-up of the same cohort over a five-year period.

**Key**: **SMS** = self-management support.

The studies were classified according to intervention type: SMS education programmes, internet-based SMS programmes, telemedicine and other SMS interventions. However, it is worth noting that many studies looked at a combination of interventions. In particular, written self-management plans, which are known to

be effective in asthma, featured in five studies, but were not assessed as standalone interventions.

This review captures all SMS interventions assessed for asthma and retrieved few conventional economic evaluations. Eleven of the retrieved studies gathered cost data as part of a randomised controlled trial (RCT) while data for one study was based on an observational cohort study. Five of the studies were limited to costing studies. The quality of the included studies was predominantly poor.

#### 5.3.2.1 Self-management support education programmes

Four articles were retrieved that assessed SMS education programmes describing three unique studies (Table A5.3). Two of the studies were based on cost data gathered as part of an RCT: one study from Finland reported the one-, three- and five- year outcomes for the same RCT cohort.[110-112] One study from Norway assessed outcomes at one year.[109] The number of participants in these studies ranged from 78 to 162. Finally, a study from Canada modelled the cost of different asthma SMS education delivery models for primary care (general practitioner [GP]) practices with populations of adult asthma patients ranging from 25 to 100 patients.[107]

The interventions described in the studies varied in format and intensity. Both the studies from Norway and Finland used a combination of group and individual visits and provided participants with written self-management plans.[109-112] The Finnish study also required patients to measure their peak flows and keep a diary. The Canadian study examined the cost, from the GP perspective of different formats and durations of education sessions with initial peak flow measurement performed at the GP surgery. The Finnish and Norwegian studies examined costs and benefits from a societal perspective.

The experimental studies measured and reported undiscounted total direct and indirect asthma-related costs during the study period. Direct costs included costs to the health system, both primary and secondary care and cost to patients. Indirect costs included productivity loss due time spent ill or to attend visits.[107;109-112] Gallefoss et al. reported total mean costs of €1,768 per patient for those who participated in the education programme compared to mean total annual costs of €1,160 per patient for the control groups. In contrast, the Finnish study found slightly higher total mean annual costs in the intervention group in the first year (€438 per patient) compared with the control group (€373 per patient). Cost savings did occur at the three and five year follow-up and were mainly driven by a reduction in unscheduled attendance costs. It is important to note that the intervention was only delivered in year one and not repeated in the following years.

Only two of the studies examined clinical outcomes.[109-112] The Norwegian study found significant improvements in forced expiratory volume in one second (FEV1) and disease-specific quality of life scores (Saint George Respiratory Questionnaire scale) in the intervention group. This, coupled with lower total costs for the intervention group, resulted in an negative incremental cost-effectiveness ratio (ICER) of €497 per 5% improvement in FEV1 and of €376 per clinically significant improvement in quality of life score (10 units on the Saint George Respiratory Questionnaire scale). Reporting on a range of clinical outcomes (lung function [FEV1, FVC, PF], bronchial hyper-responsiveness [PD15] and both generic and disease-specific health related quality of life), the Finnish study noted statistically significant improvements for the intervention group in a limited number of surrogate markers at one-year (FEV1) and three-year (FEV1, PEF, and PD) follow-up, but reported no difference in clinical outcomes between the groups at five years.

Overall, evidence for the cost-effectiveness of SMS education programmes was conflicting. Both studies that examined clinical outcomes found improvements at year one, though these were not sustained. The cost of the SMS intervention was typically low, while mean total costs were typically found to be comparable or lower in the intervention group at year one.

#### 5.3.2.2 Internet-based self-management support programme

One study, conducted in the Netherlands, evaluated the cost-effectiveness of an internet-based SMS programme (as shown in Table A5.4).[116] Two-hundred participants were enrolled in the RCT and followed up for one year. The intervention included an immediate computerised action plan based on the results of weekly monitoring of asthma control and lung function that were inputted by the participants. Other components were online and group education, and remote web communication with a specialist nurse.

The average cost of the intervention from a societal perspective was €265 per patient per year. The study found no statistically significant difference in costs or quality-adjusted life years (QALYs) between groups, but calculated an (incremental cost-effectiveness ratio) ICER of €27,829 per QALY from a societal perspective. This decreased to €1,563 per QALY if a provider perspective was adopted. Interpretation of the results of the economic analysis is complicated by the absence of a statistically significant clinical effect. As a result, the focus should be on the cost findings rather the effectiveness data.

Costs of the technological innovation (software support, electronic spirometer, Internet and mobile phone costs) were approximately 40% of the total intervention costs in year one. The fixed technological costs of software support constituted

about one third of the intervention costs, so increasing the number of users could substantially reduce the cost per user.

#### 5.3.2.3 Telemedicine

Three studies assessed a telemedicine intervention: one UK study with a three-month follow-up directly compared the cost of a telephone-based nurse consultation with that of a face-to-face nurse consultation.[114] Another study from Australia compared the cost of six follow-up telephone consultations with usual care following an initial face-to-face educational visit for all participants (Table A5.5).[108] The third study, from the Netherlands, required participants to monitor twice-daily peak flow measurements and transfer these electronically to a nurse who would advise on therapeutic changes based on a stepwise protocol.[117]

All three studies were RCTs with the number of participants ranging from 53 to 278 adults and the follow-up from three months to one year. Both the UK and Australian studies reported cost savings in the intervention group from a healthcare provider perspective. The cost of the intervention in the Australian study was €90 per patient and of this, €40 was related to the initial educational session and the remainder to the telephone follow-up.[108] They only examined readmission cost differences between the two trial components and used a fixed tariff per admission to value these. They found that the control group had much higher readmission costs having had six episodes compared to one in the intervention group at year one follow-up. In the UK study, the total cost of the telephone review service was similar to that of the surgery review.[114] However, a higher proportion of patients completed the consultation in the telephone review service, 78% vs 48%, resulting in mean cost savings of €7 per consultation.

In the study from the Netherlands, the mean healthcare costs per patient were higher in the intervention group (€2,419) than in the control group (€1,867). This difference was mainly due to the intervention costs of €589 per person, primarily comprising fixed hardware costs. The study found no statistically significant difference in quality-adjusted life years (QALYs) between groups, but calculated an ICER of €17,069 per QALY gained from a healthcare payer perspective and €34,472 per QALY gained from a societal perspective. Removing hardware costs from the analysis reduced the ICER to €1,954 per QALY from the healthcare payer perspective. The authors postulated that with fast technological advances a reduction in the cost of monitoring could increasing the cost-effectiveness of their SMS programme.

The Australian study reported a clinically significant improvement in the Modified Marks Asthma Quality of Life Questionnaire (MAQLQ-M) in the intervention group not seen in the control group, but no difference in self-efficacy scores in either trial arm.

In contrast, the UK study found similar asthma-related quality of life scores between groups at the three month follow-up.

Evidence for the cost-effectiveness of telemedicine interventions in asthma is mixed. The cost of the intervention was low for studies involving nurse-led telephone review, but fixed hardware costs were substantial in the study involving remote peak flow monitoring. One study found improvements in clinical outcomes associated with total cost savings. The remaining studies did not find significant clinical improvements, though healthcare costs in the intervention groups were higher.

#### 5.3.2.4 Other self-management support interventions

Three additional studies evaluating different SMS interventions were identified. Two studies describing two different multi-faceted interventions were RCTs from the US,[106;115] and one study examining a cognitive behavioural therapy (CBT) intervention for asthma-related anxiety from the UK.[113] All three were limited to costing studies undertaken alongside RCTs. Follow-up ranged from six months to one year.

In Castro et al., the intervention consisted of a nurse-led service for 'high-risk' patients which included patient education, psychosocial support, individualised asthma management plan and out-patient follow-up via telephone, home visits or GP review as required.[106] The definition of 'high-risk' included hospitalisation with an asthma exacerbation and a history of frequent healthcare use. Significant reduction in hospital readmissions (60%, $p<0.01$), total bed days (69%, $p<0.04$) and multiple readmissions (57%, $p=0.03$) were documented along with a non-significant increase in emergency department visits (34%, $p=0.52$) and healthcare provider visits (3%, $p=0.82$). There was no difference in health-related quality of life between the two arms. The cost of the intervention was estimated at €384 per patient. This resulted in a mean direct health care cost savings of €9,157 per patient. The reduction in cost was mainly due to lower hospitalisation costs. The total healthcare costs were noted to be lower even when indirect patient costs such as, lost workdays and non-professional caregiver costs, were taken into account.

Shelledy et al. randomised patients into three groups to compare an in-home asthma management intervention delivered by either a respiratory therapist or a specialist nurse with usual care.[115] The intervention was a five-week multi-faceted programme delivered at home and included education visits, peak flow diaries, written action plans and environmental assessments. The cost of the programme was $365 per patient. Both asthma management groups had significantly fewer hospitalisations than the usual care group. This resulted in net hospitalisation cost savings of $37,800 for the nurse-delivered group and $32,200 for the respiratory therapist delivered group. The hospitalisation cost difference between the two

intervention arms was not significant and there were no significant differences in emergency department visits amongst the three groups. Both asthma management groups showed statistically significant improvements in quality of life scores on SF-36 PCS scales and patient satisfaction surveys. However, only the respiratory therapist group had significantly higher scores in the Asthma Self-management questionnaire at six months compared with usual care, indicating improved knowledge of the management of an asthma episode in this group.

Parry et al. selected patients who displayed signs of asthma-related anxiety to be randomised to receive a combination of asthma and anxiety education, and CBT delivered by a trained psychologist or usual care.[113] The intervention cost an average of £378 to £798 per patient depending on the number of sessions attended. No cost offsets were observed which offered no treatment cost advantage. Improvements in asthma-specific fear, quality of life and depression between the intervention and control groups were noted; however, the effect was clinically modest and was not sustained at six months. Of note, only 18 of the 32 patients randomised to the intervention arm completed the full course of treatment visits.

Limited data from the US and UK suggest that multi-faceted programmes including education components aimed at patients with poorly controlled asthma may result in decreased healthcare utilisation and associated cost savings. However, the available evidence is limited to costing studies, with the RCT data underpinning the analyses based on small sample sizes and six to 12 months follow-up. The interventions evaluated varied in form, intensity and mode of delivery, therefore it is not possible to identify which components were more effective.

## 5.4 Discussion

This section discusses the main findings from the review of the clinical-effectiveness and cost-effectiveness literature.

### 5.4.1 Clinical-effectiveness

Twelve systematic reviews are included in this overview of reviews. Nine studies were identified in the PRISMS review with an additional three studies identified in the updated search. A diverse range of self-management support (SMS) interventions were assessed. The interventions differed in the frequency, intensity and mode of delivery. Despite the heterogeneity within the intervention classes, there was a tendency for their findings to be combined, so the results of the meta-analyses should be interpreted with caution.

The findings from the 2014 PRISMS systematic review and the additional findings from this updated review indicate that SMS interventions in asthma can reduce hospital admissions and urgent healthcare use (emergency department visits and

unscheduled healthcare). Of note, these findings do not take consideration of the underlying risk of hospitalisations and urgent healthcare use as these are not reported in the systematic reviews. Therefore, it is not possible to quantify the absolute benefit of the interventions. There is limited randomised controlled trial (RCT) evidence that SMS interventions improve health-related quality of life. Where recorded, it was noted that the duration of follow-up for the trials was typically short-term; it is not known if the benefits are sustained over time.

As noted, there was significant heterogeneity in the format and intensity of the SMS interventions, the study populations, study follow-up duration and assessed outcome measures which makes it difficult to formulate clear recommendations regarding the most effective form and content of SMS in asthma. However, while the optimal intervention format of SMS is not clear, it should include education supported by a written asthma action plan. Skills training which is focused on the use of inhalers and peak flow meters would help to ensure that patients receive the optimum preventative medication and could have a central role in the reduction of urgent healthcare use for adults with asthma. The HSE's National Clinical Programme for asthma plans and the 2013 Irish Asthma Control in General Practice guidelines are in line with the findings discussed above in terms of use of SMS patient education, skills training, and use of written action plans.

The included RCTs were published from 1979 to 2010 (PRISMS) and 1993 to 2011 (additional studies) and were mainly completed in Europe or North America. Given the description of the asthma patient populations and asthma epidemiology, it would appear that the evidence should be able to be applicable to the Irish healthcare setting. Potential caveats to this assumption are the extent to which the comparator (usual care) in these RCTs is representative of usual care in Ireland due to differences in the stated standards of care and how healthcare is provided. Given the increasing tendency for usual or standard of care to be determined by evidence-based clinical guidelines and the convergence of such guidelines in Western countries, the assumption that stated standard of care is similar is not unreasonable. However, differences in healthcare systems may contribute to differences in the adherence to stated standard of care. For example, usual care for asthma in the Irish primary care setting may differ to that in the UK's National Health Service (NHS) system where adherence to quality standards is incentivised by the quality of outcomes framework. Work by the HSE's National Clinical Programme for Asthma is underway to improve asthma management in Ireland. A national model of care for asthma is being finalised which includes self-management components and details a collaborative approach between primary and secondary healthcare professionals and patients to provide a safe, seamless patient experience within the heath system.[118]

Given the volume of evidence available, in the interest of efficiency this assessment of SMS interventions in adults with asthma was undertaken in the form of an overview of reviews. As discussed in Chapter 3.4.1, a disadvantage of this approach is the inability of an overview of reviews to reflect the most recent literature: following publication of an RCT, it must first be captured in a systematic review, before subsequently being captured in an overview of reviews. This approach is therefore less suitable for a fast-moving area where there are rapid advances in the technology. However, given their sample sizes, it is not appropriate to draw conclusions on the effect of an intervention based on a single, or a number of small, RCTs. Therefore it is unlikely that more recent RCTs not captured in this overview of reviews would be sufficient to substantially alter recommendations informing major policy decisions.

### 5.4.2 Cost-effectiveness

Our search identified 12 individual economic evaluations of SMS interventions for asthma. The interventions assessed were heterogeneous as most comprised several components including education, peak flow monitoring and personalised self-management plans. Three of the studies (five reports) described education programmes for SMS of asthma, but within this group, the format and duration of these programmes differed in delivery-mode, duration and intensity. The three telemedicine studies also described heterogeneous models of intervention with some incorporating elements of education or remote peak flow monitoring.

The majority of the studies had small sample sizes and collected cost data alongside RCTs. This raises inherent issues around whether their cost findings can be applicable to the broader population. In addition, most of the studies only followed participants for up to one year and it is therefore unclear how the clinical benefits and the healthcare utilisation would change over time. The Finnish study that followed participants for five years concluded that while there was a consistent tendency for the intervention (intensive education in year one) to be less costly, there were no significant differences in outcomes or costs at one, three or five years. Of note, costs and benefits were not discounted in this study.[110-112]

Six of the studies were limited to costing studies, a number of which did not report clear costing methodology, therefore it was difficult to determine their quality and to deduce the cost of different components of the interventions. Most of the studies adopted a societal perspective. However, it was not always clear whether costs were incurred by the provider or the patient (for example, medication costs). This limits the application of the findings to the Irish setting. The quality of the included studies was predominantly poor.

In summary, the review of cost-effectiveness found 12 studies, the majority of which collected cost data alongside RCT data. This is in contrast to the review of the clinical effectiveness literature which included 12 systematic reviews of 90 unique RCTs. In general, the cost per patient of the intervention was low and the majority of the studies reported some degree of cost savings in the short-term through reduced healthcare utilisation. There were four cost-utility analyses, all of which used data from RCTs and did not extrapolate the results beyond the duration of the trial follow-up. No significant difference in clinical effectiveness between the intervention and control arms was found in any of these studies, complicating interpretation of any ICER calculated. The short follow-up period and the relatively small sample sizes raise concerns regarding the sustainability of the interventions and how applicable the findings are.

## 5.5 Key points

- Twelve systematic reviews of the clinical effectiveness of self-management support (SMS) interventions in adults with asthma were identified for inclusion in this overview of reviews.
- A diverse range of interventions was identified with the largest volume of evidence obtained for a combination of asthma educational programmes plus written action plans (n=7), a range of SMS interventions (n=2) and behavioural change techniques (n=1). Other interventions assessed included text messaging (n=1) and the Chronic Care Model (n=1) for treatment and medication adherence, respectively.
- The quality of the systematic reviews was good, with six rated as being higher quality reviews.
- The primary evidence underpinning the systematic reviews was found to be generally at moderate- to high-risk of bias, meaning that studies may have over- or under-estimated the effect size. It comprised 90 unique randomised controlled trials (RCTs) published between 1979 and 2011. These were mainly completed in Europe or North America.
- Based on the quantity and quality of the systematic reviews and the underpinning primary RCTs, there is good evidence that SMS interventions can improve quality of life and reduce hospital admissions and use of urgent and unscheduled healthcare. Behaviour change techniques are associated with improved medication adherence and a reduction in symptoms. The optimal intervention format of SMS is not clear, but should include education supported by a written asthma action plan as well as well as improved skills training including the use of inhalers and peak flow monitors.
- There is very limited evidence on the cost-effectiveness of chronic disease SMS

interventions for asthma with only 12 relevant studies retrieved. These were mostly based on cost data collected alongside RCTs that used small sample sizes and short follow-up periods, limiting the applicability of the findings.

- There is limited evidence to suggest that SMS education programmes, using a combination of individual and group sessions, may be at least be cost-neutral in patients with mild to moderate disease.
- There is limited evidence to suggest that nurse-led telephone review for patients with high-risk asthma is a relatively low cost intervention that may reduce costs by reducing healthcare utilisation, although evidence of effect in the included studies was mixed.
- Based on the description of the healthcare systems, the epidemiology, and the asthma patient populations in the included studies, and assuming that what constitutes 'usual care' is similar in Western countries, it is expected that the findings of clinical effectiveness are broadly applicable to the Irish healthcare setting. The evidence of cost-effectiveness is of limited applicability to the Irish healthcare setting, with findings from the European studies being of greater relevance.

# 6 Chronic obstructive pulmonary disease (COPD)

This health technology assessment (HTA) of chronic obstructive pulmonary disease (COPD) self-management support (SMS) is one of a series of rapid HTAs assessing SMS interventions for chronic diseases. Section 6.1 provides a brief description of COPD followed by separate reviews of the clinical- (Section 6.2) and cost-effectiveness (Section 6.3) literature of SMS interventions for COPD. Brief descriptions of the background and methods used are included with full details provided in a separate document (Chapter 3). Section 6.4 includes a discussion of both the clinical- and cost-effectiveness findings. The report concludes with a list of key points in relation to COPD SMS support (Section 6.5).

## 6.1 Description of the disease

Chronic obstructive pulmonary disease (COPD) is defined as 'a common preventable and treatable disease, which is characterised by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases'.[119] The clinical course of COPD is one of gradual impairment with episodes of acute exacerbations that contribute to the deterioration of a person's health status. In the later stages of disease, use of health services often increases with frequent hospitalisations. Currently there is no cure for COPD.[120] COPD is a major cause of morbidity and mortality and it is predicted that by 2020 it will be the third leading cause of death globally.[120] Ireland has one of the highest standardised death rates for COPD in the European Union.[120;121] Ireland also has one of the highest rates of hospital admissions for exacerbations of COPD in the Organisation for Economic Co-operation and Development (OECD). This is associated with a high smoking prevalence, a major risk factor for COPD.[120;122]

To provide some context to this section, it is noted that in 2008 a draft National Respiratory (COPD) Framework was published by the Irish Thoracic Society in conjunction with the Health Service Executive (HSE) and the Irish College of General Practitioners (ICGP). It stated that pulmonary rehabilitation is acknowledged by all international guidelines as a key component of the management of COPD; helping patients to optimise their function and better manage their disease.[123] This is based on the fact that best practice guidelines recommend that patients are referred to pulmonary rehabilitation programmes at the time of diagnosis. However, it is acknowledged that in Ireland early and accurate diagnosis of COPD in primary care is difficult due to limited access to diagnostic spirometry.[124] In 2008 many areas in Ireland had no pulmonary rehabilitation programmes, others had long waiting lists, others did not accept referrals from primary care, while the location of some posed access problems for those without transport.[123] Stated aims of the HSE's National

Clinical Programme for COPD are to improve access to diagnostic spirometry and to 'implement COPD pulmonary rehabilitation programmes to improve exercise tolerance, quality of life and reduce breathlessness in patients'.[125] In addition, it has a stated aim to provide access to patient information and self-management tools.[125] However, no decision has been made by the HSE as to the optimal format of such support interventions.

## 6.2 Review of clinical effectiveness

### 6.2.1 Background and Methods

Details of the background and methods for this assessment are included in Chapters 1 to 3 of this report. Briefly, an aim of this HTA is to review the clinical effectiveness of self-management support (SMS) interventions for a number of chronic conditions including chronic obstructive pulmonary disease (COPD). Given the large volume of literature available, it was noted that an update of an existing high-quality systematic review of SMS interventions could be considered sufficient to inform decision making.

In December 2014 a high-quality overview of reviews was published by the National Institute for Health Research in the UK. The Practical systematic Review of Self-Management Support for long-term conditions (PRISMS) overview comprised an overview of systematic reviews of randomised controlled trials (RCTs) up to 1 June 2012, and was undertaken according to the principles of systematic reviewing. An update to the PRISMS report was completed by running additional searches in PubMed, Embase and the Cochrane library from 2012 to 1 April 2015, see Appendix A3.1. In accordance with the PICOS (Population, Intervention, Comparator, Outcomes, Study design) agreed with the key stakeholder, this assessment is limited to SMS interventions for adults aged 18 and over. As noted in Chapter 3.1.1, SMS interventions are typically complex interventions that include more than one component of SMS. For this reason, and consistent with the PRISMS report with the exception of education interventions, this review did not assess single component SMS (for example, simple text message appointment reminders and drug reminder packaging). Results of the updated search are reported in addition to a summary of the findings of the PRISMS report. PRISMS did not include telehealth reviews as they deemed these to be typically about mode of delivery rather than content of what was delivered. Relevant telehealth interventions that incorporated a significant component of self management support were however included in this updated review.

Data extraction and quality assurance of the systematic reviews, meta-analyses and the risk of bias associated with the primary literature was undertaken as described in Chapter 3.1.3. In summary, in order to determine the quantity, quality, strength and

credibility of evidence underpinning the various SMS interventions, quality assurance of both the systematic review methodology (R-AMSTAR score) and the meta-analyses (Higgins et al.'s quality assessment tool)[23] was undertaken. While the R-AMSTAR score was used to determine the quality of the systematic reviews, the scores were then weighted by patient or participant trial size, with the quality of evidence being downgraded if the review was based on fewer than 1,000 participants. The quality of primary evidence was not evaluated directly; where reported, information on the risk of bias of the primary studies was extracted from the systematic reviews.

### 6.2.2 Description of the interventions

A general description of self-management and typical SMS interventions is included in Chapter 2. COPD-specific interventions introduced in this Phase II report include pulmonary rehabilitation. This is a more comprehensive form of SMS and is defined by the joint American Thoracic Society and European Respiratory Society as a '…comprehensive intervention based on a thorough patient assessment followed by patient tailored therapies that include, but are not limited to, exercise training, education, and behaviour change, designed to improve the physical and psychological condition of people with chronic respiratory disease and to promote the long-term adherence to health-enhancing behaviours.'[126] The educational component of pulmonary rehabilitation focuses on collaborative self-management and behaviour change.[126] It encompasses providing information and knowledge regarding COPD; building skills such as goal setting, problem solving and decision making; and developing action plans that allow individuals to better recognise and manage the disease.[126]

### 6.2.3 Results – Clinical-effectiveness

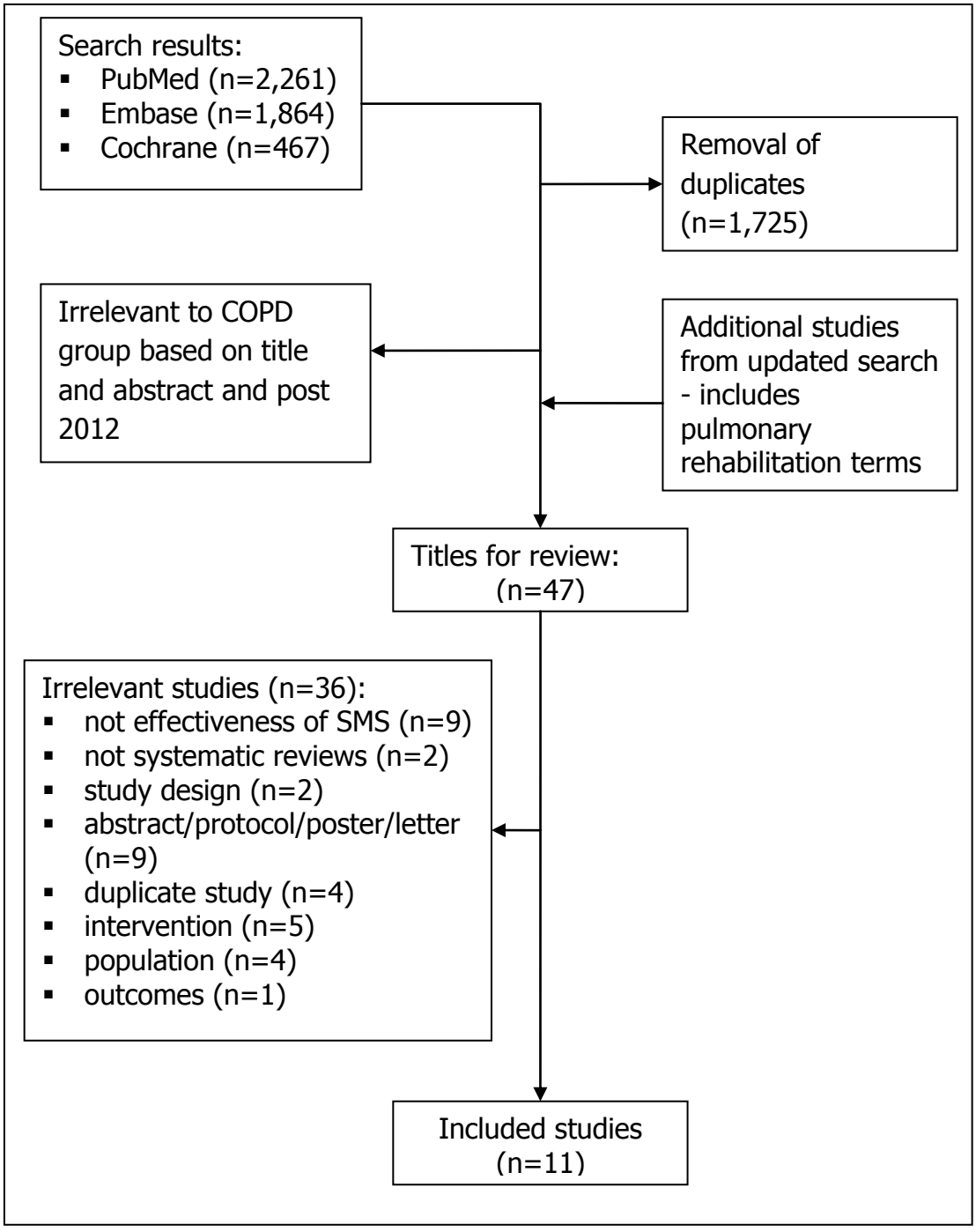
The PRISMS review retrieved a total of five systematic reviews of COPD-specific SMS interventions and generic interventions used in adults with COPD.[2] Summary details of the reviews are included in Table 6.1. The publication dates of the systematic reviews ranged from 2005 to 2012 while that of the included RCTs ranged from 1987 to 2011. The reviews included 28 individual RCTs and were conducted in Canada, the Netherlands, Sweden, France, US, UK, Australia and Hong Kong.

The PRISMS review was updated to April 2015 using the search string in Appendix A3.1. A further 11 systematic reviews were retrieved (Figure 6.1) that assessed a diverse range of SMS interventions for COPD including action plans,[127] integrated disease management (chronic care management that requires a community wide, systematic and structured multidisciplinary approach potentially employing multiple treatment modalities) ,[128] combinations of SMS interventions,[129-132] telemedicine[133-136] and pulmonary rehabilitation.[137] See Table 6.1 for details.

Study overlap is reported in Table 6.2. The results from one review by Harrison et al. (2015) are not discussed further due to large study overlap with another high-quality review by Jordan et al. (2015). The number of included RCTs per systematic review ranged from four to 65 with the number of participants ranging from 529[138] to 3,941.[129] The publication dates of the systematic reviews ranged from 2005 to 2015 while that of the included RCTs ranged from 1977 to 2013. RCT study locations were typically in Europe or North America. In total 185 unique RCTs were identified between the 16 RCTs included in this review.

The R-AMSTAR scores for the additional systematic reviews identified in the updated search ranged from 26 to 41, with scores of 31 or more indicating a high-quality systematic review. When weighted according to the number of participants in the original RCTs (less than 1,000 or greater than or equal to 1,000), nine of the systematic reviews were categorised as providing the highest quality evidence (*'three star'**** review) while four reviews each were rated as *'two-star'*** and two as *'one-star'** in terms of their quality and size. Of the 15 systematic reviews discussed, 14 included a meta-analysis of which 11 were assessed as high-quality, two as moderate quality and one as low-quality. A grading of 'low-quality' refers to studies where the conclusions are at high-risk of bias due to poor data collection or methods of data synthesis. The conclusions in studies identified as 'moderate quality' are at risk of bias, but are likely to be broadly accurate, while studies graded as 'high-quality' are very likely to have conclusions that accurately reflect the available evidence (see also Chapter 3, Table 3.1). Table 6.3 below details the number of primary studies within the review, and the quality assessment of both the systematic reviews and meta-analyses and the evidence underpinning them, and provides a summary of findings for selected outcomes from the various meta-analyses assessing the impact of SMS interventions in COPD.

**Figure 6.1 Flowchart of included studies from updated search**



## Table 6.1 Summary of systematic reviews retrieved

| Author (year) | Intervention |
|---|---|
| Reviews retrieved in PRISMS search | |
| **Education / Action Plans** | |
| Effing (2007)[139]‡ | Self-management education |
| Tan (2012)[140] | Self-management education – disease-specific |
| Turnock (2005)[141]¥ | Action plans |
| **Complex SMS interventions** | |
| Bentsen (2012)[138] | Range of SMS interventions |
| **Home care by outreach nursing programmes** | |
| Wong (2012)[142] | Home care by outreach nursing |
| Reviews retrieved in updated search | |
| **Education / Action Plans** | |
| Walters (2010)[127] ¥ | Action plans - COPD exacerbations |
| **Pulmonary rehabilitation** | |
| McCarthy (2015)[137] | Pulmonary rehabilitation |
| **Telemedicine** | |
| Cruz (2014)[133] | Home telemonitoring |
| Kamei (2012)[134] | Telehome monitoring-based telenursing |
| Lundell (2014)[135] | Telehealthcare – making pulmonary rehabilitation accessible |
| McLean (2011)[136] | Telehealthcare |
| **Complex SMS interventions** | |
| Dickens (2013)[129] | Range of complex interventions (multiple components and/or multiple professionals, with interventions (e.g., education, rehabilitation, psychological therapy, social or organisational interventions, or drug trials targeting a psychological problem) delivered by a variety of means (individual, group, telephone or computer-based) |
| Harrison (2015)[132] | Range of SMS – Following COPD exacerbation |
| Kruis (2013)[128] | Range of integrated disease management interventions (chronic care management that requires a community wide, systematic and structured multidisciplinary approach potentially employing multiple treatment modalities) |
| Zwerink (2014)[131]‡ | Range of SMS interventions |
| Jordan (2015)[130] | Range of SMS – Following COPD exacerbation. Moderate to severe COPD. |

**Key**: **COPD** = chronic obstructive pulmonary disease; **SMS** = self-management support.
¥Walter's Cochrane review (CR) (2010) is an update of Turnock's CR (2005).
‡Zwerink's CR (2014) is an update of Effing's CR (2007). Note: In Zwerink's update they chose to exclude studies with education as the only active intervention.

**Table 6.2 Study overlap between the included systematic reviews (PRISMS report plus the systematic reviews from the updated search).** Adapted from PRISMS review[2]

| | Review (year) | 1 | 2 | 3 | 4 | 5 | | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| PRISMS reviews | | | | | | | | | | | | | | | | | | |
| 1 | Bentsen (2012) | **4** | | | | | | | | | | | | | | | | |
| 2 | Effing (2007) | 2 | **13** | | | | | | | | | | | | | | | |
| 3 | Tan (2012) | 2 | 4 | **12** | | | | | | | | | | | | | | |
| 4 | Turnock (2005) | 0 | 1 | 1 | **3** | | | | | | | | | | | | | |
| 5 | Wong (2012) | 1 | 4 | 2 | 0 | **9** | | | | | | | | | | | | |
| Reviews retrieved in updated search | | | | | | | | | | | | | | | | | | |
| 6 | Cruz (2014) | 0 | 0 | 0 | 0 | 0 | | **9** | | | | | | | | | | |
| 7 | Dickens (2013) | 1 | 5 | 4 | 1 | 4 | | 1 | **32** | | | | | | | | | |
| 8 | Harrison (2015) | 0 | 0 | 2 | 0 | 1 | | 0 | 4 | **7** | | | | | | | | |
| 9 | Kamei (2012) | 0 | 0 | 0 | 0 | 0 | | 1 | 0 | 0 | **7** | | | | | | | |
| 10 | Kruis (2013) | 1 | 4 | 2 | 0 | 4 | | 1 | 1 | 1 | 0 | **26** | | | | | | |
| 11 | Lundell (2014) | 1 | 1 | 2 | 0 | 1 | | 0 | 1 | 1 | 0 | 1 | **9** | | | | | |
| 12 | Zwerink (2014) | 3 | 6 | 5 | 0 | 2 | | 1 | 7 | 1 | 0 | 6 | 2 | **29** | | | | |
| 13 | McLean (2011) | 1 | 1 | 2 | 0 | 1 | | 0 | 3 | 3 | 2 | 1 | 3 | 3 | **10** | | | |
| 14 | Walters (2010) | 0 | 2 | 1 | 3 | 0 | | 0 | 3 | 1 | 0 | 1 | 0 | 0 | 0 | **5** | | |
| 15 | Jordan (2015) | 0 | 0 | 2 | 0 | 2 | | 0 | 4 | 5 | 0 | 1 | 1 | 1 | 2 | 0 | **10** | |
| 16 | McCarthy (2015) | 0 | 3 | 0 | 0 | 1 | | 0 | 3 | 0 | 0 | 12 | 0 | 2 | 0 | 0 | 1 | **65** |

*Walter's Cochrane review (CR) (2010) is an update of Turnock's CR (2005). Note: Zwerink's CR (2014) is an update of Effing's CR (2007).

**** PRISMS review is based on a search from 1993 to June 2012. This search was updated to April 2015.

## Table 6.3 Study details, quality assurance and summary of findings from meta-analysis of impact of self-management support interventions on health-related quality of life, resource utilisation and mortality

| Study | Quality of Systematic Review | | | Primary Studies | | Quality of Meta-analysis | QoL | Hospitalisation |
|---|---|---|---|---|---|---|---|---|
| | R-AMSTAR score | Partici-pants | Quality | n | low-risk^ | | | |
| **Education / action plans** | | | | | | | | |
| Effing 2007[139] | 34 | 2,239 | *** | 13 | 3 | High | WMD –2.58 (–5.14 to 0.02) | OR 0.64 (0.47 to 0.89) |
| Tan 2012[140] | 33 | 2,103 | *** | 12 | 2 | High | WMD –3.78 (–6.82 to –0.73) | OR 0.55 (0.43 to 0.71) |
| Turnock 2005[141] | 39 | 367 | ** | 3 | 0 | High | WMD –0.32 (–3.34 to 2.70) | ‡ |
| Walters 2010[127] | 34 | 574 | ** | 5 | 1 | High | WMD –0.54 (–3.05 to 1.98) | ‡) |
| **Pulmonary rehabilitation** | | | | | | | | |
| McCarthy 2015[137] | 41 | 3,822 | *** | 65 | 17 | High | WMD –6.89 (–9.26 to –4.52) | - |
| **Telemedicine** | | | | | | | | |
| Cruz 2014[133] | 33 | 587 | ** | 9 | 2 | High | SMD –0.53 (-0.97 to -0.09) | RR 0.72 (0.53 to 0.98) |
| Kamei 2012[134] | 30 | 550 | * | 9 | 6 | Moderate | - | RR 0.80 (0.68–0.94) |
| Lundell 2014[135] | 36 | 982 | ** | 9 | 2 | Low | - | - |
| McLean 2011[136] | 39 | 1,004 | *** | 10 | 0 | High | WMD –6.57(–13.62 to –0.48) | OR 0.46 (0.33 to 0.65) |
| **Complex SMS interventions** | | | | | | | | |
| Bentsen 2012[138] | 26 | 529 | * | 4 | NR | NA | - | - |
| Dickens 2013[129] | 35 | 3,941 | *** | 32 | 8 | Moderate | - | |
| Kruis 2013[128] | 37 | 2,997 | *** | 26 | 5 | High | WMD –0.22 (–7.43 to 6.99)¥ | |
| Zwerink 2014[131] | 39 | 3,688 | *** | 29 | 9 | High | WMD –3.51 (–5.37 to –1.65) | |
| Jordan 2015[130] | 40 | 1,502 | *** | 10 | 1 | High | WMD–3.84 (–6.40 to –1.29) | |
| **Home care by outreach nursing** | | | | | | | | |
| Wong 2012[143] | 37 | 1,498 | *** | 9 | 4 | High | WMD –2.60 (–4.81 to–0.39) | OR 1.01 (0.71 to 1.44) |

**Key**: **WMD** = Weighted mean difference; **NR** = not reported; **NA** = not applicable; **QoL**, quality of life; **RR** = relative risk; **OR** = Odds Ratio;.
^ Number of the total primary studies identified as being at low risk of bias.
‡Turnock 2005 and Walters 2010 both included pooled estimates for hospitalisations, but these were not presented as relative risks. Neither found a statistically significant impact. Walters also reported a pooled estimate for ED visits (no significant impact), but no estimate of relative risk.
**¥** St. George's Respiratory Questionnaire (SGRQ) for QoL at >12 months.

**Table 6.3 (continued). Study details, quality assurance and summary of findings from meta-analysis of impact of SMS interventions on health-related quality of life, resource utilisation and mortality.**

| Study | Quality of Systematic Review | | | Primary Studies | | Quality of Meta-analysis | ED | Unscheduled/ urgent healthcare use[#] | Mortality |
|---|---|---|---|---|---|---|---|---|---|
| | R-AMSTAR score | Partici-pants | Quality | n | low-risk[^] | | | | |
| **Education / action plans** | | | | | | | | | |
| Effing 2007[139] | 34 | 2,239 | *** | 13 | 3 | High | | | |
| Tan 2012[140] | 33 | 2103 | *** | 12 | 2 | High | | | |
| Turnock 2005[141] | 39 | 367 | ** | 3 | 0 | High | | | |
| Walters 2010[127] | 34 | 574 | ** | 5 | 1 | High | | | |
| **Pulmonary rehabilitation** | | | | | | | | | |
| McCarthy 2015[137] | 41 | 3,822 | *** | 65 | 17 | High | | | |
| **Telemedicine** | | | | | | | | | |
| Cruz 2014[133] | 33 | 587 | ** | 9 | 2 | High | RR 0.68 (0.38 to 1.18) | | RR 1.43 (0.40 to 5.03) |
| Kamei 2012[134] | 30 | 550 | * | 9 | 6 | Moderate | RR 0.52 (0.41 to 0.65) | | RR 1.36 (0.77 to 2.41) |
| Lundell 2014[135] | 36 | 982 | ** | 9 | 2 | Low | | | |
| McLean 2011[136] | 39 | 1,004 | *** | 10 | 0 | High | OR 0.27 (0.11 to 0.66) | | |
| **Complex SMS interventions** | | | | | | | | | |
| Bentsen 2012[138] | 26 | 529 | * | 4 | NR | NA | | | |
| Dickens 2013[129] | 35 | 3,941 | *** | 32 | 8 | Moderate | | OR 0.68 (0.57 to 0.80) | |
| Kruis 2013[128] | 37 | 2,997 | *** | 26 | 5 | High | OR 0.64 (0.33 to 1.25) | | OR 0.45 (0.16 to 1.28) |
| Zwerink 2014[131] | 39 | 3,688 | *** | 29 | 9 | High | | | OR 0.79 (0.58 to 1.07) |
| Jordan 2015[130] | 40 | 1,502 | *** | 10 | 1 | High | not combined, low quality | | HR 1.07 (0.74 to 1.54) |
| **Home care by outreach nursing** | | | | | | | | | |
| Wong 2012[143] | 37 | 1,498 | *** | 9 | 4 | High | | | |

**Key**: **ED** = emergency department; **NR** = not reported; **NA** = not applicable; **RR** = relative risk; **OR** = Odds Ratio; **HR** = Hazard ratio.
[^] Number of the total primary studies identified as being at low risk of bias. [#] It is assumed that the definitions are similar.
‡Turnock 2005 and Walters 2010 both included pooled estimates for hospitalisations, but these were not presented as relative risks. Neither found a statistically significant impact. Walters also reported a pooled estimate for ED visits (no significant impact), but no estimate of relative risk.

### 6.2.3 Summary of findings

Detailed summaries of the systematic reviews including the intervention and comparator, outcomes assessed, duration of follow-up, sample size (number of RCTs and total number of participants), and the evidence of effect are included in Appendix A.6.1. The following are reported based on the findings from PRISMS and the additional systematic reviews retrieved in the updated search.

#### 6.2.3.1 Education / Action plans

**Three star (***) reviews**

Based on two three-star reviews, PRISMS reported that self-management education support or disease-specific education interventions were associated with a reduction in COPD-related hospital admissions.[139;140] Results from the high-quality meta-analysis showed a significant reduction in the probability of at least one hospital admission among patients receiving self-management support education compared with those receiving usual care. They also reported that the effect of education interventions on health-related quality of life is less established as a consistent and clinically significant positive effect on quality of life was not observed.

**Two star (**) reviews**

Based on the 2005 Cochrane review, PRISMS reported that action plans for COPD patients are recommended to be used only in combination with other self-management components.[141] While evidence was found that action plans improved self-management knowledge (increased recognition and appropriate reaction to an exacerbation of symptoms via the self-initiation of antibiotics or steroids), there was no evidence of significant effects on mortality, healthcare utilisation, health-related quality of life, lung function, functional capacity, symptom scores, anxiety or depression.

A 2010 update[127] to the above 2005 Cochrane review concurred with this finding. Consistent with the 2005 review, the intervention arm in this review was limited to individual action plans with limited or no self-management education (less than one hour), and excluded other broader education and exercise self-management interventions, irrespective of whether they included an action plan. No evidence was found that action plans reduce healthcare utilisation (hospital admissions, emergency department admissions or GP consultations), but evidence was found that action plan use is associated with increased initiation of corticosteroid or antibiotic treatment for acute exacerbations.

**Summary statement for education**

There is very good evidence that education in patients with COPD is associated with a reduction in COPD-related hospital admissions with limited evidence that it is associated with improvements in health-related quality of life. There is no evidence that action plans when used alone and in the absence of other self-management supports reduce healthcare utilisation or lead to improvements in quality of life.

#### 6.2.3.2 Pulmonary rehabilitation

**Three star (***) reviews**

A 2015 Cochrane review and meta-analysis by McCarthy et al.[137] of 65 RCTs compared pulmonary rehabilitation (defined as exercise training for at least four weeks with or without education and, or psychological support) with usual care on HRQoL and functional and maximal exercise capacity in persons with COPD. They reported that pulmonary rehabilitation improves functional exercise capacity and HRQoL, with improvements noted in domains related to dyspnoea and fatigue, emotional function and a sense of control over the condition. These improvements are reported as moderately large and clinically significant. The authors reported that the results strongly support inclusion of pulmonary rehabilitation as part of the management and treatment of patients with COPD. However, they also noted that large variation in the design of the pulmonary rehabilitation programmes included in the meta-analysis resulted in substantial heterogeneity. The programmes assessed ranged in duration from four to 52 weeks with the majority being eight (n=18) or 12 weeks (n=18) long. As such, they recommended that further studies should focus on identifying the components of pulmonary rehabilitation that are essential, its ideal length and location, the degree of supervision and intensity of training required, and how long treatment effects persist.

**Summary statement for pulmonary rehabilitation**

There is very good evidence that pulmonary rehabilitation which includes exercise training improves health-related quality of life and functional exercise capacity in people with COPD. Large variation in the design of pulmonary rehabilitation programmes makes it difficult to identify their optimal format.

#### 6.2.3.3 Telemedicine

**Three star (***) reviews**

A 2011 Cochrane review and meta-analysis by McLean et al.[136] reported that telehealthcare as part of a complex health intervention in COPD patients appears to decrease the number of times patients attend the emergency department and hospital. No impact on mortality rates was observed at 12 months follow up.

### Two star (**) reviews

A 2014 meta-analysis by Cruz et al.[133] assessed telehealth in COPD and found limited evidence of effectiveness, with only small positive effects for home telemonitoring to reduce healthcare utilisation and improve health-related outcomes in patients with COPD.

A 2014 meta-analysis by Lundell et al.[135] assessed a range of telehealthcare interventions for COPD (mainly focused on making pulmonary rehabilitation more accessible) and found evidence that it may lead to improvements in physical activity. However, by excluding studies that were outliers until a relatively homogeneous result was retrieved ($I^2$<60%) the authors are likely to have underestimated the degree of heterogeneity associated with this outcome and undermined the validity of the pooled estimate.

### One star (*) reviews

The 2012 meta-analysis by Kamei et al.[134] on telehome monitoring-based telenursing for patients with COPD reported statistically significant decreases in healthcare service use for patients with severe COPD. Statistically significant reductions in emergency department visits and disease exacerbations were also reported, but the intervention had no effect on mortality.

**Summary statement for telemedicine**

There is some evidence that telemedicine as part of a complex intervention decreases healthcare utilisation, with no evidence found of an impact on mortality.

#### 6.2.3.4 Complex SMS interventions

### Three star (***) reviews

A 2014 Cochrane review and meta-analysis by Zwerink et al.[131] reported that SMS interventions in patients with COPD are associated with improved HRQoL health-related quality of life (St George's Respiratory Questionnaire [SGRQ]), a reduction in respiratory-related and all-cause hospital admissions, and improvement in self-reported activity-related dyspnoea (Medical Research Council [MRC] scale). However, they assessed a diverse range of interventions (for example varying educational programmes delivered through a variety of methods (for example, group, individual, face-to-face, telephone follow-up) and were unable to determine their most effective parts.

A 2015 National Institute for Health Research (in the UK) review by Jordan et al.[130] included a review of the provision of SMS for patients shortly after being discharged from hospital with an acute exacerbation of their COPD. It concluded that there was

little evidence of benefit to providing SMS to patients shortly after discharge from hospital, although effects observed were consistent with possible improvement in HRQoL and reduction in hospital admissions. They noted that it was not easy to tease out the most effective components of SMS packages, although interventions containing exercise seemed the most effective.

A 2013 meta-analysis by Dickens et al.[129] reported that the use of urgent healthcare in patients with COPD was significantly reduced by using a range of 'complex interventions'. Such complex interventions involved multiple components and, or multiple professionals, with interventions (for example, education, rehabilitation, psychological therapy, social or organisational interventions, or drug trials targeting a psychological problem) delivered by a variety of means (individual, group, telephone or computer-based). They noted that the key components of these interventions that were associated with a reduction in urgent healthcare utilisation were education, exercise and relaxation.

A meta-analysis by Kruis et al.[128] reported that integrated disease management interventions improved disease-specific quality of life and exercise capacity. A significant improvement in self-reported activity-related dypsnoea was also reported using the MRC Dyspnoea Scale, but another study found no improvement using the Borg scale (a validated instrument assessing exercise-induced dyspnoea and used as an outcome measure in pulmonary rehabilitation programmes). The authors defined integrated disease management as interventions that contained a programme provided by caregivers from at least two different disciplines, with two different components (for example, exercise, education, self management), and concluded that there was insufficient evidence to refute or confirm the long term effectiveness of integrated disease management.

### One star (*) reviews

PRISMS did not report any conclusions based on the single one-star review they identified.

**Summary statement for complex SMS interventions**

Based on the quantity and quality of the systematic reviews and the underpinning primary randomised controlled trials (RCTs), there is good evidence that complex self-management support (SMS) interventions (involving multiple components and, or multiple professionals delivered by a variety of means) in patients with COPD are associated with improvements in health related quality of life (HRQoL). No evidence was found of a statistically significant benefit regarding mortality while there was limited evidence of reductions in health care utilisation. Although it is not clear which

components of SMS support relate to these improvements, education and exercise seem to be effective.

#### 6.2.3.5 Outreach nursing programmes

**Three star (***) reviews**

Based on a single three-star review by Wong et al.,[143] PRISMS reported that outreach nursing programmes improved health-related quality of life (although the improvement may not have been clinically significant), but their effect on hospitalisations was variable.

**Summary statement for outreach nursing programmes**

There is some evidence that outreach nursing programmes improve health-related quality of life in patients with COPD.

## 6.3 Review of cost effectiveness of self-management support interventions

A review of cost-effectiveness studies was undertaken to assess the available evidence for self-management support (SMS) interventions for people with COPD. Studies were included if they compared the costs and consequences of a SMS intervention to routine care.

### 6.3.1 Search strategy

A search was carried out to identify economic analyses of SMS interventions. In conjunction with the systematic review of clinical effectiveness, the search for economic evaluations was carried out in MEDLINE, EMBASE and the Cochrane Library. The same search terms were used with the exception of terms for systematic review and meta-analysis. In place of these, search terms and filters for economic evaluations were applied. In addition, systematic reviews of SMS interventions identified through the results of the clinical effectiveness search which included cost or economic outcomes were used to identify additional studies. The search was carried out up until 4th March 2015.

The PICOS (Population, Intervention, Comparator, Outcomes, Study design) analysis used to formulate the search is presented in Table 6.4 below.

**Table 6.4. PICOS analysis for identification of relevant studies**

| | |
|---|---|
| **Population** | Adults ≥ 18 years old with COPD. |
| **Intervention** | Any self-management support intervention that helps people with COPD through education, training or support. |
| **Comparator** | Routine care. |
| **Outcomes** | Cost or cost-effectiveness of intervention. |
| **Study design** | Randomised controlled trials, case-control studies, observational studies, economic modelling studies. |

Studies were excluded if:

- a nursing home or non-community dwelling population was included,
- it included a paediatric population,
- cost data were not clearly reported,
- published prior to 2000 due to limited relevance.

As outlined in Chapter 3.2.2 and in accordance with national HTA guidelines, assessment of the quality of the studies using the Consensus on Health Economic Criteria (CHEC)-list was performed independently by two people. For studies that included an assessment of cost-utility or an economic modelling approach, assessment of the relevance to the Irish healthcare setting and their credibility was considered using a questionnaire from the International Society of Pharmacoeconomics and Outcomes Research (ISPOR).

### 6.3.2 Results – Cost-effectiveness

The initial screening retrieved 63 papers relating to COPD. Of these, 38 studies were identified for full text review, with the remaining 25 excluded as irrelevant or unsuitable based on screening of abstract or full text. A further 13 were excluded according to the various exclusion criteria. Two additional studies were identified following hand searching of systematic reviews of clinical effectiveness included in Section 6.2, leaving 27 articles included in this review.

Five studies were conducted in Canada, six studies in the UK, four in the US and three from Spain. In addition, there were two studies from Australia and the Netherlands and one each from Belgium, Denmark, Italy, Ireland and Norway. The included studies were all published between 2001 and 2015. The characteristics of the included studies are given in Table 6.5. Costs reported in each of the studies were inflated to 2014 prices using the consumer price index for health and expressed in Irish Euro using the purchasing power parity exchange rate.[122]

## Table 6.5 Characteristics of the studies included

| Study | Country | Intervention |
|---|---|---|
| Bakerly (2009)[144] | UK | Integrated care |
| Bourbeau (2006)[145] | Canada | SMS education |
| Cecins (2008)[146] | Australia | Pulmonary rehabilitation |
| Chandra (2012)[147] | Canada | Smoking cessation* |
| Chandra (2012)[147] | Canada | Pulmonary rehabilitation* |
| Chuang (2011)[148] | US | Case management |
| De San Miguel (2013)[149] | Australia | Telemedicine |
| Dewan (2011)[150] | US | Disease management |
| Farrero (2001)[151] | Spain | Case management |
| Gallefoss (2004)[152] | Norway | SMS education |
| Gillespie (2013)[153] | Ireland | Pulmonary rehabilitation |
| Golmohammadi (2004)[154] | Canada | Pulmonary rehabilitation |
| Griffiths (2001)[155] | UK | Pulmonary rehabilitation |
| Haesum (2012)[156] | Denmark | Telemedicine |
| Hernandez (2003)[157] | Spain | Case management |
| Hoogendoorn (2010)[158] | Netherlands | Pulmonary rehabilitation |
| Jodar-Sanchez (2014)[159] | Spain | Telemedicine |
| Jordan (2015)[130] | UK | Post-discharge SMS intervention |
| Khdour (2011)[160] | UK | SMS education |
| Liu (2013)[161] | US | Case management |
| Monninkhof (2004)[162] | Netherlands | SMS education |
| Pare (2013)[163] | Canada | Telemedicine |
| Stoddart (2015)[164] | UK | Telemedicine |
| Taylor (2012)[165] | UK | SMS education |
| Tinkelman (2003)[166] | US | Case management |
| Van Boven (2014)[167] | Belgium | Pharmacy led medication adherence |
| Vitacca (2009)[168] | Italy | Telemedicine |

*The 2012 HTA by Chandra et al., separately modelled the costs and benefits of smoking cessation and pulmonary rehabilitation versus usual care and so are reported as two individual reports here.
**Key**: **SMS** = self-management support.

The studies were classified according to the type of intervention assessed: SMS education programmes, pulmonary rehabilitation, telemedicine, case management, and other SMS interventions. Of note, many interventions included more than one element such as case management plus telephonic support or education plus physical activity.

This review captures all SMS interventions assessed for COPD and retrieved few conventional economic evaluations (n=5). Seventeen of the retrieved studies gathered cost data as part of a randomised controlled trial (RCT) while data for five other studies were based on a non-randomised prospective study (n=1) or observational cohort studies (n=4). The quality of the included studies varied with eight identified as being of high-quality (see Appendix Table A6.3).

#### 6.3.2.1 Self-management support education programmes

Five studies were identified that investigated a variety of SMS education programmes, including two from the UK and one each from Canada, Norway and the Netherlands (see Table A6.4). Interventions typically involved an education programme which was delivered by a healthcare specialist at home or in a primary care setting; two studies from the UK examined a pharmacy-led SMS education programme while another was delivered by a lay person (tutor). In four of the studies the education programme was used in combination with another intervention such as an exercise programme, exercise classes, access to telephone follow up by a nurse or individual follow-up sessions.

All of the studies were based on patient data gathered from an RCT with a follow-up ranging from six months to one year. Study sizes ranged from 62 to 191 patients. Where reported, the patients' ages ranged from over 35 years to below 70 years. Four studies included those with moderate to severe disease.

Three studies reported cost savings as a result of an SMS education programme.[145;160;165] The 2006 Canadian study by Bourbeau et al.[145] described a six to eight week education programme with use of an action plan and ongoing supervision from a case manager for people with moderate to severe disease. It reported results for different caseloads of patients per case manager. Using 14 patients as its base case, it found the total cost of the intervention per patient was €2,953. Of note, this also included a pool of 20 stationary bikes which were distributed to each patient for the first two months of follow-up to increase physical activity motivation. An incremental cost-effectiveness ratio (ICER) of €3,293 per hospitalisation prevented was reported from the third-party payer perspective. For a more realistic caseload of 50 patients per case manager, they estimated a total intervention cost of €929 per patient and an ICER of €1,036 per hospitalisation prevented. The authors postulated the intervention would be less cost-effective in those with milder disease.

A mean cost of intervention of €177 per patient was reported in the 2002 Norwegian study by Gallefos et al. describing an education programme comprising both group and one-to-one education visits, and an individualised action plan. Improvements in

health-related quality of life (HRQoL) were reported and a cost-benefit ratio of 1: 4.8 was found from a societal perspective.

The 2011 study from Northern Ireland described a pharmacist-led education programme and found a non-significant mean cost saving of €1,005 in the intervention group, driven mainly by the decrease in hospitalisations and associated with a mean differential quality-adjusted life year (QALY) gain of 0.065.[160] Therefore, the education intervention was dominant (that is less costly and more effective than usual care) and an ICER was not calculated.

Two studies reported an increase in costs arising from a SMS education programme. A 2004 study from the Netherlands by Monnikhof et al. of the COPE SMS programme reported no measurable changes in HRQoL or QALYs and a slight decrease in healthcare consumption for participants enrolled in a five-week group education session, coupled with a weekly fitness programme.[162] The cost per patient of the self-management intervention was €713. The incremental cost difference from a societal perspective was €931 per patient per year in favour of usual care; the additional costs were mostly due to the high intervention costs. Participants in this study had mild disease. The 2012 UK study by Taylor et al. described a lay-led structured education programme and found that, when the total cost of providing seven courses and staff training was divided amongst all patients in the intervention group, this resulted in a cost per patient of €541.[165] However, when the 27 patients who failed to attend were excluded, the intervention cost per patient was €827. A small gain was reported in HRQoL. An ICER from a provider perspective of €16,465 per QALY gained over 6 months was calculated, however, interpretation of the ICER is complicated given the absence of a significant clinical effect size. Although the cost of the intervention was not offset by a decrease in healthcare utilisation, the authors suggested that the intervention was still cost-effective using NICE guideline threshold values.

All but one study reported potential cost savings or cost-effectiveness for patients with moderate to severe disease; however, the potential for savings depended on the efficiency with which the programme could be delivered. Potential cost savings were driven by a decrease in healthcare utilisation. However, only three studies examined HRQoL utility scores and of these, two reported small differences in favour of the intervention group in the short term.

#### 6.3.2.2 Pulmonary rehabilitation for COPD

Six studies were identified that examined the cost-effectiveness of pulmonary rehabilitation: two from Canada and one each from Australia, Ireland the Netherlands and the UK (Table A6.5). The interventions varied from four weeks to four months in duration, but in general comprised similar education and

physiotherapy exercise components. The number of weekly sessions also varied from daily to once a week. Some programmes specified input from dieticians and smoking cessation counselling, while others described inputs from physiotherapists only. Three of the studies were conducted alongside RCTs, two were pre- and post-intervention studies and one used published data to populate an economic model with a 30 year horizon. Follow-up ranged from 22 weeks to one year and the number of participants ranged from 199 to 350.

The cost of the intervention ranged from €273 per patient for twice weekly exercise classes reported by Cecins et al.[146]to €1,758 for an intensive four month programme with an additional 20 month maintenance follow-up in the study from the Netherlands.[158] The study published in Ireland, described an eight-week community-based programme provided by a nurse and physiotherapist for patients with mild to moderate disease and found a mean cost of €948 per patient.[153] This comprised €650 healthcare costs and €297 in patient costs.

Four studies conducted a cost-utility analysis. Chandra et al. modelled the cost-effectiveness of a four-week multi-disciplinary programme from a provider perspective and using a 5% discount rate, found an ICER of €12,885 per QALY and €10,502 per life year gained. Based on a two-year follow-up period, the Netherlands' study estimated an ICER of €34,548 per QALY and €26,966 per QALY from a societal and healthcare payer perspective, respectively; although the difference in QALYs between the intervention and the control groups was not significant. Excluding the additional resources for the intervention, overall healthcare utilisation was similar in the two groups at the study end point. The Irish study reported that pulmonary rehabilitation was only cost-effective when disease-specific health status scores were used (€980 per unit increase in the Chronic Respiratory Disease Questionnaire [CRQ] total score). It is important to note that though statistically significant improvements in the CRQ scores occurred at 22 week follow-up, the authors raised concerns that the confidence intervals included differences that were not clinically significant. The study did not report significant QALY gains and this is reflected in an ICER of €544,099 per QALY gained. The short follow-up of 22 weeks may also have affected this estimate by not capturing potential future cost savings. Finally, the authors of an exploratory UK study examined the potential cost-effectiveness of outpatient pulmonary rehabilitation delivered in a post-exacerbation period.[155] The main drivers of the model were the effect on hospital readmission, the duration of effect, and the cost of the self-management support programme. To be cost-effective, the authors concluded that the self-management programme post admission for an acute exacerbation would need to cost no more than GBP£2,200 (€2,749) if the relative reduction in admissions was consistent with a hazard ratio of 0.82.

As has been shown, the intensity, duration and composition of the rehabilitation programmes varied although all of them exhibited the greatest focus on exercise classes. All the included studies reported some degree of improvement in clinical outcome or utility, irrespective of disease severity. Based on the better quality studies, there is limited evidence that pulmonary rehabilitation is cost-effective in moderate to severe disease. The evidence from the one Irish study indicated that it is not cost-effective in those with mild to moderate disease. However, these findings were influenced by the choice of quality of life instrument, with speculation that the generic EQ5D instrument was not sufficiently sensitive to detect clinically meaningful differences in COPD health status. The follow-up period was limited to 22 weeks, so long-term costs and effects are uncertain.

#### 6.3.2.3 Telemedicine interventions for COPD.

Six studies were identified that assessed telemedicine SMS interventions for patients with COPD (Table A6.6). These examined telemedicine interventions requiring daily patient-self monitoring and remote transmission of repeated clinical measurements to a nurse, case manager or respiratory physician who would trigger contact with the patient as required to provide clinical advice. The studies were from Australia, Denmark, Spain, Italy, UK and Canada. All of these studies were based on RCTs with follow-up ranging from four to 21.5 months; the number of participants ranged from 45 to 256.

Of the telehealth monitoring studies, all but one required daily monitoring of vital signs and symptoms which were then transferred securely. In contrast, the Danish study described a customised monitoring frequency protocol for each patient.[156]

There were three cost-utility analyses. The Danish study, customised monitoring frequency for each patient and included monthly online telerehabilitation team case discussion. They found the intervention to be more effective and less costly than usual care when all healthcare costs from a provider perspective were considered. Using a 3% discount rate for capital costs, the cost of their intervention equipment was estimated at €597.[156] The authors cautioned that their project was small sized and conducted by a highly motivated researcher, doctors and patients thus questioning its reproducibility on a large scale. Jodar-Sanchez et al. estimated an ICER of €278,379 per QALY gained for their intervention in patients with severe COPD who took daily measurements and sent them a clinical call centre for review by a case manager.[159] The ICER, which indicated the intervention was not cost-effective, was based on the difference in all health-related hospital costs and health outcomes between trial arms over four months. Stoddart et al. examined telemedicine in a cohort of patients with mixed disease severity and reported an ICER of €182,673 per QALY. Their cost analysis was over one year and included all

healthcare costs from a provider perspective.[164] The largest proportion of costs in their study was due to equipment costs.

The three remaining studies reported cost savings associated with telemedicine. Pare et al. described daily remote telemonitoring by a case manger and focused their cost analysis on COPD-related emergency department attendances, hospitalisations and home visits. They estimated a net saving of €1,103 per patient year in the tele-homecare group mainly driven by reduction in hospitalisation and length of stay.[163] They also found that the cost of technology and nursing staff required for the intervention accounted for 20% of total healthcare costs. Of note, during the study period the control group also experienced a 38% reduction in number of hospitalisations. De San Miguel found net costs saving of €2,425 per person per year in their trial based on total healthcare cost from a provider perspective collected over six months and annualised.[149] Their participants had severe disease and the authors found that daily monitoring prompted more communication from patients with their physicians. Lastly, the Italian study looked at telemedicine in a cohort of patients with chronic respiratory failure on home ventilation or long-term oxygen therapy.[168] Only a proportion of these had COPD and were analysed separately. They found the cost of the intervention ranged from €903 to €1,008 per patient. The mean direct healthcare costs per patient excluding the intervention were €8,907 in the intervention group and €14,728 in the control over a one year period. The reduction in cost was mainly due to fewer hospitalisations, emergency department and GP visits.

The costs included in the studies vary widely with some limiting their analysis to hospital costs only, while others also include primary care costs. Some studies only examined COPD-related costs while others included all healthcare costs. This methodological variance limits the conclusions that can be gleaned from these studies.

In summary, evidence for the cost-effectiveness of telemedicine is mixed, with more applicable evidence suggesting that telemedicine interventions are not cost-effective. Interpretation of the evidence is complicated by the small study sizes, short-term follow-up (four to 12 months) and differences in disease severity between studies.

#### 6.3.2.4 Case-management interventions

Five studies were identified that assessed case management-type interventions: two from Spain[151;157] and three from the US (see Table A6.7). The interventions varied with one of the Spanish studies outlining a schedule of home visits and telephone review by a nurse for a cohort of stable COPD patients on long-term oxygen therapy, while the other described early discharge of patients with exacerbations facilitated by a limited number of nurse home visits and unlimited telephone contact in the eight-week period following discharge. One of the US studies modelled the effect of a

hypothetical home-based case management intervention aimed at early detection and treatment of exacerbations, while the second US study examined a disease management programme comprising a dedicated case manager to liaise with patients and physicians, unlimited access to a nurse-led helpline, an action plan and home visits. Finally, Chuang et al. described an intervention where nurses performed a number of regular and scheduled telephone call for educational and clinical advice purposes, as well as written educational materials, action plan and progress reports to primary care.[148]

The three better quality studies were based on RCT data and provide the basis for the remainder of this discussion. Follow-up duration in the intervention studies varied from eight weeks to one year. The number of participants ranged from 122 to 222 and all cost analysis were undertaken from the provider or third party payer perspective.

All three studies found cost savings mainly due to reduced hospitalisations and emergency department visits. Farrero et al. found the cost of their hospital-based home care programme to be 6.7 million pesetas for the one year study period. As outcomes, they examined diagnosis-related group costs of hospital resources used only and found net cost savings of 8.1 million pesetas during that time. Hernandez et al. found that the average direct healthcare costs for the intervention group at eight week follow up were 62% of the average costs estimated for the control group (€1,827 and €2,960 respectively, p=0.003).[157] These costs included the intervention costs, transport costs and both primary and secondary care costs from a public insurer perspective. Readmission rates were quite high in both groups at approximately 25%, but the cost savings achieved were driven by significantly lower lengths of inpatient stay (1.7 versus 4.2 days $p<0.001$) and a reduction in emergency department presentations (11 patients versus 21 patients, respectively). Chuang et al. examined costs from a third party payer perspective and found a reduction in all paid claims for the 141 participants of $328,766 at one year follow-up. The total programme costs were $225,012, resulting in an estimated return-on-investment of 46% from the payer perspective.

All the intervention studies examined some clinical outcomes alongside service utilisation. Farrero et al. found no significant differences between groups in quality of life scores and arterial blood gases, but reported similar and significant deterioration in lung function measured at follow-up for both groups. In contrast, Hernandez et al. found significant improvements for the intervention group in both HRQoL scores and patient satisfaction at eight week follow-up, as well as an increased proportion of patients in the intervention group with improvements in disease-related knowledge.

Evidence for case management examined heterogeneous interventions in different cohorts of patients with limited applicability to the Irish healthcare setting. All three studies that reported cost data collected alongside an RCT, found potential cost savings, but conflicting evidence regarding clinical effect. Of note, the study that reported a positive clinical effect was limited to eight week follow-up and the validity of the results is dependent on whether the effect can be sustained in the long-term.

#### 6.3.2.5 Other self-management support interventions

Five papers were identified that described a variety of other SMS interventions for COPD (Table A6.8). Two of these were from the UK,[130;144] with one each from Canada[147], Belgium[167] and the US. One study was a non-randomised prospective study with a matched retrospective control group, while the remaining four were economic models. Two studies were conducted alongside RCTs, while the other two used published estimates from various sources to populate their economic models.

Bakerely et al. described an integrated care approach to early discharge with a self-management plan for 130 patients with COPD.[144] They compared the one year costs of all hospital and community care in the integrated care group to hospital care costs in a retrospective matched group (n=95) and reported a cost saving of £600 per patient from a provider perspective.

Chandra et al. performed an economic evaluation of intensive counselling for smoking cessation compared with usual care which was described as a GP visit and leaflet.[147] They used a lifetime horizon and provider perspective with a 5% discount rate and found a lifetime cost savings of €1,674 and an increase in life years and QALYs; that is, that intensive counselling dominated (that is less costly and more effective) usual care. The report also assessed the impact of nicotine replacement therapy versus usual care, and a combination of intensive counselling plus nicotine replacement therapy versus placebo therapy, but did not directly compare the various interventions.

Dewan et al. used data from an RCT with one year follow-up to inform a post-hoc economic evaluation of a disease management programme. The intervention resulted in a significant reduction in hospitalisations and emergency department visits ($p<0.003$) and improvement in quality of life ($p<0.001$). The average cost saving per patient was US$593 after paying for the cost of disease management intervention.[150]

Van Boven et al. used the data from a three-month RCT of community pharmacy intervention to increase medication adherence to extrapolate costs and benefits for a one year period. They reported a cost saving of €227 per patient associated with a small QALY gain.[167] They then modelled the effects with a 12.5 year time horizon

for the same cohort and found the intervention remained cost saving, assuming that adherence returned to baseline levels after one year.

The second UK study used published data to populate an economic model to examine the effect of a SMS intervention delivered up to six weeks following discharge from hospital.[130] The intervention used in the base case was described as moderate to high intensity and consisted of two one-on-one education sessions, an action plan, and telephone follow up with a specialist nurse with home visits or specialist telephone review as appropriate. Using a 30-year provider perspective the ICER was found to be €10,270 per QALY gained. Of note, the authors did not specify any discount rate used. The ICER for the low-intensity intervention which comprised two telephone calls with a nurse was estimated as €1,291 per QALY gained. In contrast, the ICER for the high intensity intervention, described as four initial home education visits with an additional seven visits in the first year, was €11,569.

## 6.4 Discussion

This section discusses the main findings from the review of the clinical-effectiveness and cost-effectiveness literature.

### 6.4.1 Clinical-effectiveness

Sixteen systematic reviews comprising 185 unique RCTs are included in this overview of reviews. There was large heterogeneity across the interventions, however, to aid interpretation of the results the reviews were broadly categorised as 'a range of SMS interventions', 'education/action plans', 'pulmonary rehabilitation', 'telemedicine' and 'homecare by outreach nursing'.

The impact of SMS interventions on healthcare utilisation was assessed in several reports. Limited evidence was found that education and telemedicine-based SMS as well as self-management support comprising a range of SMS interventions (also referred to as complex SMS interventions, that is involving multi-components and, or multiple providers, with interventions delivered by a variety of means) are associated with statistically significant reductions in healthcare utilisation. The PRISMS review found that SMS via education is associated with a statistically significant reduction in COPD-related hospital admissions. The updated review found that a range of complex SMS interventions which specifically included education, exercise and relaxation therapy were also associated with a statistically significant reduction in urgent healthcare based on a Cochrane review. Another Cochrane review reported reductions in healthcare utilisation (patients treated with integrated disease management on average discharged earlier) and improvements in quality of life for a range of integrated disease management interventions. However, the interventions and patient populations varied widely making it difficult to make recommendations on the most effective content of self-management training. A third Cochrane review

of a range of SMS interventions found statistically significant reductions in respiratory-related hospitalisations and improvements in HRQoL. Again, the interventions and patient populations varied widely making clear recommendations on effective components of SMS difficult. There was little evidence of benefit in providing SMS to patients shortly after discharge from hospital, based on a large National Institute of Health Research (NIHR) review. They reported that it was difficult to tease out the most effective components of SMS packages, but that interventions containing exercise seemed most effective. Finally, some evidence was found that telehealthcare is associated with statistically significant reductions in hospitalisations.

Good evidence was found that pulmonary rehabilitation and SMS that comprises a range of SMS interventions are associated with significant improvements in health-related quality of life (HRQoL). The updated search found that pulmonary rehabilitation which includes at least four weeks exercise training is associated with clinically and statistically significant improvements in important domains of HRQoL, including dyspnoea, fatigue, emotional function and mastery (that is, the sense of control that individuals have over their condition). Clinically significant improvements were also reported for functional exercise capacity. However, it was noted that there is substantial variation in the design of pulmonary rehabilitation programmes making it difficult to identify their optimal format, duration and intensity. Some evidence was also found that nursing outreach programmes improve HRQoL in individuals with COPD. No evidence of a reduction in mortality was found for any of the SMS interventions that assessed this outcome.

Given the description of the COPD patient populations, it would appear that the evidence should be broadly applicable to the Irish healthcare setting. A potential caveat to this assumption is the extent to which the comparator (usual care) in these RCTs) is representative of usual care in Ireland. Given the increasing tendency for usual or standard of care to be determined by evidence-based clinical guidelines and the convergence of such guidelines in Western countries, this assumption is reasonable. However, differences may exist in how care is provided, impacting the adherence to recommended standard of care. For example, COPD care in the Irish primary care setting may differ to that in the UK's National Health Service system as the latter is incentivised by the quality of outcomes framework. Particular difficulties in Ireland have included delays in the diagnosis of COPD due to limited access to spirometry testing in primary care, although targets have been set by the HSE's Clinical Care Programme for COPD to address this issue.[125] Improved access to pulmonary rehabilitation has also been a focus of the programme: in 2013 there was access to structured pulmonary rehabilitation in 24 acute hospitals and 14 integrated service areas with a structured COPD outreach programme operational in 14 acute hospitals.[169]

Due to the volume of evidence available, and in the interest of efficiency, this assessment of SMS interventions in COPD was undertaken in the form of an overview of reviews. As discussed in Chapter 3.4.1, a disadvantage of this approach is the inability of an overview of reviews to reflect the most recent literature: following publication of an RCT, it must first be captured in a systematic review, before subsequently being captured in an overview of reviews. However, given their sample sizes, it is not appropriate to draw conclusions on the effect of an intervention based on a single, or a number of small, RCTs. Therefore it is unlikely that more recent RCTs not captured in this overview of reviews would be sufficient to substantially alter recommendations informing major policy decisions.

### 6.4.2 Cost effectiveness

Our review identified 27 unique studies examining a broad range of interventions. The majority of the studies reported cost data alongside an RCT and therefore used short time horizons ranging from four to 12 months for analysis. This has implications for the interpretation of the findings as firstly, a larger proportion of intervention costs are often accrued at the start of a programme while secondly, the duration may not be sufficient to capture all relevant benefits. Furthermore, for benefits that are observed, it is not certain if these are sustained in the long-term. The evidence of cost-effectiveness contrasts with that of the review of clinical-effectiveness which comprised 16 systematic reviews and 185 unique RCTs.

SMS interventions were typically compared with current standard of care. This was often poorly described and varied according to the location and date of the study. This represents an important caveat when comparing international data to the Irish healthcare setting. As noted in Section 6.4.1, while there is an increasing tendency for usual or standard of care to be determined by evidence-based clinical guidelines, differences may exist in how care is provided, impacting the adherence to recommended standard of care.

The SMS education programmes were heterogeneous including a range of elements in addition to the educational components. In contrast, the pulmonary rehabilitation programmes were more consistent: while they varied in duration, all adopted a multi-disciplinary approach. The telemedicine interventions that used remote monitoring were the most homogenous group, with regular clinical measurements remotely transmitted to a clinical case manager who would provide management feedback. The applicability of the international evidence to the Irish healthcare setting is limited, due to differences in the health system financing mechanisms and therefore the perspective adopted. The quality of the cost-effectiveness studies was variable, with only eight studies identified as higher quality studies.

In the modelling studies included, discount rates varied from 1.5% to 5% impacting the applicability of their findings to the Irish context where a discount rate of 5% for both costs and benefits is applied. The studies included a large variety of participants from those with mild disease to patients on home ventilation and long-term oxygen at home. Though examining these individually gives a good picture of cost-effectiveness across the spectrum of disease it does hinder comparison of findings between studies.

Overall, the findings for SMS interventions in COPD are encouraging, though the quality of the included economic evaluations was predominantly poor. The most consistent evidence was for SMS education programmes with the majority of studies reporting it to be cost saving for patients with moderate to severe disease, although the nature of the intervention provided was heterogeneous.

All of the included studies for pulmonary rehabilitation reported some degree of improvement in clinical outcome or utility, irrespective of disease severity. Based on the four better quality studies, there is limited evidence that pulmonary rehabilitation is cost-effective in moderate to severe disease. The evidence from the one Irish study indicated that it was not cost-effective in those with mild to moderate disease. However, these findings were influenced by the choice of quality of life instrument, with speculation that the generic EQ5D instrument was not sufficiently sensitive to detect clinically meaningful differences in COPD health status. Some of the interventions had effect sizes that were not statistically significant. Interpretation of the results of any subsequent cost-effectiveness ratios can be complicated, and should focus in these instances on the cost findings.

With regard to telemedicine, evidence for cost-effectiveness was mixed, with more applicable evidence from a UK study suggesting that telemedicine interventions are not cost-effective. There were four studies that focused on case management of COPD patients, but many of the other studies had elements of case management as adjunct to their main intervention. In general, these appeared to be cost saving for select groups of patients with severe disease.

Where reported, the per-patient cost of self-management support interventions was seen to vary according to the intensity of the intervention, with comprehensive pulmonary rehabilitation and complex SMS support packages being more costly to implement. Costs were typically low relative to the overall cost of care of patients with more severe disease. Ireland has a high prevalence of COPD, so the budget impact of implementing self-management support interventions for all eligible patients is likely to be substantial.

SMS support seems to decrease healthcare utilisation in patients with COPD, but the exact nature of that effective support is difficult to identify given the broad range of

interventions described in the included studies. The international evidence is of limited applicability to the Irish healthcare setting due to differences in the healthcare financing mechanisms and potential differences in the current standard of care.

## 6.5 Key points

- Sixteen systematic reviews of self-management support (SMS) interventions in adults with COPD were identified for inclusion in this overview of reviews.
- A diverse range of interventions were identified with the largest volume of evidence obtained for 'complex SMS interventions' (n=6), COPD educational programmes/action plans (n=4), telemedicine (n=4), pulmonary rehabilitation (n=1) and 'homecare by outreach nursing' (n=1).
- The quality of the systematic reviews varied, with nine rated as being higher quality reviews.
- The primary evidence underpinning the systematic reviews was found to be generally at moderate to high-risk of bias, meaning that studies may have over- or under-estimated the effect size. The randomised controlled trials (RCTs) were published between 1977 and 2013. These were mainly completed in Europe or North America.
- The interventions and patient populations varied widely making it difficult to make recommendations on the most effective content of self-management support.
- There is very good evidence that education in patients with COPD is associated with a reduction in COPD-related hospital admissions with limited evidence that it is associated with improvements in health-related quality of life. There is no evidence that action plans when used alone and in the absence of other self-management supports reduce healthcare utilisation or lead to improvements in quality of life.
- There is very good evidence that pulmonary rehabilitation which includes exercise training improves health-related quality of life (HRQoL) and functional exercise capacity in people with COPD. Large variation in the design of pulmonary rehabilitation programmes makes it difficult to identify their optimal format.
- There is some evidence that telemedicine as part of a complex intervention in COPD decreases healthcare utilisation, with no evidence was found of an impact on mortality.
- There is some evidence that outreach nursing programmes improve HRQoL in patients with COPD.
- Based on the quantity and quality of the systematic reviews and the underpinning primary RCTs, there is good evidence that complex SMS interventions (involving multiple components and, or multiple professionals with the intervention delivered by a variety of means) in patients with COPD are associated with improvements in

HRQoL. No evidence was found of a statistically significant benefit regarding mortality while there was limited evidence of reductions in health care utilisation. Although it is not clear which components of SMS support relate to these improvements, education and exercise seem to be effective.

- Most economic analyses were conducted alongside RCTs with small sample sizes and a short duration of follow-up, limiting the applicability and validity of the findings, and potentially failing to capture long-term benefits or to demonstrate if observed benefits and savings could be sustained.
- The interventions described by the included studies were heterogeneous and frequently comprised multiple components. Furthermore, the costing methodology and perspective adopted differed greatly between studies making it difficult to summarise and aggregate findings.
- Evidence for SMS education programmes suggest they could result in potential cost savings due to reduced healthcare utilisation in patients with moderate to severe disease, depending on the efficiency with which the programmes are run.
- There is limited evidence that pulmonary rehabilitation is cost-effective in patients with moderate to severe COPD disease.
- Evidence for the cost-effectiveness of telemedicine interventions is mixed, with more applicable evidence suggesting that telehealth monitoring is not cost-effective.
- Evidence suggests that case management may be cost saving for selected groups of patients with severe disease.
- The reported per-patient cost of self-management support interventions varied according to the intensity of the intervention, but was typically low relative to the overall cost of care of these patients. Ireland has a high prevalence of COPD, so the budget impact of implementing self-management support interventions for all eligible patients is likely to be substantial.
- The findings of the overview of clinical effectiveness are expected to be broadly applicable to the Irish healthcare setting, although recognising there may be differences in how and where care is delivered. The evidence of cost-effectiveness is of limited applicability to the Irish healthcare setting, with findings from the European studies being of greater relevance.

# 7 Diabetes Mellitus

This health technology assessment (HTA) of diabetes self-management support (SMS) is one of a series of rapid HTAs assessing SMS interventions for chronic diseases. Given their differences and the differing requirements for SMS in Type 1 and Type 2 diabetes mellitus, the clinical effectiveness of SMS supports for these conditions were assessed separately. The HTA does not cover pre-diabetes or gestational diabetes. Section 7.1 provides a brief description of diabetes followed by separate reviews of the clinical (Section 7.2) and cost-effectiveness (Section 7.3) literature for diabetes-specific SMS interventions. Brief descriptions of the background and methods used are included with full details provided in a separate document (Chapter 3). Section 7.4 includes a discussion of both the clinical and cost-effectiveness findings. The report concludes with a list of key points in relation to diabetes SMS support (Section 7.5).

## 7.1 Description of the disease

Diabetes is a progressive disease with disabling long-term complications if not properly managed. Persistently high blood sugar levels and high blood pressure can result in damage to both large and small blood vessels with ensuing eye, kidney, nerve, heart and circulatory complications. Tight control of these parameters and as well as other risk factors such as cholesterol and triglyceride levels, can reduce or delay their progression. Symptoms of diabetes include excessive excretion of urine (polyuria), thirst (polydipsia), constant hunger, weight loss, vision changes and fatigue.[170]

Type 1 diabetes (previously known as insulin-dependent, juvenile or childhood-onset) is characterised by deficient insulin production and requires daily administration of insulin.[170] The cause of Type 1 diabetes is not known.[170] Type 2 diabetes (formerly called non-insulin-dependent or adult-onset diabetes) results from the body's ineffective use of insulin.[170] Type 2 diabetes comprises 90% of people with diabetes around the world, and is largely the result of excess body weight and physical inactivity.

## 7.2 Review of clinical-effectiveness of self-management support interventions

### 7.2.1 Background and Methods

Details of the background and methods for this assessment are included in Chapters 1 to 3 of this report. Briefly, an aim of this health technology assessment (HTA) is to review the clinical effectiveness of disease-specific self-management support (SMS)

interventions for a number of chronic conditions including diabetes. Given the large volume of literature available, it was noted that an update of an existing high-quality systematic review of SMS interventions could be considered sufficient to inform decision making.

In December 2014 a high-quality overview of reviews was published by the National Institute for Health Research (NIHR) in the UK. The Practical Systematic Review of Self-Management Support for long-term conditions (PRISMS) study comprised an overview of systematic reviews of randomised controlled trials (RCTs) up to 1 June 2012, and was undertaken according to the principles of systematic reviewing. An update to the PRISMS report was completed by running additional searches in Pubmed, Embase and the Cochrane library from 2012 to 1 April 2015, see Appendix A3.1. In accordance with the PICOS agreed with the key stakeholder, this assessment was limited to SMS interventions for adults aged 18 and over. This restriction had implications for the assessment of SMS interventions in Type 1 diabetes in particular. The onset of Type 1 diabetes typically occurs in childhood, with the result that interventions (such as structured education programmes for Type 1 diabetes) primarily target a mixed paediatric and adult population. Unless disaggregated results could be retrieved, the identified studies were excluded. Results of the updated search are reported in addition to a summary of the findings of the PRISMS report for adults. The PRISMS report did not include telehealth reviews as they were typically about mode of delivery rather than content of what was delivered, however relevant telehealth interventions that incorporated a significant component of self management support were included in this updated review.

Following the PRISMS approach, reviews focusing on self monitoring of blood glucose (SMBG) were excluded as it is a thoroughly researched area with up-to-date clinical recommendations already in place.[2] Results from a 2012 Cochrane review concur with published guidelines that SMBG is beneficial in individuals who are newly diagnosed with Type 2 diabetes, but is less effective in those who have been diagnosed for one or more years.[2;171;172] In addition, following the PRISMS approach reviews combining data for Type 1 and Type 2 diabetes were also excluded. An exception was made for SMS interventions specifically targeting diabetic foot ulcer or diabetic kidney disease as the two conditions require broadly similar self-management irrespective of whether the patients has Type 1 or Type 2 diabetes.

Data extraction and quality assurance of the systematic reviews, meta-analyses and the risk of bias associated with the primary literature was undertaken as described in Chapter 3.1.3. In summary, in order to determine the quantity, quality, strength and credibility of evidence underpinning the various interventions, quality assurance of both the systematic review methodology (R-AMSTAR weighting by patient or

participant trial size) and the meta-analyses (Higgins et al.'s quality assessment tool),[23] While the R-AMSTAR score was used to determine the quality of the systematic reviews, the scores were then weighted by patient or participant trial size, with the quality of evidence being downgraded if the review was based on fewer than 1,000 participants. The quality of the primary evidence was not evaluated directly; however, where reported, information on the risk of bias in the primary studies was extracted from the systematic reviews.

### 7.2.2 Description of the interventions

A general description of self-management and typical self-management support (SMS) interventions is included in Chapter 2. Examples of generic patient self-management programmes include the Stanford chronic disease self-management programme (CDSMP) and the Expert Patient Programme in the UK which are described in Phase I of this HTA. New disease-specific interventions which are introduced in this report include Type 1 diabetes self-management education programmes. These include the 'Dose Adjustment For Normal Eating programme' (DAFNE) and Berger programme, a comprehensive diabetes self-care skills course, both delivered by healthcare professionals.[173] Both courses are currently available in Ireland.[173] However, as noted, because this HTA was limited to adults aged 18 years and over, evidence for diabetes self-management programmes that included paediatric populations was excluded unless disaggregated data were reported.

Interventions for Type 2 diabetes which are introduced in this report include disease-specific education programmes. Several diabetes self-management education programmes have been developed, with access to some of these available in Ireland. These include the 'diabetes education and self-management for ongoing and newly diagnosed' (DESMOND) programme for people with newly diagnosed Type 2 diabetes, as well as the 'Rethink Organization to iMprove Education and Outcomes' (ROMEO) and the 'Diabetes X-PERT Programme' for people with Type 2 diabetes. The Community Orientated Diabetes Education programme has also been developed by Diabetes Ireland and is a structured education programme for people with diabetes. The DESMOND, X-PERT-Ireland and Community Orientated Diabetes Education programmes are currently available in Ireland.[173]

### 7.2.3 Results – Clinical-effectiveness Type 1 diabetes mellitus

The PRISMS review retrieved a total of five systematic reviews of Type 1-specific SMS interventions and generic interventions used in patients with Type 1 diabetes mellitus.[2] However, as this assessment is limited to SMS interventions for adults aged 18 and over, only one review from PRISMS met our inclusion criteria. The PRISMS report was updated to April 2015 using the search string in Appendix 1. One

additional review was retrieved for Type 1 diabetes in our updated review (Figure 7.1).

The one eligible review identified in the PRISMS report included 11 unique randomised controlled trials (RCTs) with 516 adult participants. The review was published in 2006 with the publication date of the included RCTs ranging from 1985 to 2005. RCT study locations were mainly in the US (11 studies) with the remainder from Canada and Europe. The R-AMSTAR score was 41, with scores of 31 or more indicating a high-quality systematic review. When weighted according to the number of participants in the original RCTs (less than <1,000 or greater than or equal to ≥ 1,000), the systematic review was assigned the highest quality rating (`*three-star*', ***).[174]

The additional study identified as part of the update was a clinical guideline published in August 2015 by the National Clinical Guideline Centre in the UK. The guideline included systematic reviews of a variety of interventions, one of which was structured education programmes. The review included 15 RCTs with 1,994 participants. All 15 studies were carried out in Europe. The systematic review scored 35 on the basis of R-Amstar and was rated as high-quality (`*three-star*', ***).

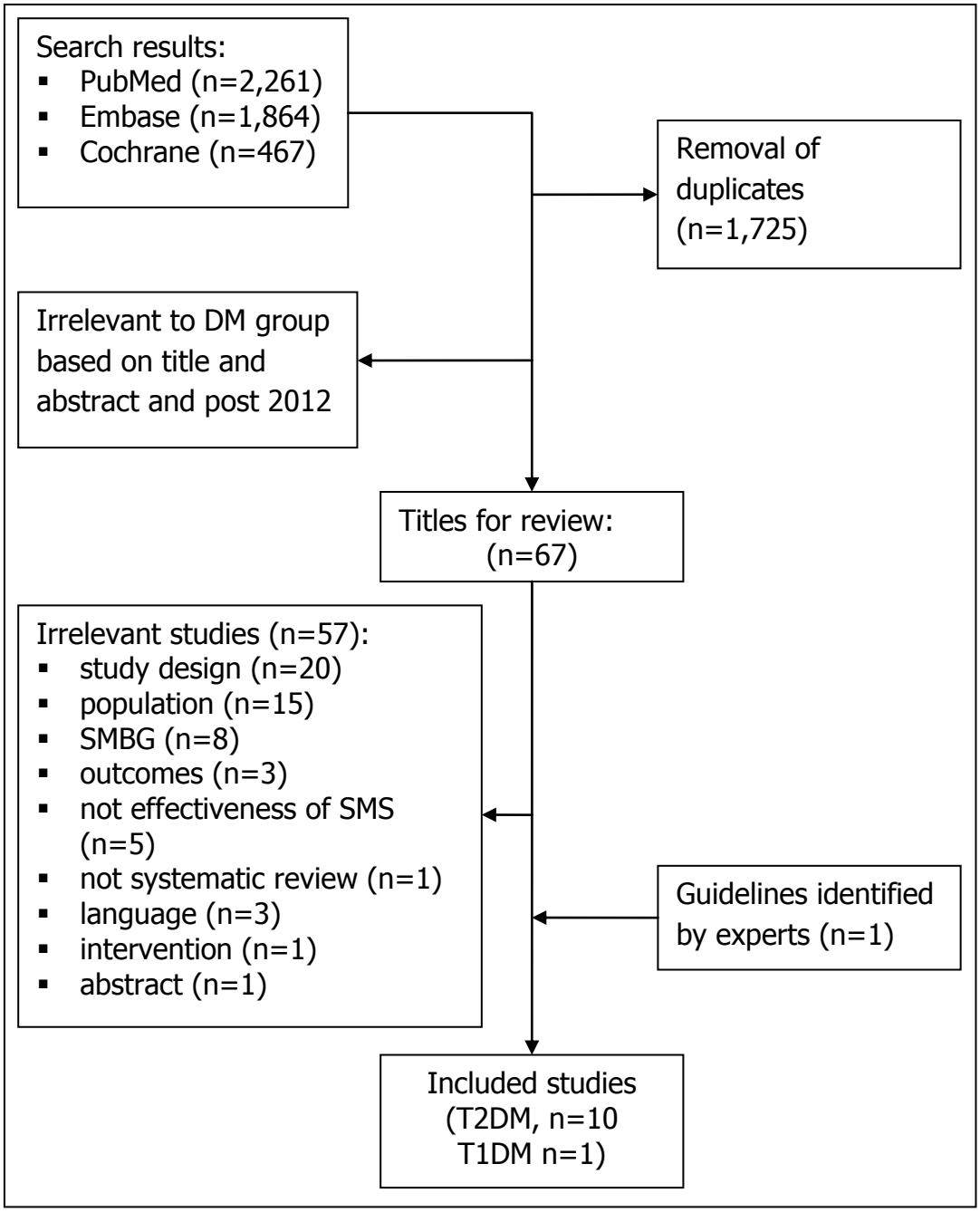
**Table 7.1 Type 1 diabetes mellitus: Summary of reviews retrieved (adults ≥ 18 years)**

| Author (year) | Intervention |
|---|---|
| **PRISMS studies retrieved** | |
| Winkley (2006)[174] | Psychological interventions |
| **Reviews retrieved in updated search** | |
| NICE (2015)[175] | Structured education programmes |

#### 7.2.3.1 Summary of findings

A detailed summary of the systematic reviews including the intervention, outcomes assessed, duration of follow-up, sample size (number of RCTs and total number of participants), and the evidence of effect is included in Appendix A.7.1. As per Chapter 3, the quality of the meta-analysis was assessed and graded. Studies graded as 'high-quality' are very likely to have conclusions that accurately reflect the available evidence (see also Chapter 3, Table 3.1). Table 7.2 below details the results of the quality assurance assessment of the single identified systematic review assessing the impact of SMS interventions in Type 1 diabetes and provides a summary of findings for selected outcomes from its meta-analysis.

**Figure 7.1 Flowchart of included studies from updated search**




Abbreviations: T1DM = Type 1 diabetes mellitus; T2DM = Type 2 diabetes mellitus

## Table 7.2 Type 1 diabetes mellitus: Summary characteristics and findings for selected outcomes for included studies

| Study | Quality of systematic review | | | Primary studies | | Meta-analysis quality | Glycated haemoglobin (SMD) |
|---|---|---|---|---|---|---|---|
| | R-AMSTAR score | Participants | Quality | n | Low risk of bias[a] | | |
| Winkley 2006[174] | 41 | 1,105 | *** | 11 | 1 | High | -0.17 (-0.45 to 0.10) |
| NICE 2015[175] | 35 | 1.194 | *** | 15 | 1 | Low | [b] |

**Abbreviations**: **SMD** = standardised mean difference;

[a] Number of the primary studies identified as being at low risk of bias.

[b] Due to potential issues with the reported outcome measures, the results of the meta-analyses are not included here.

#### 7.2.3.2 Psychological interventions

**Three star (***) reviews**

Based on one three-star review, PRISMS reported that there is no evidence for the effectiveness of psychological treatments in improving glycaemic control and reducing psychological distress in adults with Type 1 diabetes.

**Summary statement for psychological interventions**

There is no evidence of effectiveness of psychological treatments in improving glycaemic control and reducing psychological distress in adults with Type 1 diabetes.

#### 7.2.3.3 Structured education programmes

**Three star (***) reviews**

Based on one three-star review, the evidence regarding structured education programmes in adults with Type 1 diabetes was graded as low- or very low-quality. Although individual studies showed a beneficial effect of the intervention on glycated haemoglobin and severe hypoglycaemia, results were heterogeneous. Most outcomes were reported for single studies only. Individual studies showed benefits in terms of quality of life. Due to the different measures used, data could not be pooled.

**Summary statement for structured education programmes:**

There is very limited evidence of effectiveness of structured education programmes improving outcomes of severe hypoglycaemia and quality of life in adults with Type 1 diabetes.

### 7.2.4 Results – Clinical-effectiveness of Type 2 diabetes mellitus

The PRISMS review retrieved a total of 17 systematic reviews of Type 2 diabetes mellitus-specific self-management support interventions and generic interventions used in patients with Type 2 diabetes.[2] Summary details of the reviews are included in Table 7.3.

The PRISMS report was updated to April 2015 using the search string in Appendix A3.1. A further 10 systematic reviews were retrieved (Figure 7.1) which assessed a diverse range of SMS interventions for Type 2 diabetes including patient activation interventions,[176] telemedicine interventions,[177-181] motivational interviewing,[182] pharmacy care to improve medication adherence,[183] lifestyle interventions[184] and

culturally appropriate education.[185] Based on the range of SMS interventions retrieved, it was decided to classify and report the results by intervention type. The categories of systematic review include: education (which accounted for the largest body of evidence retrieved), telemedicine, self-management programmes, and other self-management support (SMS) interventions.

The number of included RCTs per systematic review ranged from two[184] to 138,[176] with the number of participants ranging from 207[186] to 33,124.[176] The study overlap between the 27 included systematic reviews is reported in Table 7.4. The publication dates of the systematic reviews ranged from 2001 to 2015, while that of the included RCTs ranged from 1985 to 2014. RCT study locations were typically in Europe or North America with 347 unique RCTs.

The quality of the systematic reviews (R-AMSTAR scores) ranged from 23 to 41, with scores of 31 or more indicating a high-quality systematic review. When weighted according to the number of participants in the original RCTs (less than <1,000 or greater or equal to ≥ 1,000), 14 of the systematic reviews were assigned the highest quality rating (*'three star'****)/11 reviews were rated as *'two star'*** and two as *'one star'** in terms of their quality and size. If a meta-analysis was completed, its quality was assessed as per Chapter 3 and graded as being of low, moderate or high-quality. A grading of 'low-quality' referred to studies where the conclusions were at high-risk of bias due to poor data collection or methods of data synthesis. The conclusions in studies identified as 'moderate quality' were at risk of bias, but were likely to be broadly accurate, while studies graded as 'high-quality' were very likely to have conclusions that accurately reflected the available evidence (see also Chapter 3, Table 3.1). In terms of the meta-analyses carried out in these reviews, 11 reviews were assessed as high-quality, six were assessed as moderate quality, and one as low-quality; no meta-analysis was undertaken in nine of the reviews.

## Table 7.3 Type 2 diabetes mellitus: Summary of systematic reviews retrieved

| Author (year) | Intervention |
|---|---|
| **PRISMS reviews retrieved** | |
| **Self-management programmes** | |
| Chodosh (2005)[187] | Self-management programmes[a] |
| **Education** | |
| Dorresteijn (2010/14)[b][188] | Education programmes – focus on foot care |
| Duke (2009)[189] | Education – individual patient education programmes |
| Li (2011)[186] | Education programmes –used for people with DKD |
| Minet (2010)[190] | Self-care SMS interventions using education or behavioural strategies |
| Norris (2001)[191] | Educational interventions |
| Norris (2002)[192] | SM Education |
| Sigurdardottir (2007)[193] | Education re diabetes self-care |
| Steinsbekk (2012)[194] | Education – group based |
| **Education – culturally tailored** | |
| Hawthorne (2008)[195] | Education – culturally tailored |
| Khunti (2008)[196] | Education – South Asian populations |
| Nam (2012)[197] | Education – culturally tailored |
| Pérez-Escamilla (2008)[198] | Education – peer nutrition and counselling for Latinos |
| **Other SMS interventions** | |
| Gary (2003)[199] | Behavioural or counselling component |
| Heinrich (2010)[200] | Multi-component aimed at SMS interventions |
| Newman (2004)[201] | SMS interventions – increase patient involvement |
| van Dam (2005)[202] | Social support interventions |
| **Reviews retrieved in updated search** | |
| **Telemedicine** | |
| Cotter (2014)[177] | Internet interventions to support lifestyle modification |
| Huang (2015)[178] | Telecare |
| Pal (2014)[179] | SMS interventions - Computer-based |
| Saffari (2014)[180] | Education via mobile phones |
| Zhai (2014)[181] | Telemedicine |
| **Education – culturally tailored** | |
| Attridge (2014)[c][185] | Education – culturally tailored |
| **Other SMS** | |
| Antoine (2014)[183] | Pharmacy care – adherence |
| Bolen (2014)[176] | Patient activation interventions |
| Schellenberg (2013)[184] | Lifestyle Interventions |
| Song (2014)[182] | Motivational interviewing |

**Abbreviations**: **DKD** = diabetic kidney disease; **SM** = self-management; **SMS** = self-management support.
[a] Programmes assessed for a range of diseases, results included for diabetes programmes only. Generic programmes were assessed for arthritis only in this review, these results are not included.
[b]Dorresteijn's Cochrane review was updated in 2014.
[c] Attridge's Cochrane review is an update to Hawthorne's CR with an additional 33 RCTs included.

## Table 7.4 T2DM: Study overlap between the included systematic reviews (PRISMS report plus the systematic reviews from the updated search).[5] Adapted from PRISMS review.[(2)]

| | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **PRISMS reviews retrieved** | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 1 | Chodosh (2005) | **26** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 2 | Dorrejstein (2010/ 14 update) | 0 | **11/ 12** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 3 | Duke (2009) | 1 | 0 | **9** | | | | | | | | | | | | | | | | | | | | | | | | | |
| 4 | Gary (2003) | 4 | 2 | 2 | **18** | | | | | | | | | | | | | | | | | | | | | | | | |
| 5 | Hawthorne (2008) | 2 | 0 | 2 | 1 | **11** | | | | | | | | | | | | | | | | | | | | | | | |
| 6 | Heinrich (2010) | 1 | 0 | 2 | 0 | 2 | **14** | | | | | | | | | | | | | | | | | | | | | | |
| 7 | Khunti (2008) | 0 | 0 | 2 | 0 | 4 | 0 | **5** | | | | | | | | | | | | | | | | | | | | | |
| 8 | Li (2011) | 0 | 0 | 0 | 0 | 0 | 1 | 0 | **2** | | | | | | | | | | | | | | | | | | | | |
| 9 | Minet (2010) | 2 | 0 | 8 | 1 | 5 | 8 | 0 | 1 | **43** | | | | | | | | | | | | | | | | | | | |
| 10 | Nam (2012) | 1 | 0 | 2 | 1 | 9 | 2 | 3 | 0 | 4 | **12** | | | | | | | | | | | | | | | | | | |
| 11 | Newman (2004) | 4 | 0 | 2 | 2 | 3 | 0 | 0 | 0 | 5 | 1 | **21** | | | | | | | | | | | | | | | | | |
| 12 | Norris (2001) | 16 | 10 | 4 | 9 | 3 | 0 | 1 | 0 | 6 | 3 | 3 | **72** | | | | | | | | | | | | | | | | |
| 13 | Norris (2002) | 8 | 4 | 4 | 7 | 3 | 0 | 1 | 0 | 6 | 3 | 3 | 30 | **31** | | | | | | | | | | | | | | | |
| 14 | Pérez-Escamilla (2008) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | **2** | | | | | | | | | | | | | | |
| 15 | Sigurdardottir (2007) | 2 | 0 | 4 | 0 | 1 | 1 | 0 | 0 | 7 | 2 | 5 | 3 | 3 | 0 | **18** | | | | | | | | | | | | | |
| 16 | Steinsbekk (2012) | 1 | 0 | 0 | 0 | 3 | 4 | 1 | 0 | 7 | 2 | 2 | 3 | 3 | 1 | 4 | **21** | | | | | | | | | | | | |
| 17 | van Dam (2005) | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 2 | 2 | 1 | 0 | 1 | 1 | **6** | | | | | | | | | | | |
| | **Reviews retrieved in updated search** | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 18 | Pal (2014) | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 2 | 1 | 0 | 0 | 0 | 0 | | **16** | | | | | | | | | |
| 19 | Song (2014) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | 0 | **10** | | | | | | | | |
| 20 | Antoine (2014) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | 0 | 0 | **6** | | | | | | | |
| 21 | Schellenberg (2013) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | 0 | 0 | 0 | **11** | | | | | | |
| 22 | Attridge (2014) (CR) | 3 | 0 | 1 | 2 | 11 | 2 | 4 | 0 | 6 | 12 | 3 | 4 | 4 | 3 | 2 | 4 | 1 | | 0 | 0 | 0 | 0 | **33** | | | | | |

[5] PRISMS review is based on a search from 1993 to June 2012. This search was updated to April 2015. Note: Dorrejstein's Cochrane review was updated in 2014 and included 1 additional RCT. The main findings of the review do not change and the updated results are included in this report.

| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 23 | Saffari (2014) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | 1 | 0 | 0 | 0 | 0 | **10** | | | | |
| 24 | Cotter (2014) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | | 2 | 0 | 0 | 0 | 1 | 0 | **9** | | | |
| 25 | Bolen (2014) | 4 | 2/2 | 4 | 3 | 2 | 8 | 0 | 1 | 18 | 1 | 3 | 10 | 8 | 1 | 3 | 8 | 1 | | 6 | 1 | 0 | 1 | 14 | 1 | 4 | **138** | | |
| 26 | Huang (2015) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | 3 | 0 | 0 | 0 | 0 | 3 | 1 | 9 | **18** | |
| 27 | Zhai (2014) | 2 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | 5 | 0 | 0 | 0 | 0 | 5 | 4 | 12 | 9 | **35** |

*Attridge's Cochrane review is an update to Hawthorne's CR with an additional 33 RCTs included.

## Table 7.5 Study details, quality assurance and summary of findings from meta-analysis of impact of self-management support interventions on blood glucose control, health-related quality of life and mortality

| Study | Quality of systematic review | | | Primary studies | | Meta-analysis quality | HbA1c (MD)[b] | Total GHb (MD) |
|---|---|---|---|---|---|---|---|---|
| | R-AMSTAR score | Participants | Rating | n | Low risk of bias[a] | | | |
| **Self-management programmes** | | | | | | | | |
| **Chodosh** 2005[(187)] | 34 | 2,579 | *** | 26 | NR | High | -0.36 (-0.52 to -0.21) | |
| **Education** | | | | | | | | |
| **Attridge** 2014[(185)] | 39 | 7,453 | *** | 33 | 5 | High | -0.30 (-0.60 to -0.10) | |
| **Dorresteijn** 2014[(188)] | 39 | 2,739 | *** | 12 | 2 | High | | |
| **Duke** 2009[(189)] | 36 | 1,359 | *** | 9 | 3 | High | -0.08 (-0.25 to 0.08) | |
| **Hawthorne** 2008[(195)] | 41 | 1,603 | *** | 11 | 3 | High | -0.10 (-0.40 to 0.20) | |
| **Khunti** 2008[(196)] | 30 | 1,004 | ** | 5 | NR | NA | | |
| **Li** 2011[(186)] | 41 | 207 | ** | 2 | 0 | High | | |
| **Minet** 2010[c(190)] | 37 | 7,677 | *** | 43 | NR | Moderate | -0.36 (-0.51 to -0.21) | |
| **Nam** 2012[(197)] | 35 | 1,495 | *** | 12 | 6 | Moderate | -0.29 (-0.46 to -0.13) | |
| **Norris** 2001[c(191)] | 27 | NR | * | 72 | NR | NA | | |
| **Norris** 2002[c(192)] | 31 | 4,263 | *** | 31 | NR | Moderate | | -0.76 (-1.18 to -0.34) |
| **Perez-Escamilla** 2008[(198)] | 25 | 214 | * | 2 | NR | NA | | |
| **Sigurdardottir** 2007[(193)] | 26 | 4,293 | ** | 18 | 7 | NA | | |
| **Steinsbekk** 2012[(194)] | 37 | 2,833 | *** | 21 | 2 | Moderate | -0.87 (-1.25 to -0.49) | |
| **Telemedicine** | | | | | | | | |
| **Cotter** 2014[(177)] | 24 | 1,913 | ** | 9 | NR | NA | | |
| **Huang** 2015[(178)] | 35 | 3,798 | *** | 18 | 4 | High | -0.54 (-0.75 to -0.34) | |
| **Pal** 2014[(179)] | 38 | 3,578 | *** | 16 | 2 | High | -0.20 (-0.40 to -0.10) | |
| **Saffari** 2014[(180)] | 35 | 960 | ** | 10 | 4 | Moderate | -0.595 (-0.833 to -0.356)<br>-0.436 -0.671 to -0.203) SMS only<br>-0.500 (-0.716 to -0.285) SMS + internet | |
| **Zhai** 2014[(181)] | 36 | 8,149 | *** | 35 | 11 | High | -0.37 (-0.49 to -0.25)<br>-0.53 (-0.81 to -0.26) Telephone based<br>-0.62 (-0.82 to -0.42) Internet based | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Other SMS** | | | | | | | | |
| **Antoine** 2014[183] | 28 | 1,025 | ** | 6 | 0 | NA | | |
| **Bolen** 2014[176] | 35 | 33,124 | *** | 138 | 43 | High | -0.37 (-0.45 to -0.28) | |
| **Gary** 2003[199] | 36 | 2,720 | *** | 18 | 5 | Moderate | -0.52 (-0.96 to -0.08) | -0.43 (-0.71 to -0.14) |
| **Heinrich** 2010[200] | 24 | 1,778 | ** | 14 | NR | NA | | |
| **Newman** 2004[201] | 23 | 2,032 | ** | 21 | NR | NA | | |
| **Schellenberg** 2013[184] | 32 | >5,145 | *** | 11 | 0 | High | | |
| **Song** 2014[182] | 29 | 2,957 | ** | 10 | 3 | Low | 0.10 (-0.04 to 0.24) | |
| **Van Dam** 2005[202] | 31 | 712 | ** | 6 | 3 | NA | | |

**Key**: **MD** = mean difference; **LT** = Long-term; **NR** = not reported; **NA** = not applicable; **QoI** = quality of life; **RR** = relative risk; **ST** = short-term; **T2DM** = Type 2 diabetes mellitus.

[a] Number of the total primary studies identified as being at low risk of bias
[b] Where multiple follow-up durations were analysed, data presented for longest duration analysed.
[c] Data on risk of bias of primary studies was reported, but not in a format that could be reliably extracted.

## Table 7.5 (continued) Study details, quality assurance and summary of findings from meta-analysis of impact of SMS interventions on blood glucose control, health-related quality of life and mortality

| Study | Quality of systematic review | | | Primary studies | | Meta-analysis quality | QoL (MD) | Mortality (RR) |
|---|---|---|---|---|---|---|---|---|
| | R-AMSTAR score | Participants | Rating | n | Low risk of bias[a] | | | |
| **Self-management programmes** | | | | | | | | |
| **Chodosh 2005**[187] | 34 | 2,579 | *** | 26 | NR | High | | |
| **Education** | | | | | | | | |
| **Attridge** 2014[185] | 39 | 7,453 | *** | 33 | 5 | High | | |
| **Dorresteijn** 2014[188] | 39 | 2,739 | *** | 12 | 2 | High | | |
| **Duke** 2009[189] | 36 | 1,359 | *** | 9 | 3 | High | | |
| **Hawthorne** 2008[195] | 41 | 1,603 | *** | 11 | 3 | High | | |
| **Khunti** 2008[196] | 30 | 1,004 | ** | 5 | NR | NA | | |
| **Li** 2011[186] | 41 | 207 | ** | 2 | 0 | High | | |
| **Minet** 2010[c][190] | 37 | 7,677 | *** | 43 | NR | Medium | | |
| **Nam** 2012[197] | 35 | 1,495 | *** | 12 | 6 | Medium | | |
| **Norris** 2001[c][191] | 27 | NR | * | 72 | NR | NA | | |
| **Norris** 2002[c][192] | 31 | 4,263 | *** | 31 | NR | Medium | | |
| **Perez-Escamilla** 2008[198] | 25 | 214 | * | 2 | NR | NA | | |
| **Sigurdardottir** 2007[193] | 26 | 4,293 | ** | 18 | 7 | NA | | |
| **Steinsbekk** 2012[194] | 37 | 2,833 | *** | 21 | 2 | Medium | 0.31 (-0.15 to 0.78) | |
| **Telemedicine** | | | | | | | | |
| **Cotter** 2014[177] | 24 | 1,913 | ** | 9 | NR | NA | | |
| **Huang** 2015[178] | 35 | 3,798 | *** | 18 | 4 | High | | |
| **Pal** 2014[179] | 38 | 3,578 | *** | 16 | 2 | High | | |
| **Saffari** 2014[180] | 35 | 960 | ** | 10 | 4 | Moderate | | |
| **Zhai** 2014[181] | 36 | 8,149 | *** | 35 | 11 | High | | |
| **Other SMS** | | | | | | | | |
| **Antoine** 2014[183] | 28 | 1,025 | ** | 6 | 0 | NA | | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Bolen** 2014[176] | 35 | 33,124 | *** | 138 | 43 | High | | OR 0.70 (0.49 to 1.01) LT<br>OR 0.90 (0.64 to 1.28) ST |
| **Gary** 2003[199] | 36 | 2,720 | *** | 18 | 5 | Medium | | |
| **Heinrich** 2010[200] | 24 | 1,778 | ** | 14 | NR | NA | | |
| **Newman** 2004[201] | 23 | 2,032 | ** | 21 | NR | NA | | |
| **Schellenberg** 2013[184] | 32 | >5,145 | *** | 11 | 0 | High | | 0.75 (0.53 to 1.06) |
| **Song** 2014[182] | 29 | 2,957 | ** | 10 | 3 | Low | | |
| **Van Dam** 2005[202] | 31 | 712 | ** | 6 | 3 | NA | | |

**Key**: **MD** = mean difference; **LT** = Long-term; **NR** = not reported; **NA** = not applicable; **QoL** = quality of life; **RR** = relative risk; **ST** = short-term; **T2DM** = Type 2 diabetes mellitus.

[a] Number of the total primary studies identified as being at low risk of bias

[b] Where multiple follow-up durations were analysed, data presented for longest duration analysed.

[3] Data on risk of bias of primary studies was reported, but not in a format that could be reliably extracted.

#### 7.2.4.1 Summary of findings

Detailed summaries of the systematic reviews including the intervention and comparator, outcomes assessed, duration of follow-up, sample size (number of RCTs and total number of participants, and the evidence of effect are included in Appendix A7.1. The following are reported based on the findings from PRISMS and the additional systematic reviews retrieved in the updated search. In order to emphasise the relevance of the findings, results are grouped by the quality of the systematic review (using the R-AMSTAR score and size of the patient population). Table 7.5 above details the results of the quality assurance assessment of the systematic reviews and provides a summary of findings for selected outcomes from the various meta-analyses assessing the impact of SMS interventions in T2DM.

The types of intervention retrieved by PRISMS included self-management programmes or multi-component interventions aimed at self-management; education; behavioural or counselling strategies and social support. PRISMS reported their findings by outcomes for all interventions and reported on blood glucose control for eight meta-analyses based on eight systematic reviews[187;189;190;192;194;195;197;199] and a further five narrative reviews.[191;196;198;201;202] They reported that there is very good evidence that SMS improves blood glucose control in the short term (less than 12 months). Longer term, they found less evidence for effectiveness, and noted that this is likely to be because of a lack of studies reporting longer-term data. They also stated that overall these SMS interventions do not appear to improve individuals' quality of life or their psychological well-being. They concluded that SMS may be provided in a variety of ways by a variety of people and that it is not possible to state definitively what the optimum mode of delivery is.

#### 7.2.4.2 Education programmes

**Three star (***) reviews**

PRISMS reported their results by outcome across a range of intervention types. Table 7.5 above shows that PRISMS reported results for interventions broadly classified as education for seven three star reviews.[188-190;192;194;195;197] Of these five reported results for HbA1c with four reporting statistically significant improvements.[190;194;195;197] One review did not find a statistically significant improvement in quality of life.[194]

In the updated search, one additional high-quality systematic review was identified. This 2014 Cochrane review by Attridge et al. compared culturally-appropriate health education with conventional health education.[185] It reported that culturally appropriate health education has short- to medium-term effects (less than 12

months) on glycaemic control and on knowledge of diabetes and healthy lifestyles. They also noted that none of the studies were long-term trials, and so clinically important long-term outcomes could not be studied. The heterogeneity of the studies made subgroup comparisons difficult to interpret with confidence.

**Summary statement for education**

Based on the quantity and quality of the systematic reviews and the underpinning primary RCTs there is very good evidence that education including culturally appropriate education improves blood glucose control in the short term (less than 12 months) in people with Type 2 diabetes.

#### 7.2.4.3 Self-management programmes

**Three star (***) reviews**

PRISMS reported their results by outcome across a range of intervention types. Table 7.5 above shows that PRISMS reported results for interventions broadly classified as self-management programmes for one three star review by Chodosh et al.. They reported that there is some evidence that a range of self-management programmes assessed in Type 2 diabetes improve blood glucose control in the short term (less than 12 months). Interventions were identified as self-management programmes if they were systematic interventions targeted at patients with chronic disease with an aim of helping them actively participate in self-monitoring (of symptoms or physiological functions) and, or decision-making (managing the disease or its impact through self-monitoring).

No additional evidence for self-management programmes assessed in Type 2 diabetes was identified in the updated search.

**Summary statement for self-management programmes assessed in Type 2 diabetes**

There is some evidence that self-management programmes assessed in Type 2 diabetes are associated with small improvements in blood glucose control in the short term.

#### 7.2.4.4 Telemedicine

PRISMS did not include telemedicine applications in their review of Type 2 diabetes, however relevant telemedicine interventions that included a significant component of self-management support were included in the updated search. Three three-star and two two-star systematic reviews relating to SMS telemedicine interventions in Type diabetes were identified.

**Three star (***) reviews**

A Cochrane review and meta-analysis by Pal et al. of 11 RCTs 2,637 participants compared computer-based diabetes self-management interventions with usual care (in five RCTs) or a range of controls (in six RCTs) to manage Type 2 diabetes.[179] The intervention included computer-based software applications that responded to user input and aimed to generate tailored content to improve one or more of the self-management domains (cognitive, behaviour and skills, and emotion) through feedback, tailored advice, reinforcement and rewards, patient-decision support, goal setting or reminders. The interface used included clinic-based touch screens and computers providing education and customised plans; home-based online peer support, education, and tailored plans; pagers; and mobile devices (primarily mobile phones) to deliver advice and personalised feedback in response to inputted self-monitoring data. All were compared with usual care. It reported a small beneficial effect on blood glucose control; this effect was larger in the mobile phone subgroup. They noted that a small treatment effect (2.3 mmol/mo or 0.2%) on HbA1c with computer-based self-management support interventions that would be important if it could be achieved and sustained across the population via the internet at a very low cost. However, this would be of limited relevance if significant nursing support and, or additional drugs were required. The results were associated with large heterogeneity indicating possible inconsistencies between the effects of the interventions. There was no evidence to show improvement in health-related quality of life. A total of three deaths were reported in 16 studies with one study reporting one dropout due to study-related anxiety. Due to the limitation of the primary studies, the authors concluded that the effectiveness of existing information technology (IT)-based interventions was unclear and difficult to attribute solely to the interventions.

A meta-analysis by Huang et al. (18 RCTs with 3,798 participants) reported that patients monitored by telecare showed significant improvement in glycemic control in Type 2 diabetes when compared with routine follow-up.[178] The intervention arm comprised self monitored transmission of glucometer data and feedback by health professionals, or automatic medical devices and was compared with routine care. Feedback was classified as human calls (that is to say, interactive phone calls), automated calls (pre-recorded voice messages), or automated text. Based on subgroup analysis, greater reductions in HbA1c levels were observed in studies with Asian populations, small sample size, baseline HbA1c less than 8.0% and human calls-based interventions when compared with those monitored by routine follow-up. No effect was observed for automated call interventions.

A meta-analysis by Zhai et al., including 36 RCTs with 8,149 participants, reported that overall, pooled results from telemedicine studies revealed a small, but

statistically significant, decrease in HbA1c following telemedicine intervention, when compared with conventional follow-up.[181] The intervention arm included telephone support in the form of a call or text message; internet-based programmes employing video-conferencing and, or informational websites; and electronically transmitted recommendations from clinicians in response to internet-based reporting of monitoring data by patients. The authors noted that significant publication bias was detected, suggesting that the literature should be interpreted with caution.

**Two star (**) reviews**

A meta-analysis by Saffari et al. reported that health education via mobile text-messaging statistically significantly improved glycemic control in patients with Type 2 diabetes.[180] The effect size was greater among studies that used both text-messaging and the internet for health education. When results were stratified by patient age, it was noted that although reductions in HbA1C remained significant in both age brackets, the effect size found in younger patients indicated a larger reduction in HbA1c than in patients over 55 years of age.

A narrative review by Cotter et al. reported that when compared with routine care, two of nine studies demonstrated improvements in diet and, or physical activity while two of nine studies demonstrated improvements in glycaemic control with web-based SMS interventions. [177]

**Summary statement for telemedicine**

There is good evidence that various forms of telemedicine are associated with improvements in blood glucose control in the short term for people with Type 2 diabetes.

#### 7.2.4.5 Other self-management supports

**Three star (***) reviews**

PRISMS reported their results by outcome across a range of intervention types. Table 7.5 above shows that PRISMS reported results for interventions broadly classified as 'other SMS' for one three star review.[199] It reported a statistically significant improvement in HbA1c.

The updated literature search identified two *'three-star'* and two *'two-star'* systematic reviews relating to a range of other SMS interventions for Type 2 diabetes.

A high-quality meta-analysis by Bolen et al. assessed activation interventions in patients with Type 2 diabetes.[176] These are a subset of behavioural interventions which actively engage patients by promoting increased knowledge, confidence and, or skills for disease self-management. They reported that patient activation

interventions modestly improve HbA1c in adults with Type 2 diabetes without impacting short-term mortality.

A meta-analysis and narrative review by Schellenberg et al. reported on lifestyle interventions for those with, and those at risk of developing Type 2 diabetes. Only the results for patients with Type 2 diabetes are presented here.[184] The control used was standard care or standard care plus a range of other SMS components. Pooled results for all-cause mortality showed no difference between the intervention and control groups at more than 10 years of follow-up. This was based on two RCTs with 'low strength of evidence'. A further narrative review of 11 RCTs reported that the evidence of benefit from comprehensive lifestyle interventions on patient-oriented outcomes is less clear.

**Two star (**) reviews**

A meta-analysis by Song et al. concluded that compared with usual care, short-term motivational interviewing (less than or equal to ≤ 6 months) is associated with reductions in HbA1c levels and improved self-management ability (diet control, exercise, foot care, glucose control, prevention and treatment of hypoglycaemia). However, the long-term effects (greater than > 6 months) are uncertain.[182] Usual care was defined as traditional diabetes health education.

A review by Antoine et al. reported that although pharmacist interventions might potentially improve adherence to Type 2 diabetes medication, high-quality studies are needed to assess effectiveness.[183] The review mainly compared pharmacist intervention to usual care or education. Possible limitations identified included differences in how pharmacists provide their adherence intervention and reduced applicability of the findings to an Irish context due to differences to the level in which pharmacists are established within the healthcare system in different counties.

**Summary statement for other self-management support**

There is good evidence that behavioural interventions are associated with modest improvements in blood glucose control (HbA1C). Based on the available evidence, it is not possible to draw conclusions in relation to the efficacy of the diverse range of other SMS interventions identified in this review.

## 7.3 Review of cost-effectiveness of self-management support interventions

A review of cost-effectiveness studies was carried out to assess the available evidence for self-management support (SMS) interventions for adults with Type 1 or Type 2 diabetes. Studies were included if they compared the costs and consequences of an SMS intervention to routine care.

### 7.3.1 Search strategy

A search was carried out to identify economic analyses of SMS interventions. In tandem with the systematic review of clinical effectiveness, the search for economic evaluations was carried out in MEDLINE, EMBASE and the Cochrane Library. The same search terms were used with the exception of terms for systematic review and meta-analysis. In place of these, search terms and filters for economic evaluations were applied. In addition, systematic reviews of SMS interventions identified through the results of the clinical effectiveness search that included cost or economic outcomes were used to identify additional studies. The search was carried out up until 4th March 2015.

The PICOS (Population, Intervention, Comparator, Outcomes, Study design) analysis used to formulate the search is presented in Table 7.6 below.

**Table 7.6 PICOS analysis for identification of relevant studies**

| | |
|---|---|
| **Population** | Adults ≥ 18 years old that had diabetes. |
| **Intervention** | Any self-management support intervention that helps patients with diabetes through education, training or support. |
| **Comparator** | Routine care. |
| **Outcomes** | Cost or cost-effectiveness of intervention. |
| **Study design** | Randomised controlled trials, case-control studies, observational studies, economic modelling studies. |

Studies were excluded if:

- a nursing home or non-community dwelling population was included,
- they included a paediatric population,
- cost data were not clearly reported,
- published prior to 2000 due to limited relevance.

As outlined in Chapter 3.2.2 and in accordance with national health technology assessment(HTA) guidelines, the quality of the studies was assessed using the Consensus on Health Economic Criteria (CHEC)-list was performed independently by two people.[24] For studies that included an assessment of cost-utility or an economic modelling approach, assessment of the relevance to the Irish healthcare setting and their credibility was considered using a questionnaire from the International Society of Pharmacoeconomics and Outcomes Research (ISPOR).[25]

### 7.3.2 Results – Cost-effectiveness

The initial search identified 118 potentially relevant articles. Three reviewers independently evaluated studies based on title, abstract and full text. Thirty eight studies were identified as applicable. Data extraction was carried out independently by two reviewers. The review includes studies relating to either Type 1 or Type 2 diabetes, or both. Studies that compared blood glucose self-monitoring to usual care were excluded on the grounds that self-monitoring is now considered part of usual care.

There were 20 studies from the United States (US), six from the United Kingdom (UK) three from Germany, two from Ireland, and one from each of Australia, Bulgaria, Canada, Denmark, India, Italy, and the Netherlands. The included studies were all published between 2001 and 2014. The characteristics of the included studies are given in Table 7.7.

**Table 7.7 Characteristics of the studies included**

| Study | Country | Intervention |
|---|---|---|
| **Albisser (2001)[203]** | US | SMS education |
| **Banister (2004)[204]** | US | SMS education |
| **Barnett (2007)[205]** | US | Telemedicine |
| **Biermann (2002)[206]** | Germany | Telemedicine |
| **Brown (2012)[207]** | US | SMS education |
| **Brownson (2009)[208]** | US | SMS education |
| **Dall (2011)[209]** | US | SMS education |
| **Farmer (2009)[210]** | UK | SMS education |
| **Fedder (2003)[211]** | US | Telemedicine |
| **Fera (2009)[212]** | US | Pharmacist |
| **Fischer (2012)[213]** | US | Telemedicine |
| **Garrett (2005)[214]** | US | SMS education |
| **Gillespie (2012)[215]** | Ireland | SMS education |
| **Gillespie (2014)[216]** | Ireland | SMS education |
| **Gillett (2010)[217]** | UK | SMS education |
| **Gilmer (2005)[218]** | US | SMS education |
| **Gilmer (2007)[219]** | US | SMS education |
| **Gordon (2014)[220]** | Australia | SMS education |
| **Handley (2008)[221]** | US | Telemedicine |
| **Ismail (2010)[222]** | UK | SMS education |
| **Jacobs-van der Bruggen (2009)[223]** | The Netherlands | SMS education |
| **Kesavadev (2012)[224]** | India | Telemedicine |
| **Kruger (2013)[225]** | UK | SMS education |
| **Kuo (2011)[226]** | US | SMS education |
| **Letassy (2003)[227]** | US | Pharmacist |
| **Mason (2006)[228]** | UK | Telemedicine |
| **Molsted (2012)[229]** | Denmark | SMS education |
| **Moreno (2009)[230]** | US | Telemedicine |

| | | |
|---|---|---|
| **O'Reilly (2007)[231]** | Canada | SMS education |
| **Palmas (2010)[232]** | US | Telemedicine |
| **Petkova (2006)[233]** | Bulgaria | Pharmacist |
| **Ritzwoller (2011)[234]** | US | SMS education |
| **Salzsieder (2011)[235]** | Germany | Telemedicine |
| **Schechter (2012)[236]** | US | Telemedicine |
| **Shearer (2004)[237]** | UK | SMS education |
| **Stock (2010)[238]** | Germany | SMS education |
| **Trento (2002)[239]** | Italy | SMS education |
| **Wiegand (2008)[240]** | US | SMS education |

The studies were classified according to the type of intervention assessed: SMS education programmes, telemedicine, and community pharmacist-based interventions. Some interventions combined elements of different intervention types. Four studies specified a population with Type 1 diabetes, 19 specified Type 2 diabetes (all, or non-insulin dependent only), and 15 included all adult patients with diabetes.

As noted, study quality was assessed using the Consensus on Health Economic Criteria (CHEC) list,[24] while the applicability of the findings from studies that included an assessment of cost-utility or an economic modelling approach, were evaluated using the ISPOR questionnaire.[25] The quality of the included studies was predominantly poor, and the following discussion sections will focus on the studies found to be of good quality. Costs reported in each of the studies were inflated to 2014 pricing levels using the local consumer price index and expressed in Irish Euro using the purchasing power parity exchange rate.[105]

#### 7.3.2.1 Education

There were 24 studies found that evaluated SMS education programmes. Of the identified studies, 15 included cost-utility analyses and the remaining nine were generally costing or cost-minimisation studies. Seven of the cost-utility analyses and one of the costing studies were found to be of good quality.

A 2009 UK study by Farmer et al. compared blood glucose self-monitoring with and without an educational component in patients with non-insulin-treated Type 2 diabetes.[210] Patients were recruited for a randomised controlled trial (RCT) in a primary care setting. Standard self-monitoring focused on clinician interpretation of monitoring results, while a more intensive alternative involved training in self-interpretation and application of the results to diet, physical activity and medication adherence. Patients were aged at least 25 years and had a glycosylated haemoglobin (A1c) greater than or equal to ≥ 6.2%. In the RCT, 150 patients were randomised to standard self-monitoring and 151 to more intensive self-monitoring. The trial results were then entered into the UKPDS model to infer the impact of

clinical results to life expectancy. This model uses data from a large UK trial to link risk factors (such as A1c) to longer term outcomes. Intervention costs for intensive self-monitoring were slightly less expensive, at €12 over 12 months, but less effective than standard self-monitoring. Both forms of blood glucose self-monitoring were found to be more costly and less effective than standardised usual care.

A 2009 study carried out in the Netherlands by Jacobs-van der Bruggen et al. evaluated lifestyle modification interventions involving nutrition or exercise programmes for adults with Type 2 diabetes.[223] The authors compared seven different interventions (DESMOND, BGI, Look AHEAD, MLP, X-PERT, ICAN, and CAN). Intervention durations ranged from six hours to 24 months. Clinical effectiveness data were extracted from published trial data and incorporated into a chronic disease model that simulated the long-term consequences of lifestyle changes in the population of the Netherlands with Type 2 diabetes. All seven modelled programmes were expected to lead to quality adjusted life years (QALY) gains (from 0.1 to 0.14 QALYs per patient). The seven interventions were considered cost-effective relative to routine care; incremental cost effectiveness ratios (ICERs) ranged from €11,414 per QALY to €49,460 per QALY. The interventions were not compared to each other, so it is not possible to state what the ICERs were relative to each other. It should also be noted that major uncertainty was identified in relation to how long improvements were sustained.

The diabetes education and self-management for ongoing and newly diagnosed (DESMOND) intervention was assessed in the UK in 2010.[217] DESMOND comprises a six-hour structured group education programme delivered in the community by two professional healthcare educators. A cost-utility analysis was undertaken by incorporating the outcomes from a 12-month multicentre, cluster RCT into the Sheffield Type 2 diabetes model. The intervention was estimated to lead to non-statistically significant reductions in A1c, total cholesterol and systolic blood pressure. The intervention was estimated to cost €282 per patient based on the 2004 trial. The ICER based on the DESMOND trial data was estimated to be €7,477 per QALY. The validity of the results depends partly on the sustainability of the effect of the programme.

Ritzwoller at al. undertook an economic evaluation of the Viva Bien trial in the US in 2011, assessing multiple-risk-factor lifestyle interventions targeting Latinas with Type 2 diabetes.[234] The trial randomised 138 patients to usual care and 142 to the intervention. The cost of the intervention per participant was €4,702, which included costs that accrued to the participants. The study estimated a cost of €7,866 per unit reduction in A1c.

A 2012 Irish study evaluated the cost-effectiveness of a peer support programme for adults with Type 2 diabetes.[215] A cost-utility analysis was undertaken by incorporating the outcomes from a two year RCT into the UKPDS diabetes model. The intervention involved group meetings led by trained peers from participants' general practices. The trial found a non-statistically significant reduction in A1c. Intervention set-up was €291 per patient. The intervention was more effective (0.09 additional QALYs) and less costly (reduction of €738) compared to routine care. The intervention was the most cost-effective option at a range of thresholds using both payer and societal perspectives.

Kruger et al. carried out an economic evaluation of the Dose Adjustment for Normal Easting (DAFNE) structured education programme in the UK in 2012 for a simulated cohort of adults with Type 1 diabetes.[225] The study used data from a trial comparing usual care to training in flexible intensive insulin therapy as provided in the DAFNE programme. The trial data were then entered into the Sheffield Type 1 diabetes model to simulate the long-term effects of the intervention. Training was associated with an increased life expectancy (0.08 life year gained per patient) and an average QALY gain of 0.03 QALYs per patient. The cost of the intervention was obtained from the literature (€432 per patient). The ICER for the intervention was estimated to be €17,432 per QALY.

A 2014 Irish study examined the cost-effectiveness of group follow-up compared to individual follow-up after participation in the DAFNE programme for adults with Type 1 diabetes.[216] The trial supporting the study was designed to evaluate whether group follow-up might be more effective at maintaining the benefits of participating in the programme longer-term. Group follow-up was less costly and less beneficial than individual follow-up. At thresholds of €20,000 and €45,000, individual follow-up was the most cost effective option. At thresholds of €15,000 and less, group follow-up was most cost effective. The findings of this study are only relevant to participants in the DAFNE programme.

#### 7.3.2.2 Telemedicine

There were 11 studies found that evaluated telemedicine programmes, including four cost-utility analyses and seven costing or cost-minimisation studies (Table A7.7). One of the cost-utility analyses and one of the costing studies were found to be of good quality.

A 2008 US study by Handley et al. evaluated a telephone self-management support intervention with nurse care management for patients with Type 2 diabetes.[221] The study was based on the results of a 12 month randomised controlled trial (RCT) involving 226 patients in a primary care setting. The SF-36 questionnaire was used to assess health-related quality of life. Start up and running costs were €436 and

€429 per patient per annum, respectively. The ICER for the intervention, including start-up costs, compared with routine care was €72,097 per QALY. Uncertainty was only assessed by varying the QALY data by plus or minus 10%.

A 2010 US study evaluated the costs associated with the IDEATel intervention, which used telemedicine case management in medically underserved patients with diabetes mellitus.[232] Project intervention costs were estimated as €662 per participant per month of intervention delivered. The mean annual payments were estimated at €9,615 for the usual care group and €10,284 for the telemedicine group. Telemedicine case management did not reduce Medicare claims for clinical services. The authors concluded that to be viable and adopted in clinical settings, less costly technology will be required, most likely incorporating mobile phone technology and computers that are owned and maintained by participants. This may not be a viable option for medically underserved patients.

#### 7.3.2.3 Pharmacist-based programmes

Three studies were identified that evaluated pharmacy-based interventions (Table A7.8). All three studies were considered poor quality and at high-risk of bias.

#### 7.3.2.4 Other self-management support programmes

A 2010 UK study evaluated motivational enhancement therapy (MET) and cognitive behaviour therapy (CBT) delivered by general nurses with additional training in these techniques.[222] Patients were adults with a confirmed diagnosis of Type 1 diabetes for a minimum duration of two years and a current A1c value between 8.2% and 15%. The study carried out a cost-utility analysis using data generated by an RCT. The unit cost for a 50-minute MET session was estimated at €74 and €73 per session including and excluding training, respectively. The respective estimates for a 50-minute session of CBT with and without training were €123 and €111, respectively. The average total cost of each treatment approach was approximately €296 for MET and €1,003 for MET in combination with CBT. Compared to usual care, MET had an ICER of €473,919 per QALY from the NHS perspective, and €244,316 per QALY from a societal perspective. Compared to usual care, MET combined with CBT had ICERs of €474,147 per QALY from the NHS perspective, and €412,385 per QALY from the societal perspective. The programme based on MET alone dominated (that is, was less expensive and more effective than) the combination of MET and CBT. The ICERs reported in this study would not generally be considered cost effective using conventional UK willingness to pay thresholds of between £20,000 per QALY and £30,000 per QALY.

## 7.4 Discussion

This section discusses the main findings from the review of the clinical-effectiveness and cost-effectiveness literature.

### 7.4.1 Clinical-effectiveness Type 1 diabetes mellitus

In accordance with the Terms of Reference, this assessment was limited to a review of the clinical effectiveness of chronic disease self-management interventions in adults aged 18 years and older. It is noted that this restriction had particular implications for the assessment of SMS interventions in Type 1 diabetes. While clinical presentation of Type 1 diabetes can occur at any age, peak incidence occurs in childhood, with only approximately 25% of cases diagnosed in adults. One review from the PRISMS report met our inclusion criteria. It found no evidence for the effectiveness of psychological treatments in improving glycaemic control and reducing psychological distress in adults. No additional reviews were retrieved in our updated search which ran to 1 April 2015. However, subsequent to this, a high-quality systematic review of structured education programmes for adults with Type 1 diabetes was published as part of a guideline by the UK's National Institute for Health Care and Excellence (NICE) on the diagnosis and management of Type 1 diabetes in adults in August 2015. Given its relevance to this health technology assessment (HTA) and the absence of other literature, this assessment was updated to include the review. Based on evidence that was graded as low- or very low-quality, the review found limited evidence to show that structured education programmes can have a beneficial effect on severe hypoglycaemia and quality of life.

Structured education programmes are currently available in Ireland for adults with Type 1 and Type 2 diabetes. A 2009 Health Service Executive (HSE) review of diabetes structured education provided a definition for structured education, specifically that it is 'a planned and graded process that facilitates the knowledge, skills and ability for diabetes self-management and empowers individuals to live healthily, to maintain and improve their quality of life and assume an active role in their diabetes care team' and outlined key criteria for structured diabetes education in Ireland. The review outlined six of the structured programmes available in Ireland (Type 1 diabetes: Berger and DAFNE programmes; Type 2 diabetes – CODE, Desmond, and X-PERT Ireland; Paediatric – BRUCIE) and noted that these should be integrated into standard diabetes care. This finding is consistent with the 2015 UK's National Institute for Health Care and Excellence (NICE) guideline which concluded that on the basis of evidence rated as being of low- or very low-quality, adults with Type 1 diabetes should be offered a structured education programme of proven benefit (and specifically recommending the DAFNE programme as an example),

stating that it should be offered six to 12 months after diagnosis. They also note that if the structured education is not taken up by 12 months that it can be offered at anytime that is clinically appropriate. The guideline also specified required components of any structured education programme for adults with Type 1 diabetes including that it be evidence-based, delivered by trained educators, quality assured and reviewed by trained competent assessors who measure it against criteria that ensure consistency, with regular audit of outcomes.[173;175]

### 7.4.2 Clinical-effectiveness Type 2 diabetes

A diverse range of SMS interventions and in particular education interventions were assessed for people with Type 2 diabetes. These differed in the frequency, intensity and mode of delivery. Despite the heterogeneity within the intervention classes, there was a tendency for their findings to be combined, so the results of the meta-analyses should be interpreted with caution. The findings from the 2014 PRISMS systematic review and the additional findings from this updated review indicate that there is consistent evidence that SMS interventions, mainly education, improve blood glucose control in the short-term. Few interventions assessed long-term follow-up with little evidence that the benefit was sustained. Expert clinical feedback noted that blood pressure control contributes as much to survival as glycaemic control in patients with diabetes.[241] Impact of SMS interventions on systolic and, or diastolic blood pressure was assessed in four systematic reviews with no evidence of effect seen for individual patient education programmes, group-based diabetes education or culturally-tailored education; a small improvement weighted mean difference (WMD) of -2.2 (95%CI -3.5 to -1.0) was observed for patient activation interventions on the basis of low- and very low-quality evidence in a systematic review by Bolen et al. (in 54 RCTs with 7,630 participants).[176]

SMS may be delivered in a huge variety of ways and by a large cast of different professionals and lay people; however, the optimal model of delivery is unclear. The PRISMS report noted that given the large number of RCTs and reviews included within its meta-review, the failure to reach any conclusion on the optimal model of delivery suggests that there may not be just one way. They noted that the evidence suggests that various models of delivery may be equally effective and consideration may instead need to be given to other factors which may influence effectiveness, such as the real-world context.

Improvement was seen for some secondary outcomes, but it generally did not persist beyond the intervention phase and the clinical significance is unclear. The evidence suggests that the SMS interventions do not impact on quality of life, which remained unaltered. PRISMS reported that the fact that quality of life remains unaltered in these interventions may be considered a positive outcome considering

the often high demands on participants' time; which could potentially impact negatively on quality of life. However, equivalence studies would be needed to confirm whether the fact that they are unchanged is significant. The PRISMS report noted that the large body of RCT evidence originating in many countries suggests that findings are likely to be highly generalisable. Impact on resource utilisation (hospitalisations, emergency department visits, or use of unscheduled care) was not evaluated in any of the reviews. As noted, there was significant heterogeneity in the format and intensity of the SMS interventions, the study populations, follow-up duration and assessed outcomes. This makes it difficult to formulate clear recommendations regarding the most effective form and content of SMS in Type 2 diabetes.

Due to the volume of evidence available, and in the interest of efficiency, this assessment of SMS interventions in diabetes was undertaken in the form of an overview of reviews. As discussed in Chapter 3.4.1, a disadvantage of this approach is the inability of an overview of reviews to reflect the most recent literature. Following publication of an RCT, it must first be captured in a systematic review, before subsequently being captured in an overview of reviews. However, given their typical sample sizes, it may not be appropriate to draw conclusions on the effect of an intervention based on a single, or a number of small, RCTs. Therefore, it is unlikely that more recent RCTs not captured in this overview of reviews would be sufficient to substantially alter recommendations informing major policy decisions.

It should also be noted that an overview of reviews makes use of pooled clinical effectiveness data, sometimes across a large number of primary studies, and that in many cases the data were very heterogeneous. Studies were often pooled despite the fact that they implemented a variety of different interventions that were only broadly similar. In many cases the pooled estimates gave an indication of the effectiveness of a broad type of intervention rather than a specific and well-defined programme. Although the pooled estimate may show limited effect, individual studies will have shown more or less effectiveness than the average effect. In the event of a policy decision to systematically provide diabetes SMS interventions, it would be advisable to consider the findings of high-quality systematic reviews and the primary evidence they included to determine which intervention might generate the greatest treatment effect.

It would appear that the evidence should be somewhat applicable to the Irish healthcare setting given the description of the diabetes patient populations and the healthcare systems in which the interventions were provided. Potential caveats to this assumption are the extent to which usual care in these RCTs is representative of usual care in Ireland, and differences in how healthcare is provided. Given the increasing tendency for usual or standard of care to be determined by evidence-

based clinical guidelines and the convergence of such guidelines in Western countries, the assumption that the stated standard of care is similar is reasonable. However, differences in healthcare systems may contribute to differences in the adherence to stated standard of care. For example, usual care for diabetes in the Irish primary care setting may differ to that in the UK's NHS system where adherence to quality standards is incentivised by the quality of outcomes framework.

As noted in Section 7.4.1, a 2009 HSE review of diabetes structured education in Ireland outlined key criteria for structured diabetes education and described five of the structured programmes available in Ireland. Of these, three were indicated for Type 2 diabetes in adults (CODE, Desmond, and X-PERT Ireland) and the review noted that these should be integrated into standard diabetes care. This recommendation is consistent with 2011 guidelines from the UK National Institute for Health and Care Excellence (NICE) which highlighted the need to use patient education programmes to improve patient outcomes by offering structured education around the time of diagnosis, with annual reinforcement and review. However, the NICE guidelines emphasise that the success of these programmes is dependent on the personal and sociological background of patients, and that such educational programmes should be tailored to patient groups or individuals.[173;242] The HSE's National Clinical Programme for Diabetes is currently developing a model of care through which it proposes all diabetes patients could have access to a structured integrated care package covering all aspects of their diabetes care.[243]

### 7.4.3 Cost-effectiveness

Thirty eight economic evaluation studies of chronic disease self-management interventions for patients with diabetes were identified as relevant. Twenty four of these were SMS education programmes, with 11 investigating telemedicine programmes and three pharmacist-led programmes). Four studies specified a population with Type 1 diabetes, 19 specified Type 2 diabetes (all, or non-insulin dependent only), and 15 included all adult patients with diabetes. The quality of the studies was generally poor. A number of the studies either used historical controls or compared outcomes to baseline data. The analysis here focused on the studies considered good quality.

The economic evaluations of SMS education programmes reported a range of results, but the majority estimated greater benefits and higher costs. The better quality studies identified in this review used data from RCTs and then extrapolated lifetime benefits using a number of chronic disease simulation programmes that estimate long-term outcomes based on patient risk-factors such as obesity, smoking, and HbA1c. Simulated results generally suggested ICERs of less than €45,000 per QALY relative to usual care. The applicability of these results depend on the extent to which the effect sizes estimated in trials, which typically involve no more than 18

months follow-up (typically six to 12 months), persist over patients' lifetimes. The results of these studies should therefore be interpreted with caution, although the general finding is of potential cost-effectiveness.

In addition, several of the evaluations were based on trials of interventions where they observed a benefit but it was not found to be statistically significant. Interpretation of the results of a subsequent economic evaluation can be complicated, and focus should in those instances be on the cost findings rather than the effectiveness data. The population of three of the evaluations of SMS education programmes was limited to adults with Type 1 diabetes.[216;225;237] The studies reported that structured education could be considered cost-effective relative to usual care. The study by Kruger et al. related to the DAFNE programme and was used to inform the 2015 NICE guideline alluded to in Section 7.4.1. A similar economic evaluation by Shearer et al. reported that a structured training and teaching programme (STTP) was more effective and less costly than usual care, while and Irish study by Gillespie et al. noted that group follow-up post structured education using DAFNE is less costly and more beneficial than individual follow-up.

In terms of telemedicine interventions, only one good quality study reported a cost-utility analysis. The study of a telephone self-management support intervention with nurse care management for patients with Type 2 diabetes reported an ICER of €72,097 per QALY relative to usual care, which would not generally be considered cost effective using conventional US willingness to pay thresholds of $50,000 per QALY. This study was based on 12 months' follow-up data from a trial of 226 patients.[221]

There was insufficient evidence of adequate quality to consider the cost-effectiveness of pharmacist-led interventions.

Some of the studies have been based on medically underserved populations or specific sub-populations. These sub-groups may be more likely to have poorly-controlled diabetes and may also have a greater probability of other risk-factors (such as smoking or obesity) than the general population. Therefore, the effectiveness of interventions may be overestimated in these studies and they may be less cost-effective when applied to a general population.

The cost per patient of interventions was highly variable, making it difficult to draw any conclusions about the typical implementation cost of self-management support programmes for people with diabetes. Higher costs may be anticipated for telemedicine programmes on account of the need for support technology. However, the cost of SMS education programmes ranges from less than €135 to €4,720 (over six months) per patient over the duration of the trial.

In summary, the review of cost-effectiveness found 38 studies where the effectiveness of interventions was generally derived from RCT evidence. This is in contrast to the review of the clinical effectiveness literature which included 27 systematic reviews of 347 unique RCTs for Type 2 diabetes and two systematic reviews of 26 unique RCTs for Type 1 diabetes. Given the diverse range of study populations, health systems and methodological approaches that have been used to estimate the cost-effectiveness of different self-management programmes for diabetes, the applicability of the available evidence to a prospective Irish programme is considered low. However, relatively recent studies from Ireland and the UK involving peer support and education programmes for patients with diabetes have reported results that would generally be considered cost-effective given conventional willingness-to-pay thresholds used in Ireland.

## 7.5 Key points

- Limited evidence was retrieved for self-management support interventions in adults with Type 1 diabetes mellitus with only two reviews being identified for inclusion in this overview of reviews. The reviews assessed psychological treatments and structured education programmes, with both rated as high-quality reviews.
- The primary evidence underpinning the systematic reviews was found to be at moderate to high-risk of bias, meaning that the studies may have over- or under-estimated the effect size. The randomised controlled trials (RCTs) were published between 1983 and 2005.
- Based on a single systematic review, there is no evidence of effectiveness of psychological treatments in improving glycaemic control and reducing psychological distress in adults with Type 1 diabetes mellitus.
- Based on a single systematic review of structured education programmes, there is very limited evidence that these interventions lead to improved outcomes in severe hypoglycaemia and quality of life in adults with Type 1 diabetes mellitus.
- Twenty-seven systematic reviews of self-management support interventions in adults with Type 2 diabetes mellitus were identified for inclusion in this overview of reviews.
- Broadly, 13 studies assessed education interventions, five assessed some form of telemedicine, one assessed self-management programmes in Type 2 diabetes and eight assessed other self-management support interventions.
- The quality of the systematic reviews was good, with 15 rated as being higher quality reviews.
- The primary evidence underpinning the systematic reviews was generally found to be at moderate- to high-risk of bias, meaning that the studies may have over-

or under-estimated the effect size. The 347 unique RCTs for Type 2 diabetes were published between 1985 and 2014.

- Based on the quantity and quality of the systematic reviews and the underpinning primary RCTs, there is very good evidence that education, including culturally-appropriate education, improves blood glucose control in the short-term (less than 12 months) in people with Type 2 diabetes.
- There is some evidence that chronic disease self-management programmes in Type 2 diabetes are associated with small improvements in blood glucose control in the short-term.
- There is good evidence that various forms of telemedicine are associated with improvements in blood glucose control in the short term for people with Type 2 diabetes.
- There is good evidence that behavioural interventions are associated with modest improvements in blood glucose control (HbA1C).
- There is evidence of improvements in blood glucose control for a diverse range of self-management support interventions; particularly educational interventions which differ in their frequency, intensity and mode of delivery.
- It is not possible to provide clear recommendations on the optimal content and format of self-management support for Type 2 diabetes. Evidence suggests that various models of delivery may be equally effective. Impact on resource utilisation was not assessed in any of the reviews. Quality of life remained unaltered.
- Thirty eight economic evaluation studies of chronic disease self-management interventions for patients with diabetes were identified as relevant. The studies evaluated self-management support education programmes, telemedicine, and pharmacist-led programmes.
- Self-management support education programmes had the greatest quantity and quality of evidence. Simulated results generally suggested ICERs of less than €45,000 per QALY relative to usual care.
- In terms of telemedicine interventions, there was only one good quality cost-utility analysis, which reported an ICER of €72,097 per QALY relative to usual care.
- There was insufficient evidence of adequate quality to consider the cost-effectiveness of pharmacist-led interventions.
- The better quality studies identified in this review used data from RCTs and then extrapolated lifetime benefits using one of a number of simulation models that predict outcomes based on risk-factors. The results of these studies should therefore be interpreted with caution.
- Based on the description of the healthcare systems and the Type 2 diabetes

mellitus patient populations in the included studies, and assuming that what constitutes 'usual care' and how it is provided is similar in Western countries, the findings of this overview of clinical effectiveness of self-management support interventions are expected to be applicable to the Irish healthcare setting. However, the applicability of some of the cost-effectiveness results to a general population is questionable due to the nature of the included trial population (for example, medically underserved populations). Therefore, the results of those studies are at risk of bias.

# 8 Stroke

This health technology assessment (HTA) of stroke self-management support (SMS) is one of a series of rapid HTAs assessing SMS interventions for chronic diseases. Section 8.1 provides a brief description of stroke followed by separate reviews of the clinical (Section 8.2) and cost-effectiveness (Section 8.3) literature for SMS interventions in stroke survivors.

Brief descriptions of the background and methods used are included with full details provided in a separate document (Chapter 3). Section 8.4 includes a discussion of both the clinical and cost-effectiveness findings. This section of the report concludes with a list of key points in relation to interventions for stroke survivors (Section 8.5).

## 8.1 Description of the disease

Stroke is the neurological condition that results from brain damage caused by either blockage or rupture of a blood vessel in the brain. About 80% of strokes occur following a blockage of a vessel (ischaemic stroke) and 20% from vessel rupture (haemorrhagic stroke).[244;245] A small number of strokes result from other causes. Transient ischaemic attack (TIA) is a related and often indistinguishable condition producing similar symptoms where the supply of blood to the brain is temporarily interrupted, but without causing permanent damage. TIAs are often a warning sign of an impending stroke. Consistent with stroke survivors, patients who experience a TIA require active risk management to reduce the risk of further TIA episodes or stroke. This may include management of other co-morbid chronic conditions (including, for example, hypertension, diabetes, coronary artery disease and obesity). However, as noted, unlike stroke survivors who require rehabilitation and physical and emotional support to deal with long-term neurological conditions, TIAs do not result in permanent neurological damage.[245]

Each year in Ireland, approximately 7,000 people are hospitalised following stroke.[246] Total annual stroke costs in Ireland were estimated to be between €489 million and €805 million in 2007, with nursing home care needs and indirect costs accounting for the largest proportion of costs.[246;247] Due to an aging population, the burden of stroke-related disease is expected to increase, with predicted increases of 11% to 15% in the proportion of the population aged 65 or older by 2021.[248] Stroke can cause a range of permanent impairments associated with movement and coordination, memory and attention, and can cause depressive symptoms, all affecting an individual's rehabilitation. It is estimated that between 30% and 40% of stroke survivors develop some degree of functional dependence requiring assistance in performing basic activities of daily living (ADLs).

## 8.2 Review of clinical-effectiveness of self-management support interventions

### 8.2.1 Background and methods

Details of the background and methods for this assessment are included in Chapters 1 to 3 of this report. Briefly, an aim of this HTA is to review the clinical effectiveness of self-management support (SMS) interventions for a number of chronic conditions including stroke. Given the large volume of literature available, it was noted that an update of an existing high-quality systematic review of SMS interventions could be considered sufficient to inform decision-making.

In December 2014, a high-quality overview of reviews was published by the National Institute for Health Research (NIHR) in the UK. The Practical Systematic Review of Self-Management Support for long-term conditions (PRISMS) study comprised an overview of systematic reviews of randomised controlled trials (RCTs) up to 1 June 2012, and was itself undertaken according to the principles of systematic reviewing. An update to the PRISMS report was completed by running additional searches in PubMed, Embase and the Cochrane Library from 2012 to 1 April 2015, see Appendix A3.1. In accordance with the PICOS (Population, Intervention, Comparator, Outcomes, Study design) agreed with the key stakeholder, this assessment is limited to SMS interventions for adults aged 18 years and over. Results of the updated search are reported in addition to a summary of the findings of the PRISMS report.

Data extraction and quality assurance of the systematic reviews, meta-analyses and the risk of bias associated with the primary literature were undertaken as described in Chapter 3.1.3. In summary, in order to determine the quantity, quality, strength and credibility of evidence underpinning the various SMS interventions, quality assurance of both the systematic review methodology (R-AMSTAR) and the meta-analyses (Higgins et al.'s quality assessment tool)[23] was undertaken. While the R-AMSTAR score was used to determine the quality of the systematic reviews, the scores were then weighted by patient or participant trial size, with the quality of evidence being downgraded if the review was based on fewer than 1,000 participants. The quality of the primary evidence was not evaluated directly. However, where it was reported, information on the risk of bias of the primary studies was extracted from the systematic reviews.

### 8.2.2 Description of the interventions

A general description of self-management and typical SMS interventions is included in Chapter 2 of this HTA. Stroke-specific interventions introduced in this Phase IIb report include stroke-specific self-management programmes and various methods of stroke rehabilitation such as telerehabilitation and virtual reality-based rehabilitation for stroke survivors. As noted in Chapter 2, generic chronic disease self-management programmes (CDSMP), for example the Stanford Programme, are behaviour-change programmes that mainly focus on improving self-efficacy and are designed to enable people to take an active part in managing their own condition. This includes necessary lifestyle adjustments to enhance quality of life, and also mechanisms to deal with the psychosocial consequences of their condition. SMS programmes specific to stroke survivors encompass a number of common SMS interventions, typically information provision, goal setting, problem solving and the promotion of self-efficacy.[249] Telerehabilitation, which stems from the broader approach of telehealth, is an alternative method of delivering conventional rehabilitation services using information and communication technologies. It typically includes some form of therapist communication at a distance. It can also encompass virtual reality interventions. Stand-alone virtual reality-based rehabilitation is a recent treatment approach in stroke rehabilitation that uses commercial gaming consoles or specifically developed consoles adopted in clinical settings.

Outcomes specific to this review include, primary activities of daily living (ADL) and extended ADL. Being able to complete fewer ADLs indicates an increased disability or dependence on the help of carers. 'Primary ADL' is typically limited to functional ability and personal care (for example, feeding, bathing and dressing measures) whereas 'extended ADL' includes more complex tasks necessary for community and domestic participation (for example, shopping, cooking and transportation use).[2]

### 8.2.3 Results — clinical-effectiveness

The PRISMS review retrieved a total of 11 quantitative systematic reviews of stroke-specific SMS interventions for stroke survivors.[2] Summary details of the reviews are included in Table 8.1. The publication dates of the systematic reviews ranged from 2003 to 2012 while that of the included RCTs ranged from 1981 to 2009. The reviews included 101 individual RCTs and were conducted in the UK, USA, China, Australia, the Netherlands, Sweden and Denmark. Not all of the systematic reviews recorded where the individual RCTs were conducted.

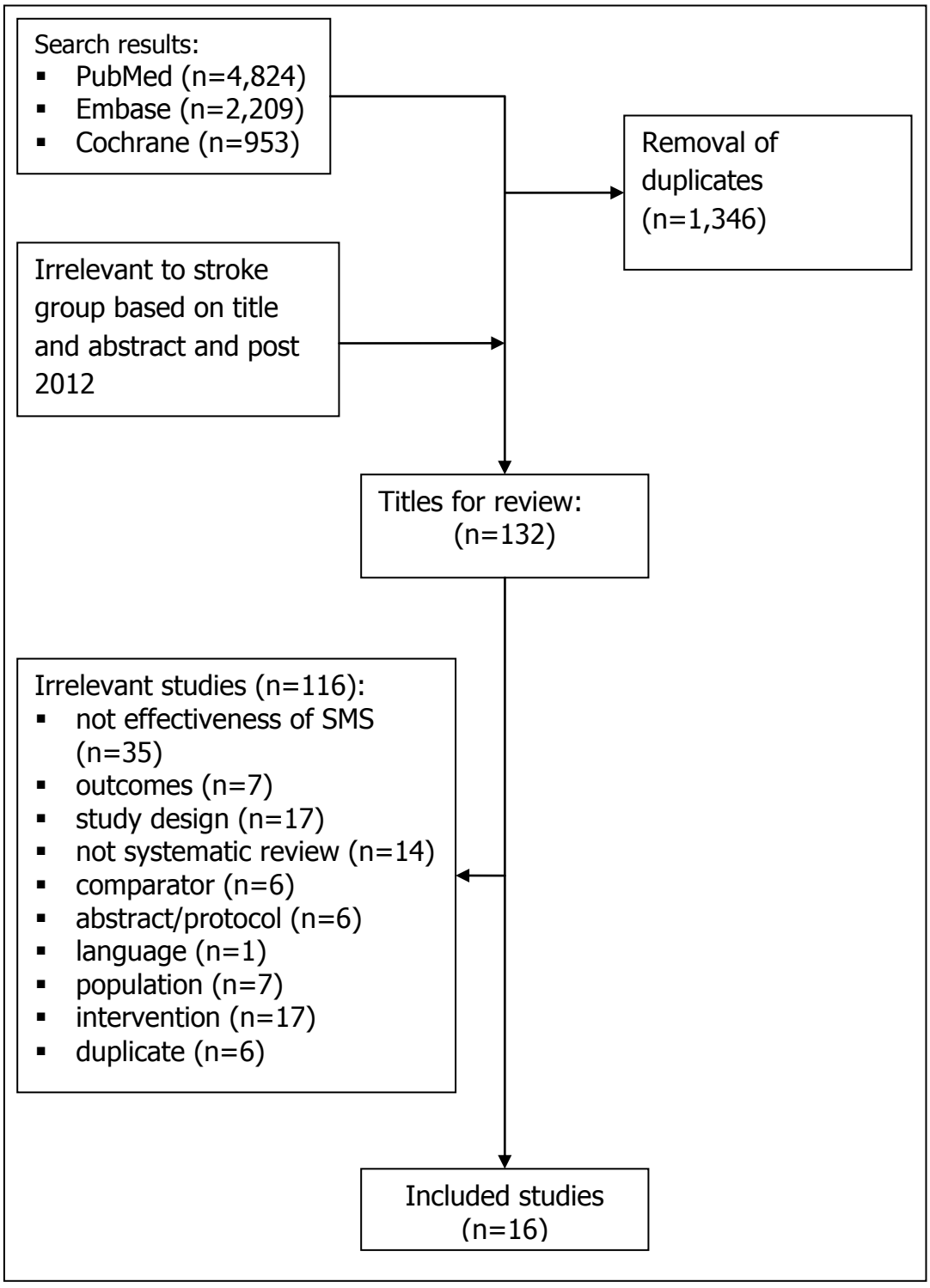
The PRISMS review was updated to April 2015 using the search string in Appendix 1. A further 16 applicable systematic reviews were retrieved (see Figure 8.1) that assessed a diverse range of SMS interventions for stroke survivors, including general stroke rehabilitation,[250] telerehabilitation[251] and virtual reality-based

rehabilitation,[252-255] self-management programmes,[249;256;257] information provision,[258] psychosocial,[259] lifestyle[260] or family-orientated interventions,[261] motivational interviewing,[262] leisure therapy[263] and multidisciplinary care[264] (see Table 8.1). Study overlap was assessed to identify studies that added little or no additional evidence. When substantial overlap was observed between two or more systematic reviews, we based our analyses on the higher quality or more comprehensive review. Based on this, the reviews by Lohse et al.,[254] Rodrigues-Baroni et al.[255] and Imam et al.[252] on virtual reality-based rehabilitation, while listed for completeness, are not discussed. Instead, the more recent comprehensive Cochrane review by Laver et al. (2015)[253] is discussed. The review by Lo et al.[256] on self-management programmes is not discussed further as the three component RCTs are included within the review by Lennon et al. (2013) on the same topic.[249] Similarly, only the results from three of the six RCTs in the narrative review by Warner et al.[257] on self-management programmes are discussed as the remaining RCTs are included in the review by Lennon et al..

For the additional systematic reviews identified in the updated search, the number of included RCTs per review ranged from 1[262] to 37[250;253] with the number of participants per systematic review ranging from 411[262] to 7,742[260]. Study overlap is reported in Table 8.2. The publication dates of the systematic reviews ranged from 2012 to 2015 while that of the included RCTs ranged from 1989 to 2014. Study locations of RCTs were typically in Asia, Europe (mainly the UK) or North America. Study location was not reported in two reviews. The R-AMSTAR scores for the additional systematic reviews identified in the updated search ranged from 24 to 38, with scores of 31 or more indicating a high-quality systematic review.

When weighted according to the number of participants in the original RCTs (<[less than] 1,000 or ≥ [greater than or equal to] 1,000), nine of the systematic reviews were categorised as providing the highest quality evidence (three star *** review) while four reviews each were rated as two-star**. Two were rated as one-star* reviews in terms of their quality and size. Of the 23 systematic reviews discussed, 13 included a meta-analysis of which 10 were assessed as high quality, and three as moderate quality. The conclusions in the latter are at risk of bias, but are likely to be broadly accurate, while studies graded as high quality are very likely to have conclusions that accurately reflect the available evidence (see also Chapter 3, Table 3.1) In total, 228 unique RCTs are included in the retrieved systematic reviews.

**Figure 8.1 Flowchart of included studies from updated search**



## Table 8.1 Stroke — summary of systematic reviews retrieved in the PRISMS review and the updated search, classified by intervention type

| Author (year) | Intervention |
|---|---|
| PRISMS studies retrieved | |
| **Rehabilitation therapy** | |
| *General Rehabilitation* | |
| Aziz (2008) CR[265] | Rehabilitation therapy — one-year post stroke |
| Hoffman (2010) CR[266] | Occupational therapy (OT) rehabilitation for cognitive impairment |
| Legg (2006) CR[267] | OT rehabilitation |
| OST (2003) CR[268] | Rehabilitation therapy |
| Poulin (2012)[269] | Rehabilitation therapy for cognitive impairment |
| Steultjens (2003)[270] | OT rehabilitation |
| Walker (2004)[271] | OT rehabilitation |
| **Stroke self-management programmes** | |
| Korpershoek (2011)[272] | Self-efficacy enhancing |
| **Information provision** | |
| Smith (2008) CR[273] | Information provision (patients and caregivers) |
| **Other SMS** | |
| Ellis (2010) CR[274] | Stroke liaison |
| Lui (2005)[275] | Caregiver problem solving |
| Reviews retrieved in updated search | |
| **Rehabilitation therapy** | |
| *General Rehabilitation* | |
| Dorstyn (2014)[263] | Leisure therapy in stroke rehabilitation |
| Zhang (2013)[250] | Stroke rehabilitation in China |
| *Virtual Reality-Based Rehabilitation* | |
| Imam (2014)[252] | Virtual reality rehabilitation |
| Laver (2015) CR[253] | Virtual reality rehabilitation |
| Lohse (2014)[254] | Virtual reality therapy |
| Rodrigues-Baroni (2014)[255] | Virtual reality-based walking training |
| *Telerehabilitation* | |
| Laver (2013) CR[251] | Telerehabilitation services (range including computer-based training programmes) |
| **Stroke self-management programmes** | |
| Lennon (2013) [249] | Stroke self-management programmes |
| Lo (2013)[256] | Stroke theory-based self-management programmes |

| Author (year) | Intervention |
|---|---|
| Warner (2015)[257] | Stroke self-management programmes |
| **Information provision** | |
| Forster (2012) CR[258]* | Information provision (patients and caregivers) |
| **Other self-management support** | |
| Cheng (2014)[259] | Psychosocial interventions (such as counselling, psychoeducation, behavioural or cognitive interventions, social support group) |
| Cheng (2015) CR[262] | Motivational interviewing |
| Fens (2013)[264] | Range of multidisciplinary care (≥2 different care professionals working together as, or supported by, a team) |
| Lennon (2013)[260] | Lifestyle interventions (including education) for secondary disease prevention |
| Vallury (2015)[261] | Family-oriented interventions to reduce post-stroke depression |

**Key**: **CR** = Cochrane review; **OT** = occupational therapy; **QA** = quality assurance.

* The CR by Forster et al. CR (2012) is an update of the 2008 CR by Smith et al..

## Table 8.2 Stroke — study overlap between the included systematic reviews (PRISMS report plus the systematic reviews from the updated search).[6] Adapted from PRISMS review[(2)]

| | Review (year) | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Aziz (2008) | **5** | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 2 | Hoffman (2010) | 0 | **1** | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 3 | Legg (2006) | 0 | 0 | **9** | | | | | | | | | | | | | | | | | | | | | | | | | |
| 4 | OST (2003) | 0 | 0 | 7 | **14** | | | | | | | | | | | | | | | | | | | | | | | | |
| 5 | Poulin (2012) | 0 | 0 | 0 | 0 | **3** | | | | | | | | | | | | | | | | | | | | | | | |
| 6 | Steultjens (2003) | 0 | 0 | 6 | 6 | 0 | **18** | | | | | | | | | | | | | | | | | | | | | | |
| 7 | Walker (2004) | 0 | 0 | 7 | 8 | 0 | 6 | **8** | | | | | | | | | | | | | | | | | | | | | |
| 8 | Ellis (2010) | 0 | 0 | 0 | 1 | 0 | 0 | 0 | **16** | | | | | | | | | | | | | | | | | | | | |
| 9 | Korpersoek (2011) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | **4** | | | | | | | | | | | | | | | | | | | |
| 10 | Lui (2005) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | **6** | | | | | | | | | | | | | | | | | | |
| 11 | Smith (2008) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | **17** | | | | | | | | | | | | | | | | | |
| Reviews retrieved in updated search | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 12 | Cheng (2014) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 3 | 2 | | **13** | | | | | | | | | | | | | | | |
| 13 | Cheng (2015) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | 0 | **1** | | | | | | | | | | | | | | |
| 14 | Dorstyn (2014) | 0 | 0 | 1 | 3 | 0 | 3 | 2 | 0 | 0 | 0 | 0 | | 0 | 0 | **8** | | | | | | | | | | | | | |
| 15 | Fens (2013) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | | 0 | 0 | 1 | **14** | | | | | | | | | | | | |
| 16 | Forster (2012) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 17 | | 3 | 0 | 0 | 0 | **21** | | | | | | | | | | | |
| 17 | Imam (2014) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | 0 | 0 | 0 | 0 | 0 | **11** | | | | | | | | | | |
| 18 | Laver (2013) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | 0 | 0 | 0 | 1 | 0 | 0 | **10** | | | | | | | | | |
| 19 | Laver (2015) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | 0 | 0 | 0 | 0 | 0 | 8 | 1 | **37** | | | | | | | | |
| 20 | Lennon (2013) SMP | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | | 2 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | **9** | | | | | | | |
| 21 | Lennon (2013) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 2 | | 0 | 0 | 0 | 2 | 2 | 0 | 0 | 0 | 2 | **17** | | | | | | |
| 22 | Lo (2013) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 0 | **3** | | | | | |
| 23 | Lohse (2014) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | 0 | 0 | 0 | 0 | 0 | 6 | 1 | 15 | 0 | 0 | 0 | **25** | | | | |
| 24 | Rodrigues-Baroni (2014) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | 0 | 0 | 0 | 0 | 0 | 5 | 0 | 3 | 0 | 0 | 0 | 3 | **7** | | | |
| 25 | Vallury (2015) | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 8 | 1 | 1 | 3 | | 1 | 0 | 0 | 1 | 3 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | **22** | | |
| 26 | Warner (2015) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 0 | 2 | 0 | 0 | 0 | **6** | |
| 27 | Zhang (2013) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | **37** |

**Notes**. 1 The Cochrane review (CR) by Forster et al. (2012) is an update of the 2008 CR by Smith et al.. 2 PRISMS included studies by Ko (2010) and Rae-Grant (2011) were excluded as there were no applicable RCTs. 3 Reviews by Lohse, Imam and Rodrigues-Baroni are not discussed further due to study overlap; the more recent, comprehensive Cochrane review by Laver (2015). The review by Lo et al. on self-management programmes is not discussed further as the RCTs overlap with the review by Lennon et al. (2013).

[6] PRISMS review is based on a search from 1993 to June 2012. This search was updated to April 2015.

#### 8.2.3.1 Summary of findings

Detailed summaries of the systematic reviews including the intervention, outcomes assessed, duration of follow up, sample size (number of RCTs and total number of participants) and the evidence of effect are included in Appendix A8.1. The following are reported based on the findings from PRISMS and the additional systematic reviews retrieved in the updated search. Based on the range of SMS interventions retrieved, it was decided to classify and report the results by intervention type.

The categories of systematic review include: rehabilitation therapy (largest body of evidence retrieved), stroke self-management programmes, information provision and other SMS interventions. In order to emphasise the relevance of the findings, results are grouped by the quality of the systematic review (using the R-AMSTAR score and size of the patient population). Table 8.3 below details the results of the quality assurance assessment of the systematic reviews and provides a summary of findings for selected outcomes from the various meta-analyses assessing the impact of SMS interventions in stroke.

## Table 8.3 Summary characteristics and findings for selected outcomes for included studies

| Study | Quality of Systematic Review | | | Primary Studies | | Quality of Meta-analysis | ADL (SMD) | Extended ADL (SMD) | Poor outcomes or death (OR) |
|---|---|---|---|---|---|---|---|---|---|
| | R-AMSTAR score | Participants | Quality | n | low-risk[a] | | | | |
| Rehabilitation therapy | | | | | | | | | |
| **General rehabilitation** | | | | | | | | | |
| **Aziz** 2008[(265)] | 40 | 487 | ** | 5 | 2 | High | NS | NS | 0.32 (0.14 to 0.71) |
| **Dorstyn** 2014[(263)] | 24 | 610 | * | 8 | | N/A | | | |
| **Hoffmann** 2010[(266)] | 35 | 33 | ** | 1 | | N/A | | | |
| **Legg** 2006[(267)] | 42 | 1258 | *** | 9 | 8 | High | 0.18 (0.04 to 0.32) | 0.21 (0.03 to 0.39) | 0.67 (0.51 to 0.87) |
| **OST** 2003[(268)] | 41 | 1617 | *** | 14 | 9 | High | 0.14 (0.02 to 0.25) | 0.17 (0.04 to 0.30) | 0.72 (0.57 to 0.92) |
| **Poulin** 2012[(269)] | 32 | 109 | ** | 3 | | N/A | | | |
| **Steultjens** 2003[(270)] | 32 | 1825 | *** | 18 | 4 | Moderate | 0.31 (0.03 to 0.60)[2] | NS | |
| **Walker** 2004[(271)] | 35 | 1143 | *** | 8 | 6 | High | OR 0.71 (0.52 to 0.98) | WMD 1.30 (0.24 to 2.79)<br>1.61 (0.72 to 2.49)[3] | NS |
| **Zhang** 2013[(250)] | 33 | 5,916 | *** | 37 | 1 | Moderate | 1.04 (0.88 to 1.21) | | |
| **Virtual reality-based rehabilitation** | | | | | | | | | |
| **Laver** 2015[(253)] | 39 | 1,019 | *** | 37 | 17 | High | 0.43 (0.18 to 0.69) | | |
| **Telerehabilitation** | | | | | | | | | |
| **Laver** 2013[(251)] | 38 | 933 | ** | 10 | 1 | High | 0.0 (-0.15 to 0.15)[4] | | |

**Abbreviations**: **ADL** = activities of daily living; **N/A** = not applicable; **NS** = non-significant; **OR** = odds ratio; **SMD** = standard mean difference; **WMD** = weighted mean difference.

**Note**: [a] Number of the total primary studies identified as being at low risk of bias.

## Table 8.3 (continued) Summary characteristics and findings for selected outcomes for included studies

| Study | Quality of Systematic Review | | | Primary studies | | Quality of meta-analysis | ADL (SMD) | Extended ADL (SMD) | Poor outcomes or death (OR) |
|---|---|---|---|---|---|---|---|---|---|
| | R-AMSTAR score | Participants | Quality | n | low-risk[a] | | | | |
| Stroke self-management programmes | | | | | | | | | |
| **Korpershoek** 2011[(272)] | 24 | 630 | * | 4 | | N/A | | | |
| **Lennon** 2013[(249)] | 29 | 1,191 | ** | 9 | | N/A | | | |
| **Warner** 2015[(257)] | 28 | <1,000 | * | 6 | | N/A | | | |
| Information provision | | | | | | | | | |
| **Smith** 2008[(273)] | 40 | 2831 | *** | 17 | 9 | High | | | NS |
| **Forster** 2012[(258)] | 39 | 3579 | *** | 21 | 2 | High | | | 0.86 (0.59 to 1.25) |
| Other interventions | | | | | | | | | |
| **Cheng** 2014[(259)] | 34 | 3,559 | *** | 18 | 2 | High | | | |
| **Cheng** 2015[(262)] | 39 | 411 | ** | 1 | | N/A | | | |
| **Ellis** 2010[(274)] | 35 | 4,759 | *** | 16 | 13 | High | NS | NS | 0.55 (0.38 to 0.81) |
| **Fens** 2013[(264)] | 29 | 2,389 | ** | 14 | | N/A | | | |
| **Lennon** 2013[(260)] | 29 | 7,742 | ** | 17 | 6 | Moderate | NS | | 1.13 (0.85–1.52) |
| **Lui** 2005[(275)] | 24 | 1,676 | ** | 6 | | N/A | | | |
| **Vallury** 2015[(261)] | 26 | 3,739 | ** | 22 | | N/A | | | |

**Abbreviations**: **ADL** = activities of daily living; **N/A** = not applicable; **NS** = non-significant; **SMD** = standard mean difference; **WMD** = weighted mean difference.

**Note**: [a] Number of the total primary studies identified as being at low risk of bias.

#### 8.2.3.2 Rehabilitation therapy

**Three star (***) reviews**

Based mainly on four three-star reviews, PRISMS reported that there is strong evidence that general rehabilitation therapy delivered in early stroke recovery has a positive impact on activities of daily living (ADL) and extended ADL, but has no impact on mood.[267;268;270;271] When delivered later in stroke recovery, there is some evidence of a beneficial effect on extended ADL, but there is some evidence to suggest no impact on ADL or quality of life (QoL). Regardless of whether rehabilitation therapy is delivered in early or late stroke recovery, there is no evidence of effect on mood. The majority of rehabilitation therapy interventions reported in the PRISMS identified systematic reviews were delivered by occupational therapists (OTs). While OTs can play an important role in delivering SMS, PRISMS noted that a more integrated whole-systems approach is needed for optimal SMS. They highlighted that a focus on longer-term support is also required.

There is good evidence that virtual reality-based rehabilitation using interactive video games is beneficial in improving upper limb function and ADL when used as an add-on to usual care. This finding is based on a Cochrane review and meta-analysis of 37 RCTs by Laver et al. published in 2015, with the author proposing that these improvements are due to an increase in overall therapy time.[253] However, they highlight that it is unclear at present which characteristics of virtual reality are most important and if the effects are sustained in the longer term.

While a high-quality systematic review and meta-analysis of a diverse range of stroke rehabilitation interventions in China was identified in the search, its results are not applicable to the Irish setting as the comparator used was no rehabilitation.

**Two star (**) reviews**

A Cochrane review and meta-analysis of telerehabilitation by Laver et al. (2013) found no significant improvements in ADL or upper limb function for post-stroke patients compared with usual care.[251]

**One star (*) reviews**

We identified a single narrative review of 32 RCTs evaluating the effect of leisure therapy on short-term psychological and leisure outcomes in adults who have sustained a stroke.[263] The review was of poor quality and found limited evidence of effect.

**Summary statement for rehabilitation therapy**

Based on the quantity and quality of the systematic reviews and the underpinning primary randomised controlled trials, there is good evidence that rehabilitation therapy provided mainly by occupational therapists and delivered in early stroke recovery has a positive impact on ADL and extended ADL. There is good quality evidence that virtual reality-based rehabilitation improves ADL and upper limb function. Based on limited evidence, telerehabilitation does not improve ADL or upper limb function for post-stroke patients compared with usual care.

#### 8.2.3.3 Stroke-specific self-management programmes

**Two star (**) reviews**

There is limited evidence of effectiveness of stroke-specific self-management programmes delivered to stroke survivors based on one narrative review by Lennon et al..[249] They reported that six out of nine RCTs showed a significant treatment effect. However, three of these RCTs are potentially not applicable due to the nature of the intervention (n=1) or the comparator used (n=2).

**One star (*) reviews**

PRISMS identified a single lower-quality narrative review of interventions to enhance self-efficacy which suggested that a chronic disease self-management course had a significant positive effect on quality of life.[272] However, this finding was based on two RCTs with the review author stating that these results should be interpreted with caution.

A single narrative review of pre-post, quasi-experimental and RCT study designs evaluating the impact of self-management programmes for stroke patients was identified.[257] The review was of poor quality and identified limited evidence of effect for a single unique RCT evaluating a programme based on a tailored nursing intervention.

**Summary statement for stroke-specific self-management programmes**

Based on the available evidence, it is not possible to draw conclusions in relation to the effectiveness of self-management programmes delivered to post-stroke patients.

#### 8.2.3.4 Information provision

**Three star (***) reviews**

The effectiveness of information provision (education) in a timely and effective format to allow for active decision-making was assessed in a Cochrane review and meta-analysis by Forster et al. (2012).[258] This review was an update to the 2008 review by Smith et al. included in the PRISMS report. Forster et al. reported that information provision improves patient and carer knowledge of stroke, and aspects of patient satisfaction. While they reported a small reduction in patient depression scores, they highlighted that this may not be clinically significant. They noted that the best way to provide information is still unclear, but that interventions using active information provision may be more effective than passive information, such as giving a patient a leaflet, for the clinically important outcomes of patient depression and anxiety symptoms. The latter included information provided on a single occasion with no subsequent systematic follow up or reinforcement, while active information interventions included a purposeful attempt to allow the participant to assimilate the information and included a subsequent agreed plan for clarification and consolidation or reinforcement. They found no evidence that information interventions are associated with improvements in activity limitation, participation or changes in service use.

**Summary statement for information provision**

There is some evidence that information provision improves patient and carer knowledge of stroke, aspects of patient satisfaction, with small reductions (which may not be clinically significant) in patient depression scores. Interventions using active information provision may be more effective than passive information, such as giving patients a leaflet, for patient depression and anxiety symptoms.

#### 8.2.3.5 Other SMS interventions

**Three star (***) reviews**

PRISMS reported some evidence that stroke liaison emphasising education and information can have a positive impact on quality of life, but that general stroke liaison has no measurable benefits for stroke survivors. This is based on one systematic review by Ellis et al. (2010) who defined a stroke liaison worker as:

> "someone whose aim is to increase participation and improve wellbeing for patients and carers. Typically they provide emotional and social support and information to stroke patients and their families and liaise with services with the aim of improving aspects of participation and quality of life for patients with stroke, their carers, or both." [274]

Stroke liaison workers are not limited to a specific professional group; the term spans both individuals from the voluntary sector and those from a range of health or social care professionals.[274]

A systematic review and meta-analysis by Cheng et al. in 2014 reported limited evidence of effectiveness of psychosocial interventions, with this term being applied to cognitive, behavioural and, or social mechanisms of action (such as counselling, psychoeducation, behavioural or cognitive interventions, social support group) that aim to improve the psychosocial and physical wellbeing of caregivers and the outcomes of stroke survivors.[259] They placed no restriction on the format (individual, group, telephone or web-based), setting (hospital, home or community), duration or frequency of intervention. A pooled analysis of two RCTs on individual psychoeducational programmes showed a small effect on improving family functioning.

### Two star (**) reviews

A 2015 Cochrane review by Cheng et al. comprising one RCT which reported insufficient evidence to support the use of motivational interviewing to improve ADL after stroke.[262]

A review and meta-analysis by Lennon et al. in 2013 concluded that there was insufficient high-quality research to support efficacy of lifestyle interventions post-stroke or transient ischaemic attack (TIA) on mortality, cardiovascular-disease event rates or cardio-metabolic risk-factor profiles.[260]

Based on one narrative review by Fens et al. in 2013, there is limited evidence of effectiveness for multidisciplinary care delivered to stroke patients living in the community.[264] Four main types of interventions were assessed: structured assessment (n=2 RCTs); assessment combined with follow-up care (n=8); rehabilitation (n=3); education (n=1).

A low-quality narrative review by Vallury et al. reported limited evidence that family-orientated models of care can be effective in reducing depression in patients and their caregivers.[261] This was based on a statistically significant reduction in post-stroke depression in five out of 22 included RCTs.

**Summary statement for other SMS interventions**

There is some evidence that stroke liaison emphasising education and information can have a significant positive impact on quality of life.

However, based on available evidence, it is not possible to draw conclusions in relation to the effectiveness of psychosocial interventions, motivational interviewing,

lifestyle interventions, multidisciplinary care or family-orientated models of care in the management of post-stroke patients.

## 8.3 Review of cost-effectiveness of self-management support interventions

A review of cost-effectiveness studies was carried out to assess the available evidence for self-management support (SMS) interventions for survivors of stroke. Studies were included if they compared the costs and consequences of a SMS intervention with routine care.

### 8.3.1 Search strategy

A search was carried out to identify economic analyses of SMS interventions. In tandem with the systematic review of clinical effectiveness, the search for economic evaluations was carried out in MEDLINE, Embase and the Cochrane Library. The same search terms were used with the exception of terms for systematic review and meta-analysis. In place of these, search terms and filters for economic evaluations were applied. In addition, 14 systematic reviews of SMS interventions were identified through the results of the clinical effectiveness search, which included cost or economic outcomes, and were used to identify additional studies. The search was carried out up until 4 March 2015.

The PICOS (Population, Intervention, Comparator, Outcomes, Study design) analysis used to formulate the search is presented in Table 8.4 below.

**Table 8.4 PICOS analysis for identification of relevant studies**

| | |
|---|---|
| **Population** | Adults ≥ [greater than or equal to] 18 years old that had experienced a stroke. |
| **Intervention** | Any self-management support intervention that helps patients with post-stroke rehabilitation through education, training or support. |
| **Comparator** | Routine care. |
| **Outcomes** | Cost or cost-effectiveness of intervention. |
| **Study design** | Randomised controlled trials, case-control studies, observational studies, economic modelling studies. |

The following study types were excluded if:

- a nursing home or non-community dwelling population was included,

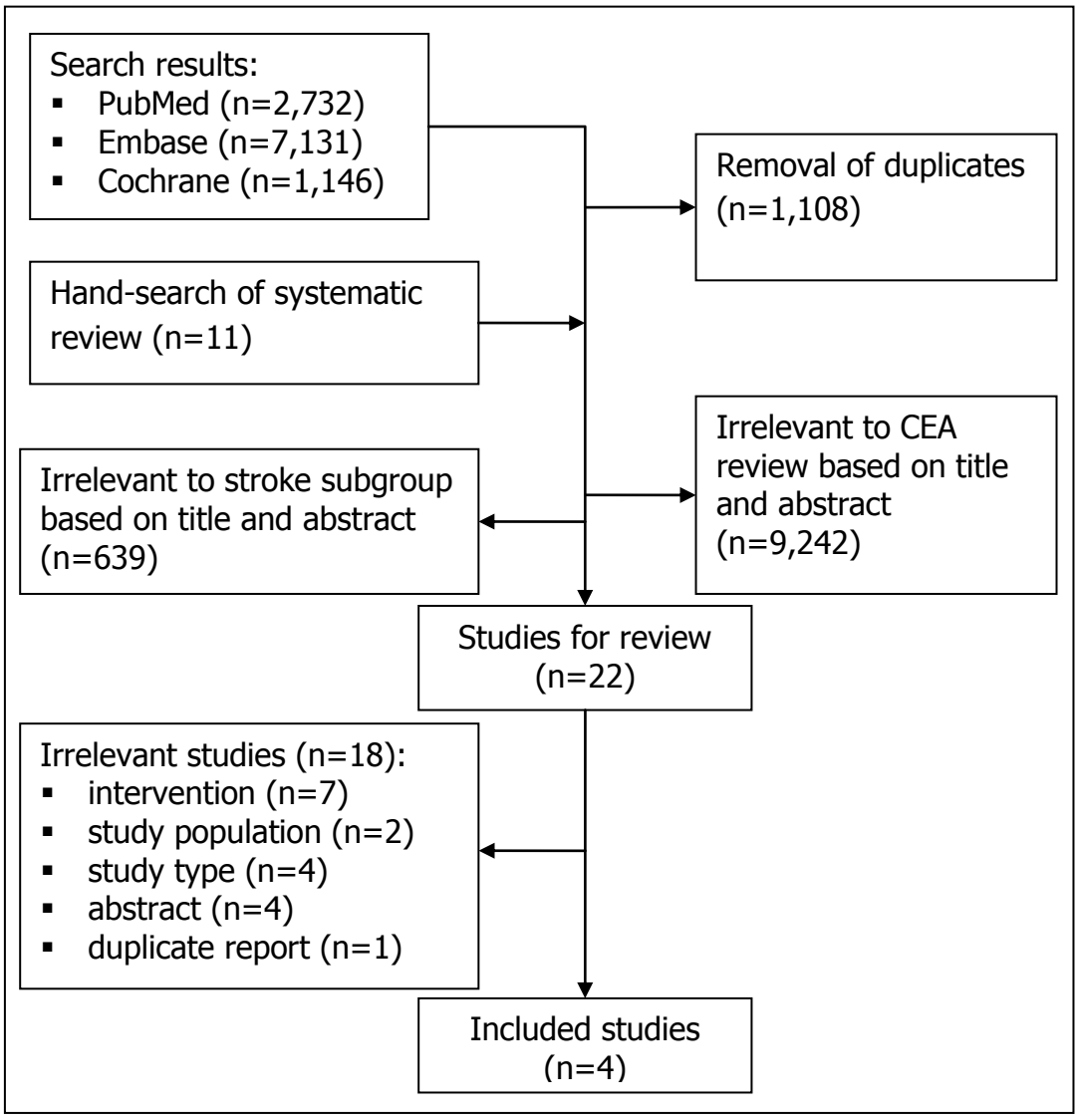
- it included a paediatric population,
- cost data were not clearly reported,
- published prior to the year 2000 (limited relevance).

As outlined in Chapter 3.2.2 and in accordance with national HTA guidelines, assessment of the quality of the studies using the Consensus on Health Economic Criteria (CHEC)-list was performed independently by two people. For studies that included an assessment of cost-utility or an economic modelling approach, assessment of the relevance to the Irish healthcare setting and their credibility was considered using a questionnaire from the International Society of Pharmacoeconomics and Outcomes Research (ISPOR).

### 8.3.2 Results – cost-effectiveness

The bibliographic search returned 11,009 studies from across the three databases, which equated to 9,901 unique studies after removal of duplicates (see Figure 8.2). After removing studies not relevant to the review of cost-effectiveness based on the titles and abstracts, 661 studies were identified that may be costing or cost-effectiveness studies. A further 639 studies were identified as not relevant to a review of stroke interventions based on title and abstract. Finally, a further 18 were excluded based on the various exclusion criteria, leaving four included studies. Assessment of eligibility of studies and data extraction was carried out independently by two people with any disagreements resolved by discussion. Costs reported in each of the studies were inflated to 2014 prices using the local consumer price index and expressed in euro using the purchasing power parity index.

**Figure 8.2 Flowchart of included studies**




Key. CEA = Cost-effective analysis.

Two of the studies were based in the UK, and one in each of Canada and Spain. The included studies were published between 2008 and 2015. The characteristics of the included studies are given in Table 8.5.

**Table 8.5 Included studies**

| Study | Country | Intervention |
|---|---|---|
| **Huijbregts (2008)**[276] | Canada | Self-management programme with land and water-based exercise |
| **Harrington (2010)**[277] | UK | Exercise and education programme |
| **Latimer (2013)**[278] | UK | Self-managed computer therapy |
| **Llorens (2015)**[279] | Spain | Virtual reality-based telerehabilitation |

The studies were classified into two intervention types: exercise-based programmes and computer-based rehabilitation therapy.

#### 8.3.2.1 Exercise-based programmes

Two trial-based costing studies were identified that evaluated exercise programmes. See Table A8.3 in the appendices for a summary of the study details and results.

A 2008 Canadian study evaluated a self-management programme with land and water-based exercise, compared with a standard six-week educational programme that is considered part of routine care in Canada.[276] The intervention consisted of 17 two-hour, group-based sessions, twice per week for eight weeks, with a booster session six weeks later. The first hour of each session involved the discussion of weekly topics, short-term goal setting, and problem solving. The second hour was devoted to exercise. Assessments at baseline, programme completion, and three-month follow-up included the Reintegration to Normal Living (RNL) Index, Activity-specific Balance Confidence (ABC) scale, exercise participation, and goal attainment (for the MOST group). Significant improvements in balance confidence at follow-up were observed in the intervention group and there was some evidence of between-group differences.

The cost of the programme per person was €313 for the intervention and €86 for routine care. Due to the marginal nature of the benefits, the cost per unit increase in balance was more expensive in the intervention group than in the control group. The study used a small sample of 30 self-selected participants, was non-randomised, and there is no indication that assessors were blinded to treatment allocation. The study is therefore at high risk of bias.

A community-based exercise and education scheme was evaluated in the UK using a randomised controlled trial (RCT).[277] The scheme comprised twice-weekly sessions for eight weeks that combined one hour of exercise with one hour of interactive education. The study included 243 stroke survivors that had returned to living in the community

for at least three months prior to the start of the study. Standard care involved a follow-up contact from a stroke coordinator at six weeks and a six-month review. Clinical improvement was measured using a variety of physical, social, activity and mobility indices. Participants in the intervention group showed greater improvements than the control group in the Subjective Index of Physical and Social Outcome (SIPSO) score and in the psychological domain of the quality of life measure. The delivery of the intervention programme cost €371 per participant, compared with €147 per participant for routine care. When all costs were taken into account, the average cost in the intervention group was €1,108 more than that for the control group.

#### 8.3.2.2 Computer-based rehabilitation therapy

There were two studies assessing computer-based rehabilitation interventions. See Table A8.4 in the appendices of this report for a summary of the study details and results.

A UK study estimated the cost-utility of self-managed computer therapy for stroke survivors with long-standing aphasia.[278] The intervention was compared with usual care which comprised general language stimulation. The evaluation used a decision-analytic model that was populated with data on 28 patients collected as part of a previous RCT. The model had three health states (initial level of aphasia, response state, and death) and followed participants to end of life. The gain in quality-adjusted life years (QALYs) were 3.07 for controls and 3.22 for the intervention. The total cost was €25,036 for controls and €25,621 for intervention participants. The incremental cost-effectiveness ratio (ICER) was therefore €4,097 per QALY. The authors concluded that there was a high likelihood of the intervention being cost-effective at a willingness-to-pay threshold of £20,000 per QALY. The utility data used in the model were not well-described in either the article or the cited trial, therefore making it impossible to determine if some of the assumptions in the model were appropriate. The underlying trial was a pilot study and used a very small sample size.[280] Hence, it is not possible to state whether the findings of the study are applicable to the Irish setting.

Additionally, a virtual reality-based telerehabilitation programme in Spain, comparing home-based and clinic-based delivery of the programme, was assessed.[279] The intervention used a computer system linked to a motion-sensing device to provide interactive exercise routines for stroke patients with residual hemiparesis (weakness of one side of the body, in its severest form, a complete paralysis of the side of the body). The data were derived from an RCT with 30 participants followed up over three months. Both intervention and control groups showed significant improvements in balance, although no significant differences were found between the groups. The mean cost per participant was €820 for the intervention, and €1,461 for controls. The clinic-based treatment required more physical therapist time and

greater patient travel costs. The home-based treatment generated greater equipment costs (US $800 [€784] per participant). The relevance of the study is questionable as the intervention is not compared with routine care.

## 8.4 Discussion

This section discusses the main findings from the review of the clinical-effectiveness and cost-effectiveness literature.

### 8.4.1 Clinical effectiveness

As a chronic disease, stroke is very different to other long-term illnesses in that it is a sudden onset disease with varying levels of sudden, potentially permanent impairments. Stroke patients typically require greater professional care initially, and where possible followed by a transition to greater responsibility by the individual for their own care. This is reflected in the stroke self-management support (SMS) clinical-effectiveness literature retrieved, which is largely focused on rehabilitation therapy. Self-management for stroke is not as clearly defined as in other chronic diseases. However, rehabilitation therapy, although not specifically termed self-management, involves varying components of self-management support such as problem solving, goal setting and improving self-efficacy and decision-making.

It was difficult to categorise the remaining reviews retrieved by intervention type as there was large heterogeneity across the interventions. However, to aid interpretation of the results the reviews were broadly categorised as 'stroke self-management programmes', 'information provision' and other 'SMS interventions'. The 'other SMS interventions' included one review per intervention and included motivational interviewing, psychosocial interventions, interventions to improve self-efficacy, caregiver problem solving, multidisciplinary care at home, lifestyle interventions (including education) and family-orientated interventions.

The duration of follow-up for all stroke-component randomised controlled trials (RCTs) was inconsistently reported by the included systematic reviews, with a maximum duration of follow-up of 12 months reported. This makes it difficult to draw conclusions in relation to the sustainability of any effect observed.

The largest evidence base retrieved by PRISMS — and in the updated search — was for rehabilitation therapy. There is strong evidence that general rehabilitation therapy delivered in early stroke recovery has a positive impact on activities of daily living (ADL) and extended ADL. The majority of general rehabilitation therapy interventions reported in the identified systematic reviews were delivered by occupational therapists (OTs). The updated search added little to the existing knowledge on general rehabilitation. However, it identified new evidence for the use of virtual reality-based and telerehabilitation interventions in post-stroke care.

PRISMS did not include telemedicine interventions in stroke based on limited evidence retrieved.

The findings for virtual reality-based interventions are based on the most comprehensive of the four systematic reviews retrieved (n=37 RCTs). It reported that the use of virtual reality and interactive video games may be beneficial in improving upper limb function and activities of daily living when used in addition to usual care as it increases overall therapy time. However, it was highlighted that it was unclear if effects are sustained in the longer term. Based on limited evidence, however, telerehabilitation does not improve activities of daily living or upper limb function for post-stroke patients compared with usual care.

Although not meeting our inclusion criteria, evidence from a Cochrane review of early supported discharge supports these findings for early delivery of rehabilitation therapy. This Cochrane review assessed any intervention that aimed to accelerate discharge from hospital for a selected group of post-stroke patients (moderate disability) via providing support (with or without a therapeutic rehabilitation intervention) in a community setting (early supported discharge). Compared with conventional care, patients who received early supported discharge returned home earlier and were more likely to be independent and living at home six months post-stroke. They were also more likely to express satisfaction with the care received, with no apparent adverse effects on mood or subjective health status of the patients or their carers.[281]

Based on one Cochrane review, the PRISMS report concluded that there is some evidence that 'information provision', particularly when provided in a way that more actively involves patients and carers, has beneficial effects on mood. Our update is broadly consistent with this finding in that the update to this Cochrane review reported a smaller, but still significant effect in terms of depression, which, however, may not be clinically significant. It is reported that there is a high incidence of mood disorders in stroke patients (31%)[282] and PRISMS qualitative analysis suggests that stroke survivors continue to struggle once their physical recovery has plateaued and their rehabilitation therapy is withdrawn. PRISMS also noted that 'information provision' using education via lectures, for example, was associated with improvements in patient and carer knowledge of stroke. The best way to provide information is reported as unclear, but that active information provision (that is, included a purposeful attempt to allow the participant to assimilate the information and included a subsequent agreed plan for clarification and consolidation or reinforcement) may be more effective than passively providing information. Findings in the updated search were consistent with this. Of note, in defining the evidence-based criteria for official certification as a European Stroke Organisation (ESO) stroke unit or ESO stroke centre, the ESO has included the provision of information

to patients and their carers as one of the stated criteria — this should include information about diagnostics, therapies, rehabilitation and prognosis.[283]

A range of other SMS interventions were identified between the PRISMS review and the updated search, each comprising one systematic review per intervention. PRISMS found some evidence that stroke liaison, emphasising education and information, can have a positive impact on quality of life. However, based on the available evidence, it is not possible to draw conclusions in relation to the efficacy of other SMS interventions including stroke self-management programmes, psychosocial intervention, motivational interviewing, multidisciplinary care or family-orientated models of care in the management of post-stroke patients.

It would appear that the evidence should be somewhat applicable to the Irish healthcare setting given the description of the stroke patient populations and the healthcare systems in which the interventions were provided. A potential caveat to this assumption is the extent to which the intervention or comparator (usual care) in these RCTs is representative of usual care in Ireland. With the increasing tendency for usual or standard of care to be determined by evidence-based clinical guidelines and the convergence of such guidelines in Western countries, this assumption is not unreasonable in relation to acute post-stroke care. However, post-stroke rehabilitation services have historically been chronically under resourced in Ireland and lacked a coherent national strategy to guide their development.

The 2010 *Cost of Stroke in Ireland* report estimated that total direct and indirect stroke costs were between €489 million and €805 million in Ireland in 2007. Nursing home costs accounted for the largest proportion of total direct costs (greater than 60%), followed by hospital costs (greater than 15%, including inpatient rehabilitation) and drug costs (approximately 3%). The report highlighted the limited availability of national data on the proportion of patients receiving inpatient and community rehabilitation, thereby making it difficult to determine gaps in service provision.[247] The HSE's National Clinical Programme for Rehabilitation Medicine was established in 2010 with an objective of extending access to specialist rehabilitation services for people with acquired disability (including stroke survivors) to enable them to maximise their ability, reduce their dependency, and increase societal participation. A model of care has been developed by the HSE that advocates a framework where patients are managed by specialist rehabilitation clinicians working as part of a managed clinical rehabilitation network (MCRN).[284] Similar to the National Policy and Strategy for the Provision of Neuro-Rehabilitation services in Ireland published by the Department of Health in 2011,[285] the draft model of care document identified key gaps in relation to the provision of supports in Ireland, specifically: an extensive shortage of key specialists involved in the provision of neurological rehabilitation services; a lack of: inpatient rehabilitation beds,

appropriate post-acute rehabilitation facilities, services in residential facilities and nursing homes and appropriate community rehabilitation; an absence of pathways to signpost appropriate services, and referral and transition processes; patchy access for patients to certain services determined by historical availability rather than clinical need; lengthy delays in effecting house adaptations; inadequate provision of essential aids, appliances and assistive technology. The proposed model of care outlines a blueprint for future provision of services that addresses these deficits.

Due to the volume of evidence available, and in the interest of efficiency, this assessment of SMS interventions in stroke survivors was undertaken in the form of an overview of reviews. As discussed in Chapter 3.4.1, a disadvantage of this approach is the inability of an overview of reviews to reflect the most recent literature; following publication of an RCT, it must first be captured in a systematic review, before subsequently being captured in an overview of reviews. However, given their sample sizes, it is not appropriate to draw conclusions on the effect of an intervention based on a single, or a number of small, RCTs. Therefore, it is unlikely that more recent RCTs not captured in this overview of reviews would be sufficient to substantially alter recommendations informing major policy decisions.

### 8.4.2 Cost-effectiveness

The four included studies provided very limited evidence regarding the costs or cost-effectiveness of self-management programmes for survivors of stroke. Only one of the studies could be considered to be high quality, although that study did not include any sensitivity analysis.

The studies gathered cost data as part of an RCT or non-randomised trial with relatively small sample sizes. A number of the studies were framed as exploratory or pilot studies, with three of the studies having samples sizes of between 28 and 30 patients. Where reported, the cost of the intervention was typically low, particularly relative to the overall cost of care. Whether costs would be similar in a programme rolled out to a larger population, or if economies of scale might apply, is unclear.

The periods of follow-up were typically short with the longest duration being 12 months. The length of follow up may have implications for estimates of both costs and clinical effectiveness. Longer-term evidence would be required to determine if benefits in intervention groups are sustained, and whether costs change over time.

Only one study was structured as a conventional economic evaluation.[278] That study was based on a small RCT with eight months of follow-up and made a number of assumptions about clinical effectiveness that may not have been supported by the evidence. That study was also specific to stroke survivors with long-standing aphasia, which is estimated to affect approximately one in three people who survive stroke.

The best evidence was generated by the UK RCT of an exercise and education programme.[277] That study used a relatively large sample size of 243 patients and collected follow-up data at 12 months. They study showed a statistically significant benefit of an individual's ability to reintegrate to a 'normal' lifestyle in terms of the Subjective Index of Physical and Social Outcome scale at 12 months and some evidence of benefit in terms of quality of life. It also showed that the cost of care was higher for the intervention group, which was only partly accounted for the by the greater cost of the intervention itself.

In summary, there is very limited evidence on the cost-effectiveness of chronic disease SMS interventions for stroke survivors, which comprised results from a number of RCTs with typically small sample sizes and short follow-up periods. This is in contrast to the review of the clinical-effectiveness literature, which included 27 systematic reviews of 228 unique RCTs. The UK study of an exercise and education intervention may be applicable in an Irish setting.[277] That study found the intervention resulted in improvements in the Subjective Index of Physical and Social Outcome scale. Costs associated with those in the intervention group were, on average, €1,108 higher over 12 months than for those in the control group. It is unlikely that the remaining three identified studies would be applicable to introducing a SMS programme for stroke survivors in Ireland.

## 8.5 Key points

- Twenty seven systematic reviews of self-management support interventions in adults with stroke were retrieved in this overview of reviews.
- A diverse range of heterogeneous interventions were identified, thereby making it difficult to categorise the results by intervention type. The largest volume of evidence (n=14) retrieved was for rehabilitation therapy (general rehabilitation therapy (n=9); virtual reality rehabilitation (n=4); and telerehabilitation (n=1). Three reviews assessed stroke self-management programmes and two assessed information provision. The remaining reviews assessed a range of interventions with one review per intervention type.
- The quality of the systematic reviews varied, with 10 rated as being higher quality reviews.
- The primary evidence underpinning the systematic reviews was found to be generally at moderate to high risk of bias, meaning that studies may have over- or under-estimated effect sizes. It comprised 228 unique randomised controlled trials published between 1981 and 2014.
- Based on the quantity and quality of the systematic reviews and the underpinning primary randomised controlled trials, there is good evidence that general rehabilitation therapy delivered in early stroke recovery has a positive

impact on activities of daily living and extended activities of daily living. Virtual reality-based rehabilitation improves upper limb function and activities of daily living when used as an add-on to usual care.

- Based on the available evidence, it is not possible to draw conclusions in relation to the effectiveness of self-management programmes delivered to post-stroke patients.
- There is some evidence that 'information provision' improves patient and carer knowledge of stroke, aspects of patient satisfaction, with small reductions (which may not be clinically significant) in patient depression scores.
- There is some evidence that stroke liaison emphasising education and information can have a positive impact on quality of life.
- Based on the available evidence, it is not possible to draw conclusions in relation to the effectiveness of psychosocial interventions, motivational interviewing, lifestyle interventions, multidisciplinary care or family-orientated models of care.
- There is very limited evidence on the cost-effectiveness of chronic disease self-management support interventions for stroke survivors with only four relevant studies retrieved. These were based on cost data collected alongside randomised controlled trials that used small sample sizes and short follow-up periods.
- Where reported, the cost of the self-management support interventions was typically low, particularly relative to the overall cost of care. However, it is unclear if costs would be similar when programmes are rolled out to a larger population or if economies of scale might apply. Longer-term evidence would be required to determine if benefits in intervention groups are sustained, and whether costs change over time.
- Based on the description of the healthcare systems, the epidemiology, and the stroke patient populations in the included studies, and assuming that what constitutes 'usual care' is similar in Western countries, the majority of findings of this overview of clinical effectiveness are expected to be applicable to the Irish healthcare setting, while results of only one cost-effectiveness study on exercise-based interventions was likely to be relevant.

# 9 Ischaemic heart disease

This health technology assessment (HTA) of ischaemic heart disease self-management support (SMS) is one of a series of rapid HTAs assessing SMS interventions for chronic diseases. Section 9.1 provides a brief description of ischaemic heart disease followed by separate reviews of the clinical (Section 9.2) and cost-effectiveness (Section 9.3) literature on such interventions for ischaemic heart disease. Brief descriptions of the background and methods used are included with full details provided in a separate document (Chapter 3). Section 9.4 includes a discussion of both the clinical and cost-effectiveness findings. The report concludes with a list of key points in relation to ischaemic heart disease SMS support (Section 9.5).

## 9.1 Description of the disease

Ischaemic heart disease (IHD) is a chronic condition characterised by narrowing and hardening of the arteries that supply blood to the heart muscle. This occurs as a result of the build up of cholesterol and other materials on the interior wall of the artery, through a process called atherosclerosis. Restriction of blood supply to the heart can result in angina or myocardial infarction. IHD claims around 5,000 lives annually in Ireland, which represents approximately half of all cardiovascular deaths.[286] As well as being associated with significant mortality, it can also weaken the heart muscle over time, which can lead to the development of heart failure and cardiac arrhythmias.

## 9.2 Review of clinical-effectiveness of self-management support interventions

### 9.2.1 Background and methods

The aim of this HTA is to review the clinical effectiveness of self-management support (SMS) interventions for a number of chronic conditions including ischaemic heart disease (IHD). Given the large volume of literature available, it was noted that an update of an existing high-quality systematic review — or a review and appraisal of previously completed systematic reviews — of the effectiveness of SMS interventions could be considered sufficient to inform decision making.

IHD was not specifically addressed in the PRISMS report, and no other existing review of reviews was identified for the disease. This report therefore presents a de novo review of systematic reviews, rather an update of an existing report. Data extraction and quality assurance of the systematic reviews, meta-analyses and the

risk of bias associated with the primary literature was undertaken as described in Chapter 3.1.3.

In summary, in order to determine the quantity, quality, strength and credibility of evidence underpinning the various SMS interventions, quality assurance of both the systematic review methodology (R-AMSTAR weighting by patient or participant trial size) and the meta-analyses (Higgins et al.'s quality assessment tool)[287] was undertaken. While the R-AMSTAR score was used to determine the quality of the systematic reviews, the scores were then weighted by patient or participant trial size, with the quality of evidence being downgraded if the review was based on fewer than 1,000 participants. In addition, while the quality of the primary evidence was not evaluated directly, where reported, information on the risk of bias in the primary studies was extracted from the systematic reviews.

### 9.2.2 Description of the interventions

A general description of self-management and typical self-management support (SMS) interventions is included in Chapter 2. Interventions specific to IHD introduced in this Phase IIb report include patient education, psychosocial or behavioural therapy and exercise programmes (including exercise based cardiac rehabilitation), as well as different methods of care provision such as home visits or via telephone or the Internet.

Cardiac rehabilitation has been defined as 'a complex intervention offered to patients diagnosed with heart disease, which includes components of health education, advice on cardiovascular risk reduction, physical activity and stress management'. Cardiac rehabilitation services are defined as 'comprehensive, long-term programmes involving medical evaluation, prescribed exercise, cardiac risk factor modification, education and counselling.'[288] While cardiac rehabilitation services may differ in format and intensity, there is consensus regarding the core components, notably: health behaviour change and education; lifestyle risk factor management (including physical activity and exercise, diet, and smoking cessation); psychosocial health; medical risk-factor management; cardio-protective therapies; long-term management; and audit and evaluation.[289] Therefore, cardiac rehabilitation includes elements of self-management support and the boundary between chronic disease self-management and what is considered 'standard' cardiac rehabilitation is often poorly defined in the literature. This is especially true for exercise-based interventions, as the terms cardiac rehabilitation and exercise-based cardiac rehabilitation are often used interchangeably. Exercise-based interventions have been included in this review in order to provide a summary of the evidence available for this particular component of cardiac rehabilitation, which may involve varying degrees of self-management depending on whether the exercise training is

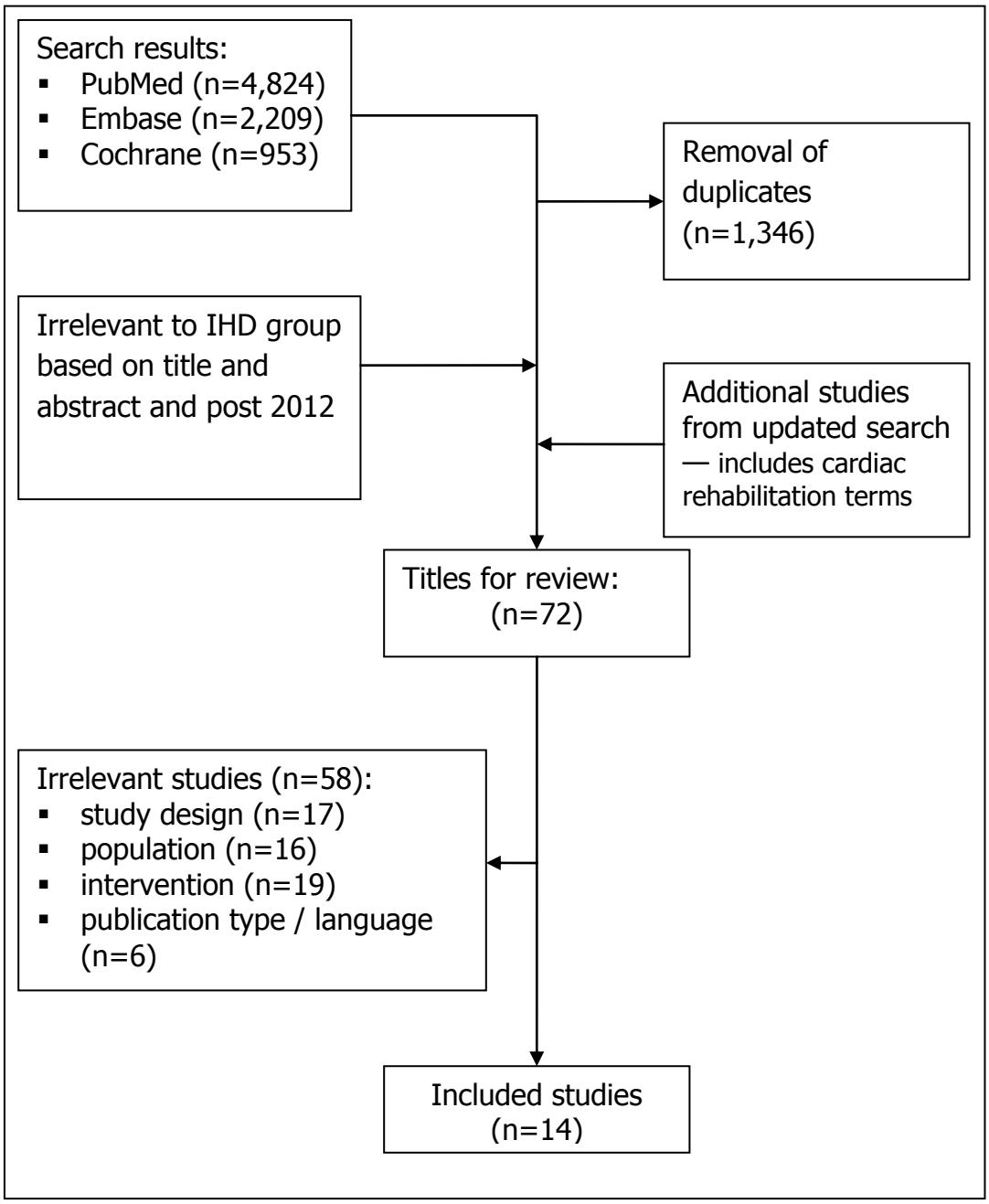
supervised or unsupervised, or takes place in an inpatient, outpatient, community or home-based setting.

### 9.2.3 Clinical effectiveness results

The search identified 14 systematic reviews of chronic disease self-management support (SMS) interventions for people with ischaemic heart disease (IHD), which were published between 2009 and 2015 and were based on randomised controlled trials (RCTs) published between 1974 and 2012 (see Figure 9.1). The quality of the systematic reviews (R-AMSTAR scores) ranged from 18 to 38 out of a maximum score of 44, with 5 out of 12 achieving a score of 31 or more, indicating a high-quality systematic review.

The identified meta-analyses were also assessed for quality with all assessed as high quality, meaning that they were very likely to have conclusions that accurately reflected the available evidence. Table 9.1 shows the different types of interventions that were assessed. Table 9.2 shows the degree of overlap between reviews and Table 9.3 summarises the results for mortality and hospital admissions.

**Figure 9.1 Flowchart of included studies from updated search**




Key: IHD = ischaemic heart disease

## Table 9.1 Summary of included reviews

| Author (year) | Intervention |
|---|---|
| **Patient Education** | |
| Ghisi (2014)[290] | Patient-education interventions |
| Brown (2013)[291] | Patient-education interventions |
| Brown (2011) CR[292] | Patient-education interventions |
| **Psychosocial or behavioural interventions** | |
| Barth (2015) CR[293] | Behavioural therapeutic changes with telephone support and self-help material |
| McGillion (2014)[294] | Supportive coaching, anxiety and stress management or counselling, exercise, nutrition planning, medication review, relaxation training and energy conservation |
| Whalley (2014)[295] | Psychological intervention |
| **Exercise** | |
| Heran (2011) CR[296] | Exercise plus educational or psychological management (or both) and exercise only |
| Lawler (2011)[297] | Supervised or unsupervised cardiac rehabilitation programmes that may have included other interventions, which took place in an outpatient, community or inpatient setting. |
| **Home Visit** | |
| Clark (2010)[298] | Home-based interventions, relating to prevention, rehabilitation and support services |
| Taylor (2010) CR[299] | Home-based cardiac rehabilitation programme |
| **Telehealth** | |
| Huang (2015)[300] | Telehealth delivered cardiac rehabilitation |
| Kotb (2014)[301] | Telephone support |
| Neubeck (2009)[302] | Telephone, videoconference or web-based interventions |
| **Combined Interventions** | |
| Cole (2011)[303] | Interventions that involved dietary changes, exercise, education, psychological or organisational changes. |

**Key**: **CR** = Cochrane review

**Table 9.2 Study overlap between the included systematic reviews**

| | Review (year) | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Barth (2015) | **40** | | | | | | | | | | | | |
| 2 | Brown (2011, 2013) | 2 | **13** | | | | | | | | | | | |
| 3 | Clark (2010) | 0 | 2 | **36** | | | | | | | | | | |
| 4 | Ghisi (2014) | 7 | 1 | 0 | **42** | | | | | | | | | |
| 5 | Heran (2011) | 1 | 0 | 5 | 0 | **47** | | | | | | | | |
| 6 | Huang (2015) | 0 | 0 | 5 | 0 | 1 | **9** | | | | | | | |
| 7 | Kotb (2014) | 5 | 1 | 6 | 1 | 0 | 0 | **26** | | | | | | |
| 8 | McGillion (2014) | 0 | 0 | 1 | 0 | 0 | 0 | 0 | **9** | | | | | |
| 9 | Neubeck (2009) | 2 | 2 | 4 | 0 | 1 | 0 | 5 | 0 | **11** | | | | |
| 10 | Taylor (2010) | 0 | 0 | 7 | 0 | 2 | 4 | 1 | 0 | 0 | **12** | | | |
| 11 | Whalley (2014) | 1 | 0 | 0 | 1 | 1 | 0 | 2 | 1 | 0 | 0 | **24** | | |
| 12 | Lawler (2011) | 3 | 1 | 3 | 0 | 15 | 1 | 0 | 0 | 1 | 2 | **1** | **34** | |
| 13 | Cole (2011) | 2 | 3 | 3 | 2 | 2 | 0 | 1 | 1 | 1 | 0 | 0 | 2 | **21** |

## Table 9.3 Quality appraisal and summary of findings from meta-analyses

| Review | Quality of systematic review | | | Primary studies | | Quality of meta-analysis | All-cause mortality | Disease-specific mortality | Hospital admissions |
|---|---|---|---|---|---|---|---|---|---|
| | R-AMSTAR Score | Participants | Quality | N = | Low-risk | | | | |
| **Patient education** | | | | | | | | | |
| **Brown (2011, 2013)**[291;292] | 34 | 68,556 | *** | 13 | 2 | High | RR 0.79 (0.55 to 1.13) | - | RR 0.83 (0.65 to 1.07) |
| **Ghisi (2014)**[290] | 18 | 16,079 | ** | 42 | - | N/A | - | - | - |
| **Psychosocial or behavioural interventions** | | | | | | | | | |
| **Barth (2015)**[293] | 33 | 7,682 | *** | 40 | - | N/A | - | - | - |
| **McGillion (2014)**[294] | 25 | 1,282 | ** | 9 | - | N/A | - | - | - |
| **Whalley (2014)**[295] | 26 | 9,296 | ** | 24 | 5 | High | RR 0.89 (0.75 to 1.05) | RR 0.80 (0.64 to 1.00) | - |
| **Exercise** | | | | | | | | | |
| **Heran (2011)**[296] | 33 | 10,794 | *** | 47 | 4 | High | RR 0.87 (0.75 to 0.99) | RR 0.74 (0.63 to 0.87) | RR 0.69 (0.51 to 0.93) |
| **Lawler (2011)**[297] | 28 | 6,111 | ** | 34 | - | High | OR 0.74 (0.58 to 0.95) | OR 0.64 (0.46 to 0.88) | - |
| **Home visit** | | | | | | | | | |
| **Clark (2010)**[298] | 24 | 8,297 | ** | 36 | 0 | High | RR 1.08 (0.73 to 1.60) | - | - |
| **Taylor (2010)**[299] | 38 | 1,938 | *** | 12 | 1 | High | RR 1.31 (0.65 to 2.66) | - | - |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Telehealth** | | | | | | | | | |
| **Huang (2015)**[300] | 26 | 1,546 | ** | 9 | 2 | High | RR 1.15 (0.61 to 2.19) | - | - |
| **Kotb (2014)**[301] | 23 | 4,081 | ** | 26 | 14 | High | OR 1.12 (0.71 to 1.77) | - | OR 0.62 (0.40 to 0.97) |
| **Neubeck (2009)**[302] | 27 | 3,145 | ** | 11 | Not reported | Moderate | RR 0.70 (0.45 to 1.10) | - | - |
| **Combined interventions** | | | | | | | | | |
| **Cole (2011)**[303] | 29 | 10,972 | ** | 21 | - | Low | RR 0.75 (0.65 to 0.87) | RR 0.63 (0.47 to 0.84) | - |

**Abbreviations**: **OR** = odds ratio; **RR** = risk ratio.

#### 9.2.3.1 Summary of findings

This section provides a narrative summary of the findings, relevance and applicability of the included reviews for each type of IHD self-management intervention. A detailed account of the data extracted from each review is provided in Appendix A9.1.

#### 9.2.3.2 Patient education interventions

Three reviews of patient education interventions were identified, all of which had combined sample sizes of over 1,000 patients.[290-292] Two reviews that had R-AMSTAR scores of 31 or more (indicating a high-quality review), were found to be duplicate reports of the same evidence.[291;292]

**Three star (***) reviews**

A 2011 Cochrane review (13 RCTs [n=68,556 patients]) of patient education in the management of coronary heart disease reported no significant effect on all-cause mortality, myocardial infarction, revascularisation rates or hospitalisation rates. While the review did find increased quality of life scores in some domains, there was no consistent evidence of superiority.[291;292]

**Two star (**) reviews**

A 2014 qualitative review (42 RCT, n=16,079 patients) examined the effect of patient education on a range of intermediate outcomes such as patient knowledge, physical activity, dietary habits and smoking cessation rates.[290] This review included observational studies as well as RCTs. Of the six RCTs that assessed patient knowledge: four reported a statistically significant positive effect compared with controls, one reported a beneficial effect at four months that had disappeared at one year, and one reported no difference in effect.

Patient-education interventions were found to be associated with a significant beneficial effect in: 77% of all studies that reported physical activity outcomes, 84% of all studies reporting dietary habits, and 65% of all studies reporting smoking cessation rates.

**Summary statement for patient education interventions**

Based on the quantity and quality of the systematic reviews and the underpinning primary randomised controlled trials, there is short-term evidence that patient-education interventions are associated with an improvement in interim outcomes such as physical activity, dietary habits and smoking cessation.

#### 9.2.3.3 Psychosocial or behavioural interventions

Three reviews examined the impact of psychosocial or behavioural interventions in ischaemic heart disease .[293-295] The total sample size in each of these was greater than 1,000. However, only one had an R-AMSTAR score of 31 or more.

**Three star (***) reviews**

A 2015 Cochrane review specifically examined psychosocial interventions for smoking cessation. Based on 40 randomised controlled trials (RCTs) (n=7,682 participants), it reported a positive effect of interventions on abstinence after 6 to 12 months, with a relative risk (RR of 1.22 [95% CI 1.13 to 1.32]).[293]

**Two star (**) reviews**

Two reviews examined the effect of psychosocial or behavioural interventions on ischaemic heart disease symptoms, quality of life and psychological outcomes. One narrative review based on nine RCTs (n=1,282) found a significant improvement in the frequency of angina symptoms, a reduction in the use of sublingual nitrates, as well as improvements in physical limitation and depression scores.[294] This review reported no effect on angina stability, disease perception, or treatment satisfaction. The other review — published the same year, 2014 — and comprising 24 RCTs (n=9,296) reported no strong evidence that psychological intervention reduced total deaths, risk of revascularisation, or non-fatal infarction.[295] However, it noted psychological intervention did result in small to moderate improvements in depression and anxiety, and there was a small effect for cardiac mortality.

**Summary statement for psychosocial or behavioural interventions**

Based on the quantity and quality of the systematic reviews and the underpinning primary randomised controlled trials, there is limited evidence to demonstrate the effectiveness of behavioural modification interventions, although some have reported positive effects on smoking cessation and symptom management.

#### 9.2.3.4 Exercise interventions

Two reviews examined clinical outcomes associated with exercise programmes. As outlined earlier (in section 9.2.3.1), exercise interventions are nowadays considered a central component of 'standard' cardiac rehabilitation programmes.

**Three star (***) reviews**

One high-quality Cochrane systematic review of exercise interventions for ischaemic heart disease was identified. The intervention arm in the studies included exercise

training alone or exercise training in addition to psychosocial and or educational interventions (that is, comprehensive cardiac rehabilitation) and could be supervised or unsupervised. The intervention arm could also be delivered in a variety of settings (inpatient, outpatient, community or home-based) and be of varying intensity.

The control arm included standard medical care such as drug therapy, but did not receive any form of structured exercise training or advice. Pooled analysis from studies with follow-up periods of greater that 12 months showed that compared with no structured exercise training or advice, exercise-based interventions reduced overall mortality and cardiovascular mortality (RR 0.87 [95% CI 0.75 to 0.99] and RR 0.74 [95% CI 0.63 to 0.87] respectively).[296]

A positive effect on hospital admissions was evident from studies with a follow-up period of less than 12 months (RR 0.69 [95% CI 0.51 to 0.93]). Exercise-based interventions did not reduce the risk of total myocardial infarction, coronary artery bypass graft (CABG) or percutaneous transluminal coronary angioplasty (PTCA). In seven out of 10 trials reporting health-related quality of life using validated measures, there was evidence of a significantly higher level of quality of life with exercise-based interventions than with usual care.[296]

### Two star (**) reviews

One other systematic review was identified that assessed exercise-based cardiac rehabilitation post-myocardial infarction. This review was judged by the HTA reviewers to be of lower quality. The intervention arm in the RCTs included: exercise-only cardiac rehabilitation, exercise-based cardiac rehabilitation as part of a comprehensive secondary prevention programme or both in two independent intervention arms, and had a minimum intervention duration of two weeks and a minimum follow up of 12 weeks.

All trials included a non-exercising control arm. This review also found evidence of a reduction in mortality associated with exercise-based programmes (OR 0.74, 95% CI 0.58 to 0.95).[297] A subgroup analysis found that this reduction was only evident in studies with a follow-up period of greater than one year. This analysis also reported statistically significant reductions in disease-specific mortality (OR 0.64, 95% CI 0.46 to 0.88) and re-infarction rates (OR 0.54, 95% CI 0.38 to 0.76).

**Summary statement for exercise interventions**

There is good evidence from studies with follow-up periods of greater than 12 months of a statistically significant reduction in mortality for exercise programmes in suitable patient cohorts. Exercise-based interventions are also associated with fewer hospitalisations, but inconsistent results have been reported in myocardial infarction rates.

#### 9.2.3.5 Home visit interventions

Two reviews of home-based interventions for the management of ischaemic heart disease were identified.[298;299] The combined sample size of each of these exceeded 1,000 patients, but only one had an R-AMSTAR score over 30.[299]

**Three star (***) reviews**

A 2010 Cochrane review found no difference in outcomes of home versus centre-based cardiac rehabilitation on mortality, cardiac events, exercise capacity or non-modifiable risk factors (blood pressure, cholesterol) or proportion of smokers at follow-up or health-related quality of life.[299] Neither was there a consistent difference in healthcare costs.

**Two star (**) reviews**

A separate systematic review of RCTs published in 2010 also found no statistically significant effect of home-based programmes on mortality or the rate of cardiovascular events.[298] However, compared with usual care, home-based interventions significantly improved quality of life, systolic blood pressure, smoking cessation and total cholesterol. Home-based secondary prevention interventions are formalised interventions for the secondary prevention of coronary heart disease (CHD) with predominant or exclusive home-based components, which can be provided in a range of ways including paper, face-to-face, electronic, or telephone-based methods.[298] Usual care was defined as normal healthcare and or risk factor management at the time the trial was undertaken without supplementary secondary prevention intervention. Cardiac rehabilitation was defined as dedicated secondary prevention programmes provided by healthcare professionals in an acute (hospital) or community care provider setting.[298] The authors reported that comparisons between home-based interventions and cardiac rehabilitation could not be made because of the small number of trials and high levels of heterogeneity.

**Summary statement for home visit interventions**

There is limited evidence that home-based and centre-based interventions have comparable outcomes.

#### 9.2.3.6 Telemedicine interventions

Three reviews of telemedicine interventions in ischaemic heart disease were identified in the search, all of which included studies with a combined total of more

than 1,000 patients. However, none had an R-AMSTAR score of greater than 31.[300-302] Two studies compared telehealth interventions to usual care and one compared telehealth interventions to supervised, centre-based programmes.

**Two star (**) reviews**

Of the two with the usual care comparator, one only included telephone-based interventions and found no difference in mortality or cholesterol levels. However, it did report fewer hospitalisations (OR 0.62 [95% CI 0.40 to 0.97]), better smoking cessation rates (OR 1.32 [95% CI 1.07 to 1.62]), reduced blood pressure and lower depression and anxiety scores (standardised mean difference (SMD) 20.10 [20.21 to 20.00] and SMD 20.14 [20.24, 20.04], respectively).[301] The other review compared any telehealth intervention (telephone, Internet, and videoconferencing) to usual care, also finding no statistically significant difference in mortality (RR 0.70 [95% CI 0.45 to 1.1]), but beneficial effects on total cholesterol levels (weighted mean difference (WMD) 0.37 mmol/l [95% CI 0.19 to 0.56]), systolic blood pressure (WMD 4.69 mmHg [95% CI 2.91–6.47]) and smoking cessation (RR 0.84 [95% CI 0.65 to 0.98]).[302]

The final review compared cardiac rehabilitation provided using telehealth to centre-based cardiac rehabilitation. This review found no statistically significant difference in any of the outcomes examined, which included mortality, blood pressure, lipid profile, smoking, exercise capacity, weight and quality of life.[300] Non-inferiority of telehealth outcomes would be advantageous if the cost of this type of intervention was lower than supervised, centre-based cardiac rehabilitation. However, the review found that although the evidence was limited, the costs of both type of intervention appear to be similar.

**Summary statement for telemedicine interventions**

There is limited evidence that telemedicine and centre-based interventions have comparable outcomes.

### 9.2.3.7 Combined interventions

**Two star (**) reviews**

One systematic review that examined the clinical effectiveness of interventions that included dietary advice, exercise, psychological or educational interventions, and organisational improvements reported statistically significant improvements in all cause and cardiovascular mortality (RR 0.75 [95% CI 0.65 to 0.87] and RR 0.63 [95% CI 0.47 to 0.84] respectively). It also reported a reduction in non-fatal cardiac events such as myocardial infarction or revascularisation procedures (RR 0.68 [95% CI 0.55 to 0.84]).[303] However, a limitation of these multifactorial interventions is an

inability to determine the relative contribution of each of the different elements of the interventions to the improved outcomes reported.

**Summary statement for combined interventions**

There is moderate quality evidence that interventions that combine multiple types of chronic disease self-management interventions are associated with improved outcomes. However, the relative impact of each component of these interventions is unclear.

## 9.3 Review of cost-effectiveness of SMS interventions

A review of cost-effectiveness studies was undertaken to assess the available evidence for self-management support interventions for patients with ischaemic heart disease . Studies were included if they compared the costs and consequences of an SMS intervention with routine care.

### 9.3.1 Search strategy

A search was carried out to identify economic analyses of SMS interventions. In tandem with the systematic review of clinical effectiveness, the search for economic evaluations was carried out in MEDLINE, EMBASE and the Cochrane Library. The same search terms were used with the exception of terms for systematic review and meta-analysis. In place of these, search terms and filters for economic evaluations were applied. The search was undertaken up until 4 March 2015.

The PICOS (Population, Intervention, Comparator, Outcomes, Study design) analysis used to formulate the search is presented in Table 9.4 below.

**Table 9.4 PICOS analysis for identification of relevant studies**

| | |
|---|---|
| **Population** | Adults greater than or equal to [≥] 18 years old that had ischaemic heart disease . |
| **Intervention** | Any self-management support intervention that helps patients with ischaemic heart disease through education, training or support. |
| **Comparator** | Routine care. |
| **Outcomes** | Cost or cost-effectiveness of the intervention. |
| **Study design** | Randomised controlled trials, case-control studies, observational studies, economic modelling studies. |

Study types were excluded if:

- a nursing home or non-community dwelling population was included
- it included a paediatric population
- cost data were not clearly reported
- published prior to the year 2000 (limited relevance).

As outlined in Chapter 3.2.2 and in accordance with national HTA guidelines, assessment of the quality of the studies using the Consensus on Health Economic Criteria (CHEC)-list was performed independently by two people. For studies that included an assessment of cost-utility or an economic modelling approach, assessment of the relevance to the Irish healthcare setting and their credibility was considered using a questionnaire from the International Society of Pharmacoeconomic Outcome Research (ISPOR).

### 9.3.2 Cost-effectiveness results

The initial screening retrieved 41 papers relating to ischaemic heart disease. Of these, fifteen studies were identified for full text review, with the remaining 27 excluded as irrelevant or unsuitable based on screening of abstract or full text. There were three studies from the US, four from the UK, two from Australia, and one from Denmark, Netherlands, Belgium, Italy and Germany. The included studies were all published between 2003 and 2015. The characteristics of the included studies are given in Table 9.5.

### Table 9.5. Characteristics of the included studies

| Study | Country | Intervention |
|---|---|---|
| **Ballegaard (2004)**[304] | Denmark | Cardiac rehabilitation |
| **Barley (2014)**[305] | UK | Case management |
| **Berndt (2015)**[306] | Netherlands | Telemedicine |
| **Briffa (2005)**[307] | Australia | Cardiac rehabilitation |
| **Dendale (2008)**[308] | Belgium | Cardiac rehabilitation |
| **Furze (2012)**[309] | UK | Lay-facilitated angina management |
| **Ito (2012)**[310] | US | Multiple interventions |
| **Jolly (2007)**[311] | UK | Cardiac rehabilitation |
| **Ladapo (2011)**[312] | US | Smoking cessation |
| **Marchionni (2003)** | Italy | Cardiac rehabilitation |
| **Reid (2005)**[313] | US | Cardiac rehabilitation |
| **Seidl (2014)**[314] | Germany | Case management |
| **Taylor (2007)**[315] | UK | Cardiac rehabilitation |
| **Turkstra (2013)**[316] | Australia | Telemedicine |
| **Raftery (2005)**[317] | UK | Nurse-led secondary prevention programme |

The studies were classified according to the type of intervention assessed: cardiac rehabilitation, case management, telemedicine, and 'other' interventions (including complex interventions, and nurse-led, pharmacist-led and lay-led education interventions). Some studies combined elements of different intervention types.

The quality of the included studies was predominantly poor, and the following discussion sections will focus on the findings of studies found to be of better quality. Cost effectiveness results from each included study reported in this section were converted to 2015 euro.

#### 9.3.2.1 Cardiac rehabilitation

Seven studies were retrieved that evaluated cardiac rehabilitation. See Table A9.3 in the appendices for a summary of the study details and results. One was a cost-utility analysis, while the remaining six were costing or cost-minimisation studies. Two of the studies were from the UK with one each from the US, Australia, Italy, Belgium and Denmark. In three studies, the comparator was no cardiac rehabilitation (routine care), while for the other four studies, the comparator was different modes of delivery of cardiac rehabilitation (home- versus hospital-based rehabilitation [n=3], and intensive versus dispersed rehabilitation [n=1]). Study follow-up ranged from nine months to 13 years.

A 2005 study carried out in Australia by Briffa et al.[307] compared an 18-session comprehensive exercise-based outpatient cardiac rehabilitation programme with conventional care (no cardiac rehabilitation) in 113 patients with ischaemic heart disease aged 41–75 years who had experienced an acute coronary syndrome. Patients allocated to rehabilitation were offered a six-week package of sessions three times a week, each comprising 60–90 minutes of supervised exercise, combined with 45 minutes of education (12 occasions) and 45 minutes of psychosocial counselling (six occasions).

Sessions were conducted in groups (maximum of 15 people) and, if necessary, additional one-to-one counselling was provided. Non-exercise sessions addressed symptom management, pharmacological treatment, healthy eating, psychosocial counselling and stress management delivered by a clinical nurse consultant, physiotherapist, clinical psychologist, dietician, social worker or pharmacist. Rehabilitation costs of €647 per patient were offset by a reduction in follow-up costs of €242, resulting in a non-significant (p=0.75) increase in costs of €405 per patient compared with the control group. Gains in utility scores from baseline were observed for both the intervention and control groups at 6 and 12 months. While the estimated improvement in utility was higher in rehabilitation patients at 12 months, the difference between improvements in the conventional and rehabilitation groups was not significant (p = 0.38). The estimated gain in QALYs was 9.289 per 1,000 patients up to 12 months for the intervention group, providing an incremental cost-effectiveness ratio (ICER) of €43,589 per QALY saved. The intervention was suggested to be an effective treatment and although non-significant advantages were reported in terms of quality of life, the cost of delivering rehabilitation was low.

A 2008 Belgian study by Dendale et al.[308] compared a cardiac rehabilitation programme for patients' post-percutaneous coronary intervention (PCI) with standard care (no cardiac rehabilitation). The intervention comprised a three-month rehabilitation programme comprising 24 one-hour supervised exercise training sessions, dietary and psychological counselling as well as counselling to participate in an eight-week smoking cessation programme where applicable. The study took the perspective of the healthcare provider and evaluated patients over a 4.5 year follow-up period. The study estimated that the cost of one cardiac rehabilitation session to be €27 per patient.

The cardiac rehabilitation programme resulted in a significant reduction in hospitalisations for angina (75% versus 45%, p<0.05) and coronary revascularisations (17% versus 7%, p<0.05). However, a significant (p<0.05) increase in non-fatal myocardial infarction was reported (2.5% versus 7.5%). Overall, the intervention resulted in a lower incidence of cardiac events with an incidence rate of 0.93 compared with 1.52 for the control group. The total cost for

the intervention and control groups were €5,655 per patient and €6,395 per patient, respectively, a difference of €636, with the difference in cost being attributed to reduced hospitalisations for angina and repeat PCI in the intervention group.

A home-based cardiac rehabilitation programme using a 'Heart Manual' was compared with conventional centre-based cardiac rehabilitation in the 2007 UK study by Jolly et al.[311]. The study recruited patients who had experienced an MI or coronary revascularisation within the previous 12 weeks from four hospitals in predominantly inner-city, multi-ethnic, socio-economically deprived areas for a randomised controlled trial with a 24-month follow-up period. The mean cost per home-based cardiac rehabilitation patient was €337, approximately 25% above that of the hospital arm of €267. No differences in primary or secondary clinical outcomes were reported during the trial period. Incremental QALYs reported after the 24-month period for home-based and centre-based care were 0.731 and 0.753, respectively, a difference of 0.022. Discounting of costs or benefits was not reported. The study reported costs from both a societal and health service perspective.

From a National Health Service (NHS) perspective, the home-based arm was more costly than the hospital-based arm. From a societal perspective, however, the inclusion of patient travel costs and travel time increased the mean cost of the hospital-based arm to €308. The study concluded that for low to moderate risk patients with ischaemic heart disease , a home-based cardiac rehabilitation programme does not produce inferior outcomes compared with the traditional centre-based programmes. With the level of home visiting in this trial, the home-based programme was more costly to the health service, because costs associated with the centre-based programmes were borne by the patients who incurred substantial out-of-pocket travel costs.

Additionally, a cost-effectiveness analysis was undertaken in the 2007 UK study by Taylor et al.[315] to evaluate home- versus hospital-based cardiac rehabilitation. Using the perspective of the healthcare system, the study compared the costs and consequences for 104 patients with an uncomplicated acute myocardial infarction and without major co-morbidity randomised to home-based ('Heart Manual') or hospital-based rehabilitation over a nine-month follow-up period. The cost of the home and hospital-based rehabilitation interventions were €279 and 328 per patient, respectively. Therefore, home-based cardiac rehabilitation was €51 per patient less than for the hospital-based group. Mean utility values for the home and hospital groups were comparable at baseline (0.76 vs. 0.74), and nine months (0.74 vs. 0.78), with no significant difference between the groups (p=0.06). Overall healthcare costs for the home and hospital-based groups did not differ significantly.

Although the evidence presented seems to favour hospital-based cardiac rehabilitation, the authors noted that the findings were not conclusive due to the small sample size, short duration of follow up and high variability in healthcare costs between patients. Further sensitivity analysis found that simulations included all four-quadrants of the cost-effectiveness plane and ranged from a small QALY gain and lower cost in favour of hospital-based rehabilitation to a small QALY gain and lower cost in favour of home-based rehabilitation.

The 2005 US study by Reid et al.[313] aimed to determine the most efficient delivery of cardiac rehabilitation. To achieve this, the study compared standard care (33 sessions over three months) with distributed care (33 sessions over 12 months) delivery. At two years, the total direct costs of the distributed rehabilitation were €6,073 (€875 for programme delivery + €5,198 for cardiac healthcare costs) versus €5,918 for standard cardiac rehabilitation (€785 for programme delivery + €5,132 for cardiac healthcare costs). There were no clinically meaningful or statistically significant differences between the groups for outcomes at 12 or 24 months; however, generic and heart disease health-related quality of life (HRQoL) were noted to improve for both groups.

#### 9.3.2.2 Telemedicine programmes

Two studies were retrieved that evaluated telemedicine programmes. Both were cost-utility studies that collected cost and utility data alongside randomised controlled trials (RCTs). The studies were from the Netherlands and Australia, and had trial follow-up periods of six months. See Table A9.4 in the appendices for a summary of the study details and results.

The 2013 Australian RCT (n=430) by Turkstra et al.[316] evaluated a telephone-delivered health-coach intervention versus usual care as secondary prevention for adult myocardial infarction patients. Primary outcome variables were health-related quality of life (HRQoL) and physical activity levels. The intervention consisted of ten 30-minute scripted telephone health coaching sessions over a six-month period from a qualified health professional or 'health coach'. Usual care involved providing existing written educational resources. The cost of the health coach was €26 per session, which accounted for little of the overall costs. The major difference in costs between groups was the cost for hospitalisation, with higher average hospitalisation costs (€4,893 versus €3,565) and total treatment costs (€7,563 versus €6,104) for patients randomised to the intervention group. Compared with usual care, the intervention was more costly (increase of €1,459) and more effective (0.012 additional quality adjusted life years [QALYs]), generating an incremental cost-effectiveness ratio (ICER) of €61,102 per QALY. It was concluded that the telemedicine intervention was not a cost-effective intervention in the short-term compared with usual care.

In a 2015 Dutch study, Berndt et al.[306] compared usual care with a combination of telephone or face-to-face smoking cessation counselling in addition to nicotine replacement therapy in ischaemic heart disease patients. This RCT (n=625) with six-month follow up included patients over 18, who were recently hospitalised and who smoked five or more cigarettes on average per day prior to admission or quit smoking less than four weeks prior to admission. Usual care comprised a risk assessment, advice to quit smoking, and occasionally written educational material; no follow up was included. Telephone counselling lasted for three months and consisted of seven telephone calls of 10 to 15 minutes each. Face-to-face counselling delivered by nurses comprised six sessions of 30 to 45 minutes each over three months and concluded with a follow-up call five weeks after the last session. Compared with usual care, a significantly higher proportion of patients in the telephone group and face-to-face-based counselling groups achieved continued abstinence (37.9%, 54.1%, 51.6%, respectively) and seven-day abstinence (41.5, 57.1, 54.9, respectively) at six-months follow-up. The cost-utility analysis was undertaken from the societal perspective with results reported as costs per QALY. Telephone counselling had lower costs and slightly higher effects than either usual care or face-to-face counselling, and thus dominated the other treatments. In contrast, face-to-face counselling was dominated by usual care as it was more costly and less effective. The reported QALYS for usual care, telephone- and face-to-face-based counselling were 0.489, 0.491 and 0.487 respectively, while societal costs were €9,372, €8,293and €9,175 respectively.

The authors concluded that assuming a willingness-to-pay of €20,000 per abstinent patient, telephone counselling combined with nicotine replacement therapy would be a highly cost-effective smoking cessation intervention assisting cardiac patients to quit. However, they highlighted the lack of consensus concerning the willingness-to-pay per quitter and noted that studies with extended follow-up periods are needed to capture late relapses and possible differences in QALYs.

#### 9.3.2.3 Case management

Two studies were identified that evaluated the cost-effectiveness of nurse-delivered case management programmes for patients with ischaemic heart disease . The studies from Germany and the UK gathered cost and utility data alongside RCTs with 12-month follow-up. See Table A9.5 in the appendices for a summary of the study details and results.

A nurse-based case management programme for elderly patients (65 years and older) with a recent myocardial infarction (n=329) was evaluated in a 2014 paper by Seidl et al.[314]. The intervention comprised at least one home visit and quarterly telephone calls, with additional visits and calls according to the patient's needs and risk levels. Usual care comprised regular physician visits, in-hospital cardiac

rehabilitation and or long-term disease management programmes offered by health insurance companies. On average, patients received 1.41 home visits and 3.85 telephone interviews in the intervention group. The cost of the intervention was estimated at €145 per patient. Utility scores measured using the EQ-5D-3L were significantly increased from baseline in the intervention group at month three (0.077) and month six (0.0509), but returned towards baseline levels by month 12.

The mean QALY difference at 12 months, adjusted for gender, age in groups and number of co-morbidities, between the intervention and control groups was -0.0163 (p=0.536). Total costs for the intervention and control groups were €9,223 and €9,881, respectively; the average overall cost difference per patient at 12 months was -€20 (p=0.9856). Direct healthcare costs were driven by hospitalisation costs (60%), which were not significantly lower in the intervention group (-€466). The study concluded that the case management intervention was not an effective or cost-effective alternative to usual care within a time horizon of one year.

A 2014 UK pilot study by Barley et al.[305] evaluated the UPBEAT programme for adults with symptomatic coronary heart disease, reporting symptoms of depression. This was a multi-centre outcome assessor-blinded, parallel group study (n=81) with eligible patients randomised to personalised care or treatment as usual for six months and followed for one year. The intervention consisted of standardised, face-to-face, biopsychosocial assessments by nurse case managers, the results of which were used to help patients to increase their self-efficacy to achieve their desired goals. Follow-up telephone interviews to determine progress and or set new goals were conducted initially weekly then at increasing intervals according to patient need. A unit cost of GBP £36 per hour was attached to the average intervention duration for each patient. The total cost of the personalised care and control groups at baseline was €2,322 and €4,721, respectively; this decreased after six months to €1,090 and €1,560, respectively, increasing after 12 months to €1,425 and €2,638, respectively. Both groups improved on all outcomes. The largest between-group difference was in the proportion no longer reporting chest pain (personalised care 37% versus control 18%; OR 2.21 95% CI 0.69-7.03) with some evidence that self-efficacy (mean scale increase of 2.5 versus 0.9) and illness perceptions (mean scale increase of 7.8 versus 2.5) had improved compared with the control group at one year.

While the intervention demonstrated good acceptability and feasibility, there were no significant differences between groups on any measure of depression, in the proportion reporting chest pain, or in resource use or utility scores at six or 12 months. This pilot study was underpowered to detect between group differences over time. The authors calculated an incremental cost-effectiveness ratio (ICER) of €39,193 per additional QALY. The point estimate of the incremental cost-

effectiveness ratio fell in the south-western (SW) quadrant, representing the situation where the personalised care group has reduced costs and worse outcomes. The authors concluded that personalised care appeared to be more cost-effective up to a QALY threshold of approximately £3,000.

#### 9.3.2.4 Other self-management support interventions

Four additional studies evaluating different SMS interventions were identified. Two economic modelling studies from the US assessed interventions to improve medication adherence and smoking cessation, respectively. The third study, also an economic modelling study, from the UK assessed a lay-facilitated angina management programme. The fourth was a UK cost-effectiveness analysis of nurse-led secondary prevention clinics for coronary heart disease based on four years' follow up of a randomised controlled trial. See Table A9.6 in the appendices for a summary of the study details and results.

A 12-week lay-facilitated angina management programme was compared with usual care (routine advice and education from a specialist nurse) in a 2012[309] pragmatic RCT (n=142) in the UK of patients with new stable angina. The intervention consisted of stress management and a relaxation programme combined with a 45-minute individual educational session delivered by trained lay facilitators that focused on goal setting to increase physical activity and reduce behavioural risks. Progress was tracked with brief follow-up telephone calls (10-15 minutes) or home visits as agreed between the facilitator and participant. There was no important difference in angina frequency at six months. The intervention group had significantly higher mean quality of life as measured by EQ-5D index scores, at both three (0.82 [0.21] versus 0.70 [0.28], p=0.01) and six months 0.82 [0.24] versus 0.68 [0.32], p=0.008). The remaining outcomes (anxiety, depression, angina misconceptions) were not significantly different between the two groups.

In the regression model, the average cost per patient in the control group was €1,743 compared with €2,071in the intervention group, however, the difference between the two groups was not significantly different. There was a statistically significant difference in average QALY per patient of 0.045 (CI: 0.005–0.085). The authors concluded that at a willingness-to-pay threshold of €27,680 per QALY, the intervention had an 80% probability of being cost-effective.

A 2012 US modelling study by Ito et al.[310] evaluated the comparative cost-effectiveness of interventions to improve adherence to prescribed secondary prevention medications among post-myocardial infarction (MI) patients. The interventions were categorised by different targets for adherence improvement: informational (mailed education), behavioural (disease management), or complex (polypill combined with either mailed education or disease management).

All the interventions were compared with usual care, defined as the absence of adherence interventions. The analysis found that all the interventions resulted in a higher total QALY gain than usual care. Compared with usual care, only mailed education had both improved health outcomes and reduced spending. In an incremental analysis, only mailed education had an ICER of less than €92,053 per QALY and was therefore identified as the optimal strategy. It was noted that polypill use, particularly when combined with mailed education, could be cost-effective, and potentially cost saving if its price decreased to less than €92 per month.

Using a Monte Carlo model, the 2011 US study by Ladapo et al.[312] evaluated a smoking cessation intervention for a hypothetical US cohort of 327,600 smokers that had been hospitalised with acute myocardial infarction. The study, which was undertaken from a societal perspective, compared routine care (consisting of advice to quit smoking) with nurse-led counselling plus supportive telephone follow-up post discharge. The programme was estimated to cost €530 per quitter and €19,447 per acute myocardial infarction avoided (considering only intervention costs), generating an ICER of €4,272 per life-year and €4,960 per QALY gained. It was concluded that nurse-led smoking cessation counselling with post-discharge support had the potential to be cost-effective relative to the usual care.

Finally, a cost-effectiveness analysis of a nurse-led secondary prevention programme for ischaemic heart disease patients that was based on four years of follow-up data from a UK RCT found that the intervention was likely to be highly cost effective, with an ICER of €2,015/QALY.[317]

## 9.4 Discussion

This section discusses the main findings from the review of the clinical-effectiveness and cost-effectiveness literature.

### 9.4.1 Clinical effectiveness

Exercise programmes were the only intervention for which a statistically significant beneficial effect on mortality was found. In the only high-quality review that reported this significant result, the control groups receiving usual care were given advice about diet and exercise, but no formal exercise programme. There was a high degree of heterogeneity in the intervention groups, which differed considerably in programme duration (range 1–30 months), exercise frequency (1–7 sessions per week), and exercise session duration (20–90 minutes per session). The effect was only evident in studies that had greater than 12-months' follow-up, which gives an indication of the minimum time frame needed in order to realise the beneficial effect of these types of programmes. This study also found reductions in hospitalisation rates over a shorter time horizon. Interestingly, despite reduced mortality and hospitalisation rates, the intervention had no significant effect on the rate of myocardial infarction or revascularisation rates (percutaneous transluminal coronary angioplasty [PTCA] or coronary artery bypass graft [CABG]). Another, moderate quality, review of exercise programmes also found a reduction in all-cause mortality, as well as a reduction in the rate of reinfarction. A review of interventions that combined multiple types of interventions, including exercise, in the same self-management programme also reported reductions in all-cause and disease-specific mortality.

The degree to which exercise-based self-management support interventions can be considered separate to standard cardiac rehabilitation is questionable, as exercise is a core component of cardiac rehabilitation programmes.[288] The evidence presented here is specific to the exercise component as it compares exercise-based interventions (including exercise-only cardiac rehabilitation and exercise as part of comprehensive cardiac rehabilitation) with a non-exercise intervention arm. It is likely that exercise interventions of some sort are already provided through cardiac rehabilitation services.

There is some evidence to show that patient education programmes may be beneficial in terms of achieving their immediate goal of raising the level of awareness and understanding that patients have about their disease, as well as their ability to make positive changes to their diet and lifestyle. However, there is a lack of evidence that these are translated into changes in meaningful clinical outcomes. This may be partly related to uncertainty about the persistence of such effect in the long

term, with a beneficial effect reported at four months not being maintained at 12 months.

A Cochrane review of service organisation for the secondary prevention of ischaemic heart disease in primary care was not included in this review as it focussed primarily on service organisation rather than self-management strategies.[318] This review did, however, include studies that looked at improving patient education along with regular planned recall of patients for appointments, structured monitoring of risk factors and prescribing, and found weak evidence that these are associated with improvements in cholesterol and blood pressure control.

Limited evidence was found to demonstrate the effectiveness of behavioural modification interventions, although some researchers have reported positive effects on smoking cessation and symptom management.

The choice of comparator is particularly important when considering the effectiveness of telehealth or home-based interventions. Studies comparing the intervention with a standard of care that does not involve a structured cardiac rehabilitation are reporting the incremental effect of both the programme and the methods used to deliver it, rather than the incremental benefit of the mode of delivery itself. A review that compared home-based interventions with usual care found improvements in quality of life, blood pressure, cholesterol and smoking cessation. It is impossible in these types of comparisons to separate the effect of the cardiac rehabilitation programme from the effect of its mode of delivery.

In contrast, another review compared home-based versus centre-based cardiac rehabilitation programmes and found that there was no discernible difference in clinical outcomes. This would imply that it is the cardiac rehabilitation, rather than the fact that it is carried out at home, that is the most important factor. Similarly, when telehealth interventions are compared with usual care there appears to be a beneficial effect on some intermediate outcomes such as blood pressure and smoking cessation. However, when the mode of delivery is examined in isolation, by providing the same basic programme to both intervention and control groups, but varying how it is delivered (telehealth or centre-based), no difference in clinical outcomes were reported.

The findings of a 2014 Cochrane overview summarising six Cochrane reviews of cardiac rehabilitation for people with heart disease (ischaemic heart disease and heart failure) are consistent with the evidence presented here. This found that exercise-based cardiac rehabilitation interventions with over 12-months' follow up were associated with a beneficial effect on both overall and cardiovascular mortality; psychological and education-based interventions appear to have little impact on mortality or morbidity, but may improve HRQL. Home- and centre-based

programmes are equally effective in improving HRQL at similar costs. The authors concluded that exercise-based cardiac rehabilitation is effective and safe in the management of clinically stable CAD patients.[319]

Assuming that the comparator (usual care) in the primary literature on which these systematic reviews are based is representative of usual care in Ireland, it would appear that the evidence should be broadly applicable to the Irish healthcare setting given the description of the patient populations and the healthcare systems in which the interventions were provided. With the increasing tendency for usual or standard of care to be determined by evidence-based clinical guidelines and the convergence of such guidelines in Western countries, this assumption is not unreasonable. However, this assumption depends on adherence to the stated standard of care and access to cardiac rehabilitation services for people with ischaemic heart disease in Ireland. The model of care developed by the national clinical programme in Ireland for acute coronary syndromes recommends that cardiac rehabilitation programmes are established within the acute setting to treat hospitalised patients prior to discharge, with follow-up secondary prevention programmes in the primary care setting. In-hospital cardiac rehabilitation should begin as soon as the patient is clinically well enough to receive it, while patients should receive an invitation to early cardiac rehabilitation services (Phase 3), within four weeks of hospital discharge. It is a stated (as of 2013) goal that 90% of eligible patients are referred.[320]

The extent to which this is in place throughout the country, and adherence levels in areas where such services are provided, was examined in a 2013 survey, which found significantly different staffing levels and resources between cardiac rehabilitation services, lengthy waiting times for some individual services and wide variation in availability of multidisciplinary teams, which meant that not all patients receive the best possible cardiac rehabilitation.[321] There is also considerable uncertainty about access to primary prevention services for patients who have not been hospitalised for an acute event or revascularisation procedure associated with ischaemic heart disease. Furthermore, international evidence suggests that even where available, uptake of cardiac rehabilitation is variable, with participation rates as low as 20% to 50% reported. Barriers to participation include poor referral rates for certain groups (women, elderly, ethnic minorities, low socio-economic classes), logistical issues, and patient factors such as multi-morbidities, obesity and psychological wellbeing.[288] As evidenced in this assessment, novel mechanisms of providing cardiac rehabilitation are emerging including alternative modes of delivery (centre-based, home or online programmes) aimed at improving uptake across all groups of cardiac patients.

### 9.4.2 Cost-effectiveness

Fifteen economic evaluation studies of chronic disease self-management support (SMS) interventions for patients with ischaemic heart disease were identified as relevant. The majority of studies evaluated cardiac rehabilitation (n=7), with the remainder investigating telemedicine (n=2), case management (n=2) and other SMS interventions (n=4). The quality of the studies was generally poor. Most economic analyses were conducted alongside RCTs with small sample sizes and a short duration of follow-up, typically six to 12 months' duration, limiting the applicability of the findings presented in this section. The interventions described by the included studies were heterogeneous and frequently comprised multiple components. What constituted usual care also differed, so that the control groups (no SMS intervention) are not necessarily comparable. Given the diverse range of study populations, health systems and methodological approaches used to estimate the cost-effectiveness of different self-management programmes for ischaemic heart disease, the applicability of the available evidence to a prospective Irish programme is considered relatively low.

The largest body of evidence was found for cardiac rehabilitation, however, the delivery and components of the programmes differed significantly across studies, as well as the choice of comparator. When compared with no rehabilitation, the intervention was found to be clinically and cost-effective. However, when comparing different modes of delivery of cardiac rehabilitation (home versus hospital-based, or intensive versus dispersed delivery), no difference in outcomes was observed, while costs were similar.

While two studies were identified that evaluated the impact of telemedicine-based self-management support interventions, the SMS interventions evaluated differed. Both comprised economic evaluations conducted alongside RCTs with short-term follow up. A health-coach delivered educational programme was found not to be clinically or cost-effective in the short-term compared with usual care, while a smoking cessation intervention (telephone-based or face-to-face counselling) found that telephone-based SMS intervention dominated (was more effective and less costly) than either usual care or face-to-face counselling. However, in the latter study, nicotine replacement therapy was also included in the intervention arms, so it is not possible to conclude if the outcomes observed were due to this treatment or the telemedicine support.

Equivocal results were found for two economic evaluations that evaluated nurse-led case management interventions. Both were conducted alongside a RCT with short-term follow-up. One study concluded that the case management intervention was not an effective or cost-effective alternative to usual care within a time horizon of

one year, while the other, which was underpowered to detect a clinical effect, concluded that case management had the potential to be cost-effective.

There was insufficient evidence of adequate quality or relevance to consider the cost-effectiveness of interventions discussed in the 'other SMS' section.

Overall, the findings for SMS interventions in ischaemic heart disease were equivocal, and the quality of the included economic evaluations was as noted, predominantly poor. The majority of studies reported either similar or reduced costs (predominantly as a result of reduced healthcare usage) for the intervention group. Clinical outcomes were typically similar between the intervention and control arms, with no significant differences in HRQOL reported in most of the studies. Several of the RCTs were noted by the authors to be underpowered to detect differences in outcomes while short follow-up periods were also noted to be limiting factors. Where reported, the cost of the SMS intervention was typically low relative to the overall cost of care.

## 9.5 Key points

- Fourteen systematic reviews of self-management support interventions in adults with ischaemic heart disease published between 2009 and 2015 were identified for inclusion in this overview of reviews.
- The quality of the systematic reviews varied, with five being rated as higher quality reviews, with an R-AMSTAR score of at least 31 out of 45.
- These reviews included five broad types of self-management support intervention, which were focused on patient education, exercise, psychosocial or behavioural changes, home-based services or telehealth. Interventions such as education, exercise and behavioural changes are core components of cardiac rehabilitation, so the boundary between standard cardiac rehabilitation services and chronic disease self-management support is ill-defined.
- The only single intervention with evidence for a statistically significant reduction in mortality is exercise programmes for suitable patient cohorts with follow-up of greater than 12 months. Exercise-based interventions are also associated with fewer hospitalisations, but there is conflicting evidence about myocardial infarction rates or revascularisation procedures.
- There is some evidence that patient education programmes are associated with an improvement in interim outcomes such as smoking cessation and reduced blood pressure, but there is uncertainty about how long any such effect persists.
- There is limited evidence to demonstrate the effectiveness of behavioural modification interventions, although some studies have reported positive effects on smoking cessation and symptom management.

- There is limited evidence that comparable home- and telehealth-based cardiac rehabilitation interventions achieve similar outcomes to centre-based interventions.
- Fifteen economic evaluation studies of chronic disease self-management interventions for patients with ischaemic heart disease were identified as relevant.
- The self-management interventions assessed in the included studies tended to be multi-faceted and therefore heterogeneous. Most economic analyses were conducted alongside RCTs with small sample sizes and a short duration of follow up, limiting the applicability and validity of the findings, and potentially failing to capture long-term benefits or to demonstrate if observed benefits and savings could be sustained. However, where reported, the cost of the self-management support interventions was typically noted to be low, relative to the overall cost of care.
- The largest body of evidence was found for cardiac rehabilitation. When compared with no rehabilitation, the interventions were found to be clinically effective and to create cost savings as a result of reductions in healthcare usage.
- Equivocal results have been reported for telemedicine-delivered self-management support interventions and nurse-led case management programmes. Due to the heterogeneity of the interventions assessed, it is not possible to draw conclusions in relation to the cost-effectiveness of these interventions.
- Based on the description of the healthcare systems, the epidemiology, and the ischaemic heart disease patient populations in the included studies, and assuming that what constitutes 'usual care' is similar in Western countries, the majority of findings of this overview of clinical effectiveness are expected to be applicable to the Irish healthcare setting. The applicability of the cost-effectiveness literature to the Irish healthcare setting was considered relatively low.

# 10 Hypertension

This health technology assessment (HTA) of hypertension self-management support (SMS) is one of a series of rapid HTAs assessing SMS interventions for chronic diseases. Section 10.1 provides a brief description of hypertension followed by separate reviews of the clinical (Section 10.2) and cost-effectiveness (Section 10.3) literature of SMS interventions in hypertension. Brief descriptions of the background and methods used are included with full details provided in a separate document (Chapter 3). Section 10.4 includes a discussion of both the clinical and cost-effectiveness findings. The report concludes with a list of key points in relation to hypertension SMS support (Section 10.5).

## 10.1 Description of the disease

The World Health Organization's *Health 2020* policy identifies high blood pressure or hypertension as the world's most prevalent, but preventable disease.[322] Research published in 2015 from the Irish Longitudinal Study on Ageing (TILDA) estimated that 64% of the population over 50 years of age in Ireland has high blood pressure, equivalent to 797,000 people.[323] National data suggest that there are approximately five adults aged over 45 years with undiagnosed hypertension for every three adults aged over 45 years with clinically diagnosed hypertension.[324] Hypertension is a serious medical condition that often has no symptoms, but significantly increases the risks of heart, brain, kidney and vascular disease.

In particular, the detection and management of hypertension is relevant to stroke prevention. Stroke is a leading cause of cardiovascular morbidity in Ireland — approximately 7,000 people are hospitalised following stroke each year in Ireland while in 2007 total annual stroke costs were estimated to be between €489 million and €805 million.[247] The Department of Health's National Cardiovascular Health Strategy (2010-2019) recommends that the effective management of hypertension should be prioritised in primary care and calls for guidelines on standards of assessment, management and review of patients based on best practice.[325]

Normal blood pressure is defined as <120/80 mmHg. Blood pressure is normally distributed in the population and there is no natural cut-off point above which hypertension definitively exists and below which it does not.[326] The risk associated with increasing blood pressure is continuous, with each 2 mmHg rise in systolic blood pressure associated with a 7% increased risk of mortality from ischaemic heart disease and a 10% increased risk of mortality from stroke.[326] The European Society of Hypertension and European Society of Cardiology guidelines for the management of hypertension define hypertension as having readings on separate occasions consistently showing your blood pressure to be ≥140 mmHg systolic blood pressure

(SBP) and or ≥90 mmHg diastolic blood pressure.[327] While a target blood pressure of below 130/80mmHg was typically recommended for individuals with kidney disease, diabetes or a condition that affects the heart and circulation,[328] the 2013 ESH/ESC guidelines relaxed blood pressure targets for high-risk hypertensive patients driven by a lack of commanding evidence for an aggressive approach.[327] However, this is a contentious issue and some argue that these blood pressure targets should not have dropped.[329]

The correct diagnosis of hypertension is essential to ensure adequate management. Guidelines, such as those developed by the National Institute for Health and Care Excellence (NICE) in the UK (2011), outline criteria for the appropriate measurement of blood pressure. They specify the type of conditions in which readings should be taken, the equipment that should be used, and the specific criteria for those with pulse irregularity and symptoms of postural hypotension. They also outline criteria for the diagnosis of hypertension (including criteria for multiple measurements and confirmatory ambulatory and self-monitoring blood pressure measurements).[326]

## 10.2 Review of clinical-effectiveness of self-management support interventions

### 10.2.1 Background and methods

Details of the background and methods for this assessment are included in Chapters 1 to 3 of this report. Briefly, an aim of this health technology assessment (HTA) is to review the clinical effectiveness of self-management support (SMS) interventions for a number of chronic conditions including hypertension. Given the large volume of literature available, it was noted that an update of an existing high quality systematic review of SMS interventions could be considered sufficient to inform decision-making.

In December 2014, a high-quality overview of reviews was published by the National Institute for Health Research (NIHR) in the UK. The Practical Systematic Review of Self-Management Support for long-term conditions (PRISMS) overview comprised an overview of systematic reviews of randomised controlled trials (RCTs) up to October 2012, and was itself undertaken according to the principles of systematic reviewing. An update to the PRISMS report was completed by running additional searches in PubMed, Embase and the Cochrane Library from 2012 to 1 April 2015, see Appendix A3.1.

In line with the PICOS (Population, Intervention, Comparator, Outcomes, Study) design agreed with the key stakeholder, this assessment is limited to SMS interventions for adults aged 18 and over. As noted in Chapter 3.1.1, SMS interventions are typically complex interventions that include more than one

component of SMS. For this reason, and consistent with the PRISMS report, with the exception of education interventions, this review did not assess single component SMS (for example, simple text message appointment reminders and drug reminder packaging). PRISMS did not include telehealth reviews as the available literature was typically about mode of delivery rather than content of what was delivered. Telehealth interventions are included in this updated review. Relevant telehealth interventions that incorporated a significant component of SMS were also included in this updated review. Results of the updated search are reported in addition to a summary of the findings of the PRISMS report.

Data extraction and quality assurance of the systematic reviews, meta-analyses and the risk of bias associated with the primary literature was undertaken as described in Chapter 3.1.3. In summary, in order to determine the quantity, quality, strength and credibility of evidence underpinning the various SMS interventions, quality assurance of both the systematic review methodology (R-AMSTAR weighting by patient or participant trial size) and the meta-analyses (Higgins et al.'s quality assessment tool)[23] was undertaken. While the R-AMSTAR score was used to determine the quality of the systematic reviews, the scores were then weighted by patient or participant trial size, with the quality of evidence being downgraded if the review was based on fewer than 1,000 participants. The quality of the primary evidence was not evaluated directly; where reported, information on the risk of bias of the primary studies was extracted from the systematic reviews.

### 10.2.2 Description of the interventions

A general description of self-management and typical SMS interventions is included in Chapter 2. Treatment recommendations for hypertension depend on the blood pressure level and the risk of developing a cardiovascular disease. Lifestyle changes are recommended for people with blood pressures slightly above 130/80mmHg and a low risk of cardiovascular disease. Treatment with medication and lifestyle changes is recommended for people with moderately high blood pressure (140/90mmHg or above) and a risk of cardiovascular disease in the next 10 years. Immediate treatment is recommended, possibly with further tests, if blood pressure is very high (180/110mmHg or above).[328]

Lifestyle changes can be extremely effective in reducing high blood pressure and include eating a healthy diet, reducing salt intake (to less than 5g daily), exercising regularly, stopping smoking and reducing alcohol consumption.[322] However, adherence with lifestyle modifications, especially dietary changes, is problematic and as such, improving adherence to lifestyle changes is a key target for behavioural interventions for enhancing SMS. Clinical guidelines recommend that lifestyle advice should be offered initially and then periodically to people undergoing assessment or treatment for hypertension. However, pharmacological intervention becomes

necessary in most hypertensive patients to achieve substantial, sustained blood pressure lowering.[326] Sustained reduction in blood pressure reduces the incidence of stroke, coronary artery disease, heart failure and mortality, with the potential to benefit being proportional to the individual's overall cardiovascular risk. In the first year of anti-hypertensive treatment, on average only 20% of patients have sufficiently high adherence to achieve benefit.[330] This may be related to the fact that a lack of symptoms makes it a difficult disease to treat. A 2015 European study estimated that increasing adherence to anti-hypertensive therapy to 70% would save a total of €332 million (CI 95%: €319-346 million) from the national payers' perspective.[331] Measures to improve adherence include simplified dosing schedules, (for example, once-daily dosing, single pill combinations), educational interventions, telephone and computer-assisted monitoring and prompts, increased convenience of care, and involvement of community healthcare professionals (nurse and, or pharmacist).[326;332] Improving adherence is also a key target for behavioural interventions for enhancing SMS.

Self-measured or self-monitoring of blood pressure (SMBP) refers to the manual measurement of BP by a patient at home or outside of a clinic setting using a blood pressure monitor, with data recorded by the patient or electronically transmitted to a healthcare provider, using telemonitoring. Self- (also known as home) monitoring of blood pressure is indicated by clinical guidelines as an adjunctive measure in the diagnosis and or management of hypertension for certain patient cohorts.[333-335] However, despite guideline recommendations, there is a lack of clarity regarding the benefits and duration of benefits for SMBP, the best way of deploying it, and the need for additional support (for example, telemedicine, education, counselling). The validity of the data generated is dependent on the degree to which the patient adheres to recommendations in relation to SMBP, including: the use of a validated device that is calibrated at regular intervals; and the extent to which they adhere to proper measurement procedures (such as when seated with arm supported at heart level and waiting at least five minutes before the first measurement; not when rushed or uncomfortable within two hours of a large meal and so on).

Patients require adequate training in both the use of the device and the interpretation of the readings. As mentioned in Section 10.1 above, the correct diagnosis of hypertension is essential to ensure adequate management.

### 10.2.3 Results — clinical-effectiveness

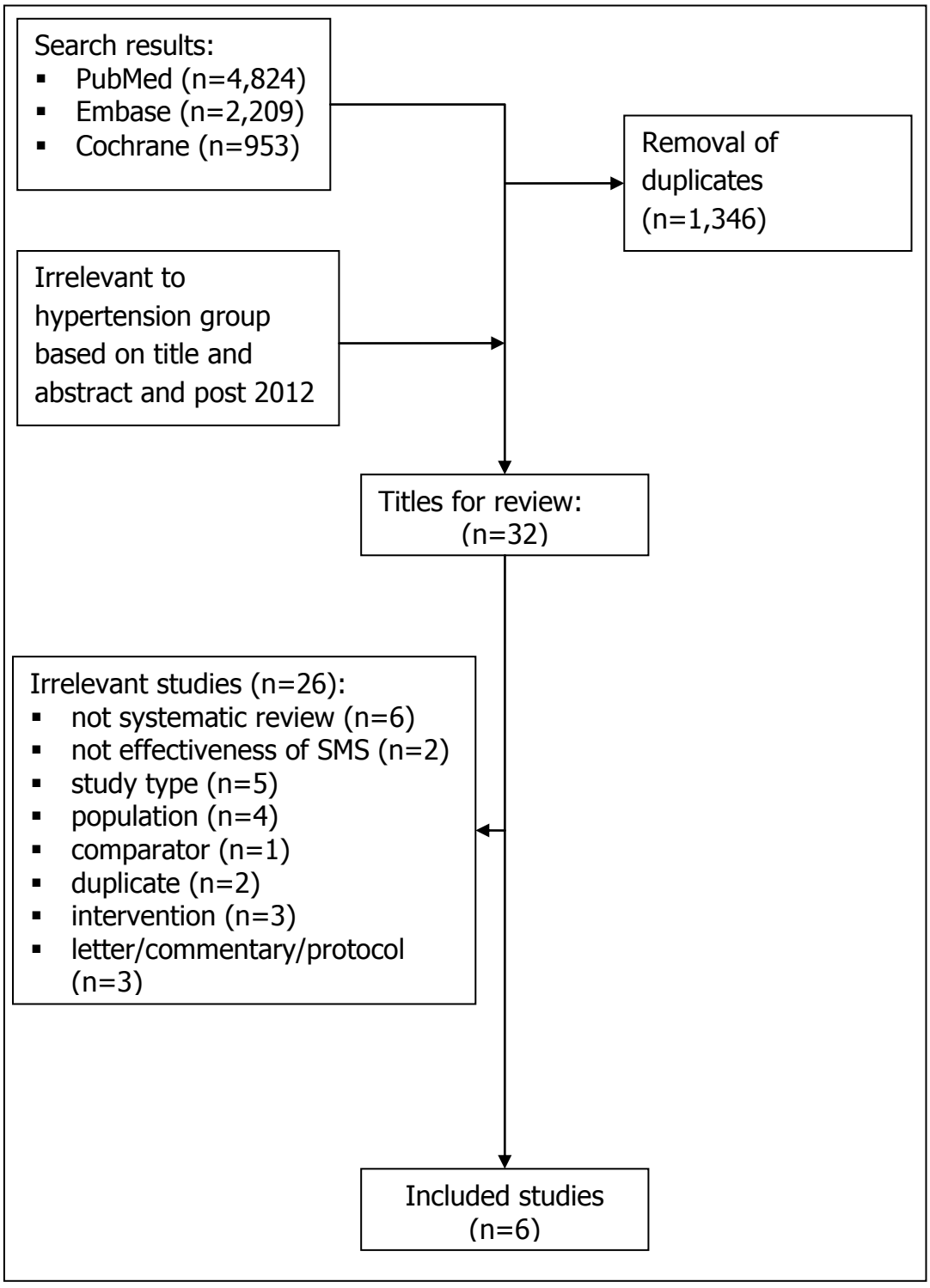
The PRISMS review retrieved a total of 10 systematic reviews of hypertension-specific SMS interventions and generic interventions used in adults with hypertension.[2] Summary details of the reviews including the intervention assessed are included in Table 10.1. The number of included RCTs ranged four[336] to 51 with the number of participants ranging from 382 to more than 87,000.[337] Study overlap

is reported in Table 10.2. The publication dates of the systematic reviews ranged from 1998 to 2011 while that of the included RCTs ranged from 1973 to 2010. Not all included systematic reviews recorded where individual RCTs had been conducted; of those that did, the greatest number was from the USA. The majority of the rest were from Europe, others were from Canada, Australia and South Africa.

The PRISMS report was updated to April 2015 using the search string in Appendix 1. A further six systematic reviews were retrieved (see Figure 10.1), details of which are included in Table 10.1. The additional six included reviews assessed a diverse range of SMS interventions for hypertension, including self-monitoring of blood pressure with or without telemedicine or additional support,[334;338;339] pharmacist-led interventions,[340] health education (in China)[341] and a range of technology interventions.[342] For the additional systematic reviews, the number of included RCTs ranged from 12 to 52 with the number of participants ranging from 2,475 to 5,400. Study overlap is reported in Table 10.2. The publication dates of the systematic reviews ranged from 2012 to 2015 while that of the included RCTs ranged from 1973 to 2014. RCT study locations were typically in Europe or North America.

The quality of the systematic reviews (R-AMSTAR scores) ranged from 12 to 33, with scores of 31 or more indicating a high-quality systematic review. When weighted according to the number of participants in the original RCTs (less than [<] 1,000 or greater and equal to [≥] 1,000), four of the systematic reviews were assigned the highest quality rating (three-star ***), while one review each rated as two-star (**) and one-star (*). The identified meta-analyses were also assessed for quality; three were assessed as high quality, four as moderate quality, and four as low quality; five reviews did not include a meta-analysis. A grading of low quality referred to studies where the conclusions were at high risk of bias due to poor data collection or methods of data synthesis. The conclusions in studies identified as moderate quality were at risk of bias, but were likely to be broadly accurate, while studies graded as high quality were very likely to have conclusions that accurately reflected the available evidence. In total, 240 unique RCTs are included in the retrieved systematic reviews from the PRISMS report and updated search. The number of primary studies within each review, and the quality assessment of both the systematic reviews and the evidence underpinning them are provided in Table 10.3 on the following pages.

**Figure 10.1 Flowchart of included studies from updated search**



## Table 10.1 Hypertension: summary of systematic reviews retrieved

| Author (year) | Intervention |
|---|---|
| **Reviews identified in the PRISMS report** | |
| **SMBP (primary intervention assessed)** | |
| **Ebrahim (1998)[343]** | Methods for improving adherence and control (results included for SMBP, patient / professional education) |
| **Glynn (2010)[337]** | Model of care that improve BP control or follow-up care of patients (SMBP, patient / health professional educational interventions, health professional (nurse or pharmacist)-led care, organisational interventions aimed at improving the delivery of care, appointment reminder systems) |
| **Ogedegbe (2006)[344]** | SMBP — Effects on adherence (2 out of 11 RCTs for SMBP alone, remaining SMBP part of complex interventions, typically education) |
| **Verberk (2011)[345]** | SMBP — Telecare for the management of hypertension (data transfer to healthcare provider via telephone, modem, internet, mail. Many RCTs included education and behavioural training also) |
| **Other SMS interventions** | |
| **Bosch-Capblamch (2007)[346]** | Contracts between practitioners and patients to improve adherence to treatment, prevention and health promotion activities |
| **Chodosh (2005)[187]** | Self management programmes for hypertension |
| **Dickinson (2006)[347]*** | Lifestyle interventions (Results for combinations of interventions only included e.g. improved diet, exercise, alcohol restriction, sodium restriction) |
| **Saksena (2010)[336]** | Computer-based education for patients |
| **Schroeder (2004)[348]** | Interventions to enhance medication adherence (education, medication regime simplification, allied health professional involvement, special monitoring such as SMBP) |
| **Takiya (2004)[349]** | Methods to improve adherence (behavioural (to change normal behaviour or routine using e.g. telephone reminders), educational or combination of both) |
| **Reviews retrieved in updated search** | |
| **SMBP** | |
| **Fletcher (2015)[338]** | SMBP effect on medication adherence and lifestyle factors (SMBP alone / with telemedicine / education) |
| **Omboni (2013)[334]** | SMBP telemonitoring (alone/with support, such as education/nurse support) |
| **Uhlig (2013)[339]** | SMBP (alone/additional support such as telemedicine, education, counselling) |
| **Other SMS interventions** | |
| **Cheema (2014)[340]** | Pharmacist-led interventions |
| **Chandak 2015)[342]** | Technology-enabled interventions |
| **Xu (2014)[341]** | Health education in China (education on diet, nutrition, exercise, physical activity, lifestyle or social support) |

**Key: QA** = quality assurance; **SMBP** = self monitoring of blood pressure; **SMS** = self-management support.
*Lifestyle interventions include exercise, alcohol restriction and salt reduction form an integral part of hypertension care and are not considered self-management support interventions. If they were interventions to improve adherence to exercise, diet modifications and so on, then they were considered applicable.

## Table 10.2 Study overlap between the included systematic reviews (PRISMS report plus the systematic reviews from the updated search)[g]

| Review (year) | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | | 11 | 12 | 13 | 14 | 15 | 16 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| PRISMS reviews retrieved | | | | | | | | | | | | | | | | | | |
| 1 | Bosch-Capblanch (2007) | **4** | | | | | | | | | | | | | | | | |
| 2 | Chodosh (2005) | 1 | **13** | | | | | | | | | | | | | | | |
| 3 | Dickinson (2006) | 0 | 2 | **6** | | | | | | | | | | | | | | |
| 4 | Ebrahim (1998) | 0 | 0 | 0 | **46** | | | | | | | | | | | | | |
| 5 | Glynn (2010) | 0 | 1 | 0 | 15 | **72** | | | | | | | | | | | | |
| 6 | Ogedegbe (2006) | 1 | 0 | 0 | 1 | 3 | **11** | | | | | | | | | | | |
| 7 | Saksena (2010) | 0 | 0 | 0 | 0 | 0 | 0 | **4** | | | | | | | | | | |
| 8 | Schroeder (2004) | 0 | 0 | 0 | 4 | 8 | 4 | 0 | **38** | | | | | | | | | |
| 9 | Takiya (2004) | 0 | 0 | 0 | 1 | 3 | 3 | 0 | 14 | **16** | | | | | | | | |
| 10 | Verberk (2011) | 0 | 0 | 0 | 0 | 2 | 0 | 1 | 1 | 1 | **9** | | | | | | | |
| Reviews retrieved in updated search | | | | | | | | | | | | | | | | | | |
| 11 | Cheema (2014) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | | **16** | | | | | |
| 12 | Chandak (2015) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | | 0 | **12** | | | | |
| 13 | Fletcher (2015) | 0 | 0 | 0 | 2 | 7 | 9 | 0 | 6 | 4 | 1 | | 0 | 2 | **28** | | | |
| 14 | Omboni (2014) | 0 | 0 | 0 | 0 | 2 | 1 | 1 | 1 | 1 | 9 | | 0 | 2 | 3 | **23** | | |
| 15 | Uhlig (2013) | 1 | 1 | 0 | 6 | 11 | 7 | 1 | 6 | 3 | 9 | | 1 | 3 | 13 | 15 | **52** | |
| 16 | Xu (2014) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | | 0 | 0 | 0 | 0 | 0 | **14** |

[g] PRISMS review is based on a search from 1993 to October 2012. This search was updated to April 2015.

#### 10.2.3.1 Summary of findings

Detailed summaries of the systematic reviews including the intervention, outcomes assessed, duration of follow-up, sample size (number of RCTs and total number of participants) and the evidence of effect are included in Appendix A.10.1. The following are reported based on the findings from PRISMS and the additional systematic reviews retrieved in the updated search. Based on the range of SMS interventions retrieved, it was decided to classify and report the results by intervention type. The categories of systematic review include: self-monitoring of blood pressure (SMBP) and other SMS interventions. PRISMS reported their results per component of SMS and not per systematic review category. As such their results are reported by component of SMS below. In order to emphasise the relevance of the findings, results are grouped by the quality of the systematic review (using the R-AMSTAR score and size of the patient population). Table 10.3 below details the results of the quality assurance assessment of the systematic reviews and provides a summary of findings for selected outcomes from the various meta-analyses assessing the impact of SMS interventions in hypertension.

## Table 10.3 Summary characteristics and findings for selected outcomes for included studies

| Study | Quality of systematic review | | | Primary studies | | Quality of meta-analysis | Effect on SBP mmHg (95% CI) | Effect on DBP mmHg (95% CI) |
|---|---|---|---|---|---|---|---|---|
| | R-AMSTAR score | Partici-pants | Quality | n | low-risk[a] | | | |
| **Self-monitoring of blood pressure** | | | | | | | | |
| Ebrahim 1998[343] | 28 | >32,000 | ** | 46 | NR | Low | –7.6 (–8.5 to –6.7) | –4.2 (–4.6 to –3.8) (SMBP)<br>–1.5 (–2.7 to –0.3) (patient ed.)[g]<br>–1.9 (–3.3 to –0.5) (prof. ed.)[h] |
| Fletcher 2015[338] | 37 | 7,021 | *** | 28 | 3 | High | | –2.02 (–2.93, –1.11) |
| Glynn 2010[337] | 35 | >87,000 | *** | 72 | 12 | High | –2.5 (–3.7 to –1.3)<br>-0.4 (-1.1 to 0.2) | –1.8 (–2.4 to –1.2) (SMBP)<br>-0.4 (-1.1 to 0.3) (Physician ed) |
| Ogedegbe 2006[344] | 27 | 1,550 | ** | 11 | | N/A | | |
| Omboni 2014[334] | 35 | 7,037 | *** | 23 | NR[e] | Moderate | –4.71 (–6.18 to –3.24)[b] | –2.45 (–3.33 to –1.57)[b] |
| Uhlig 2013[339] | 33 | 5,400 | *** | 52 | 10 | Low | –3.9[c] | –2.4[c] |
| Verberk 2011[345] | 24 | 2,501 | ** | 9 | NR[f] | Low | –5.2 | –2.1 |
| **Other SMS interventions** | | | | | | | | |
| Bosch-Capblanch 2007[346] | 32 | 382 | ** | 4 | | N/A | | |
| Chandak 2014[342] | 14 | NR | * | 12[d] | | N/A | | |
| Cheema 2014[340] | 31 | >3,032 | *** | 16 | 1 | Moderate | –6.13 (–8.44 to –3.81) | –2.51 (–3.46 to –1.55) |
| Chodosh 2005[187] | 34 | 1,557 | *** | 13 | NR | Moderate | –0.39 (–0.51 to –0.28) | –0.51 (–0.73 to –0.30) |
| Dickinson 2006[347] | 35 | 413 | ** | 6 | | High | –5.5 (–8.8 to –2.3) | –4.5 (–6.9 to –2.0) |
| Saksena 2010[336] | 28 | 1,319 | ** | 4 | | N/A | | |
| Schroeder 2004[348] | 34 | 15,519 | *** | 38 | | N/A | | |
| Takiya 2004[349] | 29 | 2,446 | ** | 16 | NR[f] | Low | - | - |
| Xu 2014[341] | 31 | 2,475 | *** | 14 | 1 | Moderate | –19.03 (–23.26 to –14.80) | –10.33 (–13.40 to –7.26) |

**Key**: ***BP** = blood pressure; **DBP** = diastolic blood pressure; Ed = education; **MD** = mean difference; **NR** = not reported; **NA** = not applicable; **QoL** = quality of life; **RR** = relative risk; **SBP** = systolic blood pressure; SMBP = self-monitoring of blood pressure; **SMS** = self-management support; [a] Number of the total primary studies identified as being at low risk of bias. [b] Office SBP/DBP; [c] SMBP alone at six months. [d] Results for two of these studies are also included in the reviews by Fletcher et al., Omboni et al. and Uhlig et al. [e] All studies were considered to be of acceptable quality. [f] Risk of bias in primary studies was not assessed. [g] Education of patients. [h] Education of physicians.

## Table 10.3 (continued) Summary characteristics and findings for selected outcomes for included studies

| Study | Quality of systematic review | | | Primary studies | | Quality of meta-analysis | Medication adherence (95% CI) | BP control, OR (95% CI) |
|---|---|---|---|---|---|---|---|---|
| | R-AMSTAR score | Participants | Quality | n | low-risk[a] | | | |
| **Self-monitoring of blood pressure** | | | | | | | | |
| Ebrahim 1998[343] | 28 | >32,000 | ** | 46 | NR | Low | | |
| Fletcher 2015[338] | 37 | 7,021 | *** | 28 | 3 | High | SMD 0.21 (0.08 to 0.34) | |
| Glynn 2010[337] | 35 | >87,000 | *** | 72 | 12 | High | | 0.83 (0.75 to 0.91) (Ed.)<br>0.54 (0.41 to 0.73) (appointment reminder) |
| Ogedegbe 2006[344] | 27 | 1,550 | ** | 11 | | N/A | | |
| Omboni 2014[334] | 35 | 7,037 | *** | 23 | NR[e] | Moderate | | RR: 1.16 (1.04 to 1.29) |
| Uhlig 2013[339] | 33 | 5,400 | *** | 52 | 10 | Low | | |
| Verberk 2011[345] | 24 | 2,501 | ** | 9 | NR[f] | Low | | |
| **Other SMS interventions** | | | | | | | | |
| Bosch-Capblanch 2007[346] | 32 | 382 | ** | 4 | | N/A | | |
| Chandak 2014[342] | 14 | NR | * | 12[d] | | N/A | | |
| Cheema 2014[340] | 31 | >3,032 | *** | 16 | 1 | Moderate | OR 12.1 (4.2 to 34.6) | |
| Chodosh 2005[187] | 34 | 1,557 | *** | 13 | NR | Moderate | | |
| Dickinson 2006[347] | 35 | 413 | ** | 6 | | High | | |
| Saksena 2010[336] | 28 | 1,319 | ** | 4 | | N/A | | |
| Schroeder 2004[348] | 34 | 15,519 | *** | 38 | | N/A | | |
| Takiya 2004[349] | 29 | 2,446 | ** | 16 | NR[f] | Low | 0.04 (-0.01 to 0.09) | |
| Xu 2014[341] | 31 | 2,475 | *** | 14 | 1 | Moderate | | |

Key: **BP** = blood pressure; **DBP** = diastolic blood pressure; **MD** = mean difference; **NR** = not reported; **NA** = not applicable; **QoI** = quality of life; **RR** = relative risk; **SBP** = systolic blood pressure; **SMS** = self-management support; [a] Number of the total primary studies identified as being at low risk of bias. [b] Office SBP/DBP; [c] SMBP alone at six months. [d] Results for two of these studies are also included in the reviews by Fletcher et al., Omboni et al. and Uhlig et al. [e] All studies were considered to be of acceptable quality. [f] Risk of bias in primary studies was not assessed.

To provide some context to the following results it is noted that the criteria used by the European Medicines Agency to assess the efficacy of blood pressure lowering medications include the percentage of patients with a normalisation of blood pressure (SBP less than [<] 140 mmHg and DBP <90mmHg) and, or reductions of SBP greater than and equal to [≥] 20 mmHg and/or DBP ≥10 mmHg.[350] Clinical guidelines have used a mean change of 5mmHg as a threshold for appreciable benefits and harms when establishing the minimal important difference for blood pressure outcomes.[326] The mean reductions in blood pressure reported in Table 10.3, although statistically significant, are of a much smaller magnitude.

#### 10.2.3.2 Self-management of blood pressure (SMBP)[8]

**Three-star (***) reviews**

Based on one three-star (Glynn et al.)[337] and three two-star systematic reviews (Ebrahim et al., Ogedegbe et al. and Verberk et al.),[343-345] PRISMS reported that SMBP is promising, but with mixed evidence of effect, and noted that it may be more successful as part of a complex intervention. They noted that SMBP using 'telecare' had been shown to improve BP control; however, they also noted that this was based on a lower quality review (Verberk et al.).[345]

In the updated search, based on three three-star systematic reviews, good evidence was found that SMBP alone, or in combination with a range of additional support, is beneficial in lowering both SBP and DBP. The use of additional supports, such as education, seems to enhance the blood pressure lowering effect of SMBP. A 2015 meta-analysis of 28 RCTs by Fletcher et al. which assessed SMBP alone or in combination with education (face-to-face or via telemedicine) reported a small, but significant improvement in medication adherence and a significant reduction in DBP.[338]

A 2014 meta-analysis by Omboni et al. comprising 23 RCTs assessed the effect of SMBP using telemonitoring alone or with combinations of patient education, nurse support or pharmacist management and physician oversight.[334] They reported that SMBP using telemonitoring resulted in statistically significant improvements in office SBP and DBP, ambulatory blood pressure and blood pressure normalisation. A significantly higher use of antihypertensive medications was also observed, but the results for quality of life (QoL) were noted to be mixed. This report by Omboni et al. represents an update of the review by Verberk et al. identified in the PRISMs study as it included all nine RCTs identified by the Verberk report. The meta-analysis was rated of moderate quality, meaning that the conclusions were at risk of bias, but were likely to be broadly accurate.

[8] For hypertension PRISMS reported their results per component of SMS and not per systematic review category.

Finally, a 2013 meta-analysis comprising 52 RCTs by Uhlig et al. assessed the effect of SMBP alone or in combination with a range of additional supports (for example, telemedicine, education or counselling).[339] They reported that SMBP, with or without additional support, lowers BP compared with usual care, but that the blood pressure effect beyond 12 months and the long-term benefits remain uncertain. They also reported that additional support enhances the blood pressure lowering effect.

**Summary statement for self-monitoring of blood pressure:**

Based on the quantity and quality of the systematic reviews and the underpinning primary randomised controlled trials, there is good evidence that self-measured or self-monitoring of blood pressure (SMBP) alone or in combination with a range of additional supports, including telemedicine, is beneficial in lowering systolic and diastolic blood pressure with the duration of effect being uncertain. Additional support seems to enhance the blood pressure lowering effect of SMBP. While statistically significant, the clinical effect of these interventions may be small.

#### 10.2.3.4 Other SMS interventions

**Three-star (***) reviews**

Based on two three-star (Glynn et al., Schroeder et al.)[337;348] and two two-star reviews (Ebrahim et al., Saksena et al.),[336;343] the PRISMS report concluded that there was limited evidence of effectiveness of patient educational interventions alone in improving medication adherence or blood pressure control. No additional systematic reviews on educational interventions relevant to the Irish healthcare system were identified in the updated search, for this reason the review by Xu et al.is not discussed further.[341]

Based on a single three-star review (Schroeder et al.),[348] PRISMS reported that there is some evidence that simplification of medication regimens may improve adherence, although they noted that the clinical effect of this may be small and that it was not supported by all studies.

Based mainly on three three-star reviews (Chodosh et al., Glynn et al. and Schroeder et al.)[187;337;348] and two two-star reviews (Ogedegbe et al. and Verberk et al.),[344;345] PRISMS reported that there was evidence of benefit for complex interventions (that is, including multiple components or modes of delivery of SMS in supporting self-management, with mixed results for the use of interventions led by allied health professionals. They noted that while the range of evidence available for complex interventions was too heterogeneous to be able to make definitive conclusions, a patient-specific approach may be the most beneficial, involving components tailored to the individual patient with hypertension.

The updated search identified one additional three-star systematic review evaluating other SMS interventions. The 2014 review by Cheema et al. included a meta-analysis that assessed the effectiveness of community pharmacist interventions including patient education on hypertension, identification of drug-related problems and lifestyle advice.[340] Rated as being of moderate quality, the meta-analysis reported statistically significant reductions in systolic and diastolic blood pressure and improvements in medication adherence. The authors concluded that community pharmacist-led interventions could be useful for improving clinical management of hypertension.

### Two-star (**) reviews

Based on a single two-star systematic review (Bosch-Capblanch et al.),[346] the PRISMS report concluded that there was little evidence for the use of contracts between practitioners and patients when used alone to improve adherence in the management of hypertension. Also based on a single two-star review (Dickinson et al.),[347] PRISMS reported that lifestyle interventions may be beneficial to patients although their clinical effect may be small. Included in this review were various combinations of lifestyle interventions (for example, targeted at weight loss, alcohol or salt restriction). However, it is not clear the extent to which they included SMS.

### One-star (*) reviews

A single narrative review by Chandak et al. assessing the effectiveness of technology-enabled interventions was identified.[342] The review reported results for three telemonitoring studies, however, based on an assessment of study overlap, only one is a unique RCT to this overview. The review was of poor quality and identified limited evidence of effect for a single unique RCT evaluating a telemonitoring programme.

**Summary statement for other self-management support interventions:**

Based on the quantity and quality of the systematic reviews and the underpinning primary randomised controlled trials, there is limited evidence of effectiveness of patient education interventions when used alone in improving adherence or blood pressure control. There is some evidence that community pharmacist interventions, which include patient education, can lead to statistically significant reductions in systolic and diastolic blood pressure. There is some evidence that simplification of medication regimens may improve adherence, although the clinical effect of this improvement may be small. There is some evidence of benefit for a range of complex self-management support interventions (that is, including multiple components or modes of delivery) in improving blood pressure control. As definitive conclusions cannot be drawn based on the available evidence, a patient-specific

approach may be the most beneficial, involving components tailored to the individual patient with hypertension.

## 10.3 Review of cost-effectiveness literature of self-management support interventions

A review of cost-effectiveness studies was carried out to assess the available evidence for self-management support (SMS) interventions for people with hypertension. Studies were included if they compared the costs and consequences of a SMS intervention to routine care.

### 10.3.1 Search strategy

A search was carried out to identify economic analyses of SMS interventions. In tandem with the systematic review of clinical effectiveness, the search for economic evaluations was carried out in MEDLINE, Embase and the Cochrane Library. The same search terms were used with the exception of terms for systematic review and meta-analysis. In place of these, search terms and filters for economic evaluations were applied. In addition, 14 systematic reviews of SMS interventions were identified through the results of the clinical effectiveness search, which included cost or economic outcomes, and were used to identify additional studies. The search was carried out up until 4 March 2015.

The PICOS (Population, Intervention, Comparator, Outcomes, Study design) analysis used to formulate the search is presented in Table 10.4 below.

**Table 10.4 PICOS analysis for identification of relevant studies**

| | |
|---|---|
| **Population** | Adults greater than and equal to [≥] 18 years old with diagnosed hypertension. |
| **Intervention** | Any self-management support intervention incorporating education, training or support. |
| **Comparator** | Routine care. |
| **Outcomes** | Cost or cost-effectiveness of intervention. |
| **Study design** | Randomised controlled trials, case-control studies, observational studies, economic modelling studies. |

Study types were excluded if:

- a nursing home or non-community dwelling population was included
- it included a paediatric population
- cost data were not clearly reported
- published prior to the year 2000 (due to limited relevance because of advances in technology and limited applicability of cost data).

After reviewing the available studies, it was found that the majority evaluated interventions based on home-based blood pressure monitoring with or without a telemedicine component.

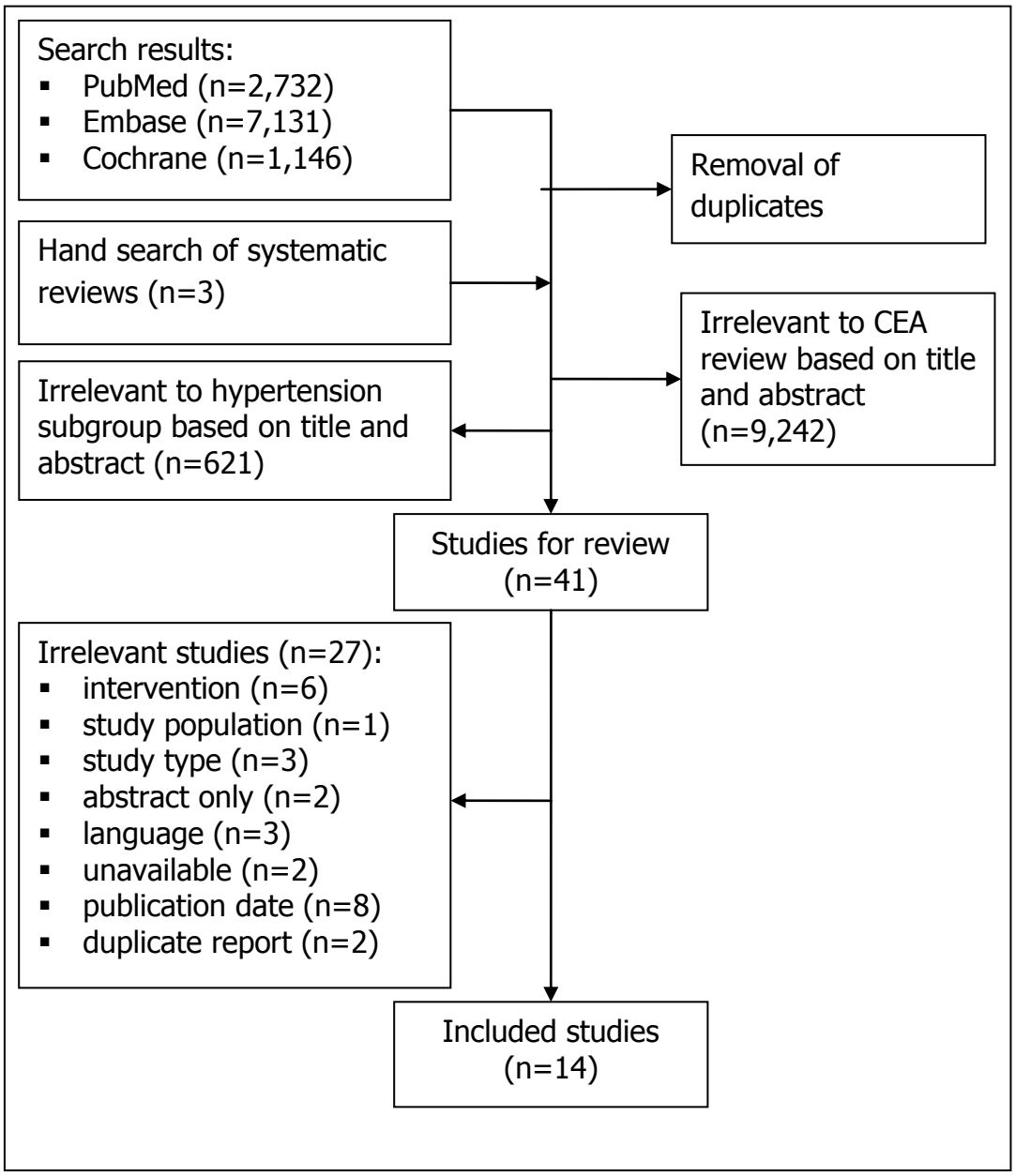
As outlined in Chapter 3.2.2 and in accordance with national HTA guidelines, assessment of the quality of the studies using the Consensus on Health Economic Criteria (CHEC)-list was performed independently by two people. For studies that included an assessment of cost-utility or an economic modelling approach, assessment of the relevance to the Irish healthcare setting and their credibility was considered using a questionnaire from the International Society of Pharmacoeconomics and Outcomes Research (ISPOR). Studies that were considered poor quality are not discussed below, although data from these studies are included in the evidence tables.

### 10.3.2 Results — cost-effectiveness

The bibliographic search returned 11,009 studies from across the three databases, which equated to 9,901 unique studies after removal of duplicates (see Figure 10.2). A further three potential studies were identified after reviewing reference lists of the systematic reviews of clinical-effectiveness. After removing studies not relevant to the review of cost-effectiveness based on the titles and abstracts, 662 studies were identified that may be costing or cost-effectiveness studies. A further 621 studies were identified as not relevant to a review of hypertension interventions based on title and abstract. Finally, a further 27 were excluded based on the various exclusion criteria, leaving 14 included studies. Assessment of eligibility of studies and data extraction was carried out independently by two people, with any disagreements resolved by discussion.

Costs reported in each of the studies were inflated to 2014 using the local consumer price index and expressed in Irish Euro using the purchasing power parity index. The one exception was the 2011 study from Argentina. As reliable inflation data are not available for Argentina and the study presented figures in US dollars, the figures have been inflated using US consumer price index data. For this reason, the price data for this study are considered unreliable. In the following text, monetary data are presented in the original study currency and then in 2014 Irish Euro equivalent in brackets.

**Figure 10.2 Flowchart of included studies**




Six of the studies were based in the US, three in the UK, and one in each of Argentina, Belgium, Denmark, Italy and the Netherlands. The included studies were published between 2004 and 2014. The characteristics of the included studies are given in Table 10.5.

Two studies were excluded because full-text articles were not readily available to adequately determine their relevance. One study evaluated the feasibility of loaning self-measurement equipment to patients.[351] The study was observational in nature and was primarily concerned with accuracy of readings rather than effect on blood pressure. Another study investigated a self-management intervention based on a software application.[352] Routine care involved a telemedicine component that was

unlikely to reflect usual care in Ireland. Exclusion of these articles is unlikely to affect the findings of this review. The studies were classified into two intervention types: exercise-based and computer-based programmes.

### Table 10.5 Included studies

| Study | Country | Intervention |
|---|---|---|
| **Arrieta (2014)**[353] | US | Home blood pressure telemonitoring |
| **Datta (2010)***[354] | US | Behavioural intervention through telemedicine |
| **Fishman (2013)***[355] | US | Home blood pressure monitoring with and without pharmacist support |
| **Kaambwa (2014)**[356] | UK | Home blood pressure monitoring with self-titration of anti-hypertensives |
| **Maciejewski (2014)***[357] | US | Nurse-led telemedicine self-management programmes |
| **Madsen (2011)**[358] | Denmark | Home blood pressure telemonitoring |
| **McManus (2005)**[359] | UK | Blood pressure self-monitoring in primary care |
| **Parati (2009)***[360] | Italy | Home blood pressure telemonitoring |
| **Perman (2011)**[361] | Argentina | Multidisciplinary antihypertensive programme |
| **Reed (2010)**[362] | US | Behavioural intervention through telemedicine with blood pressure self-monitoring |
| **Staessen (2004)**[363] | Belgium | Home blood pressure monitoring |
| **Stoddart (2013)**[364] | UK | Home blood pressure telemonitoring |
| **Trogdon (2012)**[365] | US | Collaborative hypertension intervention including home blood pressure monitoring |
| **Verberk (2007)**[366] | Netherlands | Home blood pressure monitoring |

* Studies that were considered to be low quality based on the CHEC-list and ISPOR questionnaire.

#### 10.3.2.1 Self-monitoring of blood pressure

Seven studies were retrieved that evaluated self-monitoring of blood pressure. See Table A10.3 in the appendices for a summary of the study details and results.

A US-based simulation study by Arrieta et al. was used to predict one-, three-, five- and 10-year returns on investment for home blood-pressure monitoring compared with usual care.[353] The data used in the model were mostly derived from health insurance claims data for beneficiaries with hypertension in a context of no home blood-pressure monitoring. Health outcomes were not reported, but were incorporated into the model in terms of costs associated with events and chronic conditions such as myocardial infarction, transient ischaemic attack, stable angina, stroke and congestive heart failure. Reductions in blood pressure associated with home monitoring were estimated from a previously published meta-analysis of RCTs. The analysis took into account attrition from plans as members migrate to other insurers. Certain costs, such as device validation and patient training, were excluded on the grounds that they would not be covered by the insurer. Depending on the insurance plan and age group, the estimated net saving of home monitoring ranged from €27 to €136 per member in the first year, and the return on investment ranged from €0.70 to €3.08 per dollar invested.

Madsen et al. evaluated home blood-pressure telemonitoring compared with usual care in a cohort of patients with poorly controlled hypertension.[358] The study was based on an RCT from Denmark that included 223 patients. Systolic and diastolic blood pressure reduced in both the intervention and control arms of the trial, and there was no statistically significant difference in blood pressure reduction between the groups. The intervention cost €166 per patient. The study reported ICERs of €32 per mm HG reduction in systolic blood pressure, and €81 per mm Hg reduction in diastolic blood pressure. Given the lack of statistically significant difference in blood pressure reductions, presentation of the ICERs would appear to be inappropriate.

A UK study by McManus et al. investigated the effect of enabling patients with uncontrolled hypertension to measure their own blood pressure at their general practitioner (GP) practice.[359] The study was based on an RCT of 441 patients. There was no statistically significant difference between the control and intervention groups at 12 months in terms of reductions in blood pressure. The intervention group had, on average, fewer GP consultations than the control group. Delivery of the intervention cost €42 per patient. The ICER for reduction in systolic blood pressure was presented as €7.94 per mm Hg, but this was in the absence of a statistically significant treatment effect. No secondary care costs were reported in the study.

An RCT by Staessen et al. with 400 participants was used to compare home-based and office-based blood pressure monitoring in patients with poorly controlled hypertension.[363] Patients were recruited at sites in Belgium and Ireland, although the majority (93%) were in Belgium. The trial ran for 12 months and at completion, the control group had achieved greater blood pressure reductions than the intervention group. However, a greater proportion of the intervention group had ceased antihypertensive drug treatment. The intervention cost €408 per 100 patients treated for one month. Total costs were lower in the intervention group: €4,317 compared with €4,750 per 100 patients per month.

A home-based blood-pressure telemonitoring intervention was compared with usual office-based monitoring in the UK in a population with uncontrolled hypertension.[364] The trial ran for six months and included 401 participants. The intervention group achieved a greater reduction in systolic blood pressure than the control group, and the difference was statistically significant. The intervention cost €92 per patient to deliver and the ICER was an estimated €33 per mm Hg drop in systolic blood pressure. The article reports different blood pressure targets for the intervention (<135/85 mm Hg) and control groups (<140/90 mm Hg). The reason given for the difference was that blood pressure measurements taken at home tend to be lower.

A Dutch RCT compared home-based blood-pressure monitoring with usual office-based monitoring in patients with uncontrolled hypertension.[366] The self-monitoring results were used to determine treatment decisions. The blood-pressure monitoring device cost €434 for 100 patients per month. Consistent with the findings of the report by Staessen et al., the control group had achieved a greater reduction in blood pressure than the intervention group at 12 months' follow-up. The intervention group used less antihypertensive medication and had lower costs. The authors concluded by suggesting that home blood-pressure monitoring could be used as an add-on to office-based monitoring rather than as an alternative, although that option was not tested as an alternative in the trial.

#### 10.3.2.2 Other self-management support interventions

Seven studies were retrieved that evaluated other types of SMS interventions. See Table A10.4 in the appendices for a summary of the study details and results.

A UK modelling study evaluated self-monitoring combined with self-titration of antihypertensives using data from a 12-month RCT.[356] The study modelled a cohort of patients with uncontrolled hypertension from age 66 years to 100 years of age. Equipment and training costs for the intervention arm were €298 per patient and annuitised over five years. The base case analysis assumed that blood pressure reductions achieved at 12 months would persist. Extensive sensitivity analyses were used to determine the impact of varying the duration of effect on blood pressure.

The ICERs for the intervention were estimated at €2,107 per QALY for men and €6,386 per QALY for women. The sensitivity analyses found that even with a relatively rapid reduction of effect, the intervention was still considered cost-effective by UK standards.

A multidisciplinary programme for middle-class elderly patients with hypertension was modelled using data from a quasi-experimental study in Argentina.[361] The programme included personal and telephone contact, support with diet and physical activity, educational material, and workshops. The intervention cost €13 per patient to deliver. The intervention resulted in an increased proportion of patients having well-controlled hypertension. The ICER for the intervention compared with usual care was €1,003 per life year gained. It was unclear if it was assumed that the effect of the programme would persist or if it was restricted to the follow up of the original study. There is a risk of bias due to the uncontrolled nature of the effectiveness data. It was also not apparent whether patients could move between risk states in the model. The study is of questionable applicability to the Irish setting.

Reed et al. estimated the cost-effectiveness of a telephonic behavioural self-management programme as part of an RCT. The trial ran for 24 months and included 636 participants. The trial had four arms: usual care; home blood pressure monitoring; a behavioural intervention; and a combined behavioural and home monitoring intervention. The study took a societal perspective. The cost per patient of delivering the intervention was €81 for home monitoring, €312 for the behavioural intervention, and €376 for the combined intervention. Only the combined intervention achieved a statistically significant reduction in systolic blood pressure compared with usual care. The two-year cost per unit reduction in systolic blood pressure for the combined intervention was €97 based on direct costs, and €268 when patient time costs were incorporated. Medicine costs were excluded from the study, which may impact on the results.

A US study used a modelling approach to simulate the effects of an education programme for patients with uncontrolled hypertension.[365] The model used data from a programme that had been rolled out to health plan members. Patients in the intervention group were given self-management kits that contained a variety of materials to educate on diet, promote exercise, and improve medication adherence. Usual care was modelled using baseline data for the cohort who had received the intervention. The lack of data for concurrent controls will have introduced a risk of bias in the study. Results were presented for one- and 10-year follow up. Scenario analysis was used to test assumptions about the effect of the intervention. Adverse events of hypertension included acute myocardial infarction, stroke, congestive heart failure, and renal failure. The total cost of delivering the programme was €114,821 for 534 patients, or €215 per patient. Based on the one-year follow-up data, the

intervention cost €719 per patient achieving controlled blood pressure, €379,635 per adverse event avoided, and €39,330 per life year gained. Given the observational and uncontrolled nature of the underlying data, the 10-year estimates are unlikely to be reliable.

## 10.4 Discussion

This section discusses the main findings from the review of the clinical-effectiveness and cost-effectiveness literature.

### 10.4.1 Clinical effectiveness

Sixteen systematic reviews are included in this overview of reviews of which 10 reviews were included in the PRISMS review with the additional six reviews retrieved from the updated search. A diverse range of self-management support (SMS) interventions was assessed; these differed also in the frequency, intensity and mode of delivery. Despite the heterogeneity within the intervention classes, there was a tendency for their findings to be combined, so the results of the meta-analyses should be interpreted with caution.

Compared with other chronic diseases, SMS for hypertension is not well defined within the literature. Clinical trials have shown that antihypertensive treatment can achieve blood pressure control in the majority of the patients, but that there is a gap between the treatment potential and real-life practice, possibly due to poor medication adherence. Hypertension remains a leading cause of death and cardiovascular morbidity in Ireland and elsewhere in the world. This may be related to the fact that a lack of symptoms makes it a difficult condition to treat, with hypertensive individuals being unaware of the condition or, if aware, failing to obtain or adhere to treatment. The absence of symptoms may reduce an individual's motivation to self-manage, emphasising the potential role of appropriate education and other SMS.

As noted, there was significant heterogeneity in the format and intensity of the SMS interventions, the study populations, study follow-up duration and assessed outcome measures. This makes it difficult to formulate clear recommendations regarding the most effective form and content of SMS in hypertension. The main findings from the 2014 PRISMS systematic review — and the additional findings from this updated review — indicate that SMBP with or without additional support (education, telemedicine) lowers blood pressure compared with usual care, but that the clinical significance and durability of the response remain uncertain. The main outcomes assessed in the reviews retrieved were systolic and diastolic blood pressure (SBP and DBP). In the context of criteria for efficacy used in the assessment of pharmaceuticals or the threshold for a minimal important difference (5mmHg) used

in clinical guidelines, the clinical impact of SMS support interventions appears small.[350] Results from the relevant meta-analyses indicated mean reductions in SBP ranging from 0.4 to 7.6mmHg (SMBP) and 0.4 to 4.5mmHg (lifestyle interventions) for DBP. Wide variability in changes may indicate that the evidence is not conclusive. However even small changes in blood pressure are noted to be important if there are population wide shifts. As discussed in Section 10.1, the risk associated with increasing blood pressure is continuous, with each 2 mmHg rise in systolic blood pressure associated with a 7% increased risk of mortality from ischaemic heart disease and a 10% increased risk of mortality from stroke.[326]

Complicating the picture, however, is the accuracy of the initial hypertension diagnosis and its subsequent monitoring. Data from SLÁN[367] and TILDA[368] indicate high levels of undetected hypertension and poor blood pressure control levels in Ireland. Issues include a lack of agreement on which blood pressure guidelines are to be used in the management of hypertension (European or British Hypertension Society, NICE guidelines), inability to account for white coat and masked hypertension, inaccuracy of blood pressure measuring devices and reliance on office blood pressure measurements. Further issues may include lack of a National Clinical Lead in Hypertension, funding of general practitioners and practice nurses to diagnose and manage hypertension and adequately staffed and funded blood pressure units / hypertension clinics for difficult to control or resistant hypertensive patients to be referred to. This may complicate drug treatment, leading to potential over- or under-treatment and difficulties interpreting SMBP readings.[369;370] This review assumed that patients in the primary studies had correctly diagnosed hypertension. As noted in Section 10.1, clinical guidelines outline criteria for the appropriate measurement of blood pressure and for the diagnosis of hypertension (including criteria for multiple measurements and confirmatory ambulatory and self-monitoring blood pressure measurements).[326]

The majority of the evidence should be applicable to those with diagnosed hypertension in the Irish healthcare setting based on the description of the hypertensive patient populations, epidemiology, and the healthcare systems in which the interventions were provided. A potential caveat to this assumption is the extent to which the comparator (usual care) in these RCTs is representative of usual care in Ireland. Given the increasing tendency for usual or standard of care to be determined by evidence-based clinical guidelines, and the convergence of such guidelines in Western countries, this assumption is reasonable. However, differences in healthcare systems may contribute to differences in the adherence to stated standard of care. For example, usual care for hypertension in Ireland may differ to that in the UK's NHS system where adherence to quality standards (including implementing preventive measures such as routine blood pressure checks and monitoring the proportion of patients achieving blood pressure control) is

incentivised by the quality-of-outcomes framework. The incremental benefit of new hypertension self-management initiatives in Ireland will therefore be dependent on the current adherence to stated standards of care and the level of unmet need.

Given the volume of evidence available, in the interest of efficiency this assessment of SMS interventions in adults with hypertension was undertaken in the form of an overview of reviews. As discussed in Chapter 3.4.1, a disadvantage of this approach is the inability of an overview of reviews to reflect the most recent literature. Following publication of an RCT, it must first be captured in a systematic review, before subsequently being captured in an overview of reviews. This approach is therefore less suitable for a fast-moving area where there are rapid advances in the technology. However, given their sample sizes, it is not appropriate to draw conclusions on the effect of an intervention based on a single, or a number of small, RCTs. Therefore it is unlikely that more recent RCTs not captured in this overview of reviews would be sufficient to substantially alter recommendations informing major policy decisions.

### 10.4.2 Cost-effectiveness

Of the 14 costing and cost-effectiveness studies identified in this review, seven were from Europe and six from the US.

For many of the studies, the intervention was compared with usual care which involved some form of disease management by the patient's GP. Where evaluations are based on RCT evidence with six to 24 months of follow-up, most of the health service utilisation is generated in the primary care setting. The method of reimbursement in primary care varies substantially from country to country and therefore findings may not be applicable to the Irish setting. Where reduced healthcare utilisation was reported, it was in terms of reduced GP consultations. Data on reduced hospitalisations was based on longer-term simulation studies that projected adverse events related to uncontrolled or elevated blood pressure.

The majority of studies defined the study population as adults with uncontrolled hypertension. The definition of 'uncontrolled' varied from study to study and could be based on systolic or diastolic blood pressure alone, or a combination of the two. Where interventions were applied to patients with uncontrolled hypertension, it was unclear whether the intervention should continue indefinitely if the patient achieved controlled blood pressure. If the intention is that patients would continue to receive the intervention, then there would be long-term resource implications as the size of the eligible cohort would increase over time.

The relevance of the published intervention costs to Ireland is difficult to evaluate. Many of the studies included a component of home blood-pressure monitoring with or without a telemedicine component to transmit data to their GP or a centralised

management system. Many of the studies found equipment costs to be relatively low and that devices could be reused or had life spans in the region of five years. The use of independently validated devices was not always documented. The cost of training patients in how to use equipment were not always included. For home blood pressure monitoring, the monthly cost per patient ranged from €3.50 to €27.67. For other SMS interventions, the monthly cost per patient ranged from €3.38 to €17.92. The figures are not equivalent due to differing lengths of trials and need for capital investment. However, it does indicate the relatively low cost of providing the evaluated interventions.

Data on effectiveness of interventions was generally derived from RCT evidence that was based on six to 24 months of follow-up. The simulation studies relied on assumptions regarding the duration of effect, some assuming that it would be sustained to life expectancy. Where assumptions around duration of effect were tested in sensitivity analyses, a reduced duration did not change the findings. However, the sustainability of the effect may have implications for whether patients continue to receive the intervention long-term or whether it is used as a time-limited intervention.

Many studies reported cost-effectiveness as a cost per unit reduction in blood pressure. While this may facilitate comparison across the studies, it does not allow comparison with conventional willingness-to-pay thresholds. Results in terms of cost per life year gained or cost per QALY were all based on simulation studies that predicted long-term outcomes as a function of blood pressure. This is a limitation of the included studies and a feature of hypertension interventions.

The included studies have evaluated cost or cost-effectiveness based on evidence of a positive effect either in terms of blood pressure reduction or cost-reduction. Two of the studies based their estimates on RCTs that did not find a statistically significant effect, but the point estimate showed a positive effect. Thus, there is an inherent selection bias that may not be consistent with the published clinical effectiveness data. The cost and cost-effectiveness results should therefore be considered in conjunction with the clinical effectiveness review.

In summary, the review of cost-effectiveness found 14 studies where the effectiveness of interventions was generally derived from RCT evidence. This is in contrast to the review of the clinical effectiveness literature which included 17 systematic reviews of 240 unique RCTs. Half of the cost-effectiveness evaluations were of some form of blood pressure self-monitoring. The available evidence is largely for patients with uncontrolled hypertension. The results were inconsistent across outcomes of ambulatory blood pressure, costs, and healthcare utilisation. In some studies, the intervention had a positive effect; in others it was negative,

relative to usual care. The cost per patient of delivering the interventions was generally low.

## 10.5 Key points

- Sixteen systematic reviews of the clinical-effectiveness of self-management support (SMS) interventions in adults with hypertension were identified for inclusion in this overview of reviews. A diverse range of interventions was identified with the largest volume of evidence obtained for reviews where self-monitoring of blood pressure was the main intervention (n=8). The remaining reviews assessed a range of interventions.
- The quality of the systematic reviews varied, with eight rated as being higher quality reviews.
- The primary evidence underpinning the systematic reviews was found to be generally at moderate to high risk of bias, meaning that studies may have over- or under-estimated the effect size. It comprised 240 unique randomised controlled trials (RCTs) published between 1973 and 2014. These were mainly completed in Europe and North America.
- Based on the quantity and quality of the systematic reviews and the underpinning primary RCTs, there is good evidence that self-monitoring of blood pressure alone or using a range of additional support, including telemedicine, is beneficial in lowering systolic and diastolic blood pressure. However, the clinical significance and durability of the effect are unclear. Additional support seems to enhance the blood pressure lowering effect.
- There is limited evidence of effectiveness of patient education interventions when used alone in improving medication adherence or blood pressure control.
- There is some evidence that community pharmacist interventions which include patient education can lead to statistically significant reductions in systolic and diastolic blood pressure.
- There is some evidence that simplification of medication regimens improves adherence although the clinical significance of this effect may be small.
- There is some evidence that a range of complex SMS interventions (that is involving multiple components or modes of delivery) lead to improvements in blood pressure control. As definite conclusions cannot be drawn, a patient-specific approach may be the most beneficial, involving components tailored to the individual patient with hypertension.
- The review of cost-effectiveness found 14 studies where the effectiveness of interventions was generally derived from RCT evidence. Half of the evaluations were of some form of blood pressure self-monitoring, the available evidence being largely for patients with uncontrolled hypertension.

- The cost-effectiveness results were inconsistent across outcomes of ambulatory blood pressure, costs, and healthcare utilisation. In some studies, the intervention had a positive effect; in others it was negative, relative to usual care. The cost per patient of delivering the interventions was generally low.
- The context of high levels of undetected hypertension and poor blood pressure control in Ireland must be considered when evaluating the applicability of the findings of this overview. There are substantial levels of unmet need to routine care in Ireland, which may impact the estimated incremental benefits of self-management support interventions for hypertension.

# 11 Heart failure

This Health Technology Assessment (HTA) of heart failure self-management support (SMS) is one of a series of rapid HTAs assessing SMS interventions for chronic diseases. Section 11.1 provides a brief description of heart failure followed by separate reviews of the clinical (section 11.2) and cost-effectiveness (Section 11.3) literature for SMS interventions in patients with heart failure. Brief descriptions of the background and methods used are included with full details provided in a separate document (Chapter 3). Section 11.4 includes a discussion of both the clinical and cost-effectiveness findings. The report concludes with a list of key points in relation to heart failure SMS support (section 11.5).

## 11.1 Description of the disease

Heart failure is a chronic condition characterised by an inability of the heart to pump blood effectively, due to systolic and or diastolic dysfunction. It can present as new onset heart failure in people without known cardiac dysfunction, or as acute decompensation of chronic heart failure. The condition can be caused by a range of diseases that result in damage to the heart muscle, including coronary artery disease, myocardial infarction and hypertension. Symptoms of the disease include lung congestion, fluid retention, weakness and an irregular heart rhythm. The average age at diagnosis is 76 years and the overall prevalence of heart failure in Ireland is approximately 1.1%, with a five-year mortality rate of 36%.[371-373] Prevalence is increasing due to better management of the disease and the ageing population, which has resulted in congestive heart failure becoming one of the most common reasons for emergency admission to hospitals in Ireland.[286]

## 11.2 Review of clinical effectiveness

### 11.2.1 Background and methods

The aim of this HTA is to review the clinical effectiveness of self management support (SMS) interventions for a number of chronic conditions including heart failure. Given the large volume of literature available, it was noted that an update of an existing high quality systematic review or a review and appraisal of previously completed systematic reviews of the effectiveness of SMS interventions could be considered sufficient to inform decision-making.

Chronic heart failure was not specifically addressed in the PRISMS report. This report therefore presents a completely new review of systematic reviews rather an update of an existing report. Data extraction and quality assurance of the systematic reviews, meta-analyses and the risk of bias associated with the primary literature was undertaken as described in Chapter 3.1.3. In summary, in order to determine

the quantity, quality, strength and credibility of evidence underpinning the various SMS interventions, quality assurance of both the systematic review methodology (R-AMSTAR weighting by patient or participant trial size) and the meta-analyses (Higgins et al.'s quality assessment tool)[287] was undertaken. While the R-AMSTAR score was used to determine the quality of the systematic reviews, the scores were then weighted by patient or participant trial size, with the quality of evidence being downgraded if the review was based on fewer than 1,000 participants. The quality of the primary evidence was not evaluated directly — where reported, information on the risk of bias of the primary studies was extracted from the systematic reviews.

### 11.2.2 Description of the interventions

A general description of self-management and typical SMS interventions is included in Chapter 2. Heart failure-specific interventions introduced in this Phase IIb report include patient education, psychosocial or behavioural therapy and exercise programmes, as well as different methods of care provision such as home visits or via telephone or the Internet.

Cardiac rehabilitation has been defined as 'a complex intervention offered to patients diagnosed with heart disease, which includes components of health education, advice on cardiovascular risk reduction, physical activity and stress management'. Cardiac rehabilitation services are defined as 'comprehensive, long-term programmes involving medical evaluation, prescribed exercise, cardiac risk factor modification, education and counselling.'[288] While cardiac rehabilitation services may differ in format and intensity, there is a consensus regarding the core components, notably: health behaviour change and education; lifestyle risk factor management (including physical activity and exercise, diet, and smoking cessation); psychosocial health; medical risk factor management; cardio-protective therapies; long-term management; and audit and evaluation.[289] Therefore, cardiac rehabilitation includes elements of self-management support, although the boundary between chronic disease self-management and what is considered 'standard' cardiac rehabilitation is often poorly defined in the literature. This is especially true for exercise-based interventions, as the terms cardiac rehabilitation and exercise-based cardiac rehabilitation are often used interchangeably. Exercise-based interventions have been included in this review in order to provide a summary of the evidence available for this particular component of cardiac rehabilitation. The cardiac rehab may involve varying degrees of self-management depending on whether the exercise training is supervised or unsupervised, or takes place in an inpatient, outpatient, community or home-based setting.

### 11.2.3 Results

The search identified 20 systematic reviews of chronic disease management programmes for people with heart failure, which were published between 2009 and 2015 (see Table 5.1). The quality of the systematic reviews (R-AMSTAR scores) ranged from 18 to 37, with 5 out of 20 achieving a score of 31 or more, indicating a high-quality systematic review. Table 11.1 shows the different types of interventions that were assessed, Table 11.2 shows the degree of overlap between reviews, while Table 11.3 summarises the quality appraisal of the included systematic reviews and meta-analyses and results for mortality and hospital admissions.

**Table 11.1 Summary of included reviews**

| Review | Intervention |
|---|---|
| **Patient education** | |
| **Feltner 2014**[374] | Education of patient or caregiver delivered before or after discharge |
| **Wakefield 2013**[375] | Patient educational interventions |
| **Boyde 2011**[376] | Educational interventions defined as a prespecified learning activity |
| **Ditewig 2010**[377] | Interventions containing a self-management principle and or an education component |
| **Boren 2009**[378] | Heart failure self-management educational programmes |
| **Psychosocial or behavioural interventions** | |
| **Samartizis 2013**[379] | Structured non-pharmacologic intervention conducted by health professionals focused on improving the psychological and or social aspects of a patient's health |
| **Barnason 2012**[380] | Cognitive-behavioural interventions |
| **Exercise** | |
| **Rajati 2014**[381] | Exercise self-efficacy interventions designed to increase any type of physical activity |
| **Taylor (CR) 2014**[382] | Exercise-based interventions with six months' follow-up or longer compared with a no exercise control that could include usual medical care |
| **Tierney 2012**[383] | Specific strategies/interventions to promote or improve exercise/physical activity adherence |
| **Hwang 2009**[384] | Centre-based exercise training, home-based exercise training or concurrent centre and home-based exercise training |

| Review | Intervention |
|---|---|
| **Home Visits** | |
| **Feltner 2014**[374] | Home-visiting programmes for heart failure patients |
| **Gorthi 2014**[385] | In-home visits for heart failure patients |
| **Telehealth** | |
| **Feltner 2014**[374] | Remote monitoring of physiologic data, with or without remote clinical visits |
| **Kotb 2015**[386] | Telemedicine interventions in adult heart failure patients |
| **Conway 2014**[387] | Non-invasive remote monitoring for heart failure |
| **Gorthi 2014**[385] | Structured telephone support, non-invasive and invasive telemonitoring interventions |
| **Nakamura 2013**[388] | Remote patient monitoring interventions in congestive heart failure patients |
| **Pandor 2013**[389] | Home telemonitoring or structured telephone support programmes after recent discharge in patients with heart failure |
| **Giamouzis 2012**[390] | Telemonitoring interventions in chronic HF patients |
| **Clarke 2011**[391] | Telemonitoring on patients with congestive heart failure |
| **Inglis (CR) 2010**[392] | Structured telephone support or telemonitoring programmes for patients with chronic heart failure |
| **Pare 2010**[393] | Home telemonitoring in heart failure patients |

Key: CR = Cochrane Review; HF = heart failure.

## Table 11.2 Study overlap

| # | Review | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Feltner 2014[374] | **47** | | | | | | | | | | | | | | | | | | | |
| 2 | Wakefield 2013[375] | 16 | **35** | | | | | | | | | | | | | | | | | | |
| 3 | Boyde 2011[376] | 5 | 3 | **19** | | | | | | | | | | | | | | | | | |
| 4 | Ditewig 2010[377] | 5 | 7 | 5 | **19** | | | | | | | | | | | | | | | | |
| 5 | Boren 2009[378] | 6 | 12 | 6 | 9 | **35** | | | | | | | | | | | | | | | |
| 6 | Samartizis 2013[379] | 4 | 7 | 1 | 3 | 7 | **16** | | | | | | | | | | | | | | |
| 7 | Barnason 2012[380] | 3 | 3 | 5 | 2 | 4 | 1 | **19** | | | | | | | | | | | | | |
| 8 | Rajati 2014[381] | 0 | 0 | 0 | 0 | 0 | 0 | 0 | **10** | | | | | | | | | | | | |
| 9 | Hwang 2009[384] | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | **19** | | | | | | | | | | | |
| 10 | Tierney 2012[383] | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | **9** | | | | | | | | | | |
| 11 | Taylor 2014[382] | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 7 | 1 | **33** | | | | | | | | | |
| 12 | Kotb 2015[386] | 8 | 11 | 3 | 7 | 5 | 1 | 2 | 0 | 0 | 0 | 0 | **30** | | | | | | | | |
| 13 | Conway 2014[387] | 8 | 8 | 2 | 7 | 6 | 3 | 2 | 0 | 0 | 0 | 0 | 16 | **25** | | | | | | | |
| 14 | Gorthi 2014[385] | 12 | 16 | 3 | 5 | 10 | 4 | 2 | 0 | 0 | 0 | 0 | 15 | 14 | **52** | | | | | | |
| 15 | Nakamura 2013[388] | 2 | 3 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 6 | 5 | 7 | **13** | | | | | |
| 16 | Pandor 2013[389] | 10 | 7 | 0 | 3 | 2 | 2 | 1 | 0 | 0 | 0 | 0 | 9 | 13 | 10 | 4 | **21** | | | | |
| 17 | Giamouzis 2012[390] | 2 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 6 | 4 | 7 | 5 | 3 | **12** | | | |
| 18 | Clarke 2011[391] | 3 | 4 | 1 | 1 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 5 | 6 | 10 | 4 | 4 | 4 | **13** | | |
| 19 | Inglis 2010[392] | 9 | 8 | 2 | 7 | 6 | 3 | 2 | 0 | 0 | 0 | 0 | 21 | 21 | 14 | 5 | 12 | 2 | 5 | **25** | |
| 20 | Pare 2010[393] | 3 | 4 | 0 | 2 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 3 | 3 | 3 | 0 | 3 | 0 | 0 | 3 | **17** |

## Table 11.3 Quality appraisal and summary of findings from meta-analyses

| Review | Quality of systematic review | | | Primary studies | | Quality of meta-analysis | All-cause mortality | All-cause hospital admissions | HF hospital admissions |
|---|---|---|---|---|---|---|---|---|---|
| | R-AMSTAR score | Participants | Quality | N | Low-risk | | | | |
| Patient education | | | | | | | | | |
| **Feltner 2014**[374] | 31 | <1,000 | ** | 4 | 1 | High | RR 1.20 (0.52–2.76) | RR 1.14 (0.84–1.54) | RR 0.53 (0.31–0.90) |
| **Wakefield 2013**[375] | 23 | 8,071 | ** | 35 | - | Moderate | OR 0.79 (0.69-0.92)** | SMD 0.157 (0.071-0.244) | - |
| **Boyde 2011**[376] | 22 | 2,686 | ** | 19 | - | N/A | - | - | - |
| **Ditewig 2010**[377] | 31 | 4,162 | *** | 19 | 8 | N/A | - | - | - |
| **Boren 2009**[378] | 19 | 7,413 | ** | 35 | - | N/A | - | - | - |
| Psychosocial or behavioural interventions | | | | | | | | | |
| **Samartizis 2013**[379] | 21 | 2,180 | ** | 16 | - | N/A | - | - | - |
| **Barnason 2012**[380] | 18 | 3,166 | ** | 19 | - | N/A | - | - | - |
| Exercise | | | | | | | | | |
| **Rajati 2014**[381] | 18 | 800 | * | 10 | - | N/A | - | - | - |
| **Hwang 2009**[384] | 24 | 1,069 | ** | 19 | - | N/A | - | - | - |
| **Tierney 2012**[383] | 27 | 3,231 | ** | 9 | - | N/A | - | - | - |
| **Taylor 2014**[382] | 37 | 4,740 | *** | 33 | 21 | High | RR 0.93 (0.69-1.27) | RR 0.75 (0.62-0.92) | RR 0.61 (0.46-0.80) |
| Home visit | | | | | | | | | |
| **Feltner 2014** [374] | 31 | >1,000 | *** | 16 | 1 | High | RR 0.77 (0.60–0.997) | RR 0.75 (0.68–0.86) | RR 0.51 (0.31–0.82) |
| **Gorthi 2014**[385] | 19 | >1,000 | ** | 7 | - | N/A | - | - | - |
| Structured telephone support | | | | | | | | | |
| **Feltner 2014**[374] | 31 | >1,000 | *** | 13 | 0 | High | RR 0.74 (0.56–0.97) | RR 0.92 (0.77–1.10) | RR 0.74 (0.61–0.90) |
| **Kotb 2015**[386] | 26 | 10,193 | ** | 30 | 17 | Network Meta-analysis | OR 0.80 (0.66-0.96) | OR 0.88 (0.74-1.06) | OR 0.96 (0.56-0.85) |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Conway 2014**[387] | 24 | >4,000 | ** | 25 | - | Moderate | RR 0.87 (0.75-1.01) | - | RR 0.77 (0.68-0.87) |
| **Inglis 20110**[392] | 35 | 8,323 | *** | 25 | 7 | High | RR 0.88 (0.76-1.01) | RR 0.92 (0.85-0.99) | RR 0.77 (0.68-0.87) |
| **Gorthi 2014**[385] | 19 | >1,000 | ** | 14 | - | N/A | - | - | - |
| Structured telephone support : human –human | | | | | | | | | |
| **Pandor 2013**[389] | 33 | >1,000 | *** | 21 | 10 | Network Meta-analysis | HR 0.77 (0.55-1.08) | HR 0.97 (0.70-1.31) | HR 0.77 (0.62-0.96) |
| Structured telephone support : human-machine | | | | | | | | | |
| **Pandor 2013**[389] | 33 | >1,000 | *** | 21 | 10 | Network Meta-analysis | HR 0.98 (0.41-2.33) | HR 1.06 (0.44-2.53) | HR 1.03 (0.66-1.54) |
| Telemonitoring | | | | | | | | | |
| **Feltner 2014**[374] | 31 | <1,000 | ** | 6 | 0 | High | RR 0.93 (0.25–3.48) | RR 1.11 (0.87–1.42) | RR 1.70 (0.82–3.51) |
| **Kotb 2015**[386] | 26 | 10,193 | ** | 30 | 17 | Network Meta-analysis | OR 0.53 (0.36-0.80) | OR 0.75 (0.48-1.18) | OR 0.64 (0.39-0.95) |
| **Conway 2014**[387] | 24 | >4,000 | ** | 25 | - | High | RR 0.62 (0.50-0.77) | - | RR 0.75 (0.63-0.91) |
| **Nakamura 2013**[388] | 25 | 3,337 | ** | 13 | - | Low | RR 0.76 (0.62-0.93) | - | - |
| **Giamouzis 2012**[390] | 17 | 3,877 | ** | 12 | - | N/A | - | - | - |
| **Clarke 2011**[391] | 25 | 3,480 | ** | 13 | - | Moderate | RR 0.77 (0.61-0.97) | RR 0.99 (0.88-1.11) | RR 0.73 (0.62-0.87) |
| **Inglis 2010**[392] | 35 | 8,323 | *** | 25 | - | High | RR 0.66 (0.54-0.81) | RR 0.91 (0.84-0.99) | RR 0.79 (0.67-0.94) |
| **Pare 2010**[393] | 19 | >1,000 | ** | 17 | - | N/A | - | - | - |
| **Gorthi 2014**[385] | 19 | >1,000 | ** | 14 | - | N/A | - | - | - |
| Telemonitoring - 24/7 | | | | | | | | | |
| **Pandor 2013**[389] | 33 | >1,000 | *** | 21 | 10 | Network Meta-analysis | HR 0.49 (0.20-1.18) | HR 0.81 (0.33-2.00) | - |
| Telemonitoring - Office Hours | | | | | | | | | |
| **Pandor 2013**[389] | 33 | >1,000 | *** | 21 | 10 | Network Meta-analysis | HR 0.76 (0.49-1.18) | HR 0.75 (0.49-1.10) | HR 0.95 (0.70-1.34) |

**Key**: **HF** – heart failure; **HR** – hazard ratio; **N/A** – not applicable; **OR** - odds ratio; **RR** - risk ratio.

** Correspondence with the author indicates that what was reported as mortality was actually survival, so the value included in the above table is the reciprocal of the result reported in the article

### 11.2.4 Summary of findings

This section provides a narrative summary of the findings, relevance and applicability of the included reviews for each type of heart failure self-management support intervention. A detailed account of the data extracted from each review is provided in Appendix A11.1.

#### Patient education interventions

Five reviews were identified that examined the effectiveness of patient-education interventions in chronic heart failure.[374-378] One of these were rated as high quality (R-AMSTAR greater than [>] 30 and >1,000 patients).[377] The other four were moderate quality (R-AMSTAR score less than [<] 31 and >1,000 patients or R-AMSTAR score of >30 and <1,000 patients).[374-376;378]

**Three-star (***) reviews**

One high-quality review concluded that the limitations of the available evidence made it impossible to reliably estimate the effect of patient-education interventions on mortality, all-cause hospital readmissions, chronic heart failure hospitalisation rate and quality of life in patients with chronic heart failure.[377] Of the nine studies identified in this review that reported mortality outcomes, eight found no significant difference between the control and intervention groups. It also identified four studies that reported hospital admission results, two of which found no effect.

**Two-star (**) reviews**

One moderate quality review (R-AMSTAR >30 and <1,000 patients) carried out a pooled analysis of educational interventions that found no significant effect on mortality or all-cause readmission rates, but did find a reduction in heart failure-specific readmission (RR 0.53, 95% CI 0.31 to 0.90).[374] Another moderate quality review (R-AMSTAR <31, >1,000 patients) reported that most heart failure self-management programmes had a teaching component, with the most frequent teaching topics being symptom recognition and management, medication review, and self-monitoring. However, it reported that individual interventions used in the programme are not described in sufficient detail to permit programme replication.[375] The final two reviews were more descriptive in nature, and characterised educational interventions as mainly involving one-to-one didactic sessions focused on symptom recognition and management.[376;378]

**Summary statement for patient education interventions**

Based on the quantity and quality of the systematic reviews and the underpinning primary randomised controlled trials (RCTs), there is a lack of good quality evidence that patient-education programmes are associated with improvements in mortality, hospital readmissions and quality of life in patients with chronic heart failure.

## Psychosocial or behavioural interventions

### Two-star (**) reviews

Two reviews, both of moderate quality, were identified that reported results for psychosocial or behavioural interventions in chronic heart failure.[379;380]

Neither reported results for mortality or healthcare usage. One reported that psychosocial interventions improved quality of life of heart failure patients (Standardised Mean Difference [SMD] 0.46, 95% CI 0.19 to 0.72), and that face-to-face interventions showed greater improvement compared with telephone interventions.[379] The other was an integrative review, which reported that psychosocial interventions were most frequently used to improve patient's heart failure self-care, and noted that the majority of the studies reported improvements in heart failure patients' self-care maintenance and management behaviours.[380]

**Summary statement for psychological or behavioural interventions**

Based on the quantity and quality of the systematic reviews and the underpinning primary RCTs, there is a lack of evidence that psychosocial or behavioural interventions are associated with a reduction in either mortality or healthcare usage. However, there is some evidence showing that these types of interventions, particularly when delivered face-to-face, are associated with improvements in quality of life.

## Exercise interventions

Four reviews that examined the impact of exercise interventions in the management of heart failure were identified in the search.[381-384]

### Three-star (***) reviews

One high quality Cochrane systematic review comparing exercise-based interventions (alone or in conjunction with health education and psychological interventions), with usual medical care or cardiac rehabilitation that included no exercise training, failed to find a mortality benefit at one year (RR 0.93 [95% CI 0.69 to 1.27]). However, it did report a trend toward reduced mortality in a pooled

analysis of studies with follow-up of greater than one year, though this was not statistically significant (RR 0.88 [95% CI 0.75 to 1.02]).[382] This study also reported a reduction in overall and heart failure-specific hospital admissions (RR 0.75 [95% CI 0.62 to 0.92] and RR 0.61 [95% CI 0.46 to 0.80], respectively) and improved quality of life.

### Two-star (**) reviews

One moderate quality review that specifically examined home exercise programmes found that these were associated with improvements in exercise duration, peak oxygen consumption and distances achieved in the six-minute walk test.[384] However, this review did not report pooled results for more relevant clinical outcomes.

A further moderate quality study focusing exclusively on ways to improve exercise adherence reported that although short-term benefits were achieved using exercise prescriptions, goal setting, feedback and problem-solving, longer-term maintenance of exercise was less successful.[383] The authors also reported that addressing self-efficacy may be a particularly useful area to consider. This was examined in the final, low-quality review, which reported a lack of evidence evaluating self-efficacy strategies to improve exercise in heart failure. It did report, however, that the most common strategies to improve patients' self-efficacy were performance accomplishments, vicarious experience, verbal persuasion, and emotional arousal.[381]

**Summary statement for exercise interventions**

Based on the quantity and quality of the systematic reviews and the underpinning primary RCTs, there is good evidence that exercise interventions are associated with a reduced likelihood of readmission to hospital. However, no statistically significant mortality effect was observed at 12 months' follow up.

## Home-visit interventions

One high-quality and one moderate-quality review examining the effectiveness of home-visiting interventions for heart failure patients were identified.[374;385]

### Three-star (***) reviews

A high-quality 2015 review by Feltner et al. found evidence of a statistically significant effect on both mortality and hospital readmission rates at three to six months (RR 0.77 [95% CI 0.60 to 0.996] and RR 0.75 [95% CI 0.66 to 0.86], respectively).[374] This review compared a number of different types of interventions and included a total of 47 RCTs. Eight of these reported the results of home-visit

interventions and were used to calculate the pooled estimate for mortality and readmission. While the pooled estimate of effect on mortality was significant at the p<0.05 level, no individual study reported a significant effect.

### Two-star (**) reviews

The moderate quality review published in 2014 identified seven primary studies comparing home visits with usual care, only three of which were associated with a significant improvement in hospital readmission, while none were able to demonstrate a significant reduction in all-cause mortality.[385]

**Summary statement for home-visit interventions**

Based on the quantity and quality of the systematic reviews and the underpinning primary RCTs, there is high-quality evidence that home-visit interventions are associated with a reduction in mortality and hospital readmission rates. However, one moderate-quality review failed to replicate these findings.

## Telemedicine interventions

Ten reviews assessed the effectiveness of telehealth interventions in patients with chronic heart failure.[374;385-393] Two were rated high quality (R-AMSTAR score >30 and a combined total of >1,000 patients).[389;392] The eight remaining reviews were all rated moderate quality (R-AMSTAR score <31 and a combined total of >1,000 patients or R-AMSTAR >30 and < 1,000 patients).[374;385-388;390;391;393]

### Three-star (***) reviews

A 2013 high-quality systematic review by Pandor et al. from the UK — examining home telemonitoring or structured telephone support programmes compared with standard care (primarily GP follow up) after recent discharge in patients with heart failure — failed to find a significant effect on mortality or hospital admission in a pooled analysis of studies with follow-up of between three and 15 months.[389] In contrast, a high-quality Cochrane review of structured telephone support and telemonitoring (also compared with standard care) in the management of patients with chronic heart failure published in 2010 found that telemonitoring was associated with a 34% mean reduction in all-cause mortality (RR 0.66 [95% CI 0.54 to 0.81]) and that structured telephone support was associated with a non-statistically significant 12% mean reduction in all-cause mortality (RR 0.88 [95% CI 0.76 to 1.01]).[392] The length of follow-up in the studies included in this review ranged from three to 18 months, with many studies reporting outcomes after 12 months. It also reported that both structured telephone support and telemonitoring significantly reduced heart failure-related hospitalisations (RR 0.77 [95% CI 0.68 to 0.87] and RR 0.79 [95% CI 0.67 to 0.94] respectively). Smaller, but still statistically

significant, reductions were also found for all-cause hospitalisations (RR 0.92 [95% CI 0.85 to 0.99] for structured telephone support and RR 0.91 [95% CI 0.84 to 0.99] for telemonitoring).[392]

### Two-star (**) reviews

One moderate-quality review examined remote monitoring of physiological signals with or without remote clinical consultations (such as videoconferencing) and found no significant effect in either mortality or hospital readmissions at three to six months follow-up.[374] Among the seven other moderate quality studies, there was broad agreement that telemonitoring in heart failure patients was associated with reduction in both mortality and heart failure-related hospital admissions.[385-388;390;391;393] Statistically significant estimates of the mean reduction ranged from 23% to 47% for mortality,[386;391] and 27% to 36% for heart failure-related hospital admissions.[386;387] There were a high degree of overlap between the studies included in these reviews, with 21 studies appearing in both the Inglis and Kotb studies.[386;392] There was agreement between the two moderate-quality reviews reporting a meta-analysis of structured telephone support interventions that the intervention was associated with reduced hospital admission, but while one reported a statistically significant reduction in mortality (OR 0.80 [95% CI 0.66 to 0.96]), the other found a mean decrease that was not statistically significant at the p=0.05 level (RR 0.87 [95% CI 0.75 to 1.01]).

**Summary statement for telemedicine interventions**

Based on the quantity and quality of the systematic reviews and the underpinning primary RCTs, there is high-quality evidence that telemedicine interventions are associated with a significant reduction in both mortality and hospitalisation rates. However, these findings are not shared across all high-quality reviews.

## 11.3 Systematic review of cost-effectiveness

A review of the economic literature was undertaken to assess the available evidence for self-management support (SMS) interventions for adults chronic heart failure. Studies were included if they compared the costs and consequences of an SMS intervention to routine care.

### 11.3.1 Search strategy

A search was carried out to identify economic analyses of SMS interventions. In tandem with the systematic review of clinical effectiveness, the search for economic evaluations was carried out in MEDLINE, Embase and the Cochrane Library. The same search terms were used with the exception of terms for systematic review and

meta-analysis. In place of these, search terms and filters for economic evaluations were applied. The search was carried out up until 4 March 2015.

The PICOS (Population, Intervention, Comparator, Outcomes, Study) design analysis used to formulate the search is presented in Table 11.4 below.

**Table 11.4 PICOS analysis for identification of relevant studies**

| | |
|---|---|
| **Population** | Adults greater than and equal to [≥] 18 years old with diagnosed chronic heart failure. |
| **Intervention** | Any self-management support intervention incorporating education, training or support. |
| **Comparator** | Routine care. |
| **Outcomes** | Cost or cost-effectiveness of intervention. |
| **Study design** | Randomised controlled trials (RCTs), case-control studies, observational studies, economic modelling studies. |

The following study types were excluded if:

- a nursing home or non-community dwelling population was included
- it included a paediatric population
- cost data were not clearly reported
- published prior to the year 2000 (due to limited relevance).

As outlined in Chapter 3.2.2 and in accordance with national HTA guidelines, assessment of the quality of the studies using the Consensus on Health Economic Criteria (CHEC)-list was performed independently by two people. For studies that included an assessment of cost-utility or an economic modelling approach, assessment of the relevance to the Irish healthcare setting and their credibility was considered using a questionnaire from the International Society of Pharmacoeconomics and Outcomes Research (ISPOR). Studies that were considered poor quality will not be discussed below, although data from those studies are included in the evidence tables.

### 11.3.2 Results

The initial search identified 118 potentially relevant articles. Three reviewers independently evaluated studies based on title, abstract and full text. Thirty nine studies were identified as applicable. Seven additional studies were identified following hand searching of the systematic reviews of clinical effectiveness included in Section 11.2 for primary studies that included economic outcomes, leaving a total

of 46 studies in this review, see table below. Data extraction was carried out independently by two reviewers with any disagreements resolved by discussion.

| Country | Number of studies |
|---|---|
| United States | 23 |
| Spain | 4 |
| Italy | 4 |
| Australia | 3 |
| UK | 3 |
| Netherlands | 3 |
| Germany | 2 |
| Hong Kong | 1 |
| Ireland | 1 |
| Sweden | 1 |
| Taiwan | 1 |
| Total | 46 |

The included studies were all published between 2001 and 2014. The characteristics of the included studies are given in Table 11.5.

## Table 11.5 Characteristics of the studies included

| Study | Country | Intervention |
|---|---|---|
| **Agren (2001)** | Sweden | SMS education |
| **Aguado (2010)*** | Spain | SMS education |
| **Anderson (2005)** | US | Disease management |
| **Berg (2004)** | US | Telemedicine |
| **Boyne (2013)** | Netherlands | Telemedicine |
| **Bruggink (2007)** | Netherlands | Heart failure clinic |
| **Chen (2010)** | Taiwan | Disease management |
| **Cui (2013)** | Canada | Telemedicine |
| **Dar (2009)** | UK | Telemedicine |
| **Discher (2003)** | US | Disease management |
| **Dunagan (2005)** | US | Telemedicine |
| **Giordano (2009)** | Italy | Telemedicine |
| **Gregory (2006)** | US | Disease management |
| **Hebert (2008)** | US | Disease management |
| **Hendricks (2014)** | Germany | Disease management |
| **Inglis (2006)** | Australia | Disease management |
| **Jerant (2001)** | US | Telemedicine |
| **Kasper (2002)** | US | Multidisciplinary care |
| **Klersy (2011)** | Italy | Telemedicine |
| **Koelling (2005)** | US | SMS education |
| **Krumholz (2002)** | US | SMS education |
| **Kwok (2008)** | Hong Kong | Disease management |
| **Laramee (2003)** | US | Disease management |
| **Ledwidge (2003)** | Ireland | Multidisciplinary care |
| **Lopez (2006)** | Spain | SMS education |
| **Maeng (2014)** | US | Telemedicine |
| **Mejia (2014)** | UK | Cognitive behavioural therapy |

| Study | Country | Intervention |
|---|---|---|
| **Miller (2009)**** | US | Disease management |
| **Morcillo (2005)*** | Spain | SMS education |
| **Murray (2007)** | US | Pharmacist intervention |
| **Naylor (2004)** | US | Disease management |
| **Pandor (2013)** | UK | Telemedicine |
| **Piepoli (2006)** | Italy | Multidisciplinary care |
| **Postmus (2011)** | Netherlands | Disease management |
| **Pugh (2001)** | US | Disease management |
| **Riegel (2004)** | US | SMS education |
| **Riegel (2002)** | US | Telemedicine |
| **Roig (2006)** | Spain | Disease management |
| **Scalvini (2005)** | Italy | Telemedicine |
| **Smith (2008)**** | US | Disease management |
| **Sohn (2012)** | Germany | Telemedicine |
| **Soran (2010)** | US | Telemedicine |
| **Stauffer (2011)** | US | Transitional care |
| **Stewart (2002)** | Australia | Multidisciplinary care |
| **Tsuyuki (2004)** | US | Disease management |
| **Wootton (2009)** | Australia | Telemedicine |

* The study by Aguado et al. is an update of an earlier study by Morcillo et al..
** The study by Miller et al. is modelled using data from Smith et al..

The studies were classified according to the type of intervention assessed: SMS education programmes, telemedicine, disease management, multidisciplinary care and other SMS interventions. Of note, many interventions included more than one element such as case management plus telephone-based support or education plus physical activity.

This review captures all SMS interventions assessed for chronic heart failure and retrieved few conventional economic evaluations. Thirty nine of the retrieved studies gathered cost data as part of a randomised controlled trial (RCT) while data for four other studies were based on a non-randomised study designs.

Study quality was assessed using the Consensus on Health Economic Criteria (CHEC) list.[24] For studies that included an assessment of cost-utility or an economic modelling approach, applicability of the findings were evaluated using the ISPOR questionnaire.[25] The quality of the included studies was predominantly poor, and the following discussion sections will focus on the findings of studies found to be of better quality. Where possible, costs are reported in Irish euro, and were inflated to 2014 using the local consumer price index for health before transferred into Irish euro using the purchasing power parity index.

#### 11.3.2.1 SMS education programmes

Six unique studies were identified that investigated a variety of SMS education programmes (See Appendix A11.3). The studies included one cost-utility analysis and five costing studies. All of the studies were based on patient data gathered alongside a randomised controlled trial (RCT) with a follow-up ranging from three to 24 months. Study sizes ranged from 62 to 191 patients. There was one Swedish study, two from Spain and three from the US. Interventions included education programmes delivered by a healthcare specialist at home or in a primary care setting, while a US study examined a peer-support group delivered by trained mentors.

A 2013 Swedish study by Agren et al. compared a nurse-led education and psychosocial support programme with usual care for recently discharged heart failure patients and their partners. The intervention was delivered in three face-to-face sessions and included nurse-led counselling, with educational, supportive and behavioural components two, six and 12 weeks after discharge. After 12 months, significant improvements in quality of life from baseline were observed in both groups, however, the difference between groups was not significant. The total cost of the intervention including transportation was estimated to be €15,825 or €223 per patient.

The intervention, which was assessed from a societal perspective, was not found to be cost-effective for the patient alone due to increased costs and lack of utility gains. However, when the combined costs and benefits for the patient and partner or caregiver were examined, the intervention was found to be cost-effective, with a cost per QALY gained of €16,159.

The 2010 Spanish study by Aguado et al. randomly assigned patients hospitalised with systolic heart failure to either usual care or a once-off, home-based educational session by trained nursing staff one week after hospital discharge. The RCT recruited 106 patients admitted with heart failure over a 24-month period. A significant decrease in healthcare usage was reported in favour of the intervention group after 24 months of follow-up with reductions in emergency room visits (mean 0.68 (SD

0.9) versus. 2.00 (SD1.97), p < 0.001) and unplanned readmissions (mean 0.68 (SD 1.94) versus. 1.71 (1.67) p < 0.003); no difference in mortality was observed (46.7% versus 55.4%, p=0.448). The mean cost of the educational intervention was €70.59, and included salary and travel costs for the nursing staff and the cost of educational material. The mean total cost per person was €898 for the intervention group and €2,879 for the control group, with a statistically significant difference of €1,982 (p < 0.001). The authors concluded that a single educational home visit by a nurse after discharge from hospital leads to improvements in health-related quality of life (HRQoL) and has the potential to result in cost savings as a result of decreased healthcare usage.

The 2002 US study by Krumholz et al. recruited 88 heart failure patients in a prospective RCT to investigate the impact of an education and support intervention on one-year readmission rates, mortality and costs of care. After adjusting for clinical and demographic characteristics, the intervention was associated with a significantly lower risk of readmission compared with the control group (hazard ratio 0.56, 95% CI: 0.32 to 0.96, p=0.03) as well as a decrease in the total number of readmissions (49 vs. 80, p=0.06). A significant reduction in the relative risk of readmission or death during the 12-month follow up (RR 0.69, 95%CI 0.52-0.92, p=0.01) was observed in favour of the intervention group. The intervention was estimated to cost USD $530 per patient. The total costs of hospital readmissions in the control and intervention groups were $21,935 and $14,420, respectively resulting in an estimated net reduction in the average cost of care of $6,985 per patient in the intervention group.

The 2006 Spanish study by Lopez et al. assessed the efficacy of a multi-factorial educational intervention by a pharmacist for patients with heart failure. Outcomes for 134 patients (mean age 75 years) with a low educational level were assessed during 12 months' follow-up. The intervention was found to reduce hospital readmissions (adjusted hazard ratio 0.56; 95%CI 0.32-0.97) and was predicted to prevent one readmission a year being prevented per every 6.5 patients with heart failure. Reductions in hospital bed days were observed at two (mean 1.7 vs. 3.5, p=0.034)), six (4.3 vs. 6.8, p=0.02) and 12 (5.9 versus 9.6, p>0.05) months. The cost of the intervention was €2,170 equating to a cost of €31 per patient. In terms of total costs, the intervention resulted in savings of €30,995 (€100,815- €69,820) or €578 per patient.

Koelling et al. used data from an RCT with six-month follow-up to inform a post-hoc economic evaluation of a nurse-provided education programme. The intervention group had a lower risk of hospitalisation or death, but there was no difference in the mortality rates between groups. The intervention cost €100 per subject, with the overall cost of care significantly lower in the education group €3,477.

#### 11.3.2.2 Telemedicine programmes

There were 15 studies found that evaluated telemedicine programmes (see Appendix A11.4). Of the identified studies, four were cost-utility analyses and the remaining 11 were generally costing or cost-minimisation studies. Details of the four cost-utility studies and two of the costing studies which were identified as higher quality studies are discussed.

In 2013, Boyne et al. undertook an economic evaluation of telemonitoring versus usual care for 382 heart failure patients from the Netherlands. The effectiveness of the telemonitoring programme was expressed as QALYs gained. At 12 months' follow up, no difference in HRQoL (-0.0031 QALY, 95% CI -0.0552 to 0.0578) was observed. The total cost of telemonitoring was €17,323 compared with €17,192 in the usual care group, a difference of €140 between the groups. Compared with usual care, the study reported an incremental cost-effectiveness ratio (ICER) of €41,858 per QALY gained. However, given the lack of a statistically significant difference in QALYs, presentation of an ICER would appear to be inappropriate.

A 2013 Canadian study by Cui et al. randomised 179 patients aged 40 and over with a diagnosis of chronic heart failure (levels II to IV) to one of two telemonitoring (health lines or health lines plus monitoring [HLM]) interventions or to usual care. The health lines intervention comprised standard care plus access to nurse-led telephone support that provided suggestions about the patient's daily disease management. HLM included provision of monitoring devices and instructions on how to use them in addition to the telephone support and usual care. The mean per patient cost of the intervention was €1,386 and €1,576 for health lines and HLM, respectively. When compared with usual group, the interventions were shown to result in a reduction in healthcare usage, although this finding was not significantly different between groups. The total calculated saving from averted healthcare utilisation costs through the interventions was €21,163 or €178 per patient. HRQoL, as measured by SF-6D utility scores, differed significantly between the groups ($p=0.0247$). Cui et al. reported that both interventions (health lines and HLM) dominated (cost less and were more effective than) standard care and reported an ICER of €2,224/QALY for health lines relative to HLM. The study concluded that health lines had an 85.8% probability that of being cost-effective at a willingness-to-pay threshold of €37,381.

In a 2011 study by Klersy et al. undertook a cost-effectiveness analysis of a remote patient monitoring programme compared with usual care and focusing on hospitalisations as the primary outcome. The data from 21 RCTs was collected to conduct an economic analysis of a remote monitoring intervention. Remote patient monitoring was associated with significantly fewer hospitalisations for heart failure at 12 months ($p<0.001$), however, there was no change in length of stay. The QALY

gain associated with the reduction in hospitalisations was estimated to be 0.04 for surviving patients and when this was added to the QALY gain of 0.02 for reduced mortality, the total QALY gain for remote patient monitoring was 0.06.

Remote patient monitoring was found to be a dominant strategy over existing treatments of heart failure as it resulted in cost saving and QALY gains. Sensitivity analysis that tested a variety of situations estimated that the difference in costs between remote patient monitoring and usual care ranged from about €300 to €1,000, with the intervention always being less costly than usual care. These cost savings were mostly driven by a reduction in the number of heart failure hospitalisations. The authors noted that an important caveat to this finding was the limited follow-up time of the studies considered in the meta-analysis, which restricted the time horizon for the cost-effectiveness assessment to one year.

Using results from a systematic review of the literature, a 2013 UK study by Pandor et al. modelled the cost-effectiveness of telemedicine strategies versus usual care for adults recently discharged (within 28 days) from acute care after an exacerbation of chronic heart failure. Interventions comprised either structured telephone support via human-to-machine (STSHM) interface; structured telephone support via human-to-human (STSHH) contact; or home telemonitoring (TM), and were compared with usual care. The average total cost per patient for the STSHM intervention over six months was estimated to be €963, equating to €160 per patient per month. The total cost per patient for the office hours' TM intervention for six months was estimated to be €1,416, equating to €233 per patient per month. STSHH intervention was estimated to cost €1448 over six months, equating to a monthly cost of €241 per patient. The expected costs over a lifetime (30-year time horizon) differed for each strategy, with STSHH having the highest costs at €12,938 followed by TM during office hours (€12,757), STSHM (€12,125) and usual care (€11,421). QALY gains were reported for all intervention groups. In terms of utilisation, TM with medical support during office hours or 24-seven was associated with 25% (HR 0.75, 95% CI 0.49 to 1.10) or 19% (HR 0.81, 95% CI 0.33 to 2.00) reduction in all-cause hospitalisations, respectively, whereas there was no major effect of STSHM (HR 1.06, 95% CI 0.44 to 2.53) or STS HH (HR 0.97, 95% CI 0.70 to 1.31). TM during office hours was identified as the most cost-effective strategy with an ICER of €12,871/QALY compared with usual care. STSHM was dominated by usual care. Limitations noted by the authors included considerable variability in what constituted remote monitoring and the absence of robust estimations of cost.

A 2014 study carried out in the US by Maeng et al investigated the cost-effectiveness of telemonitoring for disease management. The study analysed the impact of the telemonitoring programme using claims data related to changes in hospital admission and readmission rates as well as cost of care among the

insurance plan members with heart failure who had participated in the programme. The study found that members in the sample had experienced significant reductions in their odds of hospital admissions (23% lower) as well as 30-day and 90-day readmissions (44% and 38% lower, respectively) in a given month. The total cost of the programme was USD $1,596 per member, per month while the implementation of the heart failure telemonitoring programme was associated with approximately 11% cost savings during the study period. Maeng et al estimated that the return on investment associated with the telemonitoring programme was approximately 3.3. That is, for every $1 spent to implement the programme, there was a $3.30 return on this investment in terms of the cost savings accrued to the insurance plan. They concluded that these findings imply that telemonitoring can be an effective add-on tool for managing elderly patients with heart failure.

A 2012 Germen study by Sohn et al. undertook an economic analysis to evaluate the programme 'Telemedicine for the Heart'. The programme consisted of nurse calls to motivate patients to perform regular self-measurements (blood pressure, pulse, weight) with either their own or telemedical measuring devices provided by the programme. The primary outcome of the study was healthcare utilisation and the study reported there were fewer hospital admissions in the programme group (1.02 versus 1.30 per patient per year in the intervention and control groups, respectively). Significant cost differences in favour of the study group of up to 25% in relation to the total cost could be detected. This corresponded to a reduction of €2,633 in costs per patient per year relative to the control group. The cost saving were mainly for patients with less severe heart failure and the study found that more severe heart failure patients incurred increased costs and a cost disadvantage.

Miller et al. developed a Markov model to compare a disease management programme with usual care, over a patient's lifetime. Baseline model results indicated that patients with systolic heart failure would live an average of 0.141 years (51 days) longer with disease management than those in the control group. The corresponding discounted QALY benefit was 0.111 per patient. Discounted lifetime costs per patient averaged €91,182 and €97,156 for the control and disease management groups respectively. The average (undiscounted) per-patient cost of the disease management programme was estimated at €10,576 (€303 a month for an 18-month disease management programme or €132 a month over average patient lifetime). The estimated ICER was calculated to be €53,767 per QALY saved. The authors concluded that that disease management of heart failure patients can be cost-effective in the long term, and that short-term results from a clinical trial might not reveal long-term cost-effectiveness.

#### 11.3.2.3 Multidisciplinary care interventions

Three studies were identified that examined multidisciplinary care interventions, including one cost benefit study from Ireland and one prospective randomised controlled trial each from the US and Australia (see Appendix A11.5). All studies examined the ability of multidisciplinary care to reduce rehospitalisations for recently discharged heart failure patients.

The 2003 Irish study by Ledwidge et al. aimed to determine whether multidisciplinary care can significantly reduce rates of unplanned hospitalisations. A total of 98 New York Heart Association (NYHA) class IV heart failure patients (mean age 70.8) were randomised to multidisciplinary care (n=51) or routine care (RC; n=47). Over a three-month follow up, there was an absolute reduction of 10 rehospitalisations (12 versus 2) in favour of the intervention group. The service cost was estimated at €113 (95% CI: 185–244) per patient over three months, corresponding with a cost per hospitalisation prevented of €586, and generating a net cost saving per patient treated of €729.

A 2009 US study by Kasper evaluated the effect of a multidisciplinary outpatient management programme on hospital readmissions and mortality over a six-month period. Two hundred chronic heart failure patients with a mean age of 63 years were randomised to multidisciplinary or routine care. The intervention comprised education, support and telecare from a four-member intervention team made up of a telephone nurse coordinator, the chronic heart failure nurse, the chronic heart failure cardiologist and the patient's primary physician.

There were fewer hospital admissions for any reason in the intervention group. Quality of life, measured by the Minnesota Living with Heart Failure Questionnaire, improved in both groups, but was significantly higher at six-month follow up for the intervention group (p=00.1). The intervention, including salaries and supplies, cost €1,335 per patient. The mean outpatient pharmacy cost per patient was similar in both groups: €1,998 in the intervention group and €2,075 in the non-intervention group. Mean inpatient costs for intervention group was €16,712 and €18,522 for the non-intervention group.

A 2002 study by Stewart et al compared a multidisciplinary home-based intervention (comprising structure home visits by nurse and/or pharmacist) within 7 to 14 days of discharge) with usual care. During a median of 4.2 years follow-up, home-based intervention was associated with fewer unplanned readmissions or death (0.21 versus 0.37 per patient per month, p<0.01), longer event-free survival (7 versus 3 months, p<0.01), fewer deaths (56% versus 65%, p=0.06), and a more prolonged survival (median 40 versus 22 months p<0.05). The average cost of applying the home-based intervention, taking into account both the cost of home visits and

additional cardiology, primary care, and pharmacy consultations, was €617 per patient. The authors concluded that home-based intervention is beneficial in reducing the frequency of unplanned readmissions for heart failure, that this persists in the long term and is associated with prolongation of survival, reduced levels of hospital activity and associated costs.

#### 11.3.2.4 Disease management programmes

There were 17 studies found that evaluated disease management programmes including three cost utility analyses and 14 costing or cost-minimisation studies (see Appendix A11.6). Three cost utility studies and two of the costing studies were found to be good quality and will be examined in this section. Follow-ups ranged from three months to 10 years.

A nurse-led disease management programme was examined in the 2008 paper by Hebert et al.. The analysis focused on patients with systolic dysfunction from an ethnically diverse urban community in the US. The total cost of the intervention was €2,853 per patient with nurse and physician time accounting for the largest cost component. In terms of QALYs, the study reported a gain for the intervention group of 0.0497 QALY per person for the Health Utilities Index (HUI3, 0.6122 vs. 0.6619) and 0.0430 QALY per person for the EuroQol-5 dimension (EQ-5D, 0.6651 vs. 0.7080). The total societal cost of the intervention and usual care was €30,000 and €29,012 respectively for a total cost saving of €988 per patient. The analysis estimated an ICER of €22,994 based on the estimate of quality of life based on the EQ-5D and €19,883 for translation to HUI3. To conclude, the study found that at less than €32,768 per QALY saved, this nurse-led disease management programme was reasonably cost-effective over 12 months, especially for patients with earlier stages of heart failure.

A 2008 study carried out in the US by Smith et al. evaluated the cost-effectiveness of a telephone-based disease management programme for community dwelling heart failure patients. A total of 1,069 heart failure patients were recruited to a randomised controlled trial over an 18-month period and randomised to usual care, disease management, or augmented disease management. Subjects in the intervention arms were assigned a disease manager, a registered nurse who performed patient education and medication management with the patient's primary care provider for the full 18-month enrolment period. The mean cost of the disease management services was calculated to be €296 per patient per month. No differences were reported in clinical outcomes between the control and intervention groups. Considering all patients and all costs, the ICER was €176,762 per quality-adjusted life-year (QALY) gained, exceeding the standard of €120,353 considered the upper limit of an acceptable expenditure from a societal perspective. Subgroup analysis indicated that for patients with NYHA class III/IV symptoms and patients

with systolic heart failure, the ICERs were €81,580 and €115,203 per QALY gained, respectively. The authors concluded that telephone-based disease management did not reduce costs and was not cost-effective in community dwelling patients with heart failure, but that if programme labour costs could be reduced through technological innovation, economies of scale, or competition, carefully targeted disease management programmes may produce cost-effective improvements in heart failure outcomes.

A 2006 study carried out in Australia by Inglis et al. evaluated a home-based disease management intervention for 148 elderly patients suffering with heart failure over a 10-year follow up. The intervention was assessed in terms of the cost per life-year gained. Patients assigned to home-based intervention received the same level of care as those assigned to usual care plus the prospectively designated study intervention. Overall, the home-based intervention group accumulated more unplanned readmissions during follow-up. However, when the duration of the follow-up was adjusted; the rate of readmission was significantly lower in the home-based intervention group (intervention 2.04±3.23 versus control 3.66±7.62 admissions; $p<0.05$). The study also reported statistically fewer deaths during the follow-up period for intervention patients. The total cost to the health system of introducing the intervention was €100,138. The total cost for the intervention group and usual care group was €3,271,893 and €3,064,146, respectively, an increase of €207,460. The incremental cost effectiveness ratio of home-based intervention was estimated to be €1,731 per additional life-year gained.

The 2011 Dutch study by Postmus et al. conducted a trial-based economic evaluation of two nurse-led disease management programmes in heart failure. The intervention group received either basic or advanced disease management from a heart failure specialist nurse. This was compared with usual care (routine follow-up by a cardiologist). The study evaluated the intervention in terms of cost per QALY and per life-year gained. Postmus et al. estimated a mean quality-adjusted survival time was 287.6 days in the care-as-usual group, 296.1 days in the basic-support group, and 294.6 days in the intensive-support group. In terms of cost per life-year, basic support dominated care as usual because it generated 0.048 additional life-years while saving €79. When comparing the two disease management programmes, intensive support was found to generate 0.0022 additional life-years at an excess cost of €1,211, yielding an ICER of €547,599 per life-year. In terms of cost per quality-adjusted life-year (QALY), basic support was found to dominate both care as usual and intensive support because it generated 0.023 and 0.004 excess QALYs while saving €79 and €1,211, respectively.

A 2004 US study evaluated a two-stage multicenter disease management programme. In stage one, a pharmacist or nurse assessed each patient and made

recommendations to the physician to help treatment. In stage two, patients were randomised to usual care of a patient support programme (PSP) which involved education, telemedicine and other support. In stage one, medication adherence improved for all patients' ACE inhibitor use increasing from 58% on admission to 83% at discharge. In stage two, differences were reported in healthcare usage as cardiovascular-related emergency room visits decreased (49 versus 20, p=0.030) as did hospitalisation days (812 versus 341, p=0.003); adherence remained unchanged in this period. The total cost of care for cardiovascular-related events over the six-month follow-up period of this study was €3,798 for usual care patients compared with €1,684 for patient support programme patients, for a cost difference of €2,113 per patient. For all-cause events, the cost difference per patient was €2,057 (€5,139 for usual care and €3,082 for the patient support programme). It was concluded that the intervention was cost-saving relative to usual care due to a reduction in healthcare usage costs.

#### 11.3.2.5 Other self-management support interventions

Four additional papers were identified that described a variety of other SMS interventions for heart failure (see Appendix A11.7). Two of the papers were from the US with one each from the UK and the Netherlands. All four collected cost and resource data alongside RCTs.

A cost-effectiveness analysis of a nurse-facilitated cognitive behavioural self-management programme was evaluated in a 2014 pragmatic RCT (n=260) in the UK by Mejia et al. with follow-up at six and 12 months. The analysis reported a similar frequency of healthcare usage for both the intervention and control group. While patient-reported length of stay was lower in the self-management group, this difference was not significant (difference = 1.09, 95% CI: 1.43 to 3.61, p = 0.3941). After controlling for baseline utility data, treatment was associated with a reduction in QALY of 0.004 and an increase in costs of €128, and consequently was dominated by usual care using cognitive behavioural therapy alone. Therefore, the study concluded that the addition of nurse facilitation to a cognitive behavioural therapy for patients with heart failure is associated with no clear effect on costs or effectiveness as measured by QALYs.

The 2007 RCT by Murray et al. examined a pharmacist intervention aimed to improve medication adherence in a cohort of heart failure patients with low health literacy and limited resources. The study recruited 314 low income patients aged 50 years of age in the US. The intervention was delivered over nine months and included assessment of patient knowledge and provision of instructions in relation to medication use. The paper estimated that the intervention cost €247 per patient and was associated with a reduction in emergency department visits (mean 2.16 versus 2.28; IRR 0.82 [0.70–0.95] and a non-significant reduction in hospital admissions

[0.78 versus 0.97]; IRR 0.81 [0.64–1.04]). No difference in disease-specific quality of life was observed at six or 12 months follow-up. While, with the exception of drugs, costs across all categories (including outpatient and inpatient costs), were lower in the intervention group, these differences were not statistically significant.

A 2007 Dutch study by Bruggink et al. evaluated a physician and nurse directed heart failure clinic. The study recruited 240 patients recently discharged heart failure patients with NYHA class III or IV for an RCT. The intervention comprised one scheduled phone call and eight scheduled patient visits to a combined, intensive physician-and-nurse-directed heart failure outpatient clinic. Verbal and written comprehensive education on topics including exercise, rest, symptoms and self-management were provided in addition to optimisation of treatment, and easy access to the clinic. During the 12-month study period, the intervention was associated with a significant reduction in admissions for worsening heart failure and, or all-cause deaths (RR 0.49 [95%CI 0.30-0.81, p=0.001]; and a significant improvement in left ventricular ejection fraction [+2.6% vs. -3.1%, p=0.004]). A significant improvement (p=0.001) in health-related quality of life (HRQoL) as measured by the Minnesota Living With Heart Failure Questionnaire (MLWHFQ) was observed at three months and persisted through to 12 months' follow-up. Patients in the intervention group were hospitalised for a total of 359 days compared with 644 days for those in the usual care group (rate ratio 0.56 (95%CI 0.49 to 0.64). The difference between the costs of hospitalisation in the intervention (€65,046) and the usual care group (€202,728) was €137,682. The total cost for the heart failure clinic programme (salaries of the heart failure nurse, heart failure physician and the dietician, and for the extra laboratory and electrocardiograms [ECGs]) was €50,246. Therefore, overall costs were €87,436 lower in the intervention group, corresponding to a difference in the overall cost of care per patient of €741.

## 11.4 Discussion

### 11.4.1 Clinical effectiveness

The literature in relation to the effectiveness of different self-management support interventions for patients with chronic heart failure is characterised by a high degree of inconsistency among reviews that examined the same type of intervention. The best evidence of a beneficial effect was found in studies examining telemedicine interventions that included non-invasive telemonitoring and structured telephone support, which showed statistically and clinically significant reductions in both mortality and hospital admissions in most, but not all, reviews.

There was quite a degree of heterogeneity in the way telemonitoring and telephone support interventions were provided in the individual RCTs included in the reviews. While all were based around the concept of using of technology to send data

collected about patients to healthcare professionals for the purposes of assessment and ongoing management, there were differences in the frequency with which this information was sent (for instance, daily, weekly or monthly), the sort of information gathered (such as weight, blood pressure, pulse and pulse oximetry, ECG reading, medication, symptoms) and the type of health professionals interpreting the data (for example, nurse, physician, specialist team including cardiologist).

Some positive results were also reported for home-visit programmes, but there were only two reviews of this area and the other one failed to find a significant effect. The findings of a review of exercise interventions echoed those for coronary artery disease, where a mortality reduction did not become apparent until after 12 months. However, while the review of exercise programmes for heart failure also saw an increasing effect over longer follow-up periods, the mortality reduction observed in studies with follow up of greater than 12 months was not statistically significant.

The findings of this review of systematic reviews are consistent with similar studies that have compared a number of different approaches to managing heart failure patients.[385;394] However, even in these types of broad analyses there is a degree of inconsistency. For example, a 2014 review comparing a range of different interventions concluded that telemonitoring was not associated with a reduction in mortality or admissions and that structured telephone support should be prioritised ahead of it.[374]

The application of telemedicine in the management of heart failure patients has received a lot of attention due to its potential to increase the coverage and efficiency of heart failure management programmes. This is reflected in the number of recent narrative reviews that examine not only the available evidence, but also any unresolved questions or outstanding issues in relation to these types of interventions. A 2015 overview of systematic reviews of telemedicine in heart failure that included five studies identified in this analysis[389-393] highlighted gaps in our understanding of the process by which home telemonitoring improves outcomes. It recommends that future research be directed at identifying optimal strategies and follow-up durations, as well as investigating whether there is differential effectiveness between different subgroups of heart failure patients.[395] Other overviews have also been careful to sound a note of caution about telehealth interventions being considered the standard of care for heart failure management, citing the need for more evidence given the divergent results reported to date; a lack of clarity about specific elements of the interventions that underpinned the positive outcomes; and uncertainty about how best to integrate these processes within the context of the wider health service.[396-398]

The incremental benefit of new heart failure self-management initiatives in Ireland is dependent to a large extent on the current provision of cardiac rehabilitation

services. The HSE's clinical programme for heart failure has developed a model of care for the public health service, which describes two types of programmes that can be offered:[399]

**Model A:**

Heart failure rehabilitation programme: This model exists when there is a dedicated heart failure specialist team who coordinates and run the programme. This includes the clinical lead in heart failure, clinical nurse specialists in heart failure, physiotherapists, exercise physiologists, dieticians, psychologists, social workers, pharmacists and occupational therapists. Programmes will run for a minimum of six weeks twice weekly. Exercise will be prescribed and progressed by an exercise professional, i.e. physiotherapist or exercise physiologist. Patients should be monitored on telemetry while exercising.

**Model B:**

This is the amalgamation of existing cardiac rehabilitation services with heart failure services. The process of referral will be through the heart failure specialists. They will work with the cardiac rehabilitation specialists in responding to symptom deterioration and acute decompensation. Heart failure patients will have undergone their self-care education as part of the model of care pathway prior to initiating the programme. AACVRP guidelines (2004) classify heart failure patients as high risk of a cardiac event during exercise (25% mortality risk). Heart failure patients may be mixed in a group with the cardiac rehabilitation patients. Staffing ratios will change according to exercise risk stratification. Programmes will run for a minimum of six weeks twice weekly. Patients should be monitored on telemetry while exercising. There should be an interplay between the heart failure and cardiac rehabilitation nursing staff in staffing the exercise component of the programme. Exercise will be prescribed and monitored by an exercise professional i.e. physiotherapist or exercise physiologist. Patients should be monitored on telemetry while exercising.[399]

Telephone support is also included in the model of care, as part of early post-discharge follow up care, which would allow heart failure patients to contact a nurse specialist for advice on weight changes, review of medication or to discuss any queries or concerns they may have.[399]

The extent to which this is in place throughout the country, and adherence levels in areas where such services are provided, was examined in a 2013 survey, which found significantly different staffing levels and resources between cardiac rehabilitation services, lengthy waiting times for some individual services and wide

variation in availability of multidisciplinary teams, which meant that not all patients receive optimal cardiac rehabilitation.[400] There is also considerable uncertainty about access to primary prevention services for patients with heart failure who have not been hospitalised following an acute cardiovascular event.

### 11.4.2 Cost-effectiveness

Forty six studies relating to 45 unique economic evaluation studies of chronic disease self-management interventions for patients with heart failure were identified as relevant. The majority of studies evaluated disease management (n=17) with the remainder investigating telemedicine (n=15), SMS education programmes (n=6), multidisciplinary care (n=3) and other programmes (n=4). The quality of the studies was generally poor, with only four identified as high-quality reviews.

The majority of the studies had small sample sizes and collected cost data alongside RCTs. This raises inherent issues around the applicability of their cost findings to the Irish healthcare setting. In addition, most of the studies only followed participants for up to one year and it is therefore unclear how the clinical benefits and the healthcare usage would change over time. Six of the studies were limited to costing studies, a number of which did not report clear costing methodology, therefore it was difficult to determine their quality and derive the cost of different components of the interventions. The highest quality findings were reported in the study by Pandor et al. which estimated an ICER for a telemonitoring intervention compared to usual care of €12,871 per QALY gained.

The economic evaluations of SMS education programmes reported a range of results, but the majority estimated a reduction in healthcare usage and, as a result, cost savings for the intervention groups. The education programmes assessed in this analysis varied in the delivery of the programmes. A once-off post discharge education programme showed the greatest potential. A nurse-led programme in Sweden which used a societal perspective was only found to be cost-effective when combined costs and outcomes for the patient and caregiver were assessed; the study reported a cost gained per QALY of €16,159.

The best evidence was found in support of telemedicine interventions. Four cost-utility studies were identified. Studies supported the assumption that telemedicine is an effective intervention, reporting cost savings with improvements in HRQoL and reductions in healthcare usage up to 12 months' follow-up. Considerable variation in what constituted remote monitoring was noted as well as the absence of robust estimations of costs. The duration of any effect and the impact on long-term costs is uncertain.

Disease management programmes were assessed in 17 studies and were generally found to be cost-effective or cost saving relative to usual care. The role of

multidisciplinary care to reduce rehospitalisations in recently discharged heart failure patients was evaluated in three studies, the most relevant of which was a 2003 study from Ireland. It indicated that multidisciplinary care was cost saving due to reductions in rehospitalisations in a three-month follow-up period. The durability of this effect and the long-term impact on costs is not known.

In general, the cost per patient of the interventions was low, particularly relative to the overall cost of care, and the majority of the studies reported some degree of cost savings in the short-term through reduced healthcare usage. The short follow-up period and the relatively small sample sizes do raise concerns regarding the sustainability of the interventions and the applicability of the findings when applied to a larger population.

## 11.5 Key points

- Twenty systematic reviews of the clinical effectiveness of self-management support interventions in adults with chronic heart failure published between 2009 and 2015 were identified for inclusion in this overview of reviews.
- The quality of the systematic reviews varied, with five being rated as high-quality reviews, 14 being rated as moderate quality and one being rated as low quality.
- These reviews included five broad types of interventions, which were focused on: patient education, exercise, psychosocial or behavioural changes, home-based services or telehealth. Interventions such as education, prescribed exercise and behavioural changes are core components of cardiac rehabilitation, so the boundary between standard cardiac rehabilitation services and chronic disease self-management support is ill-defined.
- Statistically significant reductions in mortality were reported for both telehealth interventions and home-visit programmes. However, there was a lack of consistency across reviews that examined these types of interventions, with some reporting no effect.
- Statistically significant reductions in the rate of hospital readmission were reported for exercise interventions, home-visit programmes and telehealth interventions.
- There is limited evidence to demonstrate the effectiveness of patient education programmes or behavioural modification interventions.
- Despite the positive results that have been reported for telemedicine and structured telephone support interventions, concerns have been raised about these being considered the standard of care for the management of heart failure due to inconsistent findings across studies and a lack of understanding about which specific elements of the interventions contribute to the improving

outcomes.

- Forty six unique economic evaluation studies of chronic disease self-management interventions for patients with heart failure were identified as relevant.
- The interventions described by the included studies were heterogeneous and frequently comprised multiple components. The short follow-up period and the relatively small sample sizes raise concerns regarding the sustainability of the interventions and the applicability of the findings when applied to a larger population.
- Based on randomised controlled trials that showed improvements in health-related quality of life and reductions in healthcare utilisation, the majority of telemedicine interventions reported cost savings relative to usual care, although the interventions assessed were heterogeneous.
- Based on randomised controlled trials that showed reductions in healthcare utilisation, certain disease management and education programmes were found to be cost-effective or cost saving relative to usual care.
- The reported per-patient cost of self-management support interventions varied according to the intensity of the intervention, but was typically low relative to the overall cost of care of heart failure patients.
- Based on the description of the healthcare systems, the epidemiology, and the heart failure patient populations in the included studies, and assuming that what constitutes 'usual care' is similar in Western countries, the majority of findings of this overview of clinical effectiveness are expected to be applicable to the Irish healthcare setting. The applicability of the cost-effectiveness literature to the Irish healthcare setting was considered relatively low.

# 12 Discussion

A health technology assessment (HTA) is intended to support evidence-based decision-making in regard to the optimum use of resources in healthcare services. Measured investment and disinvestment decisions are essential to ensure that overall population health gain is maximised, particularly given finite healthcare budgets and increasing demands for services provided. The purpose of this HTA was to examine the clinical and cost-effectiveness of self-management support (SMS) interventions for chronic diseases. Self-management can be broadly defined as the tasks that individuals must undertake to live with one or more chronic diseases. These can broadly be defined as interventions that help patients to manage portions of their chronic disease or diseases through education, training and support.

## 12.1 Scope of the study

This HTA examined the clinical and cost-effectiveness of generic self-management support (SMS) interventions for chronic diseases and disease-specific interventions for diabetes (Type 1 and Type 2), chronic obstructive pulmonary disease (COPD), asthma, cardiovascular disease (stroke, hypertension, ischaemic heart disease [IHD] and heart failure).

For the purpose of this review, the 2003 definitions of self-management and SMS developed by the US Institute of Medicine were used. Self-management was thus defined as: 'the tasks that individuals must undertake to live with one or more chronic diseases. These tasks include having the confidence to deal with the medical management, role management and emotional management of their conditions.' SMS was defined as: 'the systematic provision of education and supportive interventions by health care staff to increase patients' skills and confidence in managing their health problems, including regular assessment of progress and problems, goal setting, and problem-solving support.'

SMS interventions may: target different recipients (for example, patients, carers, healthcare professionals); include different components (for example, education, information, practical support, providing equipment, social support, lifestyle advice, prompts, financial incentives); be delivered in different formats (for example, face-to-face, remote, web-based); be delivered by different individuals (including healthcare personnel and trained or untrained lay persons); differ in their intensity and duration.

A consistent theme is that SMS interventions are typically complex interventions that include more than one component of SMS. For this reason, with the exception of education interventions, this report did not assess single component SMS (for

example, simple text message appointment reminders and drug-reminder packaging).

The review of clinical effectiveness was restricted to SMS interventions evaluated through randomised controlled trials (RCTs) in adult populations. Given the volume of literature available, the clinical effectiveness of SMS interventions was evaluated using an 'overview of reviews' approach, where systematic reviews were reviewed rather than the primary evidence. Where existing high-quality overviews were identified, these were updated rather than undertaking a de novo overview of reviews. The cost-effectiveness of generic and disease-specific SMS interventions was evaluated by undertaking systematic reviews of the available literature for each of the disease categories.

## 12.2 Previous reviews

In December 2014, a high-quality overview of reviews was published by the National Institute for Health Research (NIHR) in the UK. The Practical Systematic Review of Self-Management Support for long-term conditions (PRISMS) study comprised an overview of systematic reviews of RCTs up to 1 June 2012, and was itself undertaken according to the principles of systematic reviewing. The PRISMS study included reviews of SMS interventions for asthma, chronic obstructive pulmonary disease, diabetes (Type 1 and Type 2), hypertension, and stroke.

In broad terms, the PRISMS study concluded that effective SMS interventions are multifaceted, disease-specific, tailored to the individual, and should be underpinned by a collaborative relationship between the patient and healthcare professional. The PRISMS study also included interventions that were applied to children, and included reviews of qualitative implementation studies. These were outside the terms of reference of this project and were not included in this report.

## 12.3 Additional evidence

This HTA updated the PRISMS reviews to April 2015. The inclusion of the most recent evidence is particularly relevant for telemedicine and computer-based interventions given the rapid rate of technological advance. We identified an additional 47 systematic reviews for the disease areas included in the PRISMS review. PRISMS did not include telehealth reviews as they deemed these to be typically about mode of delivery rather than content of what was delivered. Relevant telehealth interventions that incorporated a significant component of self-management support were, however, included in this updated review.

The PRISMS review did not include generic SMS interventions that were not tailored for specific diseases. Chronic disease self-management programmes such as the Stanford model are designed to be used in populations with a range of chronic

conditions. Generic interventions have the benefit of being potentially applicable to a large proportion of people with one or more chronic diseases. This study evaluated the evidence for generic interventions for which 26 systematic reviews were identified.

Ischaemic heart disease (IHD) and heart failure were also not included in the PRISMS review, but were identified by the HSE as relevant to the scope of this assessment. De novo overviews of reviews were carried out as part of this assessment, identifying 14 reviews of IHD interventions and 20 reviews of heart failure interventions.

Furthermore, corresponding to the reviews of clinical effectiveness, this assessment carried out systematic reviews of the cost-effectiveness literature. These reviews provide valuable evidence on the likely cost implications and cost-effectiveness of SMS interventions. We identified and reviewed 181 costing and cost-effectiveness studies.

In total, this study considered the evidence of over 2,000 RCTs as presented across 160 systematic reviews.

## 12.4 Summary of findings

The clinical effectiveness of self-management support interventions was reviewed in relation to each disease. A broad range of intervention types were assessed. Some intervention types were only applied to a single or small number of diseases.

**Generic (non-disease-specific) self-management support interventions**

As noted, a de novo overview of reviews was undertaken in respect of generic self-management support (SMS) interventions. The largest volume of evidence was retrieved for the chronic disease self-management programmes, mainly the Stanford programme. There is some evidence of short-term improvements in patient-reported outcomes such as self-efficacy, health behaviour (exercise) and health outcomes (pain, disability, fatigue, depression). Short-term improvements in health status were found for telephone-delivered cognitive-based therapy. There is insufficient evidence to determine if computer-based chronic disease self-management programmes are superior to usual care or standard programmes. There is some evidence that a range of SMS interventions can lead to a small, but significant reduction in healthcare utilisation; however, it is not possible to identify which types of SMS interventions or components contribute to this positive result. Based on the available evidence, the best possible format of generic self-management support, the diseases in which it is likely to be beneficial, and the duration of its effectiveness, if any, remain unclear.

### Asthma

Good evidence was found that SMS interventions can improve quality of life and reduce hospital admissions and use of urgent or unscheduled healthcare in patients with asthma. While the optimal intervention format is unclear, the evidence suggests that the best asthma self-management should include education supported by a written asthma action plan, as well as improved skills training including the use of inhalers and peak flow meters. Behavioural change techniques were noted to be associated with improved medication adherence and a reduction in symptoms.

### Chronic obstructive pulmonary disease (COPD)

The assessment found wide variation in the interventions and patient populations, thereby making it difficult to make recommendations on the most effective content of SMS. Very good evidence was found that education is associated with a reduction in COPD-related admissions with limited evidence found that it is associated with improvements in health-related quality of life. Very good evidence was found for pulmonary rehabilitation that included exercise therapy in improving health-related quality of life (HRQoL) and functional exercise capacity of people with COPD. However, because of the substantial variation in the design of pulmonary rehabilitation programmes, the optimal format, intensity and duration of such programmes are unclear. Good evidence was found that complex SMS interventions (that is involving multiple components including education, rehabilitation, psychological therapy, and integrated disease management and or multiple professionals delivered by a variety of means) are associated with improvements in HRQoL in patients with COPD. Some evidence was found that telehealth (as part of a complex intervention) decreases healthcare utilisation while some evidence was also found of improvements in health-related quality of life for nursing outreach programmes. Given the complexity of the interventions assessed, it is difficult to identify the optimal content of a SMS intervention for COPD. Nonetheless, the inclusion of education, exercise and relaxation therapy elements have emerged as important themes.

### Diabetes

As the scope of this HTA was limited to adults aged 18 years and older, the majority of the evidence related to the management of Type 2 diabetes. Only two systematic reviews for SMS interventions in Type 1 diabetes were identified for inclusion in this overview of reviews. Very limited evidence was found that structured educational programmes lead to improved outcomes of quality of life and episodes of severe hypoglycaemia in adults with Type 1 diabetes. Very good evidence was found that education, including culturally-appropriate education, improves blood glucose control in the short term (less than 12 months) in adults with Type 2 diabetes, although

quality of life remains unaltered. Some evidence was found that self-management programmes are associated with small improvements in blood glucose control in the short term in Type 2 diabetes, while good evidence was found that behavioural interventions are associated with modest improvements in blood glucose control (HbA1c). Evidence of improvements in blood glucose control for a diverse range of SMS interventions — and in particular educational interventions which differ also in their frequency, intensity and mode of delivery — was also found. Given the complexity of SMS interventions assessed, it is not possible to provide clear recommendations on the optimal content and format of SMS for Type 2 diabetes, other than they should include an education component, with evidence suggesting that various models of delivery may be equally effective. Impact on resource utilisation was not assessed in any of the reviews.

### Stroke

There is good evidence that general rehabilitation therapy delivered in early stroke recovery has a positive impact on activities of daily living (ADL) and extended ADL for stroke survivors. There is good evidence that virtual reality-based rehabilitation (that is, using commercial gaming consoles or specifically developed consoles adopted in clinical settings) improves upper limb function and ADL when used as an adjunct to usual care. Based on the available evidence for stroke, it is not possible to draw conclusions in relation to the effectiveness of self-management programmes or a range of interventions including motivational interviewing, psychosocial or lifestyle interventions delivered to stroke survivors. There is some evidence that provision of providing information improves patients and carers' knowledge of stroke and aspects of patients' satisfaction, with small reductions (which may not be clinically significant) in patients' depression scores. Some evidence of effect was also noted for improvements in health-related quality of life for stroke liaison emphasising education and information provision.

### Ischaemic heart disease (IHD)

Good evidence was found that exercise programmes (including exercise-based cardiac rehabilitation) are associated with a significant reduction in mortality in suitable patient cohorts with follow-up periods greater than 12 months. Exercise-based interventions were also found to be associated with fewer rehospitalisations. Some evidence was found that patient-education interventions are associated with interim outcomes such as smoking cessation and blood pressure control. Limited evidence was found to demonstrate the effectiveness of behavioural modification interventions, although there were some reported positive effects on smoking cessation and symptom management. Limited evidence was found that home- and telehealth-based cardiac rehabilitation interventions achieve similar outcomes to centre-based cardiac rehabilitation. Interventions such as education, exercise and

behavioural changes are core components of cardiac rehabilitation, so the boundary between standard cardiac rehabilitation services and chronic disease self-management support is ill-defined.

### Hypertension

Good evidence was found that self-monitoring of blood pressure, alone or using a range of additional support measures including telemedicine, is beneficial in lowering systolic and diastolic blood pressure. Limited evidence of effectiveness was found for patient-education interventions when used alone to improve medication adherence or blood pressure control. Some evidence was found that community pharmacist interventions, which include patient education, can lead to statistically significant reductions in systolic and diastolic blood pressure. However, for all interventions, the clinical significance of improvements in blood pressure control and medication adherence and the durability of the effect were unclear. As with the other chronic conditions, specific recommendations in relation to the optimal format of a SMS intervention for patients with hypertension is not possible, with evidence for a range of interventions, including education, delivered in a variety of formats. Given the heterogeneity of the patient population, tailoring the components to the individual patient may be beneficial.

### Heart failure

Statistically significant reductions in the rate of hospital readmissions were reported for exercise interventions, telehealth interventions and home-visit programmes for patients with heart failure. Similarly, statistically significant reductions in mortality were reported for both telehealth interventions and home-visit programmes. However, despite positive results for telehealth interventions, concerns have been raised about these being the consistent standard of care for patients with heart failure due to inconsistent findings across studies and a lack of understanding about which elements of the intervention contribute to improving outcomes. Limited evidence of effect was found for patient education and behavioural modification interventions for patients with heart failure. As with ischaemic heart disease it is noted that interventions such as education, exercise and behavioural changes are core components of cardiac rehabilitation, so the boundary between standard cardiac rehabilitation services and chronic disease self-management support is ill-defined.

### Evidence of cost-effectiveness

Evidence of cost-effectiveness for a wide range of SMS interventions in patients with chronic disease was generally of limited applicability to the Irish healthcare setting. To be cost-effective, an intervention must first be clinically effective; given the heterogeneity of interventions assessed in the clinical effectiveness review and the

variability in the format, intensity and mode of delivery of the interventions assessed, it is difficult to generalise the evidence. A common theme identified is that SMS interventions can typically be delivered at a relatively low cost per patient, although cost is noted to vary according to the intensity of the intervention provided. Therefore, if there is evidence of clinical benefit, typically the intervention will be cost-effective or may even be cost saving (usually driven by reductions or changes in healthcare utilisation). While international evidence suggest that self-management support interventions are potentially low cost on a per-patient level, the budget impact of these interventions could be substantial due to the large numbers of eligible patients.

## 12.5 Gaps in the evidence

One factor that may contribute to the inconsistent evidence on SMS is the lack of a clear definition of self-management across both primary studies and systematic reviews. Some of the telemedicine interventions, for example, enabled remote consultations between clinicians and patients, but the self-management aspect was a minor element of the overall intervention. The inclusion and exclusion criteria of identified systematic reviews were often based on very broad descriptions of interventions, adding to the heterogeneity of the data. A consensus on the definition of self-management would facilitate the identification of a more narrowly defined, but possibly less heterogeneous evidence-base.

With the exception of generic SMS interventions, the identified reviews related to disease-specific interventions. The included populations are likely to experience high levels of multimorbidity whereby patients have multiple chronic conditions, a number of which may be amenable to self-management. Providing a single disease-specific intervention may not be suitable for enabling successful self-management. Equally, exposure to numerous interventions may be counter-productive, placing an unsustainable burden on the individual. A systematic review of interventions for managing patients with multimorbidity found four studies that could be described as SMS interventions. The authors found that interventions that were linked to healthcare delivery or specific functional difficulties were more effective.[6] For people with multimorbidity, a coherent evidence-based approach that acknowledges their various conditions, and how they interact, is essential.

In many primary studies, interventions were implemented in addition to usual care. Because of this, many studies were structured in a manner that resulted in intervention group patients having more contact with clinical staff than the usual care group. The increased intensity of contact with health professionals may contribute to part of observed treatment effects. In some interventions, the benefit may be changing patterns of healthcare utilisation, such as the substitution of different health professionals (for instance, pharmacist support in place of general

practitioner consultations). Unfortunately, the available evidence does not support an analysis of which features of an intervention may contribute to observed effects on clinical outcomes.

Few of the included systematic reviews included outcomes of patient satisfaction. The lack of data regarding the patient experience means it was not possible to investigate the acceptability of SMS interventions to patients. As such interventions typically aim to improve or increase self-efficacy, it could be anticipated that these interventions may empower patients in their own care. However, some patients could perceive SMS negatively, for example, if they feel they have less clinician support. Further information on the patient experience would be beneficial and could give insights into why some types of SMS intervention are more effective than others.

The identified systematic reviews generally included a quality appraisal of the included primary studies, typically using the Cochrane Risk of Bias Tool or the Jadad score. These tools consider different aspects of study design such as randomisation and blinding. However, an important feature of studies is the quality of the implemented intervention, and this is not captured by the quality assessments. Poor implementation could occur in a variety of ways, such as poor quality educational material or malfunctioning equipment. Although some outcomes such as poor compliance or programme completion rates may be indicative of quality problems, they are not adequate for assessing treatment fidelity. A common audit or evaluation framework could support assessment of intervention quality, but could not be applied retrospectively. Consideration needs to be given to how the quality of intervention implementation and delivery can be evaluated.

## 12.6 Limitations

The evidence presented in this health technology assessment (HTA), and the approach used to obtain the evidence, are subject to a number of limitations that should be taken into account when considering the findings.

The review-of-reviews approach enabled an assessment of a large quantity of evidence for a range of intervention types across a number of disease areas in a relatively short period of time. Carrying out systematic reviews would not have been feasible and would have necessitated substantial resources to identify, acquire, evaluate and summarise primary evidence where others have already done this work to an acceptable standard. However, a review of reviews places one at a remove from the primary evidence and reliant on the quality of the available reviews. More recent RCTs may not be captured in this approach. However, given their typical sample sizes, it is not possible to draw strong conclusions about effectiveness based on a single RCT, or a number of small RCTs. Therefore it is unlikely that more recent

RCTs not captured in an overview of reviews would be sufficient to substantially alter recommendations informing major policy decisions. It is clear that the quality of the identified systematic reviews was variable. Reviews are, as with the primary evidence, at risk of bias. Some reviews were optimistic in their interpretation of the available evidence and concentrated on evidence showing positive effects. By evaluating the quality of the systematic reviews using a recognised method and focusing on high-quality reviews, we have minimised the risk of bias in our review.

The majority of the trials underpinning the clinical effectiveness data had relatively short-term follow-up of participants. The majority of systematic reviews were based on RCTs with no more than 12 months of follow-up. It is unclear whether effects observed at six or 12 months might be sustained over longer time horizons. Continued beneficial effects may be contingent on ongoing exposure to the intervention, and it is unclear whether good levels of compliance are likely to be maintained over longer periods. Two reviews included trials with 10 years of follow-up data, but that does not provide enough evidence to determine the potential longer-term impact of chronic disease self-management interventions. The length of follow-up also influences the types of outcomes included in studies, with some relying on risk factors or intermediate endpoints rather than clinical endpoints. Differences in mortality, for example, may be difficult to detect over six months in trials that are powered to detect differences in relation to a more common primary outcome. Trials with longer-term follow up could provide a stronger basis to evaluate both clinical outcomes and also data on whether sustained compliance is a potential issue.

Many of the primary studies were based on small sample sizes, which were sometimes presented as pilot or feasibility studies. Small sample sizes inevitably lead to imprecise effect estimates and an inability to detect a statistically significant effect. A benefit of the systematic review approach and meta-analysis techniques is that it enables the pooling of data across studies to improve precision. While this is useful for estimates of clinical effectiveness, this is less relevant for cost-effectiveness. Due to the greater variability in cost data, studies powered to detect a clinical effect are often underpowered to generate stable cost estimates. The cost-effectiveness data was mostly generated as part of an RCT, often with a small sample population. For this reason and because of differences between RCT and real world settings, cost estimates generated by RCTs should be viewed with caution.

There was a marked lack of consistency across studies in terms of the interventions, the definition of routine care, and the outcomes reported. Within a specific disease and for a particular intervention type there could still be substantial heterogeneity. This heterogeneity poses challenges in interpreting the available evidence and forming recommendations for practice. Where possible we have evaluated the

applicability of the evidence. That is, we assessed the extent to which the available data could be used to determine what would happen if the intervention was provided to the eligible patient population in Ireland. The applicability of the evidence is contingent on it reflecting the type of intervention that would be rolled out, that it was applied to similar population, that it has been compared to an approximation of routine care in Ireland, and that the outcomes are relevant to the Irish population. Due to the inconsistency of the evidence in many instances, it is only possibly to make broad statements regarding applicability.

The studies reporting costs and cost-effectiveness were generally found to be of poor quality. In many cases the studies used data collected as part of a small RCT. There is a risk of publication bias in that studies might be more likely to publish the cost data if they either observed a clinical effect or a reduction in costs. Studies that used modelling approaches made assumptions about the sustainability of effects observed with short-term follow-up. High-quality studies tested these assumptions and used sensitivity analyses to determine the impact of effects ceasing at the end of trial follow-up. The available modelling studies often extrapolated long-term outcomes on the basis of intermediate risk factors, for example, a reduction in A1c or blood pressure, using data such as the Framingham Heart Study. The cost-effectiveness data should be viewed in conjunction with the clinical effectiveness data to reduce the risk of biased interpretation, and to ensure that cost-effectiveness is only considered where there is consistent evidence of positive clinical effect.

## 12.7 Applicability of the evidence

### Clinical effectiveness

A very substantial body of literature was reviewed for this HTA, describing the clinical effectiveness of both generic and disease-specific self-management support (SMS) interventions. The applicability of the evidence is a function of the study populations, spectrum of disease, definition of routine care, health system infrastructure, and other features that impact on patient outcomes. In most cases, it was found (with caveats) that the evidence reviewed was broadly applicable to the Irish healthcare setting. A key issue was often the definition of routine care and the extent to which it corresponded to routine care as provided in Ireland.

The healthcare setting must also be considered when evaluating the applicability of the evidence. Many of the primary studies originated from the US, and due to differences in the financing and provision of healthcare, this may impact on the applicability. For example, many of the economic evaluations for SMS interventions in diabetes related to specific insurance plans, medically underserved (low income or uninsured) individuals or specific ethnic groups (for example Hispanics or Latinos), all with limited relevance to the Irish healthcare setting.

It should be borne in mind that an overview of reviews makes use of pooled clinical effectiveness data, sometimes across a large number of primary studies, and that in many cases the data were very heterogeneous. Studies were often pooled despite the fact that they implemented a variety of different interventions that were only broadly similar. In many cases the pooled estimates gave an indication of the effectiveness of a broad type of intervention rather than a specific and well-defined programme. Although the pooled estimate may show limited effect, individual studies will have shown more or less effectiveness than the average effect. Similarly, as with any healthcare intervention, within studies, some patients will have experienced a greater treatment effect than others. However, it was not possible to determine patient subgroups for which certain intervention types may be more effective. Equally it could not be stated which specific programme types might be more effective within broad intervention groupings. In the event of a policy decision to systematically provide SMS interventions, it would be advisable to consider the findings of high-quality systematic reviews and the primary evidence they included to determine what implementation might generate the greatest treatment effect.

A number of reviews included outcomes of healthcare utilisation. In some cases, studies reported either reduced utilisation or a shift in utilisation from secondary to primary care. The applicability of this evidence must be considered in conjunction with the potential for unmet need in the Irish healthcare setting. Some interventions require an element of clinician contact, for example, to carry out periodic office-based measurements. For any currently underserved patient groups, such an intervention could generate additional but appropriate utilisation. Hence, predicted reductions in service use based on international data may not translate into equivalent reductions when rolled out in Ireland.

### Cost-effectiveness

The data on costs and cost-effectiveness came from a wide range of settings, and were often RCT-based analyses. Estimates of cost-effectiveness or cost-utility, when reported, are probably of limited applicability. However, the per-patient cost of SMS interventions tended to be low, and this finding is anticipated to be applicable to the Irish setting. While per-patient costs are typically low, the overall budget impact could be substantial particularly for high-prevalence conditions.

## 12.8 Conclusions

### What did we look at?

This HTA examined the clinical and cost-effectiveness of generic self-management support (SMS) interventions for chronic diseases and disease-specific interventions. The review of clinical effectiveness was restricted to SMS interventions evaluated through randomised controlled trials (RCTs) in adult populations. The study

considered in excess of 2,000 RCTs included across 160 systematic reviews. The quality of the primary studies underpinning those reviews was often poor. In addition, the study reviewed 181 costing studies.

**What did we find?**

SMS interventions comprise a heterogeneous group with little clarity or consistency between studies. There is a clear need for an agreed definition of what constitutes self-management support. For the purpose of this review, the 2003 definitions of self-management and self-management support developed by the US Institute of Medicine were used. Self-management support interventions aim to help patients to manage portions of their chronic diseases through education, training and support. In theory, by improving self-efficacy, patients should be better able to manage their condition potentially leading to better health outcomes, fewer acute events, and reduced healthcare utilisation.

Evidence of the clinical-effectiveness of chronic disease self-management support interventions provides a complex picture. Certain forms of disease-specific interventions have been shown to improve outcomes over periods of six to 12 months. Longer-term outcome data are generally not collected. In particular, very good evidence was found that:

- Exercise programmes for patients with ischaemic heart disease are associated with a significant reduction in mortality in studies with greater than 12-months follow up. Exercise-based interventions are also associated with fewer rehospitalisations.
- Education is associated with a reduction in COPD-related hospital admissions.
- Pulmonary rehabilitation that includes exercise therapy improves quality of life and functional exercise capacity of people with COPD.
- Education, including culturally-appropriate education, improves blood glucose control in the short term (less than 12 months) in adults with Type 2 diabetes, although quality of life remains unaltered.
- Exercise interventions are associated with statistically significant reductions in the rate of hospital readmissions for patients with heart failure. Similar significant reductions in hospital readmission and mortality are noted for telehealth interventions and home-visits programmes. However, concerns have been raised in relation to telehealth interventions becoming the standard of care due to inconsistent findings across studies and lack of understanding about which elements of the intervention contribute to improving outcomes.

Good evidence was found that:

- Complex SMS interventions (that is involving multiple components including education, rehabilitation, psychological therapy, and integrated disease management and or multiple professionals delivered by a variety of means) are associated with improvements in health-related quality of life in patients with COPD.
- SMS interventions can reduce hospital admissions and use of urgent scheduled and unscheduled healthcare in patients with asthma. Optimal asthma SMS support should include education supported by a written action plan as well as improved skills training including the use of inhalers and peak flow meters
- General rehabilitation therapy delivered in early stroke recovery has a positive impact on activities of daily living and extended activities of daily living. Good evidence was also found that virtual reality-based rehabilitation improved upper limb function and activities of daily living when used as an add-on to usual care.
- Behavioural interventions (specifically patient activation interventions) are associated with modest improvements in blood glucose control in adults with Type 2 diabetes.
- Self-monitoring of blood pressure, alone or in conjunction with a range of additional support measures — including telemedicine — is beneficial in lowering systolic and diastolic blood pressure.

Some evidence of effect was noted that:

- Provision of information improves patients and carers' knowledge of stroke and aspects of patient satisfaction in stroke survivors
- Stroke liaison which emphasises education and information provision improves health-related quality of life in stroke survivors
- Self-management programmes are associated with small improvements in blood glucose control in the short term in Type 2 diabetes patients
- Community pharmacist interventions, which include patient education, can lead to statistically significant reductions in systolic and diastolic blood pressure in patients with hypertension.

Based on the available evidence, the optimal format of generic self-management support, the diseases in which it is likely to provide benefit, and the duration of effectiveness, if any, remain unclear.

There is limited evidence regarding the cost-effectiveness of chronic disease self-management support. With the exception of some telehealth interventions and more intensive rehabilitation programmes, most SMS interventions have a relatively low

cost per patient to implement and in some instances can result in modest cost savings through reductions or shifts in healthcare utilisation. However, budget impact is likely to be substantial if implemented for all eligible patients. Most economic analyses were conducted alongside randomised controlled trials, limiting their ability of determine if observed cost savings could be sustained. The costing methodology and perspective adopted differed greatly between studies making it difficult to summarise and aggregate findings.

**Is it relevant?**

The data from the primary studies was very heterogeneous, reflecting the very wide range of interventions that have been implemented. Despite the many limitations of the available evidence, the findings of the clinical effectiveness are broadly applicable to the Irish healthcare setting. The extent to which the clinical effectiveness data apply to Ireland depends on the definition of routine care, the adherence to the stated standard of care, and the similarities of the healthcare systems. Evidence of cost-effectiveness for a wide range of interventions was generally of limited applicability to the Irish healthcare setting. International data suggest a relatively low cost per patient of SMS interventions, however, consideration must be given to the size of the population, particularly for high prevalence conditions, when considering the potential budget impact of implementing SMS.

**What is the bottom line?**

SMS interventions have the potential to improve patient outcomes through improved self-efficacy. This HTA gives the evidence base for the SMS interventions that should be prioritised and for which diseases. Where chronic disease self-management support interventions are provided, it is critical that the implementation and delivery of the interventions are subject to routine and ongoing evaluation. This would help to ensure that they are delivering benefits to patients, and allow the content and format of the interventions to be refined. Evaluation will also provide a longer-term perspective not currently available in the literature and will support decisions about the optimal delivery of such interventions. The best evidence of benefit was found for the disease-specific interventions.

# Glossary of terms

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| **Action plan or written action plans (WAPs)** | These are written plans that a person with asthma develops with their doctor to help them control their condition. A WAP typically shows their daily treatment, such as the type(s) of medicine to take and when to take them. It describes how to control asthma in the long term and how to handle worsening symptoms, or attacks. The plan explains when to call the doctor or go to the emergency department. |
| **Activities of daily living (ADL) or primary ADL** | Being able to complete fewer ADLs indicates an increased disability or dependence on the help of carers. 'Primary ADL' is typically limited to functional ability and personal care (for example, feeding, bathing and dressing measures) whereas 'extended ADL' includes more complex tasks necessary for community and domestic participation (for example, shopping, cooking and transportation use).<br><br>See also **extended activities of daily living (ADL) or extended ADL.** |
| **Asthma** | Asthma is a chronic inflammatory condition of the airways characterised by recurrent episodes of wheezing, breathlessness, chest tightness and coughing. The strongest risk factors for developing asthma are inhaled substances and particles that may provoke allergic reactions or irritate the airways. Medication can control symptoms of asthma and avoidance of asthma triggers can also reduce its severity. Appropriate management of asthma can enable people to enjoy a good quality of life. |
| **Berger DM programme (T1DM)** | The Berger Programme is a comprehensive diabetes self care skills course, named after Professor Michael Berger. The programme is designed for people with Type 1 diabetes. People attending the course learn how to adjust their insulin dose depending on their food choice. The course also focuses on enhancing diabetes self management skills. It is delivered by healthcare professionals and is currently available in Ireland. |
| **Bias** | In general, any factor that distorts the true nature of an event or observation. In clinical investigations, a bias is any systematic factor other than the intervention of interest that affects the magnitude of (i.e. tends to increase or decrease) an observed difference in the outcomes of a treatment group and a control group. |

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| **BRUCIE DM programme (Paediatric)** | BRUCIE is an education programme aimed at providing adolescents over 12 years with diabetes the skills to understand the relationship between food, blood results and insulin dose adjustments. |
| **Cardiac rehabilitation** | Cardiac rehabilitation has been defined as 'a complex intervention offered to patients diagnosed with heart disease, which includes components of health education, advice on cardiovascular risk reduction, physical activity and stress management' while cardiac rehabilitation services are defined as 'comprehensive, long term programmes involving medical evaluation, prescribed exercise, cardiac risk factor modification, education and counselling. |
| **Chronic care model (CCM)** | This model was developed by Wagner in the MacColl Institute in the 1990s in response to the increasing burden of chronic disease and the varying approaches of management and care (social learning/cognitive theory). It is focused on changing a reactive system – responding mainly when a person is sick – to a more proactive system which focuses on supporting patients to self-manage. A principle part of the model is that the patient has a central role in managing their health and in particular self-efficacy. It identifies the essential elements of a health care system that encourage high-quality care including the community, the health system, self-management support, delivery system design, decision support and clinical information systems. As such, this is a higher level model than the Stanford model and UK Expert Patient Programme as self-management support is only one component of the chronic care model. |
| **Chronic disease** | The World Health Organisation (WHO) defines noncommunicable diseases (NCDs), also known as chronic diseases, as those which are not passed from person to person. They are of long duration and generally slow progression. The four main types of NCDs are cardiovascular diseases (such as heart attacks and stroke), cancers, chronic respiratory diseases (such as chronic obstructed pulmonary disease and asthma) and diabetes. |
| **Chronic disease self management programmes** | Self-management education programmes are distinct from simple education or skills training, in that they are designed to allow the patients to take an active part in the management of their own condition. Whilst early programmes may lack theoretical basis, programmes such as the Stanford CDSMP are typically based on theoretical models of behaviour. |

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| | See **Stanford CDSMP**. |
| **Chronic obstructive pulmonary disease (COPD)** | COPD is defined as 'a common preventable and treatable disease, which is characterised by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. The clinical course of COPD is one of gradual impairment with episodes of acute exacerbations that contribute to the deterioration of the patient's health status. In the later stages of disease, use of health services increases, with frequent hospitalisations. Currently there is no cure. |
| **Clinical outcome** | An outcome of major clinical importance that is defined on the basis of the disease being studied (e.g. fracture in osteoporosis, peptic ulcer healing and relapse rates). |
| **Clinical significance** | A conclusion that an intervention has an effect that is of practical meaning to patients and healthcare providers. |
| **Cochrane review** | Cochrane Reviews are systematic reviews of primary research in human health care and health policy, and are internationally recognised as the highest standard in evidence-based health care. They investigate the effects of interventions for prevention, treatment and rehabilitation. |
| **CODE DM programme** | The Community Orientated Diabetes Education (CODE) programme has also been developed by Diabetes Ireland and is a structured education programme for people with diabetes. CODE is delivered to people with Type 2 diabetes attending primary care centres by the Federation's healthcare professional staff or practice nurses with a recognised diabetes qualification who have been trained as CODE Educators. It supports people with diabetes either newly diagnosed or living with diabetes through group learning. It encourages participants to become confident in their diabetes self care management and aims to improve quality of life through informed decision making. The sessions are based on an empowering philosophy, have a stated curriculum, are quality assured and evaluated at local and national level. CODE is a programme designed for and validated on an Irish population with a view to it being part of the proposed integrated diabetes care model. This course is currently available in Ireland. |
| **Cognitive Behavioural Theory and Cognitive Behavioural Therapy** | This is a highly-structured psychotherapeutic method used to alter distorted attitudes and problem behaviours by identifying and replacing negative inaccurate thoughts and changing the rewards for behaviours. CBT attempts to help an individual |

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| **(CBT)** | make sense of overwhelming problems by breaking them down into smaller parts. CBT can take place on a one-to-one basis or with a group of people. It can be conducted from a self-help book or computer programme. The duration of the intervention can range from six weeks to six months depending on the problem and the individual; sessions usually last 30 to 60 minutes with a trained therapist. |
| **Comparator** | The technology to which an intervention is compared. |
| **Confidence interval (CI)** | Depicts the range of uncertainty about an estimate of a treatment effect. |
| **Coronary artery disease (CAD)** | CAD or ischaemic heart disease is a chronic condition characterised by narrowing and hardening of the arteries that supply blood to the heart muscle. This occurs as a result of the build up of cholesterol and other materials on the interior wall of the artery, through a process called atherosclerosis. Restriction of blood supply to the heart can result in angina or myocardial infarction. |
| **Cost per QALY** | A measure used in cost-utility analysis (CUA) to assist in comparisons among programmes; expressed as monetary cost per unit of outcome. |
| **Cost-effectiveness analysis (CEA)** | A comparison of alternative interventions in which costs are measured in monetary units and outcomes are measured in non-monetary units, e.g. reduced mortality or morbidity. (See also **Cost per QALY**). |
| **Cost-utility analysis (CUA)** | A form of cost-effectiveness analysis of alternative interventions in which costs are measured in monetary units and outcomes are measured in terms of their utility, usually to the patient, e.g. using QALYs. |
| **DAFNE DM programme (T1DM)** | The 'Dose Adjustment For Normal Eating programme' (DAFNE) programme is a structured education course delivered in a five day intensive skills based education programme to people with Type 1 Diabetes. It is delivered by healthcare professionals. In this course, people learn how to adjust their insulin dosage to suit their free choice of food, rather than having to work their life around their insulin doses. DAFNE aims to encourage and equip people who have Type 1 diabetes to manage their insulin regimens actively and independently. This course is currently available in Ireland. |
| **DESMOND DM** | The 'diabetes education and self-management for ongoing and newly diagnosed' (DESMOND) programme has a theoretical |

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| **programme (T2DM)** | basis and clearly stated philosophy based on patient empowerment.<br><br>The curriculum includes time for patients to "tell their story", information about diabetes and how it is optimally managed, the potential risks of diabetes, self-monitoring, diet, exercise, stress and emotional issues. At the end of the course people are encouraged to develop a personal action plan. DESMOND supports people in identifying their own health risks and responding to them by setting their own specific behavioural goals. DESMOND supports behaviour changes through changes in people's health beliefs. DESMOND is delivered as 6 hours of education by 2 trained Educators. People who attend the course are encouraged to bring a member of their family with them. It is targeted at people with newly diagnosed T2DM and is currently available in Ireland. |
| **Diabetes T1 and T2** | Diabetes is a progressive disease with disabling long-term complications if not properly managed. Persistently high blood sugar levels and high blood pressure can result in damage to both large and small blood vessels with ensuing eye, kidney, nerve, heart and circulatory complications; tight control of these parameters and other risk factors such as cholesterol and triglyceride levels can reduce or delay their progression. Symptoms include excessive excretion of urine (polyuria), thirst (polydipsia), constant hunger, weight loss, vision changes and fatigue.<br><br>T1DM (previously known as insulin-dependent, juvenile or childhood-onset) is characterised by deficient insulin production and requires daily administration of insulin. The cause of T1DM is not known. T2DM (formerly called non-insulin-dependent or adult-onset diabetes) results from the body's ineffective use of insulin.<br><br>T2DM comprises 90% of people with diabetes around the world, and is largely the result of excess body weight and physical inactivity. |
| **Diastolic blood pressure (DBP)** | Blood pressure is typically recorded as two numbers, written as a ratio. The bottom number measures the pressure in the arteries between heartbeats (when the heart muscle is resting between beats and refilling with blood). |
| **Economic evaluation** | The comparative analysis of alternative courses of action, in terms of their costs and consequences. |

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| **Economic model** | In healthcare, a mathematical model of the patient pathway that describes the essential choices and consequences for the interventions under study and can be used to extrapolate from intermediate outcomes to long-term outcomes of importance to patients. |
| **Effect size** | RCTs assess the effect of a treatment by comparing the outcomes in the treatment and control groups. Many measures of QoL are continuous, providing a score that varies from 0 up to a maximum based on the number and response range of the items. Comparing the mean scores of patients in the treatment and control groups gives a good indication of the impact of the treatment. A difficulty is that it takes an expert to know whether a difference of 5 points is important or not. A second problem is that studies often use different scales to measure these differences. Effect sizes overcome these difficulties by standardising and dividing the mean difference from each trial by a measure of the underlying variability of the scores on that outcome (the SD). |
| **Effectiveness** | The benefit (e.g. to health outcomes) of using a technology for a particular problem under general or routine conditions. |
| **Evidence-based medicine** | The use of current best evidence from scientific and medical research to make decisions about the care of individual patients. It involves formulating questions relevant to the care of particular patients, systematically searching the scientific and medical literature, identifying and critically appraising relevant research results, and applying the findings to patients. |
| **Expert patient programme (EPP)** | This is a modification of the Stanford model above and was introduced into the UK in 2002 and branded the EPP. |
| **Extended activities of daily living (ADL) or extended ADL** | Being able to complete fewer ADLs indicates an increased disability or dependence on the help of carers. 'Extended ADL' includes complex tasks necessary for community and domestic participation (for example, shopping, cooking and transportation use).<br><br>See also **activities of daily living (ADL) or primary ADL.** |
| **Flinders programme™** | The Flinders programme™ is a clinician-driven, behavioural change programme (based on multiple health behaviour change theories) that emphasises the role physicians have in building patient self-efficacy and the need to actively engage patients using the principles of cognitive behavioural therapy (CBT) |

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| | during patient-physician interactions (one-on-one). |
| **Glycated haemoglobin (HbA1c)** | HbA1c refers to glycated haemoglobin, it develops when haemoglobin, a protein within red blood cells that carries oxygen throughout your body, joins with glucose in the blood, becoming 'glycated'. By measuring glycated haemoglobin (HbA1c), clinicians are able to get an overall picture of what our average blood sugar levels have been over a period of weeks/months. For people with diabetes this is important as the higher the HbA1c, the greater the risk of developing diabetes-related complications. HbA1c is also referred to as haemoglobin A1c or simply A1c. |
| **HbA1c** | See **glycated haemoglobin**. |
| **Health coaching** | This is based on the trans-theoretical model of behavioural change and 'readiness to change'. It is a standalone, comprehensive intervention with a minimum of six sessions. |
| **Health outcomes** | The results or impact on health of any type of intervention (or lack of), e.g. a clinical procedure, health policy or programme, etc.. |
| **Health-related quality of life (HRQoL)** | A multi-dimensional measure comprising the physical and mental health perceptions of a patient in terms of health status, health risks, functional status, social support, and socioeconomic status. |
| **Health technology** | Any intervention that may be used to promote health, to prevent, diagnose or treat disease or for rehabilitation or long-term care. This includes the pharmaceuticals, devices, procedures and organisational systems used in healthcare. |
| **Health technology assessment (HTA)** | Health technology assessment (HTA): the systematic evaluation of properties, effects, and/or impacts of healthcare technology. It may address the direct, intended consequences of technologies as well as their indirect, unintended consequences. Its main purpose is to inform technology-related policymaking in healthcare. HTA is conducted by interdisciplinary groups using explicit analytical frameworks drawing from a variety of methods. |
| **Heart failure** | Heart failure is a chronic condition characterised by an inability of the heart to pump blood effectively, due to systolic and, or diastolic dysfunction. It can present as new onset heart failure in people without known cardiac dysfunction, or as acute decompensation of chronic heart failure. The condition can be |

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| | caused by a range of diseases that result in damage to the heart muscle, including coronary artery disease, myocardial infarction and hypertension. Symptoms of the disease include lung congestion, fluid retention, weakness and an irregular heart rhythm. |
| **Heterogeneity** | In meta-analysis, heterogeneity refers to variability or differences in the estimates of effects among studies. Statistical tests of heterogeneity are used to assess whether the observed variability in study results (effect sizes) is greater than that expected to occur by chance. |
| **Hypertension** | The WHO Health 2020 policy identifies high blood pressure or hypertension as the world's most prevalent, but preventable disease. Having hypertension is a serious medical condition that often has no symptoms, but significantly increases the risks of heart and kidney disease. Normal blood pressure is defined as <120/80 mmHg. Blood pressure is normally distributed in the population and there is no natural cut-off point above which hypertension definitively exists and below which it does not. The risk associated with increasing blood pressure is continuous, with each 2 mmHg rise in systolic blood pressure associated with a 7% increased risk of mortality from ischaemic heart disease and a 10% increased risk of mortality from stroke. |
| **Incremental cost** | The additional costs that one intervention imposes over another. |
| **Incremental cost-effectiveness ratio (ICER)** | The ratio of incremental costs to incremental benefits (difference in effect of patient outcome) obtained when comparing two technologies, e.g. additional cost per QALY. |
| **Ischaemic heart disease (IHD)** | See **coronary artery disease.** |
| **Literature review** | A summary and interpretation of research findings reported in the literature. May include unstructured qualitative reviews by single authors as well as various systematic and quantitative procedures such as meta-analysis. (Also known as overview.) |
| **Mean (arithmetic mean)** | The average value, calculated by summing all the observations and dividing by the number of observations. |
| **Median** | The middle value in a ranked group of observations. This can be a better estimate of the average value if there are extreme outlying values that may skew the arithmetic mean. |

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| **MEDLINE** | An electronic database produced by the United States National Library of Medicine. |
| **Meta-analysis** | Systematic methods that use statistical techniques for combining results from different studies to obtain a quantitative estimate of the overall effect of a particular intervention or variable on a defined outcome. |
| **Methodological quality** | The extent to which the design and conduct of a study are likely to have prevented systematic errors (bias). |
| **Motivational interviewing** | This is based on the trans-theoretical model of behavioural change and 'readiness to change'. It uses a brief approach such as 60 minutes of counselling and education to increase motivation and commitment to change; once that is achieved, other approaches are pursued. |
| **Outcomes** | Components of a patients' clinical and functional status after an intervention has been applied. |
| **Patient activation interventions** | These are a subset of behavioural interventions which actively engage patients by promoting increased knowledge, confidence and, or skills for disease self-management. |
| **p value** | In hypothesis testing, the probability that an observed difference between the intervention and control groups is due to chance alone if the null hypothesis is true. |
| **Personalised care planning or 'building the house of care'** | Personalised care planning is described as a collaborative process in which patients and clinicians identify and discuss problems caused by, or related to the patient's condition, and develop a plan for tackling these.<br><br>In the UK, the King's Fund describe the 'house of care' in 2013, a metaphor which was devised to help those working in primary care adapt the chronic care model to their own situation. It encompasses all people with long-term conditions; and assumes an active role for patients, with collaborative personalised care planning at its heart. |
| **PICOS** | Population, Intervention, Comparator, Outcomes, Study design. |
| **PubMed** | A service of the National Library of Medicine that includes over 14 million citations for biomedical articles back to the 1950s. |
| **Pulmonary rehabilitation (PR)** | PR is a more comprehensive form of SMS and is defined by the joint American Thoracic Society and European Respiratory Society as a '…comprehensive intervention based on a thorough |

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| | patient assessment followed by patient tailored therapies that include, but are not limited to, exercise training, education, and behaviour change, designed to improve the physical and psychological condition of people with chronic respiratory disease and to promote the long-term adherence to health-enhancing behaviours.' The educational component of PR focuses on collaborative self-management and behaviour change. It encompasses providing information and knowledge regarding COPD; building skills such as goal setting, problem solving and decision making; and developing action plans that allow individuals to better recognise and manage the disease. |
| **Quality of evidence** | Degree to which bias has been prevented through the design and conduct of research from which evidence is derived. |
| **Quality of life (QOL)** | See **Health-related quality of life**. |
| **Quality-adjusted life year (QALY)** | A unit of healthcare outcomes that adjusts gains (or losses) in years of life subsequent to a healthcare intervention by the quality of life during those years. |
| **Randomised controlled trial (RCT)** | An experiment of two or more interventions in which eligible people are allocated to an intervention by randomisation. The use of randomisation then permits the valid use of a variety of statistical methods to compare outcomes of the interventions. |
| **Relative risk (RR) (risk ratio)** | The ratio of (statistical) risk in the intervention group to the risk in the control group. A relative risk of one indicates no difference between comparison groups. For undesirable outcomes an RR that is less than one indicates that the intervention was effective in reducing the risk of that outcome. |
| **SD** | See **Standard deviation**. |
| **Selection bias** | Error due to systematic differences in characteristics between those who are selected for study and those who are not. |
| **Self-efficacy** | Self-efficacy, one of the core concepts of social cognitive theory, focuses on increasing an individual's confidence in their ability to carry out a certain task or behaviour, thereby empowering the individual to self-manage. |
| **Self-management** | Self-management is defined as 'the tasks that individuals must undertake to live with one or more chronic diseases. These tasks include having the confidence to deal with the medical management, role management and emotional management of their conditions'. Self-management support (SMS) is thus defined as 'the systematic provision of education and supportive |

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| | interventions by health care staff to increase patients' skills and confidence in managing their health problems, including regular assessment of progress and problems, goal setting, and problem-solving support. |
| **Self-management support (SMS) interventions** | Self-management support (SMS) interventions are any interventions that help patients to manage portions of their chronic disease(s) through education, training and support. |
| **Self-measured or self-monitoring of blood glucose (SMBG)** | SMBG refers to the measurement of blood glucose by a patient at home or outside of a clinic setting. It can be manually measured and recorded by the patient or electronically transmitted to a healthcare provider, using telemonitoring. |
| **Self-measured or self-monitoring of blood pressure (SMBP)** | SMBP refers to the measurement of blood pressure by a patient at home or outside of a clinic setting. It can be manually measured and recorded by the patient or electronically transmitted to a healthcare provider, using telemonitoring. |
| **Social Learning/ Social Cognitive Theory** | This theory proposes that behaviour change is affected by environmental influences, personal factors, and attributes of the behaviour itself. A central component of this theory is also self-efficacy. As well as belief in the behavioural change, the individual must value the outcomes they believe will occur as a result. |
| **Standard deviation (SD)** | A measure of the dispersion of a set of data from its mean. |
| **Statistical significance** | Statistical significance: a conclusion that an intervention has a true effect, based upon observed differences in outcomes between the treatment and control groups that are sufficiently large so that these differences are unlikely to have occurred due to chance, as determined by a statistical test. |
| **Stanford chronic disease self-management programme (CDSMP)** | The Stanford chronic disease self-management programme (CDSMP) is a generic programme developed by Professor Lorig in Stanford University. The term generic means that it can be used for patients with a range of chronic diseases. It is based on the fact that people with chronic disease have similar concerns and, with specific skills and training, can effectively manage aspects of their own conditions. The programme consists of two and a half hour workshops once a week for six weeks and while generally administered in community settings, is also available online. |
| **Stroke** | A stroke is caused by poor blood flow to the brain resulting in |

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| | cell death. Poor blood flow is usually the result of a clot causing a blockage (this is termed ischaemic stroke, accounting for over 80% of all cases) or as a result of a weakened blood vessel which bursts (haemorrhagic stroke). Stroke can cause a range of permanent impairments associated with movement and coordination, memory and attention, and can cause depressive symptoms, all affecting an individual's rehabilitation. |
| **Systematic review (systematic overview)** | A form of structured literature review that addresses a question that is formulated to be answered by analysis of evidence, and involves objective means of searching the literature, applying predetermined inclusion and exclusion criteria to this literature, critically appraising the relevant literature, and extraction and synthesis of data from the evidence base to formulate findings. |
| **Systolic blood pressure (SBP)** | Blood pressure is typically recorded as two numbers, written as a ratio. The top number measures the pressure in the arteries when the heart beats (when the heart muscle contracts). |
| **Telemedicine** | Telemedicine literally means 'healing at a distance' and signifies the use of information and communication technology (ICT) to improve patient outcomes by increasing access to care and medical information. However, there is no one universally accepted definition of telemedicine, so that the literature in this area describes a myriad of interventions delivered through different mechanisms for different purposes. Telemedicine typically comprise four major elements: supply of medical care, use of technology, mitigation of issues of distance, and provision of benefits. The World Health Organisation has adopted the following broad description:<br>'The delivery of health care services, where distance is a critical factor, by all health care professionals using information and communication technologies for the exchange of valid information for diagnosis, treatment and prevention of disease and injuries, research and evaluation, and for the continuing education of health care providers, all in the interests of advancing the health of individuals and their communities.'<br><br>Telemedicine is constantly evolving to incorporate new advancements in technology and to respond and adapt to changing health needs. Telemedicine applications typically have two formats, synchronous which involves real-time interaction (that is, via the telephone or videoconferencing) or asynchronous communication (not real-time, for example via text messages, email or devices that permit store-and-forward transmission of data [for example, a home glucose metre]). |

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| | Asynchronous methods that use store-and-forward transmission typically forward the data to a health professional who reviews the data and uses their clinical judgement to make recommendations to the individual. Telemedicine also includes internet- or web-based support (sometimes referred to as e-health). This can include internet versions of, for example, the online version of the Stanford CDSMP. Internet-based support offers an alternative to face-to-face interventions which could be beneficial if resources are limited. |
| **Theory of Reasoned Action and Theory of Planned Behaviour** | This social cognitive theory of reasoned action states that individual performance of a target behaviour is determined by the person's intention to perform that behaviour based on their attitude toward the behaviour and the influence of their social environment or subjective norm. The shared components are behavioural beliefs and attitudes, normative beliefs, subjective norms and behavioural intentions. The Theory of Planned Behaviour adds to the Theory of Reasoned Action, the concept of perceived control over the opportunities, resources, and skills necessary to perform a behaviour. These are considered to be critical in behavioural change. This is congruent with the concept of self-efficacy. |
| **Trans-Theoretical Theory** | This model is based on the theory that behaviours can be modified. It is related to a person's readiness to change, the stages that they progress through to change and doing the right thing (processes) at the right time (stages). As such, tailoring interventions to match a person's readiness or stage of change is said to be essential. The model comprises emotions, cognitions and behaviours, and includes measures of self-efficacy and temptation. It has been used to modify target behaviour such as smoking cessation and stress management. |
| **Transient ischaemic attack (TIA)** | TIA is a stroke related condition where the supply of blood to the brain is temporarily interrupted. TIAs are often a warning sign of an impending stroke. |
| **X-PERT DM programme** | The X-PERT Ireland (Patient Education versus Routine Treatment) programme, is a specially designed dietetic structured patient education programme. It provides people with the confidence, knowledge and skills necessary to self manage their diabetes. It is a Health Service Executive (HSE) programme for all adults with Type 2 Diabetes either newly diagnosed or with established diabetes. It involves attending 6 x 2.5 hour group education sessions with approximately 16 hours of dietetic support over the course of the programme. |

# Appendix A3

# Appendix A3.1 – Search details

**Clinical Effectiveness Review Basic search terms:**

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|---|---|
| **Chronic disease terms** | (Chronic disease[Mesh], chronic health/condition/ illness, long term illness/disease/ condition, diabetes[Mesh], asthma[Mesh], chronic obstructive pulmonary disease[Mesh], stroke[Mesh], hypertension[Mesh], heart failure[Mesh], coronary artery disease[Mesh], ischemic heart disease[Mesh]) |

AND

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| **Self-management terms** | (self care[Mesh], self management, self monitor, self help, self medication, self administration, diagnostic self evaluation[Mesh], self regulation, self treat, self test, self efficacy[Mesh]) (telemedicine[Mesh], e-Health, m-Health, telecare, e-Therapy, telenursing, telemonitor, Computer-Assisted Instruction[Mesh], telephone[Mesh], Cell Phones[Mesh]), Text Messaging[Mesh]), SMS, Self help groups[Mesh], group based, Social learning theory, Behaviour change theory, Behaviour change program, Behaviour change model, motivational interview, peer led, peer support, lay led, lay support, health coach, Action plan, Care plan, Patient education as topic[Mesh], Flinders program/model, chronic care model, expert patients programme, Stanford model/program, internet[MeSH Terms], pulmonary rehab, cardiac rehab) |

AND

| | |
|---|---|
| **Systematic review terms or filter** | (systematic review, review[Publication Type]), Meta-analysis[Publication Type], Meta-Analysis as Topic[Mesh], meta review, meta-synthesis, overview of reviews, review of reviews, cochrane review) |

**Clinical Effectiveness Review Basic search strategy:**

| | |
|---|---|
| **Phase I** | Search from 2009 to February 2015. |
| **Phase IIa** | Use PRISMS results prior to 2012.<br>New search from 2012 to April 2015. |
| **Phase IIb** | Stroke and hypertension: Use PRISMS results prior to 2012.<br>New search from 2012 to April 2015. |
| | Heart failure and ischaemic heart disease: Search from 2009 to April 2015. |

# Appendix A4 – Generic self management support interventions for a range of chronic diseases

## Appendix A4.1 – Search details

Clinical Effectiveness Review (see Appendix A3.1 for detailed search terms).

**Basic search strategy:**

Chronic disease term

AND

Self-management term

AND

systematic review term or filter.

**Figure A4.1.1 Clinical effectiveness - flowchart of included studies**

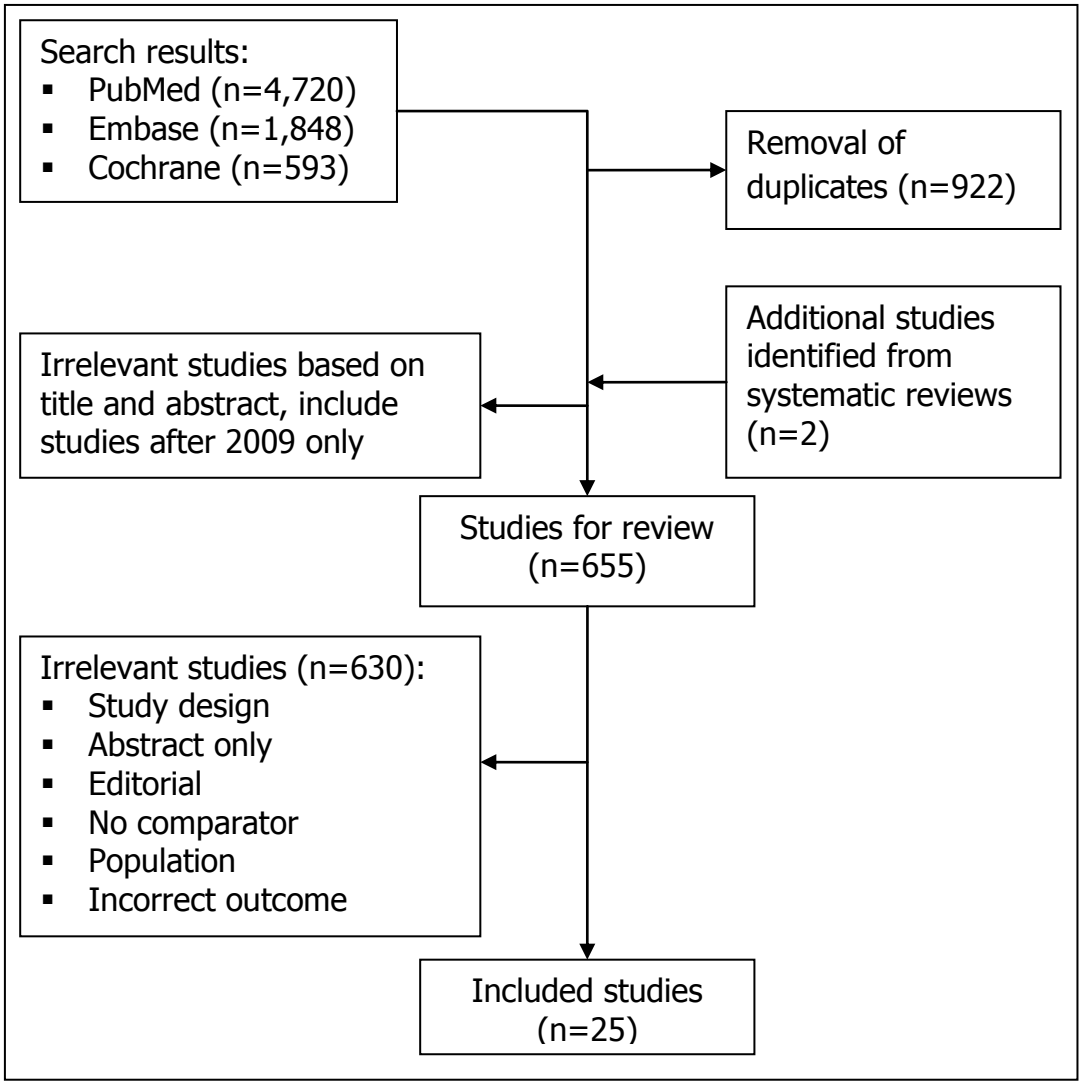
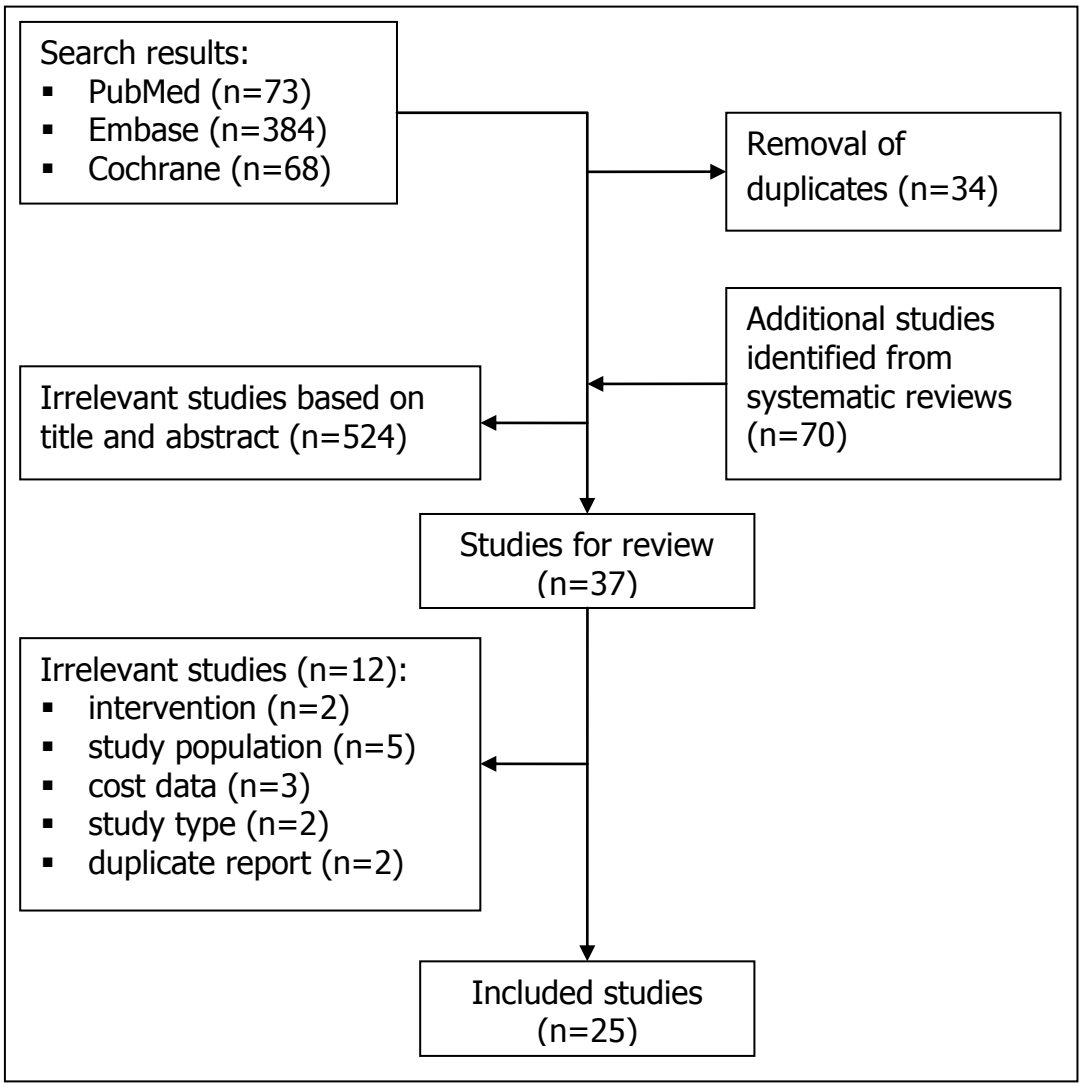


**Figure A4.1.2 Cost-effectiveness - flowchart of included studies**



# Appendix 4.2 – Evidence tables

## Table A4.2.1 CDSMPS: Summary of scope of reviews

| Review (year) | Intervention | Chronic diseases / population | Comparator | Included studies | | | Total participants | Synthesis |
|---|---|---|---|---|---|---|---|---|
| | | | | SR /MA | RCTs, n (n Stanford model) | Level of evidence from SR | | |
| **Quinones** (2014)[31] | Educational group visits for the management of chronic health conditions | One section on multiple chronic conditions | Usual care | - | 4 (4) | Moderately strong evidence for 2 US trials. | 2,593 | Narrative review |
| **Franek** (2013)[28] | SMS interventions – mainly Stanford CDSMP | Multiple chronic conditions in some specific populations (e.g. Hispanic, Bangladeshi, UK, Netherlands) | Usual care | - | 10 (9) | See below tables for each statement. | 6,074 | Meta-analysis |
| **NZGG** (2011)[7] | Health behaviour change for chronic care – multiple conditions section focuses on generic models, mainly Stanford CDSMP | DM, COPD, asthma, hypertension, stroke and multiple conditions | Range of comparators including: usual care, wait list control, exercise training, and educational material. | 3 | 10 (6) | See below tables for each statement. | > 1,000 | Narrative review |
| **Jonker** (2009)[30] | Self-management focusing on the CDSMP | In vulnerable older people with multiple conditions (combination of DM, asthma, CVD, lung diseases, cancer, low back pain) | Usual care | - | 8 (8) | Not stated | 4,284 (range: 109-954) | Narrative review |
| **Boult** (2009)[27] | Comprehensive care model – a component of which is CDSM which includes analysis of the Stanford CDSMP | CVD (3), multiple conditions-(6), OA(1) | Not specified | 1 MA | 10 (3) | Not stated | Not reported | Narrative review |
| **Inouye** (2011)[29] | Self-management<br>12 cognitive behavioural therapies, 3 health education (CDSMP), 6 alternative therapies | Asian/Pacific Islanders with chronic conditions<br>arthritis (4), cancer (2), HIV (2), DM (6), weight loss (1), COPD (1), HF (3), comorbid section includes Stanford CDSMP (3/21 Stanford model) | Range of comparators. For example, usual care, wait list control, a course of NSAIDS, course of injections, home exercise. | - | 21 (3) | 11 poor quality<br>10 good quality | > 1,000 | Narrative review |

**Key: CBI =** Cognitive Behavioural Intervention; **COPD** = Chronic obstructive pulmonary disease; CVD = Cardiovascular Disease; DM = Diabetes Mellitus; **HF =** Heart failure; **HIV =** Human Immunodeficiency Virus; **MA** = Meta-analysis; **NR =** Narrative review; **OA =** Osteoarthritis; **SMS =** Self-management support; **SR =** Systematic-review;

## Table A4.2.2 CDSMP: Summary of results

| Review (year, synthesis) | R-AMSTAR score (/44) | Outcomes measured | Follow -up | Results [Evidence appraisal] | Number of RCTs |
|---|---|---|---|---|---|
| **Franek** (2013, Meta-analysis)[28] | 28 | GP visits | Range 4 to 12 months | No SD between CDSMP and usual care (SMD, −0.03; 95% CI: −0.09 to 0.04; P = 0.41). [GRADE: Very Low] | 6 |
| | | ED visits | | No SD (SMD, −0.05; 95% CI: −0.18 to 0.09; P = 0.49). [GRADE: Very Low] | 4 |
| | | Days in hospital | | No SD (SMD, −0.06; 95% CI: −0.13 to 0.02; P = 0.14 / WMD, −0.27; 95% CI: −0.75 to 0.20; P = 0.26). [GRADE: Very Low] | 5 |
| | | Hospitalisation | | No SD (SMD, −0.09; 95% CI: −0.24 to 0.05; P = 0.20). [GRADE: Very Low] | 2 |
| | | Self efficacy | | Small SS increase (higher is better) in favour of CDSMP (SMD, 0.25; 95% CI: 0.12 to 0.39; P = 0.002). [GRADE: Low] | 6 |
| | | Self-rated health | | Small SS reduction (lower is better) in favour of CDSMP (SMD, −0.24; 95% CI: −0.40 to −0.07; P = 0.006). [GRADE: Low] | 6 |
| | | HRQoL | | Data on health-related quality of life were sparsely reported and difficult to interpret collectively. | N/A |
| | | Health distress | | Small SS reduction in favour of CDSMP (SMD, −0.20; 95% CI: −0.29 to −0.12; P < 0.001). [GRADE: Low] | 6 |
| | | Cognitive symptom management | | Small SS increase in cognitive symptom management (SMD 0.34; 95% CI: 0.20 to 0.47; p<0.001) [GRADE: Low] | 3 |
| | | Communication with health professional | | Small statistically significant increase in communication (SMD, 0.11; 95% CI: 0.02 to 0.21; P = 0.02) [GRADE: Low] | 6 |
| | | Aerobic exercise | | Small SS increase in aerobic exercise in favour of CDSMP (SMD, 0.16; 95% CI: 0.09 to 0.23; P < 0.001) [GRADE: Low] | 5 |
| | | Pain | | Small SS reduction in favour of CDSMP (SMD, −0.11; 95% CI: −0.17 to −0.04; P = 0.001). [GRADE: Low] | 6 |
| | | Disability | | Small SS reduction in favour of CDSMP (SMD, −0.14; 95% CI: −0.24 to −0.05, P = 0.004). [GRADE: Low] | 4 |
| | | Fatigue | | Small SS reduction in favour of CDSMP (SMD, −0.15; 95% CI: −0.22 to −0.08; P < 0.001). [GRADE: Low] | 5 |
| | | Dyspnoea | | Non-significant trend towards reduction in shortness of breath in favour of CDSMP (SMD, −0.10; 95% CI: −0.21 to 0.01; p = 0.08). [Very Low] | 4 |
| | | Depression | | Small SS reduction in favour of CDSMP (SMD, −0.15; 95% CI: −0.28 to −0.03; p = 0.01). [GRADE: Low] | 5 |
| **NZGG** (2011, Narrative | 28 | Health service resource use | Authors stated majority of the included | 1 SR (Foster, 2007) reported no difference between intervention and control groups (meta-analysis of 9 RCTs). This included 5 RCTs for Stanford CDSMP, 3 on the arthritis version (ASMP) and 1 disease-specific RCTs. There is no | 9 |

| Review (year, synthesis) | R-AMSTAR score (/44) | Outcomes measured | Follow -up | Results [Evidence appraisal] | Number of RCTs |
|---|---|---|---|---|---|
| Review)[7] | | | studies had short-term (6 months) follow-up | difference for the standard programme alone. | |
| | | | | No SD between groups in RCTs based on Stanford model alone (meta-analysis of 5 RCTs). | 5 |
| | | QoL | | 1 SR (Foster, 2007) reported no difference based on 3 RCTs (WMD -0.03, 95% CI -0.09 – 0.02; NS). This is based on 1 ASMP, 2 CDSMP. No difference for CDSMP alone. | 3 RCTs |
| | | | | No evidence of difference between groups for mental component of health status measure (n=1), in overall QoL measures (n=2) or in self-reported health status (n=1). | 6 (Stanford or variant) |
| | | Health distress | | 1 SR (Foster, 2007) reported greater improvement in interventional group based on 3 RCTs for the CDSMP (SMD -0.25, 95% CI -0.34 - -0.15, P<0.00001) | 3 |
| | | | | Statistically significant improvement in intervention group (n=2, 6 months, 1 year), decreased health distress (n=1). | 3 |
| | | Self-efficacy/self-control/empowerment | | 1 SR (Foster, 2007) reported significant improvement in intervention group (p<0.00001) in 10/17 trials. P<0.0029 for CDSMP alone (n=5 RCTs). | 10 |
| | | | | Statistically significant improvement at 6 months but not at 1 year follow-up (1SR). | 1 |
| | | | | No difference in 2 trials, significant improvement in 2 trials, similar improvements (1 trial), significantly improved (1 trial in short term but not at 1 year). EPP reported that those at low self-efficacy at baseline were more likely to improve. | 6 |
| | | Physical activity | | 1 SR (Foster, 2007) reported a small but statistically significant effect in favour of intervention group (SMD -0.20, 95% CI -0.27 to -0.12, p<0.00001). This is based on 2 ASMP, 4 CDSMP and 1 disease specific. P< 0.00001 for CDSMP alone (n=4 RCTs). [good quality based on risk of bias] | 1 SR (6 RCTs) |
| | | | | 1SR reported not effective. [mixed quality based on risk of bias] | 1 SR |
| | | | | Mixed results. [mixed quality based on risk of bias] | 4 RCTs |
| | | Improving diet | | 1SR reported not effective. | 1 SR |
| | | | | No difference. [mixed quality based on risk of bias] | 1 |
| | | Medication adherence | | No evidence of difference. | 2 |
| | | Depression | | 1 SR (Foster, 2007) reported a small but statistically significant effect in favour of intervention group (SMD -0.16, 95% CI -0.24 to -0.07, p=0.00036). This is based on 3 ASMP, 2 CDSMP and 1 disease specific. P=0.099 for CDSMP alone | 1 SR (6 RCTs) |

| Review (year, synthesis) | R-AMSTAR score (/44) | Outcomes measured | Follow -up | Results [Evidence appraisal] | Number of RCTs |
|---|---|---|---|---|---|
| | | | | (n=2 RCTs). [good quality based on risk of bias] | |
| | | | | No evidence of difference. | 3 RCTs |
| **Inouye** (2011, Narrative Review)[29] | 26 | Hospital stay | Baseline 4 or 6 months | Shanghai CDSMP (Fu et al.) improved hospital stay [Jadad score: 10] | 1/3 |
| | | Self-efficacy | | Significant increase in 2 studies [Jadad score: 9, 12] and an increase in the third [Jadad score: 10]. | 3 |
| | | Self-care behaviour | | Significant increase in 1 study [Jadad score: 12] | 1 |
| | | (Cognitive) symptom management | | Significant increase in 1 study [Jadad score: 9], improved in another [Jadad score: 10] | 2 |
| | | Exercise | | Significant increase in 1 study [Jadad score: 9], improved duration of aerobic exercise in another [Jadad score: 10] | 2 |
| | | Pain | | Significantly better outcomes [Jadad score=9], improved [Jadad score: 10] | 2 |
| | | Fatigue | | Significantly better outcomes [Jadad score=9], improved [Jadad score: 10] | 2 |
| | | Health distress | | Significantly better outcomes [Jadad score=9], improved [Jadad score: 10] | 2 |
| | | Energy | | Significantly better outcomes [Jadad score=9] | 1 |
| | | General health | | Significantly better outcomes [Jadad score=9], improved [Jadad score: 10] | 2 |
| | | Pain/disability/shortness of breath, social and role activity limitations | | Improved outcomes [Jadad score: 10] | 1 |
| **Jonker** (2009, Narrative Review)[30] | 21 | Hospitalisation | <1 year | Fewer hospitalisations in 1 study (Lorig), no improvement in 2 | 3 |
| | | Physician/ED visits | 1 year | Fewer visits in 1 study (Lorig), no improvement in 5 | 6 |
| | | Self-efficacy | <1 year | Improvement in 5 studies, no improvement in 2 | 7 |
| | | Cognitive symptom management | <6 months | Improvement in 3, no improvement in 1 | 4 |
| | | Mental stress management | <6 months | Improvement in 1, no improvement in 0 | 1 |
| | | Self-care | 4-6 months | Improvement in 2, no improvement in 1 | 3 |
| | | General (self-rated) health | <6 months | Improvement in 4, no improvement in 3 | 7 |
| | | QoL | 4-6 months | Improvement in 1, no improvement in 1 | 2 |
| | | Communication | <6 months | Improvement in 3, no improvement in 3 | 6 |
| | | Health distress | <1 year | Improvement in 5, no improvement in 0 | 5 |
| | | Anxiety | 4-6 months | Improvement in 0, no improvement in 2 | 2 |
| | | Emotional, physical & psychological well-being | 4-6 months | Improvement in 2, no improvement in 1 | 3 |

| Review (year, synthesis) | R-AMSTAR score (/44) | Outcomes measured | Follow -up | Results [Evidence appraisal] | Number of RCTs |
|---|---|---|---|---|---|
| | | Exercise | <1 year | Improvement in 5 studies, no improvement in 1 | 6 |
| | | Healthy diet | 4-6months | Improvement in 0, no improvement in 1 | 1 |
| | | Tobacco | ~1 year | Improvement in 1, no improvement in 1 | 2 |
| | | Pain | <1 year | Improvement in 3 studies, no improvement in 5 | 8 |
| | | Disability/ mobility | <1 year | Improvement in 2, no improvement in 3 | 5 |
| | | Fatigue / energy | 4-6 months | Improvement in 4, no improvement in 2 | 6 |
| | | Discomfort | 4-6 months | Improvement in 0, no improvement in 1 | 1 |
| | | Shortness of breath | 4-6 months | Improvement in 1, no improvement in 3 | 4 |
| | | Depression | 4-6 months | Improvement in 1, no improvement in 3 | 4 |

**Key: ASMP =** Arthritis self-management programme; **CDSMP =** Chronic disease self-management programme; **ED =** Emergency Department; **ES =** Effect size; **GP =** General Practitioner; **MA =** Meta-analysis; **NR** = Narrative review; **SD =** Significant difference; **SMD =** Standardised Mean Difference; **SR =** Systematic Review; **(HR)QoL =** (Health related) Quality of Life; **SS =** Statistically Significant ; **WMD =** Weighted Mean Difference ; **SD =** Significant difference; **CI** = Confidence interval.

## Table A4.2.3 Telemedicine: Summary of scope of reviews

| Review (year) | Intervention and population | Chronic diseases / population | Comparator | Included studies | | | Total participants | Synthesis |
|---|---|---|---|---|---|---|---|---|
| | | | | SR /MA | RCTs, n | Level of Evidence from SR | | |
| **Beratarrechea** (2014)[32] | Mobile Health Interventions (cell phone voice communication, text messaging) | Chronic diseases in developing countries | Not specified | 0 | 9 | 6 low or unclear risk of bias; 3 some risk of bias | 4,604 | Narrative Review |
| **Muller** (2011)[33] | Telephone-delivered CBT of varying intensities | SLE (1), CVD (1), End stage respiratory disease (2), RA or OA (1), MS (1), breast cancer (2). 45-61 year olds, more females | Any other intervention and/or routine care | 0 | 8 | 7 unclear risk of bias; 1 low risk of bias | 1,093 | Meta Analysis |
| **Wootton** (2012)[34] | Telemedicine (20 years) | Asthma (20), COPD(11), DM (39), HF (57), hypertension (14) | Usual care | 22 | 141 | Not stated | 37,695 | Evidence synthesis |

**Key: CBT =** Cognitive behavioural therapy; **COPD =** Chronic Obstructive Pulmonary Disease; **CVD =** Cardiovascular Disease; **DM =** Diabetes Mellitus; **HF =** Heart failure; **MA** = Meta-analysis; **MS =** Multiple Sclerosis; **NR** = Narrative review; **OA** = Osteoarthritis, **SR =** Systematic-review; **SLE =** Systemic Lupus Erythematosus; **RA =** Rheumatoid Arthritis.

## Table A4.2.4 Telemedicine: Summary of results

| Review (year, synthesis) | R-AMSTAR score (/44) | Outcomes measured | Follow -up | Results [Evidence appraisal] | Number of RCTs |
|---|---|---|---|---|---|
| **Beratarrechea** (2014)[32] | 30 | HRQoL | 3-6 months (1 study) | Improvements in HRQoL in 2 studies. [not stated] | 2 |
| | | Asthma (expiratory volume in 1s, cough & night symptoms)<br>HF (6 min walk test distance, physical impairment, symptoms)<br>DM (glycaemic control) | Not specified | Improvement in 4 trials studying clinical outcomes. | 5 |
| **Muller** (2011)[33] | 28 | Health status | 2-6 months | MA of the 8 studies revealed a significant change in health status following telephone-delivered CBT. The sample-weighted pooled effect size was d=0.225 (95% CI: 0.105, 0.344). | 8 |
| **Wootton** (2012)[34] | 22 | Asthma (n=20): Commonly healthcare utilisation, symptoms and quality of life.<br>COPD (n=11): Commonly hospital admissions and quality of life.<br>DM (n=39): Commonly HbA1c, QoL and self-efficacy.<br>HF (n=61): Commonly mortality, hospital admissions, quality of life and healthcare costs.<br>Hypertension (n=17): Commonly blood pressure and healthcare costs. | | RCTs: 73% of studies were favourable to the intervention, 26% were neutral, and 1% were unfavourable. [not stated] | 141 |
| | | QoL, ED visits, Hospitalisation, Mortality, HbA1c, Severe hypoglycaemia, Diabetic ketoacidosis | | SRs: Approximately half of the SRs provided a qualitative summary; none concluded negatively, i.e. telemedicine unhelpful in CD management. [not stated] | Approx 11/22 |
| | | | | SRs: 12 SRs provided 23 pooled estimates of effect, of which approximately half showed telemedicine to provide significantly better outcomes than the control condition. [not stated] | 12/22 |
| | | | | SRs: The other half of the pooled estimates showed telemedicine to be no better than the control condition. This emphasises the rather weak and unsatisfactory conclusions which can be drawn from the systematic reviews presently available. [not stated] | 10/22 |

**Key: CVD:** Cardiovascular Disease; **CD**: Chronic Disease; **CBT:** Cognitive Behavioural Therapy; **COPD**: Chronic Obstructive Pulmonary Disease; **DM:** Diabetes Mellitus; **ES:** Effect Size; **ED**: Emergency Department; **HbA1c:** Glycated Haemoglobin; **HF:** Heart Failure; **(HR)QoL:** (Health related) Quality of Life; **MA**: Meta-analysis; **NR**: Narrative review; **SD:** Significant difference; **SR**: Systematic Review.

## Table A4.2.5 Web-based: Summary of scope of reviews

| Review (year) | Intervention | Chronic diseases / population | Comparator | Included studies Total | | | participants | Synthesis |
|---|---|---|---|---|---|---|---|---|
| | | | | SR /MA | RCTs, n | Level of evidence | | |
| **McDermott** (2013)[39] | Computers to deliver CDSMP | Type I or II DM (3), asthma (3), HF (2), HIV (1), TIA or minor stroke (n1), RA (1). | Equivalent 'standard' CDSMP delivered by staff, usual care or no intervention | 0 | 11 RCTs (from 15 articles) | Variable risk of bias across studies | 1,506 | Narrative review |
| **Bossen** (2014)[35] | Self-Guided Web-Based Physical Activity Interventions | DM (11), HF (n 3), COPD (1), CVD (1), cancer (1), and mixed patient groups (CVD, lung disease, type 2 DM; n1). | No or minimal treatment | 0 | 5 RCTs, 2 pilot RCTs | 5 high-quality, 2 low quality | Ranged from 22 to 463 | Narrative review |
| **Kuijpers** (2013)[38] | Web-Based Interventions for Patient Empowerment and Physical Activity | DM (11), HF (3), COPD (1), CVD(1), cancer(1) and CD(1) | Similar patient group (receiving another intervention or usual care) | 0 | 18 (19 studies) | | 5,204 | Narrative review |
| **De Jong** (2014)[36] | Internet-based asynchronous communication between health providers and patients | Unspecified chronic illnesses (4), chronic pain (2), DM (4), asthma (2), COPD (n=1), chronic neurological conditions (1), HF (1) | Usual care | 0 | 15 | 3 high risk of bias; 12 low risk of bias | 6,067 | Narrative review |
| **Paul** (2013)[40] | Web-based approaches (CBT or information websites or access to expert advice ) impact on psychosocial health | Mental health (19), DM (7), cancer (7), CVD (1), obesity (1) and multiple chronic conditions (1) | Usual care or face-to face CBT | 0 | 36 | Not stated | 9,814 | Narrative review |
| **Samoocha** (2010)[41] | Web-based Interventions effectiveness on patient empowerment | CVD (2), mental health (3), infertility (2), COPD (1),ABI (1), arthritis(1), DM (1), CD(1),back pain (1) | Usual care or no care | 0 | 13 RCTs, 1 quasi-RCT | 6 fair quality, 7 good quality, 1 excellent quality | 3,417 | Meta-analysis |
| **Eland de Kok** (2011)[37] | E-health interventions (interactive websites, internet) (monitoring, treatment instructions, self-management training (coaching) and general information and web-based messaging) | DM (9), 1 atopic dermatitis (1), co-morbidity (1), CVD (1) | Usual care | 0 | 12 | 4 low; 4 mod; 4 high | 11,203 | Narrative Review |

**Key: ABI =** Acquired Brain Injury; **CD =** Chronic Disease; **COPD =** Chronic Obstructive Pulmonary Disease; **CVD =** Cardiovascular Disease; **DM =** Diabetes Mellitus; **HF =** Heart failure; **HIV =** Human Immunodeficiency Virus; **MA** = Meta-analysis; **NR** = Narrative review; **SR =** Systematic-review; **RA =** Rheumatoid arthritis; **TIA =** Transient ischemic attack.

## Table A4.2.6 Web-based: Summary of results

| Review (year, synthesis) | R-AMSTAR score (/44) | Outcomes measured | Follow -up | Results [Evidence appraisal] | Number of RCTs |
|---|---|---|---|---|---|
| **McDermott** (2013)[39] | 26 | Behavioural (e.g. dietary habits) | 0 to 6 months | Computer-based PSMP more effective when compared to no intervention or a control with no PSM element specified than when compared to standard PSMP for behavioural outcomes: 100% v 60% of studies, 77% v 25% of analyses. [not stated] | 11 |
| | | Clinical (e.g. glycosylated hemoglobin) | 3 to 12 months | Computer-based PSMP more effective when compared to no intervention or a control with no PSM element specified than when compared with standard PSMP for clinical outcomes: 100% v 50% of studies, 33% v 17% of analyses. [not stated] | 11 |
| **Bossen** (2014)[35] | 28 | Physical activity | 1 to 12 months | 3 [high-quality] studies reported significant increase for the intervention, 4 [2 high quality, 2 low quality] studies reported no SD. ES range from 0.13-0.56. | 7 |
| **Kuijpers** (2013)[38] | 26 | Patient empowerment | 1 to 18 months | Increased significantly (p<.05) in intervention group compared with usual care or observation in four studies; increase reported for both groups in 3 studies; mixed results in 2 studies; no significant change in patient empowerment in four studies. [not stated] | 13 |
| | | Patient satisfaction | Not reported | High in general | 10 |
| | | Physical activity | 1 to 18 months | Significant improvement (p<.05) for intervention group compared with usual care in 2 studies; increases for both groups but no difference between groups in 6 studies. | 14 |
| **De Jong** (2014)[36] | 29 | Health care utilisation | Not reported | Decrease, but not statistically significant. [not stated] | 4 |
| | | Self-efficacy/self-management | Not reported | Increase in self-efficacy self-care managing dyspnoea found in 2 of three studies. [not stated] | 3 |
| | | General health behaviour | Not reported | Improvements when using the intervention. [not stated] | 7 |
| | | Health outcomes e.g. HbA1c | 6 weeks in 1 study, 8 weeks in 1 study, not specified for remaining studies | Ten of the 11 studies report statistically significant improvements in one or more health outcomes. | 11 |

| Review (year, synthesis) | R-AMSTAR score (/44) | Outcomes measured | Follow -up | Results [Evidence appraisal] | Number of RCTs |
|---|---|---|---|---|---|
| **Paul** (2013)[40] | 28 | Psychosocial outcomes | Not reported for all studies, examples include 1 month, 6 months and 12 months. | Significant positive in favour of web-based intervention found in 21 studies; mixture of positive and null findings in 4 studies; no positive effect found in 11 studies. | 36 |
| **Samoocha** (2010)[41] | 33 | General self-efficacy | 8 weeks to one year | SMD 0.05 (95% CI - 0.25 to 0.35)<br>no statistically SD between Web- based interventions and usual care in increasing general self-efficacy [low quality] | 3 (combined n=293) |
| | | | | There are improvements in mastery and self-efficacy when disease specific measurement tools or scales are used but not when general ones are used. | 1 |
| **Eland-de Kok** (2011)[37] | 24 | Health care use | Not reported | *In addition to usual care:* There were only small effects shown on health care use. [not stated] | 1 |
| | | Resource use | Not reported | *In addition to usual care:* No SD in resource use between the intervention and control group were shown in two studies. [not stated] | 2 |
| | | DM(HbA1c)<br>CVD (cardiovascular related events) | Not specified | *Compared with usual care:* All 4 studies in patients with DM showed a greater reduction in HbA1c. 1 study showed greater improvement in clinical outcomes in patients with CVD and fewer cardiovascular-related events as measured after six months. However, not all outcomes improved in the 5 studies, and in some measures, comparable effect sizes were seen in both groups. [not stated] | 5 |
| | | Physical health outcomes<br>Primary health outcomes | Not specified | *In addition to usual care:* e-health programme resulted in significantly improving physical health outcomes with small to moderate ES on primary health outcomes of patients with DM. In two studies, e-health was not associated with improved health outcomes. [not stated] | 7 |

**Key: MA** = Meta-analysis; **NR** = Narrative review; **SS =** Statistically Significant; **SD =** Significant difference; **SMD =** Standardised Mean Difference; **ES =** Effect Size; **PSMP =** Patient Self-Management Programme; **HbA1c =** Glycosolated Haemoglobin.

## Table A4.2.7 Complex SMS interventions: Summary of scope of reviews

| Review (year) | Intervention | Chronic diseases / population | Comparator | Included studies | | | Total participants | Synthesis |
|---|---|---|---|---|---|---|---|---|
| | | | | SR /MA | RCTs, n | Level of evidence | | |
| **Panagioti** (2014)[43] | SMS interventions – 'Mixed problems' section includes the Stanford CDSMP. Remaining RCTs are not programmes or are disease-specific | Arthritis = 8%, CVD= 29%, DM=6%, mental health=16%, mixed problems=7%, respiratory=24%, pain=11% | Usual care | 0 | 9 (mixed problems) | Variable allocation concealment | 4,695 | Meta-analysis |
| **Desroches** (2013)[42] | Interventions to enhance adherence to dietary advice | CVD(9), hypertension (5), DM (6), renal (6), obesity (6), IBS (1) | No intervention (control); usual care; multiple interventions | 0 | 38 | Variable risk of bias | 9,445 | Narrative review (Cochrane review) |
| **Simmons** (2014)[44] | Personalised health care (effect of patient engagement) | DM (6),CV (1), MS (1),asthma (1), arthritis (1), bronchiectasis (1) | Usual care (60%), attention control, enhanced usual care or a wait-list control (40%). | 0 | 10 | 6 low quality; 4 high quality | 3,023 | Narrative review |

**Key: CD =** Chronic Disease; **COPD =** Chronic Obstructive Pulmonary Disease; **CR =** Cochrane review; **CVD =** Cardiovascular Disease; **DM =** Diabetes Mellitus; **IBS =** Irritable Bowel Syndrome; **MA =** Meta-analysis; **MS =** Multiple Sclerosis; **NR =** Narrative review; **SMS =** Self-management Support

## Table A4.2.8 Complex SMS interventions: Summary of results – Health care utilisation

| Review (year, synthesis) | R-AMSTAR score (/44) | Outcomes measured | Follow -up | Results [Evidence appraisal] | Number of RCTs |
|---|---|---|---|---|---|
| **Panagioti** (2014)[43] | 36 | Hospital use | 5 to 12 months | Small but significant reductions in hospital use. ES=– 0.12 (– 0.20 to – 0.03). A minority of self-management support studies reported reductions in health-care utilisation in association with decrements in health. | 9 |
| | | QoL | 4 to 12 months | Small, but significant improvements in QoL. ES= 0.13 (0.02 to 0.24) | 9 |
| | | Medication adherence | Not specified for all studies | No significant effect of pharmacist led interventions for medication reconciliation or for enhanced medication adherence. | 3 MA (2, 4, 9 RCTs) |
| **Desroches** (2013)[42] | 36 | Diet adherence | <6->12 months | 32/98 DA outcomes favoured the intervention group. 4 favoured the control group and 62 had no significant difference between groups. | 38 |
| **Simmons** (2014)[44] | 31 | Patient engagement | 1 to12 months | Improvements in all components of patient engagement (knowledge, skills, confidence, and at least one behaviour). [4/10 'high' methodological quality (Jadad score≥3)] | 9/10 |
| | | | | No changes in any component of patient engagement, and improvements in knowledge/confidence/skills but not behaviour. [4/10 'high' methodological quality (Jadad score≥3)] | 1/10 |
| | | Self-reported health status | 1 to 18 months | All studies reported improvements in self-reported health status. | 3/3 |
| | | Clinical markers of disease | Not reported | Five studies reported reduction in clinical markers of disease (for example HbA1C). [4/10 'high' methodological quality (Jadad score≥3)] | 5/10 |

**Key: MA =** Meta-analysis; **NR =** Narrative review; **SD =** Significant difference; **HRR =** Hospital readmission rates; **(HR)QoL =** (Health related) Quality of Life; **DA =** Diet adherence

## Table A4.2.9 Other SMS: Summary of scope of reviews

| Review (year) | Intervention and population | Chronic diseases / population | Comparator | Included studies | | | Total participants | Synthesis |
|---|---|---|---|---|---|---|---|---|
| | | | | SR /MA | RCTs, n | Level of evidence | | |
| **Kivela** (2014)[45] | Health coaching by health care professional (telephone only, internet, combination of telephone, face-to-face, internet or e-mail) | DM (3), mix conditions (3), CVD(2), overweight (2), RA (1), cancer(1) | Not specified | 0 | 13 (11 RCTs, 2 quasi-RCTs) | All studies fair quality or above | Range 22 to 1755 | Narrative review |
| **Ontario** (2013)[46] | In-home care (care in the home, community, supportive housing, or long-term care facilities.) | DM (1), stroke (1), COPD (1),multi-morbid (3- based on 2 RCTs), HF (6) | No home care or usual care/care received outside the home | 1 HTA, 4 SRs | 12 (2) | See below for each statement | Range <100 to >300 per trial | Meta-analysis & Narrative review |
| **O'Halloran** (2014)[47] | Motivational interviewing for increasing physical | obesity or CVD (7), MS (1), fibromyalgia (1) | Usual care | 0 | 10 | See below for each statement | 1176 | Meta-analysis |
| **van Camp** (2013)[48] | Nurse-led interventions to enhance medical adherence (mainly counseling via face-to-face, groups or electronic messages) | HIV (7), depression (1), 1 hypertension (1), arthritis(1) | Usual care | | 10 | All studies acceptable to high quality | 2,587 | Meta-analysis |
| **Chang** (2014)[49] | Information motivation behavioural skills, for adherence to therapy or to target risky sexual behaviour | HIV (9),DM (1), CVD (1), cancer (1) | Various interventions relating to the information construct, motivation construct and behavioural skills construct. For example, instructural pamphlets, motivational interviewing techniques, instruction or role playing | 0 | 12 | All studies fair quality | 2,605 | Narrative review |
| **Coulter** (2015)[11] | Personalised care planning All studies included components intended to support behaviour change, either face-to-face or telephone support. | DM (12), mental health (3), HF (1), end stage renal disease (1), asthma (1), various conditions (1) | Usual care | 0 | 19 (16 included in MA) | Moderate | 10,856 | Meta-analysis |

**Key: COPD =** Chronic Obstructive Pulmonary disease; **CVD =** Cardiovascular disease; **DM =** Diabetes Mellitus; **HF =** Heart Failure; **HIV =** Human Immunodeficiency Virus; **HTA =** Health Technology Assessment; **MA =** Meta-analysis; **MS =** Multiple sclerosis; **NR =** Narrative review; **SR =** Systematic-review; **RA =** Rheumatoid Arthritis;

## Table A4.2.10 Other SMS: Summary of results

| Review (year, synthesis) | R-AMSTAR score | Outcomes measured | Follow-up | Results [Evidence appraisal] | Number of RCTs |
|---|---|---|---|---|---|
| **Kivela** (2014)[45] | 29 | Physical health status | 6 weeks to 24 months | Significantly improved results reported in 3/4 studies (6 weeks, 6/8 months), non-significant outcome in 1 (at 12, 24 months). | 4 |
| | | Self-efficacy | 6 to 24 months | SS positive outcome in 2/3 studies (at 6 and 8 months), non-significant outcome in 1 (at 12, 24 months). | 3 |
| | | Satisfaction of treatment | 12 to 36 weeks | SS positive outcome in 2/2 studies. | 2 |
| | | Mental health | 6 weeks to 6 months | SS positive outcome in 2/3 studies, non-significant outcome in 1. | 3 |
| | | Weight loss | 3 to 18 months | Significantly improved results reported in 3/3 studies. | 3 |
| | | Physical activity | 3 weeks to 18 months | Significantly increased physical activity in 6/10 studies. | 10 |
| | | HbA1c | 12 weeks to 12 months | Significantly improved results reported in 2/4 studies, non-significant outcome in 1. | 4 |
| **Ontario** (2013)[46] | 29 | Mortality | 1 month to 10 years | No difference between in-home care and usual care for all-cause mortality in chronically ill multimorbid patients (Mean difference: 0.80; 95% CI: 0.54 to 1.19; p= 0.28). [Moderate evidence] | 1 |
| | | Activities of daily living | | Mean difference -0.14 [-0.27, -0.01]. (favours home care) [Moderate evidence] | 1 |
| | | Mobility | | Mean difference -0.12 [-0.29, 0.05] favours home care [Moderate evidence] | 1 |
| | | instrumental activities of daily living | | Mean difference favours home care -0.13 [-0.29, 0.03] [Moderate evidence] | 1 |
| **O'Halloran** (2014)[47] | 33 | Physical activity | 3 to 18 months | MI increased physical activity levels for people with health conditions with a small but significant effect observed immediately following the intervention (SMD = 0.19, 95% CI 0.06 to 0.32, p= 0.004, $I^2$ = 0%) [Moderate quality trials] | 8 |
| | | Cardio-respiratory fitness | | No effect of intervention with a SMD of –0.07 (95% CI –0.56 to 0.43, p= 0.79, $I^2$= 52%) [very low quality] | 3 |
| | | Functional exercise capacity | | No SD between the groups were observed (SMD 0.13, 95% CI –0.08 to 0.34, p= 0.22, $I^2$ = 0%) [moderate quality] | 2 |
| **van Camp** (2013)[48] | 29 | Medication adherence | Short term immediately post intervention | 9/10 found their interventions enhanced adherence, 4 significantly. The difference in adherence in favour of the intervention group varied from +5 to 11 %. | 10 |

| Review (year, synthesis) | R-AMSTAR score | Outcomes measured | Follow-up | Results [Evidence appraisal] | Number of RCTs |
|---|---|---|---|---|---|
| | | | (3 to 12 months) | The pooled mean differences were +5.39 (1.70–9.07) in favour of the intervention groups (p=0.004).<br>[Quality rates acceptable to high for all included studies] | |
| | | | Long term – after end of interventions | 8/8 authors found their intervention effect was sustained in the long term and some were further increasing, 4 significantly.<br>The pooled mean differences were +9.46 (4.68–14.30) in favour of the intervention groups (p<0.001).<br>[Quality rates acceptable to high for all included studies] | 8 |
| **Chang** (2014)[49] | 29 | Behavioural outcomes | 3 to 12 months | 10/12 reported significant behaviour changes at the first post-intervention assessment. | 12 |
| | | Medication adherence | - | 5/6 intervention groups showed significantly higher medication adherence than the control groups. | 6 |
| | | Measured biological variables | 0 to 12 months | 2/5 improved results in the intervention group. | 2/5 |
| **Coulter** (2015)[11] | 38 | Depression | 1.5 to 12 months | SMD of -0.36 (95% CI -0.52 to -0.20), a small effect in favour of personalised care [moderate quality evidence] | 5 |
| | | HRQoL | | No effect on the physical component summary score SMD 0.16 (95% CI -0.05 to 0.38) or the mental component summary score SMD 0.07 (95% CI -0.15 to 0.28) [moderate quality evidence] | 3 |
| | | Condition-specific health status | | No difference between the intervention and control groups, SMD -0.01 (95% CI -0.11 to 0.10) [moderate quality evidence] | 4 |
| | | HbA1c | 6 to 12 months | Mean difference -0.24% (95% confidence interval (CI) -0.35 to -0.14), a small positive effect in favour of personalised care planning compared to usual care [moderate quality evidence] | 9 |
| | | Systolic blood pressure | | Mean difference of -2.64 mm/Hg (95% CI -4.47 to -0.82) favouring personalised care [moderate quality evidence]. | 6 |
| | | Diastolic blood pressure | | No significant effect, MD -0.71 mm/Hg (95% CI -2.26 to 0.84) | 4 |
| | | Cholesterol | | No evidence of an effect on cholesterol (LDL-C), standardised mean difference (SMD) 0.01 (95% CI -0.09 to 0.11) | 5 |
| | | Body mass index | | No evidence of an effect , MD -0.11 (95% CI -0.35 to 0.13) | 4 |

**Key: ES =** Effect Size; **MA =** Meta-analysis; **NR =** Narrative review; **(HR)QoL =** (Health related) Quality of Life; **SS =** Statistically Significant; **MI =** Motivational Interviewing; **NR =** Narrative review; **SD =** Significant difference; **SMD =** Standardised Mean Difference; **HbA1C =** Glycosolated hemoglobin.

# Appendix A4.3.1 – Appraisal of study quality for included cost-effectiveness studies

| Study | Quality | Reasons for downgrading |
|---|---|---|
| **Aanesen (2011)** | Low | Results are dependent on the alternative to the intervention, namely living without it or the requirement to live in a nursing home. No sensitivity analyses. |
| **Ahn (2013)** | Low | Effectiveness based on change from baseline with no concurrent control group. No assessment of uncertainty undertaken. |
| **Bendixen (2009)** | Low | Retrospective, matched comparison study design. Significant variance in the results could not be attributed to the analysed variables, indicating a large error component for this study design. |
| **Battersby (2007)** | Low | Poorly reported cost data. No sensitivity analysis. |
| **Dimmick (2000)** | Low | Poorly reported study. Very small patient sample with unclear methodology regarding analysis. |
| **Doolittle (2000)** | Low | Poorly reported. No concurrent controls. |
| **Elliott (2008)** | High | |
| **Finkelstein (2006)** | Low | Cost data was not related to year of cost. Small study population. |
| **Graves (2009)** | High | |
| **Griffiths (2005)** | Moderate | Poor uptake of participation in underlying RCT, hence results are at risk of bias. |
| **Henderson (2013)** | Moderate | Data based on non-random subsample of trial population. |
| **Jerant (2009)** | Low | Poorly reported cost and outcome data. No sensitivity analysis. |
| **Johnston (2000)** | Low | Poorly reported. Unclear source of cost data. No sensitivity analysis. |
| **Katon (2012)** | High | |
| **Lorig (2001)** | Low | Waiting-list control group. The cost data are based on simplistic estimates of health care utilisation costs. The study uses a longitudinal design format, along with simple ER and hospitalisation cost multipliers, to estimate costs and cost savings. |
| **Moczygemba (2012)** | Low | Based on quasi-experimental study data. No sensitivity analysis. |
| **Noel (2000)** | Low | Based on pilot study data. |
| **Noel (2004)** | Moderate | Based on small RCT. |
| **Page (2014)** | Low | Data based on cost surveys. |
| **Pare (2013)** | Low | Data relating to post outcomes extrapolated from 157 to 244 days. No detail of extrapolation method given. No sensitivity analysis. |
| **Richardson (2008)** | High | |
| **Schwartz (2010)** | High | |
| **Scott (2004)** | High | |
| **Steventon (2013)** | High | |
| **Tousignant (2006)** | Low | Based on pilot study to establish proof of concept and a cost analysis of the intervention. |

## Appendix A4.3.2. Studies investigating CDSM programmes

| Study | Study design | Intervention | Comparators | Population | Findings |
|---|---|---|---|---|---|
| **Ahn (2013) US**[64] | Observational study with 12 months follow-up (n=1,170). | Chronic Disease Self-Management Programme | Routine care at baseline. | Community dwelling with chronic condition (mean age 67). | Potential cost savings estimated at €335 per person. Potential savings of $3 billion if the programme reached 5% of individuals with one or more chronic conditions. |
| **Battersby* (2007) Australia**[65] | Costing study alongside 4 RCTs (n=4,603) in 4 regions over 2 years | SA HealthPlus generic model of chronic illness care including service coordinators and behavioural and care planning | Routine care | Patients with chronic and complex medical conditions requiring high service demand (≥8 GP visits +≥4 ED /OPD visits ± ≥1 inpatient admission in 12mo. pre-enrolement. | The trial of coordinated care demonstrated that individual health and well being can be improved through patient-centered care. Any savings in admissions to acute care did not compensate for the coordination costs and additional community services with the intervention group showing a deficit of AUS$4,842,898 (1998 costs) (adjusted) compared with usual care. |
| **Griffiths (2005) UK**[72] | RCT with 4 months follow-up (n=476). | Expert patient programme | Routine care. | Bangladeshi adults with diabetes, cardiovascular disease, respiratory disease or arthritis (mean age 48.5). | The programme cost €192 per participant to deliver. The intervention group had greater improvements in self-efficacy and self-care than the control group. There were no differences between groups in terms of healthcare utilisation. |
| **Lorig (2001) US**[77] | Longitudinal design as 2 year follow-up to a randomised trial (n=831). | Chronic Disease Self-Management Programme | Routine care at baseline. | Individuals with heart disease, lung disease, stroke or arthritis (mean age 64.9). | Two-year savings of between €511 and €682 per participant (based on health service utilisation and programme delivery costs). |
| **Page (2014) US**[81] | Costing study (n=1,612). | Six-week group education and support programme. | None (costing study). | Individuals over the age of 60 who are living with chronic health problems in the community. | Costs for implementation per programme participant were €172. |
| **Richardson (2008) UK**[83] | RCT with 6 months follow up (n=520). | Expert Patients Programme (EPP), a self-care group to teach self-care support skills. | Routine care. | Individuals with a (self-defined) long-term condition being treated in a community setting (mean age 55.4). | The intervention was associated with a QALY gain (0.020 [95% CI 0.007 to 0.034]) and a reduction in average cost per patient (€41 less [95% CI: €559 more to €642 less]), resulting in an ICER of -€2,0522 per QALY. |

**Key**: **CDSM** = chronic disease self-management; **ICER** = incremental cost-effectiveness ratio; **RCT** = randomised controlled trial; **QALY** = quality-adjusted life year.
* An output of this research was the Flinders' model of self-management support programme.

## Table A4.3.3 Studies investigating telemedicine interventions

| Study | Study design | Intervention | Comparators | Population | Findings |
|---|---|---|---|---|---|
| **Aanesen (2011) Norway**[63] | Modelling study. | Smart house technology and video visits. | Routine care (physical visits and no smart home technology or video visits). | Elderly patients diagnosed with a chronic condition (mean age 70). | Smart home technology may be cost-effective. Video visits only cost-effective if there are significant reductions in time costs for home care providers. |
| **Bendixen (2009) US**[66] | Observational study with 24 months follow-up (n=9,977). | Telerehabilitation. | Standard care in matched comparison group followed over 2 years. | Home dwelling elders with chronic conditions (mean age 72.4). | No significant difference in costs pre- and post-intervention.<br>Much greater use of preventive medicine in intervention group. |
| **Dimmick (2000) US**[67] | Case study with 12 months follow-up (n=14). | Rural telemedicine programme. | Routine care involving face to face nurse visits. | Suitable community patients with chronic disease and history of high healthcare utilisation. | The programme was associated with a reduction of 28 minutes per patient consultation and potential mileage reimbursement and drive time savings of $49.33(€70) per visit. |
| **Doolittle (2000) US**[68] | Costing study. | A telehospice service providing hospice care in the home. | Traditional hospice care. | Patients requiring hospice care. | The cost per traditional care visit was between $126(€180) and $141(€201). The average telehospice visit cost was $29(€41). |
| **Elliott (2008) UK**[69] | RCT with 2 months follow-up (n=500). | Telephone-based pharmacy advisory service. | Routine care control group. | Community dwelling elders suffering from stroke, cardiovascular disease, asthma, diabetes, or rheumatoid arthritis (mean age 67). | ICER of -£2.168 (-€3,296) per extra adherent patient. |
| **Finkelstein (2006) US**[70] | RCT with 6 months follow-up (n=68). | Telemedicine delivered home healthcare using videoconferencing and physiologic monitoring. | Patients receiving traditional nursing care at home or virtual visits through video-conferencing. | Patients receiving nursing care at home. | The mean cost per visit was $48.27(€53) for in-person visits, $22.11 (€24) for video visits, and $33.11(€37) for video visits with physiologic monitoring. |

## Table A4.3.3 continued.

| Study | Study design | Intervention | Comparators | Population | Findings |
|---|---|---|---|---|---|
| **Graves (2009) Australia**[71] | Cluster-randomised trial with 12 months follow up (n=434). | Telephone counselling for physical activity and diet. | Usual care (provided literature and feedback) and 'real control' (baseline data). | Adults with type 2 diabetes or hypertension (mean age 58) from a disadvantaged community. | Telephone counselling vs. Usual care = $78,489 (€115,352)/QALY. Usual care vs. real control = $12,153(€17,861)/QALY. (Threshold = $64k (€94,000)/QALY). No evidence to support long term effect of usual care strategy. |
| **Henderson (2013) UK**[73] | RCT with 12 months follow-up (n=965). | Telehealth monitoring system | Routine care. | Individuals with a long-term condition (heart failure, COPD, or diabetes). | The intervention cost €581 per participant to deliver. The intervention was associated with reduced healthcare utilisation costs. Overall, the intervention was associated with higher costs than usual care.<br>The ICER for the intervention was €119,337 per QALY. |
| **Johnston (2000) US**[75] | Quasi-experimental study, unclear length of follow-up (n=212). | Remote video technology for home health care (with 24 hour access). | Routine care control group (home visits and telephone contact). | Newly referred patients with congestive heart failure, chronic obstructive pulmonary disease, cerebral vascular accident, cancer, diabetes, anxiety, or need for wound care (mean age 70). | Delivery of home care was an average $663(€946) more in the intervention group, but hospital care costs were $726(€1,036) lower, indicating a modest reduction in costs. Capital costs were not amortised in the calculations. |
| **Moczygemba (2012) US**[78] | Self selecting trial with 12 month follow-up (n=120) | Pharmacist-provided telephone medication therapy management | Routine care | Medicare beneficiaries who were eligible for medication therapy management (mean age 72.6) | Significant difference in the number of problems resolved (54% intervention versus 20% control) and in annual drug cost savings (drug costs decreased by $682(€695) ± $2,141(2,181) in the intervention group and increased by $119(€121) ± $1,763(€1,796) in the control group) |
| **Noel (2000) US**[79] | Costing study (n=19) | Telemedicine integrated with nurse case management for the homebound elderly. | Nurse case management | Elderly patients who were high resource users in the 6 months preceding enrolment, with at least three chronic conditions (mean age 69.4) | There were no differences in clinical outcomes and costs decreased by a comparable amount in both the intervention and treatment arms. |

## Table A4.3.3 continued.

| Study | Study design | Intervention | Comparators | Population | Findings |
|---|---|---|---|---|---|
| **Noel (2004) US**[80] | Randomised trial with 6 to 12 months follow-up (n=104). | Home telehealth programme. | Routine care (control group). | Community-dwelling participants with complex heart failure, chronic lung disease, and/or diabetes mellitus. | The mean cost per patient in the intervention group was $8,278 (€10,364) at 6 months pre-study and $4,849 (€6,071) at 6 months post-study. The mean cost per patient in the control group was $12,386 (€15,507) at 6 months pre-study and $5,832(€7,302) at 6 months post-study. |
| **Pare (2013) Canada**[82] | Cost minimisation analysis with 9 months follow up (n=95). | Telehomecare programme for elderly patients with chronic health problems. | Routine care. | Elderly patients (mean age 70) with congestive heart failure, diabetes, COPD or hypertension. | Significant reduction in overall healthcare utilisation and costs per patient (annual cost savings of CAD$1,557(€1,058) per patient). |
| **Steventon (2013) UK**[86] | Cohort with matched controls with 12 months follow-up (n=5396). | Telephone health coaching service (Birmingham OwnHealth). | Routine care. | Patients from local general practices with chronic disease and a history of inpatient or outpatient hospital use (mean age 65.5). | Emergency and outpatient admissions increased more quickly among intervention participants than matched controls (0.05, 95% CI 0.00 to 0.09, P=0.046 and 0.37, 95% CI 0.16 to 0.58, P<0.001), as did secondary care costs (£175(€236), £22(€30) to £328(€443), p=0.025). |
| **Tousignant (2006) Canada**[87] | Non-randomised study with 2 months follow-up (n=4). | Rehabilitation through teletreatment. | Homecare visits. | Community-living older adults due to be discharged with a prescription for physiotherapy follow-up. | Physiotherapy rehabilitation delivered through telemedicine cost an average of $100 (€74) less than home visits. |

## Table A4.3.4. Studies investigating internet-based telemedicine

| Study | Study design | Intervention | Comparators | Population | Findings |
|---|---|---|---|---|---|
| **Schwartz (2010) US**[84] | Cohort with matched controls using 5 years of claims data (n=773). | Online chronic disease self-management programme. | Routine care. | Adult members of a US health insurance programme (mean age 47). | Health care costs per person per year were €743 ($757) less than predicted for participants relative to matched nonparticipants, yielding a return on investment of €10 ($9.89) for every dollar spent on the programme. |

## Table A4.3.5. Studies investigating other SMS approaches

| Study | Study design | Intervention | Comparators | Population | Findings |
|---|---|---|---|---|---|
| **Jerant (2009) US**[74] | Costing study alongside randomised trial with 12 months follow-up (n=415) | One-to-one home-based, peer-led chronic illness self-management training 'Homing in on Health' (HIOH) delivered in homes or by telephone for weekly for 6 weeks | Usual care | People aged 40 years and older with ≥1 of 6 common chronic illnesses (arthritis, asthma, COPD, CHF, depression, diabetes) | There was no significant effect of HIOH delivered in the home on health care expenditures. Mean (SD) was $14,105 (20,279) for home, $12,422 ($14,241) for telephone and $11,493 ($10,972) for usual care. Authors concluded that despite leading to improvements in self-efficacy, one-on-one in-home peer-led CDSM had a limited sustained effect on only one secondary health status measure and no effect on healthcare utilisation and as such is of questionable cost-effectiveness from the health system perspective. |
| **Katon (2012) US**[76] | Randomised trial with 24 months follow-up (n=214). | Multi-condition collaborative treatment programme. | Usual primary care. | Home dwelling patients with poorly controlled diabetes mellitus, CHD, or both and co-morbid depression (mean age 56.8). | Mean cost saving of €1,741 ($1,773) per QALY and €5 ($5.26) per depression-free day. |
| **Scott (2004) US**[85] | RCT over 24 months (n=294). | Group outpatient model for chronically ill, older patients. | Usual care | Private health insurance members aged 60 and older with one or more chronic conditions (mean age 74.1). | Intervention group patients had fewer hospital admissions (0.44 vs.0.82 p=.013), emergency visits (0.66 vs.1.1 p=.008), and professional services (5.9 vs.10.3 p=.005). Intervention group patients' costs were €60 () per member per month less than for controls. |

# Appendix A5 - Asthma

## Table A5.1 Results of meta-analyses from the PRISMS review plus from the update search. Table adapted from PRISMS review

| Reference and weighting Outcome | Intervention and comparator | Outcome | Time (from initiation of intervention) | Sample size (# of RCTs; # of patients) | Significance [a] | Effect Size (95% CI) |
|---|---|---|---|---|---|---|
| **Bailey** (2009)[95]** | Culturally orientated programmes vs. control | Asthma specific QoL | NR | 2 RCTs; 293 | +* | WMD 0.25 (0.09 to 0.41) |
| **Gibson** (2002)[98]*** | Asthma self-management and educational programmes (including asthma education, self-monitoring of peak expiratory flow or symptoms, regular medical review and a written action plan) vs. control | Hospital admissions | NR | 12 RCTs 2,418 | +++ | **RR** 0.64 (0.50 to 0.82); p=0.0003 |
| | | ED visits (dichotomous) | NR | 13 RCTs; 2,902 | ++ | RR 0.82 (0.73 to 0.94); p=0.003 |
| | | ED visits (mean number) | NR | 8 RCTs; 731 | +* | SMD–0.36 (–0.50 to–0.21) |
| | | Unscheduled doctor visits (dichotomous) | NR | 7 RCTs; 1,556 | +* | RR 0.68 (0.56 to 0.81) |
| | | Unscheduled doctor visits (mean number) | NR | 7 RCTs; 1,042 | 0 | SMD–0.07 (–0.19 to 0.06) |
| | | Work/school absenteeism (dichotomous) | NR | 7 RCTs; 32 | +* | RR 0.79 (0.67 to 0.93) |
| | | Work/school absenteeism (mean number) | NR | 13 RCTs; 1,728 | +* | SMD–0.18 (–0.28 to–0.09) |
| | | Nocturnal asthma | NR | 5 RCTs; 1,136 | +* | RR 0.67 (0.56 to 0.79) |
| | | FEV1 | NR | 7 RCTs; 1,072 | 0 | SMD 0.10 (–0.02 to 0.22) |
| | | PEFR | NR | 10 RCTs; 1,346 | +* | SMD 0.18 (0.07 to 0.29) |
| | | QoL | NR | 6 RCTS; 515 | +* | SMD 0.29 (0.11 to 0.47) |

| Reference and weighting Outcome | Intervention and comparator | Outcome | Time (from initiation of intervention) | Sample size (# of RCTs; # of patients) | Significance [a] | Effect Size (95% CI) |
|---|---|---|---|---|---|---|
| **Powell** (2002)[99]*** | Asthma education and self-management vs. control | Mean FEV1 | NR | 3 RCTs | 0 | SMD 0.19 (–0.05 to 0.25) |
| **Tapp** (2007)[97]*** | Education vs. control | Hospital admissions | NR | 5 RCTs; 572 | +* | **RR** 0.50 (0.27 to 0.91) Average NNT=9 Stratified by risk: lower risk NNT=20, moderate risk NNT=8, high risk NNT=4 |
| | | ED visits | NR | 8 RCTs; 946 | +* | RR 0.66 (0.41 to 1.07) |
| | | Scheduled clinic attendance | NR | 2 RCTs; 198 | +* | RR 1.73 (1.17 to 2.56) |
| | | Lung function, PEFR | NR | 3 RCTs | 0 | 16.89 l/minute (–11.59 to 45.73 l/minute) |
| | | Work/school absenteeism | NR | 2 RCTs; 171 | 0 | RR 0.88 (0.44 to 1.73) |
| **Toelle** (2004)[102]** | Peak flow-based action plans vs. symptom-based action plans | Unscheduled doctor visits | NR | 2 RCTs; 207 | +* | RR 1.34 (1.01 to 1.77) NNT: 7 favours symptom based |
| | | Hospital admissions | NR | 3 RCTs; 283 | 0 | RR 1.17 (0.31 to 4.43) |
| | | ED visits | NR | 3 RCTs | 0 | RR 0.86 (0.44 to 1.67) |
| | | | | | | |
| **Denford** (2014)[93]*** | Behaviour change techniques in asthma self-care interventions. | Unscheduled health care use | 2 to 18 months (median 12 months) | 23 RCTS; | ++ | OR 0.71 (95% CI 0.56 to 0.90) |
| | | Medication adherence to preventative medication | | 16 RCTs; | +++ | OR 2.55 (95% CI 2.11 to 3.10) |
| | | Reduction of symptoms | | 27 RCTs; | +++ | SMD -0.38 (95% CI -0.52 to -0.24) |
| **Blakemore** (2015)[94]*** | Complex interventions to reduce use of urgent healthcare in adults with asthma. These involved multiple components | Urgent healthcare use | 6 weeks to 36 months (mean = 10.8 months) | 33 RCTs; 4,246 | + | The odds of urgent healthcare use were 21% lower in the intervention group, OR 0.79 (95% CI 0.67 to 0.94) |

| Reference and weighting Outcome | Intervention and comparator | Outcome | Time (from initiation of intervention) | Sample size (# of RCTs; # of patients) | Significance [a] | Effect Size (95% CI) |
|---|---|---|---|---|---|---|
| | and/or multiple professionals, and could be delivered on an individual or group basis, or using technology such as telephone or computer. Interventions could include education, rehabilitation, psychological therapy, social intervention (social support, support group), organisational intervention (such as collaborative care or case management), and drug trials which targeted a psychological problem, e.g. anxiety or depression. | | | | | |

**Key**: **NR** = Not reported; **SMS** = Short Messaging Service;

The significance rating is per Appendix 1 using the scale from the PRISMS review.

## Table A5.2 Summary of results from systematic reviews in the PRISM review plus the systematic reviews from the updated search, Table extracted from PRISMS review.

| Reference and weighting Outcome | Intervention | RCTs, n; Participants, n; Date range | Synthesis | Main results | Main conclusions (review author); *Important quality concerns (review author)* |
|---|---|---|---|---|---|
| **Bailey** (2009)[95]** | Culturally orientated programmes vs. usual care or limited/non-specific education | 4 RCTs; 617; 2000–8 | Meta-analysis (2RCTs) | A significant benefit in asthma QoL was found in intervention compared with control. | The available evidence suggests that culturally orientated education programmes for adults and children from minority groups are effective in improving asthma QoL in both adults and children, and rates of asthma exacerbations and asthma control in children.<br>Authors theorise that culturally specific programmes allow participants to fully engage in education, which has positive effects on QoL.<br>*This review is limited by a small number of studies and small sample sizes in two of the studies.* |
| | | | Other | No differences between intervention and control were found in any measure of adult exacerbation.<br>Evidence for ED visits was conflicting. | |
| **Gibson** (2002)[98]*** | Self-management and educational programmes vs. usual care | 36 RCTs; 6090; 1986–2001 | Meta-analysis | A significant impact was found on hospitalisation rates, emergency hospital visits, unscheduled doctor visits, days off work/school, nocturnal asthma, PEFR and QoL in the intervention group compared with control. No differences in FEV1 values were found between intervention and control. | Self-management educational programmes delivered to adults with asthma result in clinically important improvements in asthma health outcomes including reduced health-care utilisation, improvement in nocturnal asthma and reduced days off work.<br>These benefits are most pronounced with interventions which involve a WAP, self-monitoring and regular medical review.<br>Interventions which are less intensive, especially those that do not include a WAP, are less effective. |
| | | | Other | Subgroup analysis found optimal self-management (involving provision of WAPs) led to significant reductions in asthma-related hospitalisations and ED visits. Two interventions which included regular review of medication also found significantly reduced ED visits. Six studies reported on unscheduled doctor visits, with none finding a significant effect between groups.<br>Nocturnal asthma was explored in four studies, three finding a significant | |

| Reference and weighting Outcome | Intervention | RCTs, n; Participants, n; Date range | Synthesis | Main results | Main conclusions (review author); *Important quality concerns (review author)* |
|---|---|---|---|---|---|
| | | | | improvement whereas one found no significant change. Oral corticosteroids and QoL were both assessed in four studies with mixed effect | |
| **Gibson** (2004)[100]** | WAPs vs. usual care | 26 RCTs; 1987–2002 | Other | Hospital admissions were significantly reduced in participants using action plans based on both personal best PEFR and % predicted PEFR compared with control. Emergency room visits were significantly reduced, and airway caliber improved, in intervention arms using personal best PEFR compared with control; however, no significant benefit was seen with plans based on % predicted PEFR. Benefits were found for any number of action points (two to four).<br>The traffic light system was not consistently better than conventional presentation. Use of inhaled and oral steroids were consistently beneficial.<br>Efficacy of incomplete and non-specific action plans was inconclusive | The findings of this review strongly support the use of individualised complete WAPs. Effective action plans can be based on symptoms or PEFR and use two, three or four action points. PEFR-based plans should use personal best PEFR and not % predicted PEFR for the action point. Treatment instruction should include both inhaled and oral steroids<br><br>*In some cases there were insufficient studies to allow a comparison and hence a type II error is possible. However, review authors report that they were cautious in their interpretation of the data.* |
| **Moullec** (2012)[103]** | Interventions for improving use of inhaled corticosteroids (ICS) vs. usual care (Chronic Care Model components categorised as: self-management education, behavioural support, decision support, and delivery system design). | 18 RCTs; 3006; 1990–2010 | Other | Subgroup analysis found the smallest pooled ES in adherence measures for interventions with only one component of the chronic care model (CCM).<br>ES for adherence measures were larger for interventions with two CCM components, and larger still for interventions with four CCM components. All adherence effects were statistically significant. Out of 13 studies exploring one CCM, three found significant effects, two out of five studies exploring two CCM components found significant effects, and two out of three studies exploring four CCM components | This review concludes that the more CCM components included within interventions, the greater the effects on ICS adherence outcomes. This review also suggests that interventions which include motivational support, such as through joint decision making, may show the greatest promise in improving adherence. However, more research is needed to confirm this A small number of studies were included, particularly for subgroup analysis on interventions with four CCM components.<br>Also, the review authors acknowledge that a small number of CCM component |

| Reference and weighting Outcome | Intervention | RCTs, n; Participants, n; Date range | Synthesis | Main results | Main conclusions (review author); *Important quality concerns (review author)* |
|---|---|---|---|---|---|
| | | | | found significant effects. One study compared joint decision-making negotiated between clinician and patient, with decision made by physician alone. This study found a significant effect to support joint decision-making. | combinations were tested, which limits the ability to determine which components were most important for success. |
| **Newman** (2004)[104]** | Self-management interventions vs. standard care/basic information, or direct comparison between self-management interventions | 18 RCTs; 2004; 1997–2002 | Other | 8 out of 14 studies showed some improvement in lung function. Most of these used education with an action plan, but others that used this approach did not find any improvements. A writing intervention for emotional expression and a stress management intervention also improved lung function, suggesting methods directed at stress and emotions can improve lung function.<br>Half of the studies measuring QoL reported significant benefits. There was no particular pattern between those that did and did not impact on QoL. Of those interventions targeting some aspect of behaviours, 57% reported a significant change in behaviour. 7 out of 11 interventions showed reduction in health-care use; all but one used education and action plans. Only one study to use this approach did not find any reduction. No differences seen with or without action plans. Little difference recorded between use of symptoms or PEFR to guide use of medication | Review authors conclude that it should be recognised that one therapy or programme might not be suitable for all patients Evidence suggests importance of action plans in combination with education for improved lung function and reduced health-care utilisation. However, no clear patterns can be established as to the optimal self-management provision<br><br>*Review authors state a potential limitation of their review to be their decision to only include papers published between 1997 and 2002. They also report that not all outcomes (in particular all clinical outcomes) were included in this review* |
| **Ring** (2007)[101]*** | Interventions encouraging use of action plans vs. usual care | 14 RCTs; 4588; 1993–2005 | Other | Self-management education interventions were explored in five RCTS: four reported a significant increase in the number of people/ parents with action plans; one reported significantly higher action plan use. Telephone consultation to reinforce action | Primary care professionals could encourage the ownership and use of action plans through the implementation of proactive practice-based organisational systems. Highlights the lack of robust evidence on the best ways for GPs and practice nurses to |

| Reference and weighting Outcome | Intervention | RCTs, n; Participants, n; Date range | Synthesis | Main results | Main conclusions (review author); *Important quality concerns (review author)* |
|---|---|---|---|---|---|
| | | | | plan use was investigated in two RCTS: one study reporting a significant increase in people having action plans; both RCTs reporting greater understanding of how to use their plans. Asthma clinics were used in two interventions, both reporting increased ownership at 6 months post intervention, although only one was statistically significant. Asthma management systems were used in two studies: one finding more children received action plans (NNT=5); the other reporting significantly higher action plan use. Two studies looked at interventions aimed at HCPs. One study educated HCPs, with results suggesting this may facilitate action plan use for up to 2 years post intervention. Another RCT implemented quality improvement and found no overall effect | sustain action plan use among patients in the long term. Patient self-management education, reinforcement and prompting, school asthma clinics and asthma management systems all increase patient ownership or initial use of action plans up to 1 year post intervention. However, more research is needed to determine use of action plans over the longer term Some interventions used nurses with specialist asthma training; however, not all clinical nurses providing asthma care have received such training. Research interventions may also have extra resources not otherwise available. These factors may mean reduced effectiveness in a 'real-world' setting.<br><br>*The authors acknowledge the possibility of publication bias in their review; however, they state that steps were taken to minimise this possibility* |
| **Powell** (2002)[99]*** | Asthma education and self-management vs. usual care or one element of self-management (regular review/basic education/self-monitoring only | 15 RCTs; 2460; 1990–2001 | Meta-analysis | Those in the intervention had significantly better PEFR than those in the control arm. There was no significant difference in mean FEV1between intervention and control | Optimisation of asthma control by adjustment of medications may be facilitated either by self-adjustment with the aid of a WAP or by regular medical review. Individualised WAPs based on PEFR are equivalent to action plans based on symptoms These findings are clinically important as they enable interventions to be tailored to patient preference, patient characteristics and the resources available. Reducing the intensity of self-management education or level of clinical review may reduce its effectiveness |

| | | | | | |
|---|---|---|---|---|---|
| **Tapp** (2007)[97]*** | Asthma education after acute asthma exacerbation event vs. usual care | 13 RCTs; 2157; 1979–2009 | Meta-analysis | Significant benefits in terms of hospital admission rates, ED attendance and scheduled clinic attendance were reported in the intervention group compared with the control. No statistically significant difference was found for PEFR or days off work/school | Although the evidence is supportive of educational interventions to reduce readmission following an episode of acute asthma in adults, the review does not provide evidence to suggest that other important markers of long-term asthma morbidity are affected |
| | | | Other | Two RCTS detected no difference in QoL between education and control in any domain. One RCT found no difference between intervention and control in various symptom measures. One RCT found suggestive improvements in inhalation technique and awareness of PEF readings | Adults may have limited opportunities to attend educational sessions in practice due to work and child care commitments, and the format, content and uptake of educational interventions still requires quantitative and qualitative evaluation *Review authors acknowledge the possibility of publication bias, although steps were taken to avoid this* |
| **Toelle** (2004)[102]** | Individualised WAP vs. no plan; or symptom-based plan vs. peak flow-based plan | 7 RCTs; 967; 1990–2001 | Meta-analysis | Participants in intervention arms had significantly fewer unscheduled doctor visits compared with control. No significant effects were found on hospitalisation or ED visit rates | Authors state that it is not possible to conclude whether or not use of written management plans alone leads to an improvement in asthma management behaviours. They go on to comment that in order to deliver benefit to the patient, programmes must be comprehensive and include education, a written self-management plan and regular review Authors acknowledge that the small number of included studies that contributed data for the meta-analysis and the small number of patients recruited in the studies have limited the ability to draw conclusive findings. |
| | | | Other | Two of three RCTs found increased adherence in the peak flow-based plan compared with the symptom-based plan. Oral corticosteroid use was reported in two RCTs comparing peak flow with symptom-based plans, finding mixed results. Days lost from school/work were reported in two studies, with no significant difference found | |
| | | | | | |
| **Denford** (2014)[93]*** | Behaviour change techniques in asthma self-care interventions. | 38; 7,883 | Meta-analysis and meta-regression | Meta-regression analyses found that some behaviour change techniques may modify the effect size. | Interventions targeting asthma self-care are effective. Active involvement of participants is associated with increased intervention effectiveness, but the use of stress management techniques may be counterproductive. Existing recommendations about the "optimal" content of asthma self-care interventions were tested but were not supported by the data. [Low to moderate risk of bias] |
| **DiBello** (2014)[92]* | Text messaging programmes, effect on adherence to | 5 RCTs and 1 observational study; | Narrative synthesis | Small statistically significant differences favoring text messaging in medication adherence were reported in 2 RCTs (n=15 and | Text messaging may have a positive impact on medication adherence rates as well as measures of lung function. However, these results are based on |

| | | | | | |
|---|---|---|---|---|---|
| | treatment and medication | 475 | | n=22). One RCT showed a statistically significant difference in peak expiratory flow variability between groups (n=16). One RCT compared lung function within each arm of the study from the beginning to the end showing a statistically significant difference within the text messaging group as opposed to the control group (n=16). One RCT showed no difference in ED usage across intervention groups and one showed a change that did not reach statistical significance. Three of the six studies reviewed made a note of participant satisfaction with the text messaging intervention. | a small number of studies, small sample sizes and short-term follow-up. There is no statistical evidence clearly indicating if the number of ED visits will decrease or increase with the use of a text messaging intervention. |
| **Blakemore** (2015)[94]*** | Complex interventions to reduce use of urgent healthcare in adults with asthma. | 33 RCTs; 4,246 | Meta-analysis | When study effects were grouped according to the components of the interventions used, significant effects were seen for interventions that included general education, skills training and relapse prevention. In multivariate meta-regression analysis, only skills training remained significant. | The odds of urgent healthcare use were 21% lower in the intervention group. Of the interventions assessed, skills training, may be particularly effective in reducing the use of urgent healthcare in adults with asthma. |

**Key**: **CCM** = Chronic Care Model; **ED** = Emergency department; **HCP** = Health care professionals; **ICS** = inhaled corticosteroids; **NNT** = Numbers needed to treat; **OR** = Odds ration; **PEFR** = Peak expiratory flow rate; **QoL** = Quality of life; **RCT** = Randomised controlled trial; **SMD** = Standardised mean difference; **WAPs** = Written action plans;

## Table A5.3 Cost-effectiveness studies investigating SMS education programmes in asthma.

| Study | Intervention | Population | Analysis Details | Clinical & QALY Outcomes | Costs | Results |
|---|---|---|---|---|---|---|
| **Corrigan** (2004)[107] | Enhanced care (standard of care plus GP-delivered asthma education (group or individual) plus spirometry | Adult asthma patients | Country: Canada<br>Study design: Costing study for three alternative size practices (25,50 or 100 patients)<br>Perspective: GP<br>Discount rate: N/A<br>Time Horizon: N/A<br><br>CAD$ 2003 | Not assessed | For population size of 25, 50 and 100 patients:<br>Individual visit scenario: net mean cost/pp was $107 (€85),$100 (€80), $96(€76), respectively. Group visit scenario: net mean cost/pp (year 1) $85(€68), $78 (€62), $74 (€59), respectively and $39 (€31), $32(€25),$28 (€22) (subsequent years). | Authors concluded that cost of providing asthma education and spirometric testing are significant; in the absence of funding, this may act as a significant disincentive for physicians to provide these services. |
| **Gallefoss** (2001)[109] | Asthma education programme (group & individual education & individual management plan ) | Adults aged 18 to 70 yrs with mild to moderate asthma. Mean age 42.5 years | Country: Norway<br>Study design: CEA alongside RCT (n=78)<br>Perspective: Societal<br>Discount rate: N/A<br>Time Horizon: 1 year<br><br>NOK 1994 | At 12 month follow-up, SGRQ total score was 16.3 units lower in the intervention group ($p<0.001$). FEV1 improved by 6.1% in the intervention group relative to the control ($p<0.05$). The NNE to make one person symptom-free (self-reported) was 2.2. | Mean total costs including the intervention were NOK16,000 (€1,768)/pp and NOK 10,500 (€1,160)/pp for the intervention and control groups, respectively.<br><br>Education programme cost NOK916 (€101)/pp. | ICER of NOK-3,400 (-€376) / 10-unit improvement in SGRQ total score<br>ICER NOK -4,500 (-€497) / 5% improvement in FEV1in the intervention group compared to the control group during a 12 month follow-up.<br>Authors concluded that a patient education programme in asthmatics improved patient outcomes and reduced costs over a 12-month follow-up. |
| **Kauppinen** (1998, 1999, 2001)[110-112] | Intensified education (additional individual (n=1) and group (n=2) sessions in year 1) | Newly diagnosed adults (18-76) yrs with (mild) asthma. Mean age 42.7 years | Country: Finland<br>Study design: CEA alongside RCT (n=162)<br>Perspective: Societal<br>Discount rate: N/R<br>Time Horizon: 5 years<br><br>(FIM 1993, 1£=8 FIM) | Relative to the CG, there were statistically significant improvements in (FEV1) only at 12 months; in FEV1 and PEF, at 3 years; but there were no significant differences at 5 years in lung function, bronchial hyper-responsiveness or in HRQOL scores. | There were no significant differences in mean total annual cost FIM 2757 (€438) in IG vs FIM 2351 (€373) in CG) at 1 year, 3 years £464 (€589) in IG vs £476 (€605) in CG or at 5 years £381 (€484) in IG vs £457 (€581) in CG). | As no significant differences in outcomes or costs, ICER was not calculated.<br>Authors concluded that there was a consistent tendency for the intervention (intensive education in year 1) to be less costly, however there were no significant differences in outcomes or costs at 1, 3 or 5 years. |

**Key**: **CEA** = Cost-effectiveness analysis; **CI** = Confidence Interval; **CG** = Control Group; **EQ_5D** = EuroQol 5D health related scores; **GP** = General Practitioner; **FEV1** = Forced Expiratory volume at 1 second; **HRQOL** = Health related quality of life; **ICER** = Incremental cost-effectiveness ratio; **IG** = Intervention group; **NNE** = number needed to educate; **NR** = not reported; **PEF** = peak expiratory flow; **QALY** = Quality adjusted life year; **RCT** = Randomised Control trial; **SMS** = Self-management support; **SGRQ** = Saint George respiratory questionnaire.

## Table A5.4 Cost-effectiveness studies assessing internet SMS interventions for asthma

| Study | Intervention | Population | Analysis Details | Clinical & QALY Outcomes | Costs | Results |
|---|---|---|---|---|---|---|
| **Van der Meer** (2011)[116] | Internet-based SMS programme plus usual vs usual care | 18-50 year olds with recent prescription for inhaled steroids. Mean age 36.5 years | Country: The Netherlands<br>Study design: Non-blinded RCT with one year follow-up (n=200)<br>Perspective: Societal<br>Discount rate: N/A<br>Time Horizon: 1 year<br><br>($US 2007) | There was no significant difference in EQ-5D score at 3-month (0.037 (95% CI -0.007 to 0.081) or 12 months follow-up 0.006 (95% CI -0.042 to 0.054), or in QALYs: 0.024 (95% CI, -0.016 to 0.065). | Total intervention costs were $254(€265) (95% CI, $243-$265 (€253 to €276) per patient during the period of 1 year.<br>Societal perspective: cost difference was $641 (€668) (95% CI, -$1957 to $3240 (€2,040 to €3,377) in favour of usual care.<br>Health care perspective:, cost difference was $37 (€39) (95% CI,-$874 to $950 (-€911 to €990) | ICER = $26,700 (€27,829) /QALY (societal) and ICER =$1,500 (€1,563)/QALY (health care perspective with a 62% and 82% probability of being cost-effective at a willingness-to-pay threshold of $50,00 (€52,114) per QALY compared with usual care.<br>Authors concluded that internet-based self-management of asthma can be as effective as current asthma care and that costs are similar |

**Key**: CI = Confidence Interval; EQ_5D = EuroQol 5D health related scores; ICER = Incremental cost-effectiveness ratio; QALY = Quality adjusted life year; RCT = Randomised Control trial; SMS = Self-management support.

## Table A5.5 Cost-effectiveness studies assessing telemedicine interventions for asthma

| Study | Intervention | Population | Analysis Details | Clinical & QALY Outcomes | Costs | Results |
|---|---|---|---|---|---|---|
| **Donald** (2008)[108] | Nurse-led telephone review | 18-55 year old adults previously admitted to hospital with asthma<br>Mean age: N/R | Country: Australia<br>Study design: costing study alongside RCT with 1-year F/U (n=71)<br>Perspective: N/R<br>Discount rate: N/A<br>Time Horizon: 1 year<br><br>(Aus $ 2002) | At 12 months, there was a clinically important difference in HRQoL (MAQLQ-M) in the IG not seen in the CG. There was no significant difference in self-efficacy score between the IG and CG | Mean cost per participant for the intervention was $90 (€90). There was a non-statistically significant reduction in readmissions in the intervention group leading to a large reduction in readmission costs. $2,063 (€2,063) vs $41,272 (€41,281) | The authors concluded that telephone-based management is a low-cost alternative to usual care that is well accepted by patients and may result in clinically important differences in HRQoL, with costs potentially offset by reductions in re-admissions in the intervention group |
| **Pinnock** (2005)[114] | Nurse-led telephone review vs face-to-face review with asthma nurse | Symptomatic asthma patients (18-65 years) that had not been reviewed in previous 12 months<br>Mean age: N/R | Country: UK<br>Study design: CEA alongside RCT with 3 months follow-up<br>Perspective: Healthcare payer<br>Discount rate: N/R<br>Time Horizon: 3 months<br><br>(GB £ 2000) | Asthma-related quality of life and morbidity at 3 months were similar for the intervention and control groups and patients were equally satisfied with the consultations. | Total cost of intervention was similar for IG and CG £725.84 (€1,302) vs. £755.70(€1,356), as were total respiratory health care costs, however participation rate was higher for IG (78% vs 48%) resulting in a saving of £3.92 (€7) per consultation. | Authors concluded that nurse-led telephone consultations enable a greater proportion of asthma patients to be reviewed thereby improving access and reducing cost per consultation achieved. |
| **Willems** (2007)[117] | Nurse-led telephone review with remote peak flow monitoring vs usual care | 18-65 year old adults with persistent mild-moderate asthma)<br>Mean age 45.8 years | Country: The Netherlands<br>Study design: CEA alongside RCT with 1 year follow up (n= 53 adults)<br>Perspective: healthcare and societal<br>Discount rate:<br>Time Horizon: 1 year<br>(Netherlands € 2002) | There was no significant difference in generic HRQoL between the intervention and control groups | The annual cost of the intervention was €530 (€589)pp. Mean healthcare costs were higher in the intervention and control groups. | The mean ICER was €15,366 (€17,069)/QALY gained from the healthcare perspective and €31,035 (€34,476)/QALY gained from the societal perspective. |

**Key**: **CEA** = cost-effectiveness analysis; **CG** = control group; **CI** = Confidence Interval; **EQ_5D** = EuroQol 5D health related scores; **ICER** = Incremental cost-effectiveness ratio; **IG** = intervention group; **QALY** = Quality-adjusted life year; **RCT** = Randomised Control trial; **SMS** = Self-management support.

## Table A5.6 Cost-effectiveness studies assessing other SMS interventions for asthma

| Study | Intervention | Population | Analysis Details | Clinical & QALY Outcomes | Costs | Results |
|---|---|---|---|---|---|---|
| **Castro** (2003)[106] | Nurse-led multifaceted intervention (including asthma education and action plan, psychological support, OPD planning, telephone and phone visits) | Hospitalised 'high-risk' asthma patients aged (18-65)<br>Mean age: 36.4 years | Country: US<br>Study design: Cost study alongside RCT (n=96)<br>Perspective: N/R (assume societal)<br>Discount rate: N/R<br>Time Horizon: 1 year<br><br>(US $ 1991) | There was a significant reduction in hospital readmissions (60%, p<0.01), total bed days (69%, p<0.04) and multiple readmissions (57%, p=0.03), and a non-significant increase in ED visits (34%, p=0.52) and healthcare provider visits (3%, p=0.82). HRQol did not differ between the intervention and control groups | Mean intervention cost was $186 (€384) per patient. Overall savings (direct and indirect) of $6,462 (€13,358) per patient were noted including a savings of $4,430 (€9,157) in direct healthcare costs per patient primarily due to a reduction in readmissions. | The authors concluded that a programme focusing on asthma patients with high healthcare use can result in improved asthma control and reduced hospital use with substantial cost savings. However, they were unable to identify which specific component of the intervention is most effective. |
| **Parry** (2012)[113] | Cognitive behavioural therapy including a minimum of 5 to 7 sessions at weekly or fortnightly intervals. | 12-65 year olds with clinical diagnosis of asthma and a HADS anxiety score ≥8.<br>Mean age 45.3 years | Country: UK<br>Study design: Costing study alongside RCT with 1 year follow up (n= 53 adults)<br>Perspective: Healthcare provider<br>Discount rate: N/A<br>Time Horizon: Six months | Slight increase in GP visits in intervention group. Reduction in asthma specific fear and improvements in asthma QoL in intervention group. There were also significant improvements in asthma specific QoL and depression following CBT compared with controls, but these were not maintained at six month follow up. | The intervention cost between £378 and £798 per participant depending on the number of sessions attended. No cost offsets were reported.<br><br>Cost year N/R | The authors concluded that the study supported the short term and longer term efficacy of a CBT intervention in reducing panic fear in asthma, though the clinical significance of the effect was modest. |
| **Shelledy** (2009)[115] | Five-week in-house multi-faceted intervention by respiratory therapist (AMP-RT) vs nurse-led intervention (AMP-RN) vs usual care | 18-64 year olds with recent asthma-related ED visits. Mean age 42.8 years. | Country: US<br>Study design: Costing study alongside RCT with 6-month follow-up (n= 166)<br>Perspective: N/R (assume provider)<br>Discount rate: N/R<br>Time Horizon: 6-month<br>Cost year N/R | There were no significant differences (p > 0.05) in most measures of pulmonary function, dyspnoea or symptoms scores between the three groups at six months. Both asthma-management programme groups had significantly higher SF-36 and PS change scores when compared to the control group (p<0.005). | Intervention cost $365. The net hospitalisation direct cost savings for for the subjects in the AMP-RN groups was approximately $37,800, while the net cost savings for the AMP-RT group was $32,200. | The authors concluded that an in-home asthma management programme can be effectively delivered by respiratory therapists or nurses and may reduce hospitalisations, cost, and improve the quality of life and patient satisfaction in a population prone to asthma exacerbation. |

**Key**: **AMP** = asthma management plan; **CBT** = cognitive behavioural therapy; **FEV1** = Forced Expiratory volume at 1 second; **HRQOL** = Health related quality of life; **N/R** = not reported; **PEF** = peak expiratory flow; **QALY** = Quality adjusted life year; **RCT** = Randomised Control trial; **RN** = registered nurse; **RT** = respiratory therapist; **SMS** = Self-management support.

# Appendix A5.7 Appraisal of study quality for included cost-effectiveness studies

| Study | Quality | Reasons for downgrading |
|---|---|---|
| **Castro (2003)** | Low | Costing study alongside RCT with one year follow-up of 96 patients. Poorly reported cost and outcome data. |
| **Corrigan (2004)** | Low | Poorly described costing study. Insufficient information to determine if all relevant costs were included. No outcome data considered. |
| **Donald (2008)** | Low | Costing study based on small RCT. Incomplete reporting of costs |
| **Gallefos (2001)** | Low | Effectiveness data from single RCT with one year follow-up of 78 patients. Inadequate analysis of the impact of uncertainty. |
| **Kauppinen (1998, 1999, 2001)** | High | Perspective uncertain. Discounting of costs only and limited to sensitivity analysis |
| **Parry (2012)** | Low | Costing study alongside single RCT with one year follow-up of 53 patients. Poorly reported cost and outcome data. |
| **Pinnock (2005)** | Moderate | Based on small RCT with 3-month follow-up. Limited reporting of outcome data |
| **Shelledy (2009)** | Low | Costing study alongside single RCT with 6-month follow-up of 166 patients. Poorly reported cost and outcome data. |
| **Van der Meer (2011)** | Moderate | Based on small RCT with 12-month follow-up. Inadequate analysis of the impact of uncertainty. |
| **Willems (2007)** | Low | Based on small RCT (n=53) of 4 months with results extrapolated to 12-month. |

# Appendix A6 - COPD

## Table A6.1 Results of meta-analyses from PRISMS review and the systematic reviews from the updated search. Table adapted from the PRISMS review.

| Reference and weighting Outcome | Intervention and comparator | Outcome | Time (from initiation of intervention) | Sample size | Significance | ES (95% CI) |
|---|---|---|---|---|---|---|
| **Effing** (2007)[139]*** | Self-management education and usual care<br><br>(Note: In the majority of studies included in meta-analyses, action plans for self-treatment of exacerbations were assessed). | **Hospital admissions:** | | | | |
| | | COPD-related hospital admissions vs. regular care | - | 7 RCTs | ++ | OR 0.64 (0.47 to 0.89); p=0.007 |
| | | **HRQoL:** | | | | |
| | | SG-RQ total vs. usual care | - | 7 RCTs | + | WMD–2.58 (–5.14 to–0.02); p=0.05 |
| | | SG-RQ impact vs. usual care | - | 7 RCTs | +* | WMD–2.83 (–5.65 to–0.02) |
| | | SG-RQ symptom score vs. usual care | - | 7 RCTs | 0 | WMD–1.45 (–4.41 to 1.51) |
| | | SG-RQ PA vs. usual care | - | 7 RCTs | 0 | WMD–2.88 (–5.90 to 0.13) |
| **Tan** (2012)[140]*** | Disease-specific education and usual care | **Hospital admissions:** | | | | |
| | | COPD-related admissions vs. usual care | 12 months | 4 RCTs | +++ | OR=0.55 (0.43 to 0.71); p<0.00001 |
| | | **HRQoL:** | | | | |
| | | SG-RQ impact vs. usual care | 12 months | 6 RCTs | + | WMD–3.78 (–6.82 to–0.73); p=0.02 |
| | | SG-RQ total and other domains vs. usual care | 3 and 6 months | 6 RCTs | 0 | NR |
| **Turnock** (2005)[141]** | Action plans and usual care | **Hospital admissions:** | | | | |
| | | Hospital admissions vs. usual care | 12 months | 2 RCTs | 0 | WMD 0.16 (–0.09 to 0.42) |
| | | **HRQoL:** | | | | |
| | | SG-RQ overall vs. usual care | 6 months | 2 RCTs | 0 | WMD–1.91 (–5.46 to 1.63) |
| | | SG-RQ symptoms vs. usual care | 6 months | 2 RCTs | 0 | WMD–4.78 (–10.81 to 1.24) |
| | | SG-RQ activity vs. usual care | 6 months | 2 RCTs | 0 | WMD–2.43 (–7.37 to 2.50) |
| | | SG-RQ impact vs. usual care | 6 months | 2 RCTs | 0 | WMD–0.62 (–4.45 to 3.21) |
| | | SG-RQ overall vs. usual care | 12 months | 2 RCTs | 0 | WMD–0.32 (–3.34 to 2.70) |

| Reference and weighting Outcome | Intervention and comparator | Outcome | Time (from initiation of intervention) | Sample size | Significance | ES (95% CI) |
|---|---|---|---|---|---|---|
| | | SG-RQ symptoms vs. usual care | 12 months | 2 RCTs | 0 | WMD 1.87 (–3.27 to 7.00) |
| | | SG-RQ activity vs. usual care | 12 months | 2 RCTs | 0 | WMD–2.82 (–6.84 to 1.19) |
| | | SG-RQ impact vs. usual care | 12 months | 2 RCTs | 0 | WMD 1.16 (–2.21 to 4.53) |
| **Wong** (2012)[143]*** | Home care by outreach nursing vs. usual care, without respiratory nurse/health worker input | **Hospital admissions:** | | | | |
| | | Hospitalisations vs. routine care | – | 5 RCTs | 0 | Peto OR 1.01 (0.71 to 1.44); p=0.95 |
| | | **HRQoL:** | | | | |
| | | SG-RQ total vs. routine care | – | 4 RCTs | + | MD–2.60 (–4.81 to–0.39); p=0.02 |
| | | SG-RQ activity vs. routine care | – | 3 RCTs | 0 | NR |
| | | SG-RQ impact vs. routine care | – | 3 RCTs | 0 | NR |
| | | SG-RQ symptoms vs. routine care | – | 3 RCTs | 0 | NR |
| | | | | | | |
| **Walters** (2010)[127]** | Action plans with limited patient education only for exacerbations of COPD (Cochrane review) | Health care utilisation - hospital admission | 12 months | 2 RCTs; 205 participants | 0 | MD 0.23; 95% CI -0.03 to 0.49 |
| | | ED visits | 12 months | 2 RCTs; 201 participants | 0 | MD 0.37 (95% CI -0.50 to 1.24); $I^2$=81% |
| | | GP visits | 12 months | 3 RCTs; 256 participants | 0 | MD 0.53; -0.45, 1.50 |
| | | Use of medications (number of courses of oral corticosteroids) | 12 months | 2 RCTs; 200 participants | + | MD 0.74; 95% CI 0.12 to 1.35; $I^2$=0% |
| | | Use of medications (treated with at least one course of antibiotics for an acute exacerbation) | 6-12 months | 3 RCTs; 349 participants | ++ | OR 2.02; 95% CI 1.29 to 3.17 |
| | | HRQoL - SGRQ | 6 months and 12 months | 4 RCTs; 412 participants | 0 | 0.54 (-1.98. 3.05) ; $I^2$=3.1% (NS at 6 months or 12 months alone) |
| **Cruz** (2014)[133]** | Home telemonitoring effectiveness in COPD | **Health care utilisation:** | | | | |
| | | Hospitalisation rates | | 6 RCTs, 2 NRCTs; 486 participants | + | RR =0.72 (95% CI 0.53 to0.98); Z=2.12; p=0.034; $I^2$=4.73% |
| | | Mean number of hospitalisations | | 3 RCTs, 1 NRCT; 244 participants | 0 | SMD=-0.06 (95% CI-0.32 to0.19); Z=0.50; p=0.617; $I^2$=16.42%) |
| | | Length of hospital stay | | 3 RCTs, 1 NRCT; 244 participants | 0 | SMD=0.06 (95% CI -0.19 to0.31); Z=0.48; p=0.635; |

| Reference and weighting Outcome | Intervention and comparator | Outcome | Time (from initiation of intervention) | Sample size | Significance | ES (95% CI) |
|---|---|---|---|---|---|---|
| | | | | | | $I^2$=0% |
| | | ED visit rates | | 4 RCTs; 194 participants | 0 | RR=0.68 (95% CI 0.38 to1.18); Z=1.34; p=0.179; $I^2$=22.53% |
| | | Mean number of ED visits | 4-6 months | 1 RCT, 1NRCT; 160 participants | 0 | SMD=0.20 (95% CI -0.49 to0.88); Z=0.56; p=0.576). $I^2$=74.81% |
| | | **Health outcomes:** | | | | |
| | | Mortality rates | | 3 RCTs, 1 NRCT; 294 participants | 0 | RR=1.43 (95% CI 0.40 to 5.03);Z=0.55; p=0.582; $I^2$=0% |
| | | Mean change (i.e., posttest–pretest) of total and sub-dimension scores of the SGRQ | | 2 RCTs ; | + | SMD =0.53 (95% CI -0.97 to-0.09); Z=2.35; p=0.019; I $I^2$=17.74% |
| **Dickens** (2013) [129]*** | Complex interventions that reduce urgent care use in COPD | Use of urgent healthcare | 1-24 months | 32 RCTs; 3,941 participants | +++ | The odds of urgent healthcare use were 32% lower in the intervention group; OR=0.68 (95% CI 0.57 to 0.80). $I^2$=37.4% |
| **Kamei** (2012)[134]* | Telehome monitoring-based telenursing for patients with COPD (included patients with mainly severe COPD) | **Health care utilisation** | | | | |
| | | Hospitalisation in patients with severe and very severe COPD | 3-12 months | 4 RCTs, 2 NRCT; 450 participants | ++ | RR=0.81; 95% CI=0.69–0.95; $I^2$=0% |
| | | Hospitalisation in patients with moderate COPD | 3-12 months | 4 RCTs, 2 NRCT; 100 participants | 0 | RR=0.55; 95% CI=0.22–1.36; $I^2$ not reported. |
| | | Hospitalisation in all COPD patients | 3-12 months | 4 RCTs, 2 NRCT; 550 participants | + | RR=0.80; 95% CI=0.68–0.94; $I^2$=0% |
| | | Comparison of hospitalisation by THMTN duration for patients receiving THMTN for ≤3, 6 and 12months compared to CT/C | ≤3 months<br>6 months<br>12 months | 137 patients<br>155 patients<br>258 patients | 0 | RR=0.64; 95% CI=0.31–1.33;<br>RR=0.78; 95% CI=0.50–1.20;<br>RR=0.80; 95% CI=0.64–1.01; |
| | | Number of emergency department visits | 3-12 months | 4 RCTs; 335 participants | +++ | RR=0.52; 95% CI=0.41–0.65; $I^2$=0% |
| | | Disease exacerbations in severe and very severe COPD patients 3 months after THMTN | 3-12 months | 2 RCTs; 138 participants | +++ | RR=0.57; 95% CI=0.41–0.79; $I^2$=0% |
| | | Mean number of hospitalisations in severe COPD patients | 6-12 months | 5 RCTs; 453 participants | ++ | MD=-0.14; 95%; CI=-0.19 to -0.09; P<0.001; $I^2$=0% |

| Reference and weighting Outcome | Intervention and comparator | Outcome | Time (from initiation of intervention) | Sample size | Significance | ES (95% CI) |
|---|---|---|---|---|---|---|
| | | Mean duration of bed days of care in moderate to very severe COPD patients | 1-6 months | 2 RCTs; 215 participants | ++ | MD=-0.76; P<0.001; 95% CI=-0.79 to-0.73 |
| | | Mortality in moderate to very severe COPD patients | 1-12 months | 5 RCT; 374 patients | 0 | RR=1.36; 95% CI=0.77–2.41; P=0.29; $I^2$=0% |
| **Kruis** (2013)[128]*** | Integrated disease management interventions (chronic care management) and controls (varying from usual care or no treatment to single interventions, mono-disciplinary interventions) | **QoL:** | | | | |
| | | SGRQ – Short term | 3-12 months | 13 studies; 1425 participants | +++ (p<0.001) | MD -3.71 in favor of IDM (95% CI of -5.83 to -1.59); $I^2$ = 56% |
| | | SGRQ – Long term | 18, 24 months | 2 studies; 189 participants | 0 | MD -0.22; 95% CI -7.43 to 6.99, $I^2$ = 54% |
| | | **Exercise capacity:** | | | | |
| | | 6MWD – Short term | 12 months | 14 studies; 871 participants | +++ | Improved 6MWD by a statistically and clinically relevant 43.86 meters (95% CI 21.83 to 65.89); $I^2$ = 83%. Restriction to studies with adequate allocation concealment reduced effect estimate to 15.15 meters, still statistically significant (95% CI 6.37 to 23.93, P < 0.001), but no longer clinically relevant. |
| | | 6MWD – Long term | 24 months | 2 studies; 184 participants | ++ | Improved 6MWD by 16.8 meters (MD 16.84; 95% CI 3.01 to 30.67), $I^2$ = 0% |
| | | Maximal exercise capacity (Watts) using the cycle ergometer test | | 4 studies; 298 participants | +++ | IDM statistically significantly improved the maximal exercise capacity by 7 Watts (MD 6.99; 95% CI 2.96 to 11.02, P < 0.0001) |
| | | **Exacerbations:** | | | | |
| | | Number of patients experiencing at least one exacerbation - short-term | 12 months | 2 studies; 407 participants | 0 | OR 1.21 (95% CI 0.77 to 1.91); homogenous. P=0.42; No statistically or clinically relevant difference between |

| Reference and weighting Outcome | Intervention and comparator | Outcome | Time (from initiation of intervention) | Sample size | Significance | ES (95% CI) |
|---|---|---|---|---|---|---|
| | | | | | | groups |
| | | Number of patients experiencing at least one exacerbation - long-term | 24 months | 2 studies; 301 participants | 0 | OR 1.53; 95% CI 0.90 to 2.60, P = 0.12; homogenous. |
| | | Hospital admissions, all causes - short-term | 12 months | 2 studies; 226 participants | 0 | OR 0.62; 95% CI 0.36 to 1.07, P = 0.49. $I^2$= 0% |
| | | Hospital admissions, all causes - long-term | 24 months | 2 studies; 283 participants | 0 | OR 0.78; 95% CI 0.38 to 1.57; P=0.50; $I^2$ = 53% |
| | | Respiratory-related admissions - short-term | 12 months | 7 studies; 1153 participants | + | OR 0.68; 95% CI 0.47 to 0.99, P = 0.04; homogenous |
| | | Respiratory-related admissions - long-term | 24 months | 1 study; 179 participants | 0 | OR 0.59; 95% CI 0.28 to 1.22, P = 0.16 |
| | | Hospital days per patient - short-term | 12 months | 6 studies; 741 participants | ++ | Patients treated with IDM on average discharged nearly 4 days earlier compared to control, CI 6 to 2 days (MD -3.78; 95% CI -5.90 to -1.67, P < 0.001); $I^2$ = 55%. |
| | | Hospital days per patient - long-term | 24 months | 1 study; 175 participants | 0 | MD 0.60; 95% CI -3.01 to 4.21, P = 0.74 |
| | | Emergency Department (ED) visits - short-term | 12 months | 4 studies; 1161 participants | 0 | OR 0.64; 95% CI 0.33 to 1.25; $I^2$ = 71% |
| | | Dyspnoea - MRC Dyspnoea Scale | | 3 studies; 345 participants | +++ | Dyspnoea improved in IDM group by -0.30 points (MD -0.30; 95% CI -0.48 to -0.11, $I^2$ = 0%, P < 0.001) |
| | | Dyspnoea – Borg score | | 3 studies; 145 participants | 0 | MD 0.14; 95% CI -0.70 to 0.98, P = 0.74, $I^2$ = 39%) |
| | | Mortality | 12 months (4)<br>24 months (1) | 4 studies; 1,113 participants<br>1 study; 122 participants | 0 | Short-term (OR 0.96; 95% CI 0.52 to 1.74, P = 0.33; $I^2$ = 59%). Long-term (OR 0.45; 95% CI 0.16 to 1.28, P = 0.13) |
| | | Lung function | | 10 studies | 0 | - |

| Reference and weighting Outcome | Intervention and comparator | Outcome | Time (from initiation of intervention) | Sample size | Significance | ES (95% CI) |
|---|---|---|---|---|---|---|
| | | Anxiety and depression - HADS | | 2 studies; 316 participants | 0 | Anxiety (MD 0.22; 95% CI -0.41 to 0.85, $I^2$ = 0%), depression (MD 0.21, 95% CI -0.39 to 0.81, $I^2$ = 0%) |
| | | Anxiety and depression - MACL | | 1 study (55 participants) | 0 | - |
| **Lundell** (2014)[135]** | Telehealthcare for COPD (making pulmonary rehab more accessible) | Physical activity | 12 months | 1 RCT; 125 participants | +++ | SMD -0.081 (95% CI: -0.918 to 0.755) |
| | | **Physical capacity:** | | | | |
| | | 6MWD | | 6 RCTs; 533 participants | 0 | MD-1.3 m (95% CI: -8.1 to 5.5) |
| | | **Dyspnoea:** | | | | |
| | | Chronic Respiratory Questionnaire, Dyspnoea subscale (CRQ-D), Medical Research Council (MRC) Dyspnoea scale, and Shortness of Breath Questionnaire (SOBQ) | | 7 RCTs; 826 | 0 | SMD, 0.088; 95% CI 0.056 to 0.233; P=0.232 |
| **Zwerink** (2014)[131]*** | Self management for patients with COPD (Cochrane review) | **Hospitalisations:** | | | | |
| | | Respiratory-related hospitalisations vs. usual care or active intervention | 2-24 months | 10 studies; 1749 participants | +++ | OR 0.57, 95% CI 0.43 to 0.75; P<0.001 |
| | | All cause hospitalisations vs. usual care or active intervention | 2-24 months | 7 studies, 1365 participants | + | OR 0.60, 95% CI 0.40 to 0.89; P=0.011 |
| | | **HRQoL:** | | | | |
| | | SGRQ intervention vs. usual care or active intervention | 2-24 months | 10 RCTs; 1413 participants | +++ | MD -3.51, 95% CI -5.37 to -1.65, P<0.001 |
| | | **Mortality:** | | | | |
| | | | 2-24 months | 9 studies; 2134 participants | 0 | OR 0.79, 95% CI 0.58 to 1.07, P=0.13 |
| | | **Dyspnoea:** | | | | |
| | | Medical Research Council Scale ((m)MRC) intervention vs. usual care or active intervention | 2-24 months | 3 studies; 119 participants | ++ | MD -0.83, 95% CI -1.36 to -0.30; P=0.002 |

| Reference and weighting Outcome | Intervention and comparator | Outcome | Time (from initiation of intervention) | Sample size | Significance | ES (95% CI) |
|---|---|---|---|---|---|---|
| | | **Exercise capacity:** | | | | |
| | | 6MWD vs. usual care or active intervention | 2-24 months | 6 studies; 570 participants | 0 | MD 33.69 m, 95% CI -9.12 to 76.50; P=0.12 |
| **McLean** (2011)[136]*** | Telehealthcare for COPD (Cochrane review) | Quality of life: SRGQ | | 2 RCTs; 253 participants) | 0 | MD -6.57, 95% CI -13.62 to 0.48, P=0.07 minimally clinically significant change although the CIs are very wide |
| | | Emergency department visits | 12 months | 3 RCTs; 449 participants | ++ | OR 0.27 (95% CI 0.11 to 0.66) P=0.005 |
| | | Hospitalisations | 12 months | 4 RCTs; 604 participants | +++ | OR 0.46 (95% CI 0.33 to 0.65); P < 0.00001 |
| | | Deaths | 12 month | 3 RCTs; 503 participants | 0 | OR 1.05 95% CI 0.63 to 1.75; P=0.86 |
| **Jordan** (2015)***[130] | Supported self-management for patients with moderate to severe COPD | All-cause mortality | | 6 RCTs; 1179 participants | 0 | HR 1.15 (95% CI 0.79 to 1.67); P=0.47; $I^2$=0% +++ moderate quality |
| | | Hospital admissions | | 7 RCTs; 1217 participants | 0 | HR 0.78 95% CI 0.52 to 1.17; P=0.23; $I^2$= 70.9% ++; low quality |
| | | ED visits | | 5 RCTs; 932 participants | - | Not combined RR ranged from 0.27 to 1.06 ++; low quality |
| | | HRQoL: SGRQ | | 6 RCTs; 845 participants | ++ | MD 3.84-point improvement (95% CI 1.29 to 6.40 points); P=0.003; |
| **McCarthy** (2015)[137]*** | Pulmonary rehabilitation for COPD | HRQoL: CRQ - Fatigue: | | 19 RCTs; 1291 participants | +++ | MD 0.68, 95% CI 0.45 to 0.92; P<0.001; Tau² = 0.15; I² = 64% |
| | | HRQoL: CRQ - Emotional function: | | 19 RCTs; 1291 participants | +++ | MD 0.56, 95% CI 0.34 to 0.78; P<0.001; Tau² = 0.12; I² = 58% |
| | | HRQoL: CRQ - Mastery: | | 19 RCTs; 1212 participants | +++ | MD 0.71, 95% CI 0.47 to 0.95; P<0.001; Tau² = 0.16; I² = 63%; |
| | | HRQoL: CRQ - Dyspnoea: | | 19 RCTs; 1283 | +++ | MD 0.79, 95% CI 0.56 to 1.03; |

| Reference and weighting Outcome | Intervention and comparator | Outcome | Time (from initiation of intervention) | Sample size | Significance | ES (95% CI) |
|---|---|---|---|---|---|---|
| | | | | participants | | 19 trials; 1283 participants; P<0.001; Tau² = 0.15; I² = 63%; |
| | | HRQoL: SGRQ total | | 19 trials; 1146 participants; | +++ | MD -6.89, 95% CI -9.26 to -4.52; P<0.001; Tau² = 13.17; I² = 59%; |
| | | HRQoL: SGRQ symptoms | | 19 trials; 1153 participants; | +++ | MD -5.09, 95% CI -7.69 to -2.49; P<0.001; Tau² = 7.79; I² = 26%; |
| | | HRQoL: SGRQ impact | | 19 trials; 1149 participants; | +++ | MD -7.23, 95% CI -9.91 to -4.55; P<0.001; Tau² = 17.94; I² = 58%; |
| | | HRQoL: GRQ activity | | 19 trials; 1148 participants; | +++ | MD -6.08, 95% CI -9.28 to -2.88; P<0.001; Tau² = 27.01; I² = 64%; |
| | | Maximal exercise capacity | | 16 studies; 779 participants | ++ | MD 6.77, 95% CI 1.89 to 11.65; P=0.007; Tau² = 40.97; I² = 74%; |
| | | Functional exercise capacity – 6MWD | | 38 trials; 1879 participants: 1012 actively treated, 867 controls | +++ | MD 43.93 m, 95% CI 32.64 to 55.21; P<0.001; Tau² = 713.49; I² = 74%; |
| | | Functional exercise capacity – ISWT | | 8 trials; 694 participants | | MD 39.77, 95% CI 22.38 to 57.15; P<0.001; Tau² = 181.56; I² = 32% |

**Key**: **NR** = Not reported; **SMS** = Short Messaging Service; **SGRQ** = St. George's Respiratory Questionnaire;* **6MWD** = 6 minute walking distance; **MACL** = Mood Adjective Check List; **CT/C** = Conventional treatment/care; **ISWT** = Incremental shuttle walk test;

** The SGRQ is a disease-specific, validated questionnaire (scale from 0 (good health) to 100 (worse health status)). A negative sign indicates improvement, and the minimal clinically important difference (MCID) is -4 points.

## Table A6.2 Summary of results from systematic reviews, Table extracted from PRISMS review and systematic reviews from updated search.

| Reference and weighting Outcome | Focus | RCTs, n; Participants, n; Date range | Synthesis | Main results | Main conclusions (review author); *Important quality concerns (review author)* |
|---|---|---|---|---|---|
| **Bentsen** (2012)[138]* | Self-management interventions that improve COPD patients' HRQoL . | 4 RCTs; 529; 2003–11 | Narrative | Self-management interventions reduced the burden on patients and improved patient activity and total health.<br>Note: The SMS interventions included patient education (group and individual), exercises (group and individual), a self-help book, an individual action plan and discussion therapy group. | Self-management interventions tend to improve QoL of patients with COPD. Further RCTs are recommended to confirm these benefits. Involvement of nursing in health-care services is suggested to develop these interventions.<br>*Narrative synthesis broad and unclear on how RCT findings are related to conclusions made.*<br>*Potential bias towards nurses rather than general HCPs* |
| **Effing** (2007)[139]*** | Settings, methods and efficacy of COPD self-management education programmes on health outcomes and use of health-care services | 13 RCTs; 2239; 1987-2005 | Meta-analysis | **Hospital admissions:** clinically and statistically significant reduction in probability of at least one hospital admission among patients receiving self-management education compared with those receiving regular care [OR 0.64 (95% CI 0.47 to 0.89)]<br>**HRQoL:** SG-RQ total and domain scores in the self-management groups were all lower (indicating a better HRQoL) or equal to the scores in the usual care groups. The differences on the SG-RQ total [WMD –2.58 (95% CI–5.14 to–0.02)] and impact scores [WMD –2.83 (95% CI–5.65 to–0.02)] reached statistical significance at the 5% level, but did not reach the clinically important difference of 4 points.<br>No significant relevant difference was found on the SG-RQ symptom score [WMD–1.45 (95% CI–4.41 to 1.51)] or the SG-RQ domain PA [WMD–2.88 (95% CI –5.90 to 0.13)] | Self-management education is associated with reduction in hospital admissions with no indication of detrimental effects on other outcomes. Because of heterogeneity in interventions, study populations, follow-up time and outcome measures, data are insufficient to formulate clear recommendations regarding form and contents of self-management education programmes in COPD. There is an evident need for more large RCTs with a long-term follow-up, before more conclusions can be drawn.<br><br>*Publication bias was not measured.* |
| | | | Narrative | Hospital admissions: in the 3 studies which could not be meta-analysed no significant differences found between the two arms. | |

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| | | | | Though 24-month results on hospital admission (all causes) in one of the trials showing a significant reduction of –0.44 hospitalisations per patient/year in favour of the self-management education group HRQoL: No differences in SG-RQ scores after 12 months of follow-up were found. With the CRQ, two out of four HRQoL dimensions (fatigue and mastery) showed a significant improvement after a follow-up of 12 months General QoL: evidence showed significant improvement in total function measured by the SIP in the control group, better physical function and total function in favour of the intervention group. There is also a suggestion of significantly improved scores for the well-being dimension and the perceived III in one of the intervention groups (nurse-assisted collaborative management) compared with usual care. | |
| **Tan** (2012)[(140)]*** | Disease-specific education in COPD | 12 RCTs; 2103; 1997–2010 | Meta-analysis | **Hospital admissions:** there was a significant reduction in hospital admission rates among patients receiving a disease-specific education programme compared with those receiving usual care [fixed effects model, OR 0.55 (95% CI 0.43 to 0.71);p<0.00001]<br>**HRQoL:** the SG-RQ total and domain scores in the disease management groups were all lower (indicating higher HRQoL) or equal to the usual care groups scores at the 12-month intervention period. At 12-months follow-up only SG-RQ impact was significantly better, with no significant differences in other SG-RQ scores.<br>Results after a 3- or 6-month intervention: no statistically significant changes were observed in any of the SG-RQ scores. The statistical heterogeneity for the outcome (SG-RQ impact scores after 6-month intervention) may be related to the outlying effects reported in one study. Its removal led to a lower statistic (59% | A meta-analysis on these studies revealed a positive relationship between disease-specific education programmes and HRQoL scores (as measured by the SG-RQ). Although significant effects were not detected across all HRQoL, findings suggest that education programmes have the potential to be a valuable intervention for COPD patients. Results provide a foundation for future research in this area, with more rigorously designed, large, randomised studies. |

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| | | | | vs. 0%). One trial could not be used in the meta-analysis because of a lack of data | |
| **Turnock** (2005)[141]** | Action plans for the management of COPD | 3 RCTs; 367; 1997–2004 | Meta-analysis | **Hospital admissions:** no evidence of a significant effect on the number of hospital admissions over 12 months from two studies [WMD 0.16 (95% CI–0.09 to 0.42)]<br>**HRQoL (at 6 months):** no statistically significant differences between groups for HRQoL. Overall HRQoL [WMD –1.91 (95% CI–5.46 to 1.63)]; symptoms [WMD –4.78 (95% CI–10.81 to 1.24)]; activity [WMD –2.43 (95% CI–7.37 to 2.50)]; impacts [WMD–0.62 (95% CI –4.45 to 3.21)]<br>**HRQoL (at 12 months):** no statistically significant difference between groups for HRQoL. Overall HRQoL [WMD –0.32 (95% CI–3.34 to 2.70)]; symptoms [WMD 1.87 (95% CI –3.27 to 7.00)]; activity [WMD –2.82 (95% CI–6.84 to 1.19)]; impacts [WMD 1.16 (95% CI –2.21 to 4.53) | Action plans to date have not shown any significant reduction in the use of health-care resources, or improved clinical outcomes. However, the lack of evidence to support the role of action plans in COPD management should not be necessarily seen as the evidence of lack of efficacy, at this time a WAP without a broader self-management plan cannot be recommended for widespread adoption in primary care. |
| **Wong** (2012)[143]*** | Outreach respiratory health-care worker programmes for COPD patients | 9 RCTs; 1498; 1987–2006 | Meta-analysis | **Hospital admissions (meta-analysis):** no significant change in the number of hospitalisations with the intervention [Peto OR 1.01 (95% CI 0.71 to 1.44)]<br>**Hospital admissions (subgroup analysis):** after excluding an outlying study, a statistically significant increase in the number of hospitalisations in patients receiving the intervention was reported [Peto OR 1.59 (95% CI 1.02 to 2.47)]<br>**HRQoL:** significantly improved with the intervention [MD –2.60 (95% CI–4.81 to–0.39)]. No statistically significant reductions in SG-RQ subscores of activity, impact and symptom | Outreach nursing programmes for COPD improved disease-specific HRQoL. However, the effect on hospitalisations was heterogeneous, reducing admissions in one study, but increasing them in others, therefore we could not draw firm conclusions for this outcome. Other narrative findings regarding HRQoL were more heterogeneous |
| | | | Narrative | **HRQoL:** across other individual studies that could not be pooled, there were heterogeneous findings for the 'physical score' in the SIP and a range of HRQoL scores | |

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| **Walters** (2010)[127]** | Action plans with limited patient education only for exacerbations of COPD (Cochrane review) | 5 RCTs; 574 participants; 1997–2008 | | No evidence that action plans reduced health care utilisation; assessed by hospital admission, emergency department visits and GP visits. Use of action plans associated with increased initiation of treatment for acute exacerbations. Oral corticosteroid use increased over 12 months with a significant increase in odds of being treated with antibiotics over 12 months. | There is evidence that action plans with limited COPD education aid recognition of, and response to, an exacerbation with initiation of antibiotics and corticosteroids. Note: They interpret increased medication use as a positive effect. |
| **Cruz** (2014)[133]** | Home telemonitoring effectiveness in COPD | 7 RCTs + 2 NRCTs; 587 participants; 2006–2013 | Meta-analysis | Significant differences found for hospitalisation rates (RR =0.72; 95% CI=0.53–0.98; p=0.034). No differences in other healthcare utilisation outcomes observed. | The findings provide limited evidence of the effectiveness of home telemonitoring to reduce healthcare utilisation and improve health-related outcomes in patients with COPD. Although this intervention appears to have a positive effect in reducing respiratory exacerbations and hospitalisations and improving HRQOL, there is still no clear indication that it reduces healthcare utilisation and associated costs. *One limitation of this review concerns the exclusion of six studies written in languages other than English, Portuguese and Spanish, since they could be relevant for the scope of the review. The number of studies included in the meta-analysis was insufficient (n<5) to measure publication bias* |
| **Dickens** (2013)[129]*** | Complex interventions that reduce urgent care use in COPD | 32 RCTs; 3941 participants; 1988–2012 | Meta-analysis | When study effects were grouped according to the components of interventions used, significant effects seen for interventions that included general education (OR=0.66, 95% CI=0.55, 0.81), Exercise (OR=0.60, 95% CI=0.48, 0.76) and relaxation therapy (OR=0.48, 95% CI=0.33, 0.70) | Use of urgent healthcare in patients with COPD was significantly reduced by complex interventions. Complex interventions among people with COPD may reduce the use of urgent care, particularly those including education, exercise and relaxation. *The effects of different complex interventions were moderately heterogeneous, so the pooled effect from all included studies must be interpreted with caution. The pooled effects across a wide range of complex interventions of varying intensities, delivered in varying settings by different professionals tells us little about which interventions might be most effective in reducing the use of urgent care. We focused entirely on reduction in use of urgent care and we did not* |

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| | | | | | *record medical outcomes, such as health status, morbidity of HRQoL. As such we can draw no inferences about effects of these complex interventions in these other domains and cannot determine whether the reductions in the use of urgent care were due to a reduction in the need for urgent care, due to improved health, or simply due to the substitution of urgent care by scheduled care, delivered as part of the study intervention.* |
| **Kamei** (2012)[134]* | Telehome monitoring-based telenursing for patients with COPD (included patients with mainly severe COPD) | 9 RCTs; 550 participants; 2006–2011 | Meta-analysis | THMTN decreased hospitalisation rates, emergency department visits, exacerbations, mean number of hospitalisations, and mean duration of bed days of care in severe and very severe COPD patients. Hospitalisation rates and emergency department visits were comparable between patients undergoing THMTN of different durations. In addition, THMTN had no effect on mortality. | THMTN significantly decreases the use of healthcare services; however, it does not affect mortality in severe and very severe COPD patients. |
| **Kruis** (2013)[128]*** | Integrated disease management interventions (chronic care management) | 26 trials; 2997 participants; 1991–2011 | Meta-analysis | **QoL:** Pooled data showed statistically and clinically relevant improvements in disease-specific QoL on CRQ in IDM group: dyspnoea (MD 1.02; 95% CI 0.67 to 1.36); fatigue (0.82; 95% CI 0.46 to 1.17); emotional (0.61; 95% CI 0.26 to 0.95) and mastery (0.75; 95% CI 0.38 to 1.12). All domains (dyspnoea, fatigue, emotional and mastery) exceeded the minimum clinically relevant difference until 12 months follow-up. Only 2 studies measured long-term results on CRQ, positive effect maintained for fatigue, emotion and mastery domains at 24 months follow-up.<br>**Functional exercise capacity:** Improvement of 7 Watts and 44 meters in favor of the IDM group. Sensitivity analysis of 6MWD lowered effect to 15 meters.<br>Note: The clinical significance of these findings is unclear.<br>**Hospitalisations:** Total number of patients with at least one respiratory related hospital | In these COPD participants, IDM not only improved disease-specific QoL and exercise capacity, but also reduced hospital admissions and hospital days per person.<br>It is possible that patients who have learned from education and have an action plan may recognise exacerbations at an early stage and can start medical treatment directly. It is therefore likely that<br>further worsening of health status and hospital admissions can be prevented in these patients. |

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| | | | | admission decreased from 27 per 100 to 20 per<br>100 patients in favor of intervention group, with NNT of 15 patients to prevent 1 being admitted to hospital over 3 to 12 months. | |
| | | | Meta-analysis | Evidence for efficacy of integrated disease management (IDM) programmes of at least 3 months, for up to 12 months follow-up.<br>**QoL, exercise capacity:** Positive effects on disease-specific QoL and exercise capacity in studies containing an exercise program, suggesting exercise training is an important element in an IDM program. Long-term effects still unclear, only a few studies evaluated these. Magnitude of improvement in disease-specific QoL clinically relevant, especially using the Chronic Respiratory Questionnaire (CRQ).<br>**Hospital admissions:** 7 hospital admissions related to respiratory problems can be prevented for every 100 patients treated with IDM for 3 to 12 months, NNT of 15 patients to prevent 1 being admitted. Hospitalisation decreased by 3 days in patients treated with IDM compared to controls. Effects of IDM on the total number of patients suffering at least one exacerbation still remain unclear. | |
| **Lundell** (2014)[135]** | Telehealthcare for COPD (making pulmonary rehab more accessible) | 9 RCTs; 982; 1996–2013 | Meta-analysis | Physical activity level: significant effect favoring telehealthcare (MD, 64.7 min; 95% CI, 54.4–74.9). No difference between groups was found for physical capacity (MD, 1.3 m; 95% CI,8.1–5.5) and dyspnoea (SMD, 0.088; 95% CI,0.056–0.233). | The use of telehealthcare may lead to improvements in physical activity level in patients with COPD although the results should be interpreted with caution given the heterogeneity in studies. |
| **Zwerink** (2014)[131]*** | Self management for patients with COPD (Cochrane review) | 29 studies (23 on 3189 participants vs. usual care; 6 on 499 participants vs. different | Meta-analysis | **HRQoL:** significant improvement with intervention [MD -3.51, 95% CI -5.37 to -1.65]<br>**Respiratory related hospitalisations:** significant reduction [OR 0.57, 95% CI 0.43 to 0.75]<br>**All cause hospitalisations:** Some evidence in favour of intervention [OR 0.60; 95% CI | Self management interventions in patients with COPD are associated with improved HRQoL as measured by the SGRQ, a reduction in respiratory-related and all cause hospital admissions, and improvement in dyspnoea as measured by the (m)MRC. No statistically significant differences were found in other outcome parameters. |

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| | | components of self management). Primary analysis restricted to RCTs. 1998–2011 | | 0.40 to 0.89]<br>**Mortality:** No significant effect of intervention [OR 0.79, 95% CI 0.58 to 1.07]<br>**Dyspnoea:** Strong evidence in favour of intervention [MD -0.83, 95% CI -1.36 to -0.30]<br>**Exercise capacity:** No significant effect of intervention [MD 33.69 m, 95% CI -9.12] | However, heterogeneity among interventions, study populations, follow-up time and outcome measures makes it difficult to formulate clear recommendations regarding the most effective form and content of self management in COPD. |
| **McLean** (2011)[136]*** | Telehealthcare for COPD (Cochrane review) | 10 RCTs; 1004; 1990–2009 | Meta-analysis | | Telehealthcare in COPD appears to have a possible impact on the number of times patients attend the ED and hospital. |
| **Jordan** (2015) [130]*** | Supported self-management for patients with moderate to severe COPD | 10 RCTs; 1533; 2000-2012 | Meta-analysis | Meta-analysis identified no evidence of benefit of post-discharge SM support on admissions [hazard ratio (HR) 0.78, 95% confidence interval (CI) 0.52 to 1.17], mortality (HR 1.07, 95% CI 0.74 to 1.54) and most other health outcomes. A modest improvement in HRQoL was identified but this was possibly biased due to high loss to follow-up. | There was little evidence of benefit of providing SMS to patients shortly after discharge from hospital, although effects observed were consistent with possible improvement in HRQoL and reduction in hospital admissions. It was not easy to tease out the most effective components of SMS support packages, although interventions containing exercise seemed the most effective. |
| **McCarthy** (2015)[137]*** | Pulmonary rehabilitation for COPD | 65 RCTs; 3822; 1997-2013 | Meta-analysis | | Results of the meta-analysis strongly support pulmonary rehabilitation, including at least four weeks of exercise training, as part of the spectrum of treatment for patients with COPD. We found clinically and statistically significant improvements in important domains of HRQoL, including dyspnoea, fatigue, emotional function and mastery, in addition to the six minute walk/distance test - a measure of functional exercise. |

**Key**: **CCM** = Chronic care model; **ED** = Emergency department; **HCP** = Health care professionals; **NNT** = Numbers needed to treat; **OR** = Odds ration; **PEFR** = Peak expiratory flow rate; **QoL** = Quality of life; **RCT** = Randomised controlled trial; **SMD** = Standardised mean difference; **WAPs** = Written action plans.

## Table A6.3 Summary of quality appraisal of cost-effectiveness studies.

| Study | Quality | Notes |
|---|---|---|
| **Bakerly** (2009) | Moderate | GP costs not included in retrospective group |
| **Bourbeau** (2006) | Moderate | Relatively short time horizon (1 year), small RCT, no sensitivity analysis |
| **Cecins** (2008) | Poor | Lack of data on how costs were calculated |
| **Chandra** (2012) | High | |
| **Chuang** (2011) | Poor | Lack of data on how costs and benefits were estimated |
| **De San Miguel** (2013) | Poor | Relatively short time horizon (6 months), no sensitivity analysis |
| **Dewan** (2011) | High | |
| **Farrero** (2001) | Poor | GP costs omitted, lack of data on how cost and benefits were valued |
| **Gallefoss** (2004) | Moderate | Relatively short time horizon (1 year), no health-related quality of life data, sensitivity analysis unclear |
| **Gillespie** (2013) | Moderate | |
| **Golmohammadi** (2004) | Poor | No disaggregation of costs, perspective unclear, poor applicability |
| **Griffiths** (2001) | High | |
| **Haesum** (2012) | Moderate | Relatively short time horizon (10 months), no sensitivity analysis |
| **Hernandez** (2003) | Moderate | Eight week follow up, unclear valuation of costs and benefits |
| **Hoogendoorn** (2010) | High | |
| **Jodar-Sanchez** (2014) | Moderate | Short time horizon (4 months) and no GP costs included |
| **Jordan** (2015) | High | Exploratory study only due to substantial uncertainty surrounding efficacy of intervention. |
| **Khdour** (2011) | High | |
| **Liu** (2013) | Poor | Lack of data on cost and benefits included |
| **Monninkhof** (2004) | Moderate | Relatively short time horizon (1 year) |
| **Pare** (2013) | Moderate | Lack of data on how hospitalisation costs were calculated, no discounting, no sensitivity analysis |
| **Stoddart** (2015) | High | |
| **Taylor** (2012) | Moderate | Relatively short time horizon (6 months) |
| **Tinkelman** (2003) | Poor | Lack of data on how costs were estimated |
| **Van Boven** (2014) | High | |
| **Vitacca** (2009) | Poor | Relatively short time horizon (1 year), not all patient costs included, no sensitivity analysis |

## Table A6.4 Cost-effectiveness studies investigating SMS education programmes

| Study | Intervention | Population | Study Design | Clinical outcomes and QALYs | Costs | Results |
|---|---|---|---|---|---|---|
| **Bourbeau** (2006)[145] | Multi-faceted education programme with phone follow-up, WAP, on demand access to a case manager and an exercise bike | Patients with moderate- severe COPD and a history of ≥hospitalisation for exacerbation in the preceding year. Mean age 69.5 years | Country: Canada<br>Study design: RCT (n=191)<br>Perspective: Health care payer<br>DR:N/A<br>Time horizon: 1 year<br><br>(CAD$ 2004) | Decrease in frequency of hospitalisations, ED visits, unscheduled visits and days in hospital in the IG relative to usual care | Based on a case management load of 14 patients pa, the cost of the self management intervention was $3,778 (€2,953)/pp; the net difference in total healthcare costs (healthcare plus intervention costs) was $440 (€344) (p=0.68) between the IG and the CG.<br>Scenario analysis indicated that the intervention became cost-saving with increasing case management load (case load 50 patients pa: net difference = $2149 (-€1,680) (CI $38-$4258 (€30-€3,328) (p=0.046) | At a case-load of 14 patients pa. ICER $4214 (€3,293) hospitalisation prevented, reducing to $1326 (€1,036)/hospitalisation prevented at a case-load of 50 patients per annum. |
| **Gallefoss** (2002)[152] | Education programme (2 x 2hr group sessions, 1 individual education session plus 1-2 individual physiotherapist sessions) plus WAP | Adults < 70 years without severe disease. Mean age 57.5 years | Country: Norway<br>Study design RCT (n=62) Perspective: Societal<br>DR: N/A<br>Time horizon:1 year<br><br>(NOK 1994) | Relative to CG, IG had 85% decrease in GP visits (mean 0.5 vs 3.4 p<0.0001), increased satisfaction with GP (100% vs 78%, p=0.023), and a reduction in use of rescue medications (p=0.003), reductions in days in hospitals and absenteeism were not significant | The mean cost of the intervention was NOK 1600 (€177) per patient consisting of NOK 900 (€99) for education and NOK 700 (€77) for patient time costs. Mean annual total costs for the CG and IG were NOK 19,900 (€2,199) vs NOK 10,600 (€1,171), p=0.581) There was a significant reduction in total costs relative to the CG (p=0.003) The savings in total costs per patient excluding the intervention costs were NOK 7700 (€851) | Cost benefit from societal perspective is 214:1031, meaning that for every NOK spent on patient education, there was a saving of NOK 4.8 (€1). |

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|---|---|---|---|---|---|---|
| **Khdour** (2011)[160] | Pharmacy-led education with WAP and two follow-up phone calls and two follow up OPD visits vs usual care (2 OPD visits in one year) | Adult COPD patients over 45 years (>86% moderate-severe COPD) Mean age 66.4 years. | Country: N. Ireland Study design: RCT one year follow-up (n=127) Perspective: Healthcare provider DR: N/A Time horizon: 1 year<br><br>(GB£ 2006/07) | Mean differential QALY (EQ5D) was 0.065 (p=0,051); and decrease in hospital bed days (60%, p=0.007), ED visits (48%, p=0,016), unscheduled GP visits 38% p=0.003 and the mean number of antibiotic/steroid courses 23% p=0.023; no difference in scheduled GP visits. | Mean cost pp of the self management intervention was £381 (€571). Total mean healthcare cost were £671 (€1,005) lower (p=0.065) for the IG (i.e. cost saving relative to CG). | Education was found to be dominant, that is less expensive and more effective than usual care during one year follow-up |
| **Monninkhof** (2004)[162] | Education programme with physiotherapy-led exercise classes (1-2/week x 2 years) and self-management plan (COPE SMS programme) | Patients aged 40-75 years old with moderate to severe COPD. Mean age 65 years | Country: The Netherlands Study Design CUA alongside RCT with one year follow-up (n=248) Perspective: Societal Discount: N/A Time horizon: 1 year<br><br>(Netherlands € 2002) | No measurable beneficial effects were found for QALYs or HRQoL (SGRQ) scores. | The self-management programme-specific costs amounted to €642 (€713) per patient. The incremental cost difference amounted to €838 (€931) per patient per year in favour of usual care. | Authors concluded that the COPE self-management programme is not efficient in the management of patients with moderate to severe COPD |
| **Taylor** (2012)[165] | 7-week SMS educational programme delivered by lay tutor (BELLA) plus usual care vs usual care | COPD patients >35 years, with ≥ unscheduled visit in previous year (moderate-severe COPD) Mean age 69.5 years | Country: UK Study design RCT 6 month follow-up (n=116) Perspective: Healthcare payer Discount: N/A Time horizon: 6 months<br><br>(GB£ 2008) | EQ-5D scores deteriorated in both groups from baseline, but the decline was smaller in the intervention group (difference 0.12, 95% CI -0.02 to 0.26) | Total cost of the intervention was £30,000 (€42,181) for seven courses. Mean total cost of health care (including intervention) in intervention arm was £877/pp (€1,233) SD £1218 (€1,713) compared to £395/pp (€555) SD: £822 (€1,156) in control. | The ICER was £11,710 (€16,465) per QALY gained over 6 months from a provider perspective. |

Key: **CDSM** – chronic disease self-management; **CI** Confidence Interval; **CG**: Control Group; COPD – chronic obstructive pulmonary disease; **HRQoL** – health related quality of life **ICER** – incremental cost effectiveness ratio; **pa** – per annum; **pp** – per patient; **IG**: intervention group; **QALY** – quality adjusted life year; **RCT** – randomised controlled trial; **SD**: Standard Deviation; **SMS** – self-management support; **SGRQ**-St George respiratory questionnaire; WAP – written action plan.

## Table A6.5 COPD: Studies assessing pulmonary rehabilitation programmes for COPD

| Study | Intervention | Population | Study Design | Clinical outcome and QALY | Costs | Results |
|---|---|---|---|---|---|---|
| **Cecins** (2008)[146] | Pulmonary rehabilitation programme with twice weekly exercise classes for 8 weeks. | Adults with stable moderate to severe COPD Mean age 67.5 years. | Country: Australia<br>Study design: Pre-and Post-intervention design with 1 year follow-up (n=256)<br>Perspective: N/R<br>Discount rate: N/R<br>Time horizon: 1 year<br>(AUS $ 2003) | Clinically significant improvement in 6MWD and all domains CRDQ (p<0.001) | 51% reduction in total hospital admissions resulted in net savings in hospitalisations of $397,032 (€370,520). Estimated cost of providing rehab to 256 participants was $93,440 (€87,200) $292 (€273)/per patient). | Authors concluded savings achieved far outweighed cost of the programme. |
| **Chandra** (2012)[147] | Pulmonary rehabilitation 4 week programme with full MDT input including social worker and GP vs usual care | Start age 68 years, 46% females, mix of moderate and severe COPD | Country: Canada<br>Study design: Modelling study<br>Perspective: Healthcare provider<br>Discount:5%<br>Time Horizon: Lifelong<br>(CAN $ 2008) | Incremental life years 0.4 and incremental QALYs 0.3 | The incremental intervention cost per patient was $1,527 (€1,097). | The ICER was calculated to be $17,938 (€12,885) per QALY and $14,616 (€10,502) per life year |
| **Gillespie** (2013)[153] | Pulmonary rehabilitation 8-week programme with nurse and physiotherapist only vs usual care | Adults with mild to moderate disease from GP practice | Country: Ireland<br>Study design: Cost-effectiveness alongside cluster RCT with 22 week follow-up (n=350) Perspective: Healthcare provider<br>Discount: N/A<br>Time Horizon: 22 weeks<br><br>(Irish € 2009) | There was a higher CRQ score in the intervention arm of 1.11 (0.35, 1.87 p<0.01) and 0f 0.002 (-0.006, 0.11; p=0.63) QALYs compared to control group. | The cost of the intervention was estimated at €822 (€948) per participant €564 (€650) healthcare costs + €258 (€297) for patient costs). The intervention group had an increased total mean healthcare cost of €944 (€1,088) and €261 (€301) in total patient costs. | The ICER was €850 (€980) per unit increase in the CRQ Total score and €472,000 (€544,099) per additional QALY gained. Therefore cost effective for disease specific scores only. |
| **Golmohammadi** (2004)[154] | Pulmonary rehabilitation 6 to 8 week programme with 2-3 weekly classes with MDT input vs usual care | Adults older than 45 years with varying severity of COPD | Country: Canada<br>Study design: Pre- and post-intervention costing study (n=210) Perspective: Healthcare provider<br>Discount: N/A<br>Time Horizon:1 year<br><br>(Can $ 2003) | Overall improvement in SGRQ scores was 4.85% (p=0.001) or about 193 units. | The average cost for each person who started the programme was $1092 (€869). The average reduction of total health care costs after the programme was $344 (€274) per person per year. (p=0.02) | Authors concluded pulmonary rehabilitation is cost-effective in the community. |

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|---|---|---|---|---|---|---|
| **Griffiths (2001)**[155] | Outpatient multidisciplinary 6-week pulmonary rehabilitation programme (18 x 1/2 day visits) including education, exercise, individual goal setting, dietary intervention, physiotherapy and occupational therapy versus standard care. | Patients with COPD (mainly) or other chronic disabling pulmonary pathologies (FEV1 < 60% predicted with < 20% reversibility to inhaled β agonist) referred by primary and secondary care physicians for rehabilitation | Country: UK<br>Study design: CUA alongside RCT with one year follow-up, n=200 patients.<br>Perspective: Health service (primarily)<br>Time horizon: 12 months (cost year not reported - RCT published in 2000) | The incremental utility of adding pulmonary rehabilitation was 0.030 (95% CI 0.002 to 0.058) QALYs per patient, p=0.03. | Rehabilitation programme for up to 20 patients cost £12,120 (64% staff costs, 4% equipment and consumables, 15% transport, 17% overhead) equating to £725 per patient based on an attendance of 17 patients /programme.<br>The mean incremental cost saving of adding rehabilitation to standard care was £152 (95% CI –881 to 577) per patient, p=NS.<br>No significant difference was observed in the overall cost of care between the control and rehabilitation groups. | Authors concluded that outpatient pulmonary rehabilitation produces cost per QALY ratios within bounds considered to be cost effective and is likely to result in financial benefits to the health service.<br>The cost-effectiveness acceptability curve indicated the probability of the cost per QALY generated for the intervention being < £17,000 is 0.95, with a probability of 0.64 that it is cost saving. |
| **Hoogendoorn** (2010)[158] | Community rehabilitation programme with twice weekly physiotherapy sessions for four months and nurse education and dietician, followed by 20 month maintenance vs usual care | Adults with gold stage 2 or 3 | Country: Netherlands<br>Study design: RCT with 2 year follow up (n=199) Perspective: Societal and third party payer<br>Discount: N/A<br>Time Horizon: 2 years<br><br>(Dutch € 2007) | Net improvement in intervention group of 13% in SGRQ score and -17% in control. Incremental QALY of 0.08 (95% CI -0.01-0.18) | The cost of the intervention for two year was €1,650 (€1,758) per patient. Mean total costs for two years, irrespective of whether they were related to COPD or not, were €13,565 (€14,453)/pp for the INTERCOM group and €10,814 (€11,522)/pp for the usual care group. Total direct healthcare costs were €2,751 (€2,931) (95% CI- €631-€6372) (-€672-€6,789) higher in the INTERCOM group. | ICER was €32,425 (€34,548) per QALY from societal and €25,309 (€26,966) per QALY from a third party payer's perspective |

**Key**: **COPD** = chronic obstructive pulmonary disease; **CRQ** = chronic respiratory disease questionnaire; **ICER** = incremental cost-effectiveness ratio; **MDT** = multi-disciplinary team; **pp** = per patient; **QALY** = quality-adjusted life year; **SGRQ** = St George's Respiratory Questionnaire.

## Table A6.6 Cost-effectiveness studies examining telemedicine interventions

| Study | Intervention | Population | Study design | Clinical outcomes and QALY | Costs | Findings |
|---|---|---|---|---|---|---|
| **De San Miguel** (2013)[149] | Telehealth monitoring with nurse monitoring and advice and website accessible to GP | Members with a diagnosis of COPD and receiving domiciliary oxygen. Mean age 72.5 years | Country: Australia<br>Study design: Costing study alongside RCT (n= 80)<br>Perspective: Healthcare provider<br>Discount rate: N/A<br>Time horizon: 1 year<br><br>(Aus $ 2005) | There was no statistically significant difference in CRQ-SAS scores between groups, except for mastery domain. | The annualised net savings in the telehealth group was $2,931 (€2,425) per person (driven by fewer hospitalisations) | Authors concluded that remote monitoring resulted in fewer health service contacts and thus in cost savings. |
| **Haesum** (2012)[156] | Telehealth monitoring from a range of healthcare professionals and monthly telerehabilitation team meetings online | Adult COPD patients<br>Mean age 68 years. | Country: Denmark<br>Study design: CUA alongside RCT (n=111)<br>Perspective: Healthcare provider<br>Discount rate:3% for capital costs<br>Time horizon:10 months<br><br>(Danish KOR 2010 (reported as € where 100€=750 DKK)) | Incremental QALY gain for intervention group was 0.013 and -0.014 for control. | Total healthcare costs were €7862 (€6,394) (95% CI €4,818-€10,906) (€4,249-€9,621) for intervention group (including intervention equipment costs of €677 (€597) and €8,150 (€7,188) (95% CI €5879-€10420) (€5,185; €9,189) for control group | Intervention was less costly and more effective than rehabilitation in control group. |
| **Jodar-Sanchez** (2014)[159] | Telehealth monitoring by a call centre with case manager review of results | Severe COPD with LTOT<br>Mean age 72.7 years | Country: Spain<br>Study design: CUA alongside RCT (n=45)<br>Perspective: Healthcare provider<br>Discount rate; N/A:<br>Time horizon:4 months<br><br>(Spanish € 2014) | The average QALY gain was 0.0059 for the TG and 0.0006 for the CG, resulting in an incremental QALY gain of 0.0053. | The average total cost was €2300 (€2862)/pp in the intervention group and €1103 (€1372)/pp for the controls resulting in an incremental cost of €1196 (€1488) (95% CI €-498-€2892 (-620; 3,598)). | The ICER was €223,726 (€278,379) per QALY gained |

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|---|---|---|---|---|---|---|
| **Pare** (2013)[163] | Telehealth monitoring with case manager advice and pre-programmed computer generated advice. | Severe COPD<br>68% females<br>Mean age 68.2 years | Country: Canada<br>Study design: Costing study alongside RCT (n=120)<br>Perspective: healthcare provider<br>Discount rate: N/R<br>Time horizon: 21.5 months<br><br>(CAD $ 2010) | Reduced hospitalisations and length of stay | There was a net saving of $1613 (€1,103) per patient year in the tele-homecare group compared to controls, resulting in a net gain of 14%. | Authors concluded that despite positive results future research needed to confirm cost-effectiveness. |
| **Stoddart** (2015)[164] | Telehealth monitoring with telephone follow-up by responsible physician | Adults with an admission for exacerbation of COPD in the previous year with varied disease severity<br>Mean age 68.9 years | Country: UK<br>Study design: CUA alongside RCT (n= 256)<br>Perspective: Healthcare provider<br>Discount rate: 3.5% for equipment cost<br>Time horizon: 1 year<br><br>(GB £ 2010) | The mean difference in QALYs was 0.0167 when adjusted for baseline differences. | The mean overall cost of tele-homecare was £568 (€756) per patient. The mean overall health care costs per patient were £11906 (€15,834) in the telemonitoring arm and £9613 (€12,792) in the usual care arm. | The mean ICER was £137,277 (€182,673) per QALY. |
| **Vitacca** (2009)[168] | Telehealth monitoring | Chronic respiratory failure with HMV or LTOT<br>Mean age 61.1 years | Country: Italy<br>Study design: Costing study alongside RCT (n=101)<br>Perspective: Healthcare provider<br>Discount rate: N/A<br>Time horizon: One year<br><br>(Italy € cost year NR) | Fewer hospitalisations in intervention group | The cost of the intervention ranged from €903 to €1008 per patient. The mean direct healthcare costs per patient excluding the intervention were €8,907(+/-€17,580) and €14,728(+/-€28,694) in the IG and CG respectively | Authors concluded that in severe and frail chronic respiratory failure patients a nurse-led tele-assistance programme can reduce hospitalisations. |

**Key**: **CG** = control group; **COPD** = chronic obstructive pulmonary disease; **CUA** = cost-utility analysis; **ICER** = incremental cost-effectiveness ratio; **IG** = intervention group; **LTOT** = long term oxygen treatment; **RCT** = randomised controlled trial.

## Table A6.7 Cost-effectiveness studies assessing case management interventions

| Study | Intervention | Population | Study design | Clinical outcomes and QALY | Costs | Findings |
|---|---|---|---|---|---|---|
| **Farrero** (2001)[151] | Home case management with quarterly home visits and monthly telephone reviews by nurse | Adults receiving LTOT<br>Mean age 69 years. | Country: Spain<br>Study design: Costing study alongside RCT (n=122)<br>Perspective: Provider<br>Discount rate: N/A<br>Time horizon: 1 year<br><br>(Pesetas cost year NR) | No difference in QoL scores or arterial blood gases.<br>Similar and significant decreases in FVC and FEV at f/up | The cost of the intervention was estimated at 6.7 million pesetas and this resulted in net savings of 8.1 million pesetas for the study period, mainly driven by reduced hospitalisations and ED visits in intervention group. | Authors concluded that for selected group of patients with severe COPD such as those receiving LTOT, hospital based case management can be cost-effective |
| **Chuang** (2011)[148] | Regular (at least weekly) telephone education and management calls from nurse, with written action plan and liaison with GP | Members of care organisation with confirmed diagnosis of COPD. | Country: USA<br>Study design: Costing study alongside RCT (n=141)<br>Perspective: Insurance provider<br>Discount rate: N/A<br>Time horizon: 1 year<br><br>(US$ cost year NR) | Decreased healthcare utilisation in intervention group but not statistically significant | Total programme costs were $225,012. The saving in all paid claims at twelve months was $328,760 resulting in a 46% return in investment. | Authors concluded their programme provided high-quality cost-effective care. |
| **Hernandez** (2003)[157] | Case management facilitating early discharge through initial nurse home visit and continued home or telephone follow-up for eight weeks post-discharge | Adults presenting to ED with COPD exacerbation (moderate disease)<br>Mean age 70.8 years | Country: Spain<br>Study design: Costing study alongside RCT (n=222)<br>Perspective: Public insurer<br>Discount rate: N/A<br>Time horizon:8 weeks<br><br>(Spain € 2000) | Intervention group showed higher improvement in HRQL, a higher percentage of patients in the home hospitalisation group had a substantial improvement in knowledge of the disease, compliance on inhalation technique and rehabilitation at home compared to control | The average overall healthcare cost per patient in the intervention group was only 62% of the average cost calculated for control patients; €1255 (€1827) and €2033 (€2960), respectively (p=0.003) | Authors concluded that home hospitalisation of selected COPD exacerbations can result in better outcomes at lower costs than conventional care. |

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|---|---|---|---|---|---|---|
| **Liu** (2013)[161] | Home-based case management daily measurements, telephone review and home visits as required | Cohort 1 is a mix of disease severity, Cohort 2 is mix of end stage disease | Country: USA<br>Study design: Economic evaluation, modeling study<br>Perspective: Public insurer<br>Discount rate: 3.5%<br>Time horizon: Cohort 1 for 20 years, cohort 2 for 10 years<br><br>(US $ 2011) | Cohort 1 had incremental life years gained of 0.48 and QALY of 0.4; Cohort 2 had incremental life years of 0.36 and QALY of 0.22 | Cohort 1: incremental lifetime saving per person of $2,900 (€2651)<br>Cohort 2: incremental $16,100 (€14,719) lifetime saving per person | Base case analysis showed a mean cost saving of $7,250 (€6,628) per QALY gained in cohort 1 and mean cost savings of $73,187 (€66,909) per QALY gained in cohort 2. |
| **Tinkelman** (2003)[166] | Case management with access to helpline, regular telephone review, personalised action plan, educational materials and home visits | 35-89 year old in national Jewish disease management programme with a range of disease severity. Mean age 64 years. | Country: USA<br>Study design Pre and post intervention (n= 349)<br>Perspective: N/R<br>Discount: N/A<br>Time horizon: 1 year<br><br>(US$ 1996) | Activity component improved by 7.0 units (10.2%, p < 0.001), symptoms by 4.4 units (8.7%, p < 0.002) and total score by 1.9 units (3.7%, p = 0.057). | The cost of the programme was $223,500 (€358,268) (average of $635 (€1,018) per patient). Savings from reduced hospitalisations and ED visits of $672,000 (€1,077,208). | Case management is supportive of physician care and can be cost effective. |

**Key**: **COPD** = chronic obstructive pulmonary disease; **CUA** = cost-utility analysis; **ICER** = incremental cost-effectiveness ratio; **LTOT** = long term oxygen treatment; **QALY** = quality-adjusted life year; **RCT** = randomised controlled trial.

## Table A6.8 Cost-effectiveness studies examining other SMS interventions

| Study | Intervention | Population | Study design | Clinical outcomes and QALYs | Costs | Results |
|---|---|---|---|---|---|---|
| **Bakerly** (2009)[144] | Integrated care with education session, early discharge and self-management plan shared with GP. | Adult COPD patients with moderate disease | Country: UK<br>Study design: Non-randomised study (n=225) with and matched retrospective control group<br>Perspective: Healthcare provider<br>Discount rate: N/A<br>Time horizon: 1 year<br><br>(GB£ Mixed cost years 2006 and 2007) | None reported | The total mean healthcare cost per patient in the integrated care group was £1653 (95%CI, £1521–1802) compared to £2256 (95%CI, £2126–2407). Resulting in savings of £600. (p<0.001) | Authors concluded further research was needed due to changing commissioning landscape and difficulties with study design |
| **Chandra** (2012)[147] | Intensive counseling for smoking cessation 90 minute duration | Start age of 48 years, 37% females with moderate COPD | Country: Canada<br>Study design: Economic modeling study<br>Perspective: Healthcare provider<br>Discount rate:5%<br>Time horizon: Lifelong<br><br>(CAD $ 2006) | 0.62 life years gained and 0.58 QALY gained | The intervention resulted in incremental lifetime cost savings of $2,245 (€1,674) | Intervention was dominant being less costly and more effective than usual care. |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Jordan** (2015)[130] | Low, moderate or high intensity nurse-led SMS programme delivered within six weeks of hospital discharge for an acute exacerbation compared with usual care | Cohort with a start age of 72 years, 47.4% male with 39.4% current smokers | Country: UK<br>Study design: Economic evaluation modeling<br>Perspective: Healthcare provider<br>Discount rate: N/R<br>Time horizon:30 years<br><br>(GB£ 2012) | Incremental QALY was 0.0831 | Incremental cost was £683 (€854).<br>The ICER was £8,218 (€10,270) per QALY gained. Applying the high intervention estimate of £671 (€839) per patient increased the ICER to £9,257 (€11,568). Applying the low estimate of £85 (€106) decreased the ICER to £1033 (€1291). | Considerable uncertainty was noted around the impact on readmissions, the authors highlighted that the model-based analysis should be viewed as speculative The main drivers of the model were the effect on hospital readmissions, duration of the effect, and the cost of the programme. To be cost-effective, the programme needed to cost no more than £2,200 (€2,749) if there was an18% reduction in readmissions. The sensitivity analysis suggested that SM support had a probability of 68% of being cost-effective at a threshold ICER of £20,000 (€24,994) per QALY. |
| **Van Boven** (2014)[167] | Community pharmacy intervention to improve medication adherence | Cohort with mean age of 70 years, 66% male | Country: Belgium<br>Study design: Modeling study based on RCT with 3 month follow up (n=734),<br>Perspective: Healthcare payer<br>Discount Rate:3% cost, 1.5% effect<br>Time horizon: 1 year<br><br>(Belgian € 2013) | In the intervention group inhalation scores were improved with 13.5% (95%CI: 10.8-16.1; P < 0.0001); medication adherence was improved from 85.70% to 94.21% (difference: 8.51%, 95%CI: 4.63-12.4; P < 0.0001) and there was a lower hospitalisation rate was observed (9 vs 35; Rate ratio: 0.28, 95%CI: 0.12-0.64; P = 0.003) Small QALY increase was observed (<0.001 QALY) | Cost saving of €227 (€227) (95% CI €58-€403 (€58-€403)) per patient in the intervention group within the one year time horizon. The total costs per patient for intervention and usual care were €2,221 (€2,219) and €2,448 (€2,446) respectively. | Authors concluded that improving inhaler adherence in community pharmacies is a cost-saving strategy compared with usual care. |

# Appendix A7 - Diabetes

## Table A7.1 T1DM: Results of meta-analyses.

| Reference and weighting Outcome | Intervention and comparator | Outcome | Time (from initiation of intervention) | Sample size | Significance | ES (95% CI) |
|---|---|---|---|---|---|---|
| Reviews retrieved by PRISMS (QA completed by PRISMS) | | | | | | |
| **Winkley** (2006)[174]*** | Psychological interventions | GHb (adult only) | NR | 11 RCTs; 516 participants | 0 | SMD–0.17 (–0.45 to 0.10); p=0.22 |
| | | Psychological distress (adult) | NR | Six RCTs | 0 | SMD–0.25 (–0.51 to 0.01); p=0.059 |
| Additional reviews retrieved (QA completed by HIQA) | | | | | | |
| **NICE** (2015)[175]*** | Structured education programmes | ¥ | ¥ | ¥ | ¥ | ¥ |

**Key: GHb:** Glycohemoglobin; **NR:** Not reported; **QA:** Quality Assured; **RCT:** Randomised Controlled Trial; **SMD:** Standard Mean Difference
**¥**: Due to potential issues with the reported outcome measures, the results of the meta-analyses are not included here.

## Table A7.2 T1DM: Summary of results from quantitative systematic reviews. Table adapted from PRISMS review.

| Reference and weighting Outcome | Focus | RCTs, n; Participants, n; Date range | Synthesis | Main results | Main conclusions (review author); *Important quality concerns (review author)* |
|---|---|---|---|---|---|
| Reviews retrieved by PRISMS (QA completed by PRISMS) | | | | | |
| **Winkley** (2006)[174]*** | Psychological interventions | 29 RCTs; 1,709 participants; 1985–2005 | Meta-analysis | No significant effect found to support a real reduction in GHb and psychological distress for adult populations. | This review provides no evidence for the effectiveness of psychological treatments in improving glycaemic control and reducing psychological distress in adults. |
| | | | Narrative | Restriction to group cognitive behavioural therapy delivered to adults resulted in a pooled ES [SMD 0.02 (95% CI–0.41 to 0.44); p=0.95] | |
| Additional reviews retrieved (QA completed by HIQA) | | | | | |
| **NICE** (2015)[175]*** | Structured education programmes | 15 RCTs; 1,994 participants; 1983-2013 | Narrative | Some trials showed a positive effect on outcomes including glycated haemoglobin, severe hypoglycaemia, and quality of life. In the broader educational programmes, the results of the DAFNE and PRIMAS studies were superior to others. | GRADE analysis suggested that the data on structured education programmes is generally of low or very low quality. |

**Key: ES**: Effect size; **GHb**: Glycohemoglobin; **NR**: Not reported; **QA**: Quality Assured; **RCT**: Randomised Controlled Trial; **SMD**: Standard Mean Difference

## Table A.7.3T2DM: Results of meta-analyses from PRISMS review and HIQA review Adapted from PRISMS review.[2]

| Reference and weighting Outcome | Intervention and comparator | Outcome | Time | Sample size | Significance | ES (95% CI) |
|---|---|---|---|---|---|---|
| PRISMS reviews retrieved (QA completed by PRISMS) | | | | | | |
| **Self-management programmes** | | | | | | |
| **Chodosh** (2005)[187]*** | Self-management programmes for older adults | HbA1c | NR | 20 RCTs | + | –0.36 (–0.52 to–0.21) |
| | | Fasting blood glucose | NR | 13 RCTs | + | –0.28 (–0.47 to–0.08) |
| | | Weight | NR | 17 RCTs | 0 | –0.04 (–0.16 to 0.07) |
| **Education** | | | | | | |
| **Duke** (2009)[189]*** | Individual patient education systematic programmes v usual care | HbA1c | <12 months | 3 RCTs; 295 participants | 0 | WMD–0.2% (–0.5% to–0.03%);p=0.08 |
| | | | ≥12 months | 4 RCTs; 632 participants | 0 | WMD–0.1% (–0.3% to 0.1%);p=0.33 |
| | | SBP | ≥12 months | 3 RCTs; 625 participants | 0 | WMD–2 mmHg (–5 to 1 mmHg);p=0.19 |
| | | DBP | ≥12 months | 3 RCTs; 624 participants | 0 | WMD–2 mmHg (–3 to 0 mmHg);p=0.05 |
| | | Cholesterol | ≥12 months | 3 RCTs; 627 participants | 0 | WMD–0.03 mmol/l (–0.2 to 0.1 mmol);p=0.66 |
| | | BMI | ≥12 months | 2 RCTs; 312 participants | 0 | WMD–0.2 kg/m$^2$ (–1.0 to 0.62 kg/m$^2$ ); p=0.62 |
| | individual education vs. group education | HbA1c | <12 months | 2 RCTs; 148 participants | +++ | WMD 0.8% (0.3% to 1.3%); p=0.0007 |
| | | | ≥12 months | 2 RCTs; 112 participants | 0 | WMD 0.03% (–0.02% to 0.10%);p=0.22 |
| | | SBP | ≥12 months | 2 RCTs; 95 participants | 0 | WMD 4 mmHg (–4 to 12 mmHg |
| | | DBP | ≥12 months | 2 RCTs; 95 participants | 0 | WMD 2 mmHg (–4 to 7 mmHg) |
| | | BMI | <12 months | 2 RCTs; 169 participants | 0 | WMD–0.1 kg/m$^2$ (–0.9 to 0.7 kg/m$^2$ ); p=0.77 |
| | | | ≥12 months | 2 RCTs; 123 participants | 0 | WMD–0.01 kg/m$^2$ (–0.8 to 0.7 kg/m$^2$); p=0.98 |

| Reference and weighting Outcome | Intervention and comparator | Outcome | Time | Sample size | Significance | ES (95% CI) |
|---|---|---|---|---|---|---|
| **Gary** (2003)[199]*** | Clear behavioural or counselling component | GHb (total GHb, HbA1, HbA1c) | NR | 18 RCTs | ++ | –0.43 (–0.71 to–0.14); p=0.003 |
| | | Fasting blood glucose | NR | 12 RCTs | 0 | WMD–12.22 mg/dl (–25.1 to 0.67 mg/dl) |
| | | Total GHb | NR | 6 RCTs | 0 | WMD–0.4% (–0.73% to 0.08%) |
| | | HbA1 | NR | 7 RCTs | 0 | WMD–0.77% (–1.88% to 0.34% |
| | | HbA1C | NR | 5 RCTs | + | WMD–0.52% (–0.96% to–0.08%); p=0.02 |
| | | Weight | NR | 7 RCTs | 0 | WMD–4.64 lb (–9.95 to 0.66 lb) |
| **Minet** (2010)[190]*** | Self-care management interventions | HbA1c | Overall | 43 RCTs; 7677 participants | + | MD 0.36% (0.207% to 0.509%) |
| **Norris** (2002)[192]*** | Self-management education | GHb | Immediate | 20 RCTs | + | –0.76% (–0.34% to–1.18%) |
| | | | 1–3 months | 9 RCTs | 0 | –0.26% (–0.73% to 0.21%) |
| | | | ≥4 months | 8 RCTs | + | –0.26% (–0.48% to–0.05%) |
| **Sigurdardottir** (2007)[193]** | Education | HbA1c | NR | NR | ++ | p=0.008 |
| **Steinsbekk** (2012)[194]*** | Group-based diabetes education | HbA1c | <12 months | 13 RCTs; 1827 participants | +++ | MD–0.44% (–0.69% to–0.19%); p=0.0006 |
| | | HbA1c | 12 month | 11 RCTs; 1503 participants | +++ | MD–0.46% (–0.74% to–0.18%); p=0.001 |
| | | HbA1c | 2 years | 3 RCTs; 397 participants | +++ | MD–0.87% (–1.25% to–0.49%); p<0.00001 |
| | | Fasting blood glucose | <12 months | 3 RCTs; 401 participants | 0 | NR |
| | | | ≥12 months | 5 RCTs | +++ | MD–1.26 mmol/l (–1.69 to–0.83 mmol/l); p<0.00001 |
| | | QoL | <12 months | 3 RCTs; 473 participants | 0 | SMD 0.31 (–0.15 to 0.78); p=0.19 |

| Reference and weighting Outcome | Intervention and comparator | Outcome | Time | Sample size | Significance | ES (95% CI) |
|---|---|---|---|---|---|---|
| | | Self-efficacy | <12 months | 2 RCTs; 326 participants | ++ | SMD 0.28 (0.06 to 0.5); p=0.01 |
| | | Self management behaviours | <12 months | 4 RCTs; 534 participants | ++ | SMD 0.55 (0.11 to 0.99); p=0.01 |
| | | SBP | <12 months | 5 RCTs; 815 participants | 0 | –0.34 mmHg (–5.19 to 4.51 mmHg) |
| | | DBP | <12 months | 5 RCTs; 815 participants | 0 | –0.46 mmHg (–2.31 to 1.39 mmHg) |
| | | SBP | ≥12 months | 2 RCTs | 0 | –3 mmHg (95% CI –7 to 2 mmHg) |
| | | DBP | ≥12 months | 2 RCTs | 0 | 0.17 mmHg (–4.46 to 4.80 mmHg) |
| | | Total cholesterol | <12 months | 7 RCTs; 1161 participants | 0 | –0.06 mmol/l (–0.23 to 0.12 mmol/l) |
| | | Triglycerides | <12 months | 7 RCTs; 1161 participants | 0 | –0.05 mmol/l (–0.19 to 0.08 mmol/l) |
| | | Total cholesterol | ≥12 months | 4 RCTs | 0 | 0.07 mmol/l (–0.09 to 0.20 mmol/l) |
| | | Triglycerides | ≥12 months | 4 RCTs | 0 | 0.03 mmol/l (–0.42 to 0.48 mmol/l) |
| | | HDL | <12 months | 6 RCTs; 932 participants | 0 | 0.01 mmol/l (–0.05to 0.03 mmol/l) |
| | | LDL | <12 months | 6 RCTs; 932 participants | 0 | 0.05 mmol/l (–0.2 to 0.1 mmol/l) |
| | | Body weight | <12 months | 3 RCTs; 433 participants | 0 | –2.08 kg (–5.55 to 1.39 kg); p=0.24 |
| | | BMI | <12 months p=0.51 | 7 RCTs; 1159 participants | 0 | 0.21 kg/m$^2$ (–0.86 to 0.43 kg/m$^2$); |
| | | Body weight | ≥12 months | 4 RCTs; 492 participants | + | MD–1.66 kg (–3.07 to– 0.25 kg);p=0.02 |
| | | BMI | ≥12 months | 7 RCTs; 1092 participants | 0 | –0.22 kg/m$^2$(–1.13 to 0.69 kg/m$^2$); p=0.63 |
| | | Mortality | NR | NR | 0 | OR 1.10 (0.37 to 3.29) |

| Reference and weighting Outcome | Intervention and comparator | Outcome | Time | Sample size | Significance | ES (95% CI) |
|---|---|---|---|---|---|---|
| **Hawthorne** (2008)[195]*** | Culturally tailored education | HbA1c | 3 months | Five RCTs | + | WMD–0.3% (–0.6% to–0.01%) |
| | | HbA1c | 6 months | Six RCTs | + | WMD–0.6% (–0.9% to–0.4%) |
| | | HbA1c | ≥12 months | Three RCTs | 0 | WMD–0.1% (–0.4% to 0.2%) |
| | | QoL | <12 months | Three RCTs | 0 | NR |
| | | Self-efficacy | NR | Three RCTs | 0 | NR |
| | | BP | Overall | Four RCTs | 0 | NR |
| | | Total cholesterol | <12 months | NR | 0 | NR |
| | | HDL | <12 months | NR | 0 | NR |
| | | LDL | <12 months | NR | 0 | NR |
| | | Total cholesterol | ≥12 months | Three RCTs | + | WMD–0.39 g/dl (–0.64 to–0.14 g/dl) |
| | | Triglyceride | <12 months | Three RCTs | 0 | NR |
| | | BMI | Overall | Three RCTs | 0 | NR |
| **Nam** (2012)[197]*** | Culturally tailored education | HbA1c | Overall | 12 RCTs | + | –0.29 (–0.46 to–0.13) |
| | | | 3 months | Eight RCTs | 0 | –0.21 (–0.47 to 0.05) |
| | | | 6 months | Five RCTs | + | –0.41 (–0.61 to–0.21) |
| | | | ≥12 months | Two RCTs | 0 | –0.14 (–0.39 to 0.11) |
| Additional reviews retrieved (QA completed by HIQA) | | | | | | |
| **Pal** (2014) (CR)[179]*** | Computer-based DM self-management interventions | HbA1c | 2-12 months | 11 RCTs; 2637 participants | ++ | Small, statistically significant difference of 2.3 mmol/mol. MD -0.2% (95% CI -0.4 to -0.1); $I^2$ = 58%; P=0.009 |
| | | HbA1c - mobile phone subgroup | 2-12 months | 3 RCTs; | +++ | -5.5 mmol/mol or -0.5% (95% CI -0.7 to -0.3); $I^2$ = 0%; P<0.001 |
| | | HbA1c – longer term (> 6 months) | > 6 months | 6 RCTs; | 0 | -1.5 mmol/mol or -0.1% (95% CI -0.3 to 0.1); P=0.33 |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Song** (2014)[182]** | Motivational interviewing effect on self-management | Self-management ability: Diet control | 6 months (not reported in 1 RCT) | 3 RCTs; 280 participants | +++ | MD, 2.46 95% CI, 1.58-3.34; p<0.00001; $I^2$ =0%; |
| | | Self-management ability: regular exercise | | | ++ | MD 2.41 95% CI 0.64 to 4.19; p=0.008 |
| | | Self-management ability: medication adherence | | | + | MD 1.53 95% CI -0.10 to 3.16; p=0.07 |
| | | Self-management ability: glucose monitoring | | | ++ | MD 2.12 95% CI 0.81 to 3.42; p=0.001 |
| | | Self-management ability: foot care | | | +++ | MD 2.67 95% CI 1.67 to 3.68; p<0.00001 |
| | | Self-management ability: prevention and treatment of hyperglycaemia and hypoglycaemia | | | ++ | MD 3.23 95% CI 1.30 to 5.17; p=0.001 |
| | | HbA1c | 3 months of MI | 2 RCTs; 160 participants | +++ | WMD -0.66; 95% CI -1.02 to -0.30; p=0.0003 |
| | | | 6 months of MI | 6 RCTs; 714 participants | ++ | WMD -0.44; 95% CI -0.73 to -0.15; P=0.003; $I^2$ = 73%; |
| | | | 12 months of MI | 2 RCTs; 845 participants | 0 | WMD 0.10; 95% CI -0.04 to -0.23; p=0.16 |
| | | | 14 months of MI | 1 RCT; 940 participants | 0 | WMD -0.10; 95% CI 0.50 to 0.10; p=0.19 |
| | | | 18 months of MI | 1 RCT; 217 participants | 0 | WMD 0.00 95% CI -0.28 to 0.28; p=1.00 |
| | | | 24 months of MI | 1 RCT | 0 | WMD -0.20; 95% CI -0.50 to 0.1; P=0.19 |
| **Schellenberg** (2013)[184]*** | Lifestyle Interventions for Patients With and at Risk for T2DM (results for patients with diabetes only included) | All-cause mortality: (strength of evidence rated as low for this outcome) | > 10 years follow-up | 2 RCTs; 5305 participants | 0 | RR 0.75 [CI, 0.53 to 1.06] P=0.10 |
| **Attridge** (2014) (CR)[185]*** | Culturally appropriate health education for people in ethnic minority groups | HbA1c | 3 months | 14 trials; 1442 participants; | ++ | MD -0.4% (95% CI -0.6 to -0.1); P=0.003; $I^2$ = 45%. [high-quality evidence] |
| | | | 6 months | 14 trials; 1972 participants; | +++ | MD -0.5% (95% CI -0.7 to -0.4); P<0.001; $I^2$ = 37%. [high-quality evidence] |
| | | | 12 months | 9 trials; 1966 participants | + | MD -0.2% (95% CI -0.3 to -0.04); P=0.015; $I^2$ = |

| | | | | | | |
|---|---|---|---|---|---|---|
| | | | | | | 17%. |
| | | | 24 months | 4 trials; 2268 participants; | + | (MD -0.3% (95% CI -0.6 to -0.1); P=0.019; $I^2$ = 61%. [moderate-quality evidence] |
| | | Knowledge scores | 3 months | 10 trials; 936 participants; | ++ | SMD 0.4 (95% CI 0.1 to 0.6); P=0.005; $I^2$=65% |
| | | | 6 months | 9 trials; 994 participants; | +++ | SMD 0.5 (95% CI 0.3 to 0.7); P<0.001; $I^2$ = 43%. |
| | | | 12 months | 2 trial; 328 participants; | ++ | SMD 0.4 (95% CI 0.1 to 0.6); P=0.002; $I^2$ = 0%. |
| **Saffari** (2014)[180]** | Health education via mobile phones (SMS only, SMS plus internet) | HbA1c | | 10 trials; 960 participants | +++ | SMD -0.595 (95% CI -0.833 to -0.356); p<0.001; |
| | | HbA1c – SMS only | | 6 trials; | +++ | SMD -0.595 (95% CI -0.671 to -0.202); p<0.001; |
| | | HbA1c – SMS + internet | | 4 trials; | +++ | SMD -0.500 (95% CI -0.716 to -0.285); p<0.001; |
| **Bolen** (2014)[176]*** | Patient activation interventions | Long-term Mortality | > 2 years | 6 RCTs; 2,733 participants | 0 | OR 0.70 (95% CI 0.49 to 1.01); $I^2$ = 60%. |
| | | Short-term mortality | ≤ 24 months | 38 RCTs; | 0 | OR 0.90 (95% CI 0.64 to 1.28) |
| | | A1c (%) | > 3 months | 111 RCTs; 12,780 participants | | WMD -0.37 (95% CI -0.45 to -0.28) |
| | | SBP (mmHg) | > 3 months | 54 RCTs; 7,630 participants | | WMD -2.2 (95% CI -3.5 to -1.0) |
| | | CVD morbidity | > 3 months | 1 RCT; 141 participants | | RD: 20% less CVD morbidity in intervention group |
| | | LDL-c (mg/dL) | > 3 months | 37 RCTs; 4,845 participants | | WMD -4.2 (95% CI -6.9 to -1.5) |
| | | HDL-c (mg/dL) | > 3 months | 34 RCTs; 4,908 participants | | WMD 0.03 (95% CI -0.8 to 0.8) |
| | | Body weight (pounds) | > 3 months | 43 RCTs;5,749 participants | | WMD -2.3 (95% CI -3.2 to -1.3) |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Huang** (2015)[178]*** | Telecare interventions | HbA1c | 3 to 60 months | 18 RCTs; 2,793 participants | + | WMD -0.54 95% CI -0.75 to -0.34; p<0.05 |
| | | BMI | | 4 RCTs; 346 participant | 0 | WMD -0.59kg/$m^2$ 95% CI -1.52 to 0.34; p=0.21 |
| | | Weight change | | 4 RCTs; 724 participants | 0 | WMD 1.01 pounds 95% CI -3.31 to 5.33; p=0.65. |
| **Zhai** (2014)[181]*** | Telemedicine | HbA1c | 3 to 60 months | 35 RCTs; 8,149 participants | +++ | MD -0.37 95% CI -0.49 to -0.25; p<0.001 |
| | | HbA1c – telephone based interventions | | 12 RCTs | +++ | MD -0.53 95% CI -0.81 to -0.26; p<0.001 |
| | | HbA1c – internet based interventions | | 19 RCTs | +++ | MD -0.62 95% CI -0.82 to -0.42; p<0.001 |

**Key: CVD:** cardiovascular disease; **DM:** diabetes mellitus **HbA1c:** Haemoglobin A1c (specific portion of four-part haemoglobin molecule); **NR:** Not reported; **SBP:** Systolic blood pressure; **SMD:** Standard Mean Difference; **WMD:** weighted Mean Difference. **BMI**: Body Mass Index

## Table A.7.4 T2DM: Summary of results from quantitative systematic reviews from PRISMS and updated reviews. Table adapted from PRISMS review.[2]

| Reference and weighting Outcome | Focus | RCTs, n; Participants, n; Date range | Synthesis | Main results | Main conclusions (review author); *Important quality concerns (review author)* |
|---|---|---|---|---|---|
| **Chodosh** (2005)[187]*** | Self-management programmes, interventions that aim to improve active participation in either self-monitoring, or decision-making, or both | 26 RCTs; 2579; 1983–2004 | Meta-analysis | Compared with control, a statistically significant reduction in HbA1c (ES –0.36) and blood glucose (ES–0.28) were found. Interventions were not found to impact on weight when compared with control. | Chronic disease self-management programmes improved glycaemic control.<br>Feedback associated with improvement in HbA1c<br>Possible publication bias. |
| | | | Additional | Feedback the only factor associated with a significant improvement in HbA1c. Did not identify any other elements significantly associated with greater efficacy of self-management programmes. | |
| **Duke** (2009)[189]*** | Individual patient education systematic programmes, delivered face to face which addressed a wide range of self-management issues | Nine RCTs; 1359; 1996–2007 | Meta-analysis | Individual education interventions had no significant effect on HbA1c, BP, cholesterol or weight compared with usual care Compared with individual education, group education had a greater impact on HbA1c reduction in the short term (WMD 0.8%). No differences in BP or BMI outcomes were found between individual and group education. | Group education more effective than individual education in reducing HbA1c short term.<br>However, for people with higher baseline HbA1c, individual education may be more effective.<br>Included studies were generally poor quality with the majority having a high-risk of bias. |
| | | | Additional | For people with HbA1c>8%, individual education suggested to be most effective Impact on QoL unclear, small tentative suggestion that group education may produce greater improvements in QoL than individual education. | |
| **Gary** (2003)[199]*** | Clear behavioural or counselling component aimed at improving long-term diabetes | 18 RCTs; 2720; 1984–9 | Meta-analysis | Strong evidence on GHb reduction compared with control (ES–0.43). Also evidence of reduction in HbA1c (WMD –0.52). No effect was found on other measures of glycaemic control or weight. | Educational or behavioural interventions improved glycaemic control. Physician-led interventions may cause greater improvements in HbA1c; however, authors suggest this may be due to manipulation of medical regimens.<br>Possible publication bias. |
| | | | Additional | Physician led interventions may cause larger improvements in HbA1c than those led by | |

| Reference and weighting Outcome | Focus | RCTs, n; Participants, n; Date range | Synthesis | Main results | Main conclusions (review author); *Important quality concerns (review author)* |
|---|---|---|---|---|---|
| | self-care behaviour | | | nurses or dieticians. | |
| **Heinrich** (2010)[200]** | Multi-component interventions aimed at self-management. Interventions had to target at least two behaviours or had to be focused on self-management or diabetes in general | 14 RCTs; 1778; 2001–9 | Narrative synthesis | Dietary changes appear to be the outcome most responsive to interventions, regardless of intervention form Interventions most successful in increasing PA focused on self-management behaviours and lifestyle changes SMBG frequency appears reactive to interventions regardless of intervention form. | Dietary change and SMBG appear reactive to multi-component interventions. Suggests interventions aiming to increase PA should focus on self-management behaviours and lifestyle changes. |
| **Minet** (2010)[190]*** | Self-care management interventions using educational or behavioural strategies (mainly face-to-face) | 43 RCTs; 7677; 1988–2007 | Meta-analysis | Evidence of benefit in HbA1creduction compared with control (MD 0.36%) | Self-care management interventions improve glycaemic control. Greater improvements found in those RCTs with shorter follow-up, suggesting reduced impact long-term. More compact interventions may also be of greater benefit. Three studies had several intervention groups, with each intervention arm compared with the control group and considered as an individual study. |
| | | | Additional | Interventions with shorter follow-up found larger improvements in HbA1c. Some suggestion that educational techniques are more effective than behavioural or psychosocial techniques for improving HbA1c. In addition, suggestion that interventions of shorter duration are more effective than those lasting more than 9 months | |
| **Newman** (2004)[201]** | Interventions that aim to increase patients' involvement and control in their lives with chronic illness | 21 RCTs; 2032; 1997–2002 | Narrative | Majority of interventions reduce HbA1cat some point, evidence suggests that reductions can be sustained after 6 months Little effect on QoL found No difference in psychological well-being between intervention and control, evidence suggests cognitive–behavioural components to be most effective for improving psychological well-being Interventions identified positive changes in self-management behaviours compared with | Interventions improve glycaemic control and self-management behaviours. Little effect on QoL, and no difference in psychological well-being. Long-term effectiveness unclear. |

| Reference and weighting Outcome | Focus | RCTs, n; Participants, n; Date range | Synthesis | Main results | Main conclusions (review author); *Important quality concerns (review author)* |
|---|---|---|---|---|---|
| | | | | control.<br>Few interventions assessed outcomes long-term, and in those that did, many found benefits not to be sustained at long-term follow-up. Of those interventions that had long-term effectiveness, design varied, suggesting there is no one correct approach. | |
| **Norris** (2001)[191]* | Educational interventions, or multi-component interventions where the effects of the educational component could be examined separately | 72 RCTs; NR; 1981–99 | Narrative synthesis | Evidence shows improved short-term glycaemic control compared with usual care. Less evidence to support improvements longer term. Group support meetings focusing on coping skills may be beneficial in improving glycaemic control.<br>Beneficial effects were found for weight loss, dietary change, and frequency and accuracy of SMBG.<br>Benefits for psychological outcomes, QoL, BP, cholesterol and PA were all mixed, as were interventions focusing on foot care.<br>Characteristics of interventions demonstrating greater effect: shorter follow-up periods; collaborative; repetitive; ongoing; interactive; individualised. It remains unclear if the use of computers and videos for education is advantageous. | Interventions improve glycaemic control short term. Also benefits for weight loss, and self-management behaviours. |
| **Norris** (2002)[192]*** | Teaching individuals to manage their diabetes through self-management education | 31 RCTs; 4263; 1981–99 | Meta-analysis | Evidence of benefit in GHb after 4 months or more compared with control (ES–0.26%) | Self-management education interventions improve glycaemic control short term No study fulfilled all reviewer quality criteria for bias. |
| | | | Additional | On average, 23.6 hours of contact between the educator and patient are needed to achieve a 1% reduction in GHb.<br>Duration of contact time between educator and patient was the only significant predictor of effect. | |
| **Sigurdardottir** (2007)[193]** | Education which aims to enhance | 18 RCTs; 4293; 2001–5 | Meta-analysis | Strong evidence of reduction in HbA1c compared with control | Educational interventions improve glycaemic control. Greater reduction in those with high baseline HbA1c. |
| | | | Additional | There is strong evidence to suggest greater | |

| Reference and weighting Outcome | Focus | RCTs, n; Participants, n; Date range | Synthesis | Main results | Main conclusions (review author); *Important quality concerns (review author)* |
|---|---|---|---|---|---|
| | diabetes-related self-care | | | reduction in HbA1c in individuals with baseline HbA1c≥8% compared with individuals with baseline HbA1c<8% | |
| **Steinsbekk** (2012)[194]*** | Group-based diabetes education | 21 RCTs; 2833; 1988–2007 | Meta-analysis | Very strong evidence of effect on HbA1c Short term (SMD–0.44%), at 12 months (SMD –0.4%) and long-term (SMD–0.87%). Also strong evidence of reduction in fasting glucose long-term (SMD –1.26 mmol/l). Some evidence of benefit on self-efficacy (SMD 0.28) and self-management behaviours (SMD 0.55). Suggestive evidence of benefit on body weight long-term (SMD 1.66 kg). No evidence of benefit on QoL, BP, cholesterol or mortality. | Group-based education improves glycaemic control short and long-term.<br>Some evidence of benefit on self-efficacy, self-management behaviours and body weight Two studies were classified as having a low risk of bias, 12 studies as having moderate risk of bias, and seven studies were classified as having a high-risk of bias. |
| | | | Additional | Suggests the following factors to be associated with reduced effectiveness: reporting theoretical model; combination of different educator types; baseline HbA1c≥7%; include follow-up; completed education delivery in 12 months; 9–12 hours education; family member or friend invited to participate; fewer than 6 or more than 10 sessions Suggests the following factors to be associated with increased effectiveness: diabetes specialist nurse or dietician as only educator; conducted in primary care settings; lasting 1–10 months; provide 19–52 hours education; between 14–18 participants per group; between 6 and 10 sessions | |
| **Van Dam** (2005)[202]** | Social support interventions which may be emotional support, appraisal support, | Six RCTs; 712; 1991–2002 | Narrative synthesis | No beneficial effect of social support on glycaemic control. Findings suggest social support to help increase self-management behaviours, lifestyle adjustments and psychosocial functioning support from spouse may help weight loss in women, but not in men. | Social support does not improve glycaemic control, but may increase self-management behaviours, weight loss and psychosocial well-being. |

| Reference and weighting Outcome | Focus | RCTs, n; Participants, n; Date range | Synthesis | Main results | Main conclusions (review author); *Important quality concerns (review author)* |
|---|---|---|---|---|---|
| | informational support or tangible assistance | | | | |
| **Dorresteijn** (2010)[188]*** | Educational programmes which aim to promote foot self-care and to prevent the occurrence of foot lesions | 11 RCTs; 3114; 1986–2008 | Narrative synthesis | Found foot education interventions not to be associated with increased self-management behaviours. However, small but inconclusive suggestion that intensive educational interventions or foot education tailored to individual needs are associated with increased self-management behaviours. | Foot education not found to be effective; interventions should be tailored or intensive to increase likelihood of changing behaviour. |
| **Li** (2011)[186]** | Educational programmes (or programmes which include education) used for people with DKD | Two RCTs; 207; 2002–5 | Narrative synthesis | Suggest that interventions may improve some aspects of QoL Unclear effects on self-efficacy; some suggestion of benefits for specific forms of self-efficacy Some suggestion of improvement in self-management behaviours.<br>No effect on mortality was found. | Educational programmes for people with DKD may improve some aspects of QoL and self-management behaviours. |
| **Hawthorne** (2008)[195]*** | Education tailored to the cultural or religious beliefs and linguistic skills of the community being approached | 11 RCTs; 1603; 1997–2007 | Meta-analysis | Positive effect of intervention compared with control on HBA1cshort term (WMD –0.6%) and total cholesterol long-term (WMD–0.39 g/dl). No evidence of benefit on QoL, self-efficacy, BP or BMI. | Education tailored to cultural or religious beliefs improves glycaemic control short-term and cholesterol long-term. Better outcomes found when combinations of providers and approaches used.<br>Possible publication bias. |
| | | | Additional | Health educator type appears to make no difference. Better outcomes with combinations of provider and approaches. No difference found between one to one and one to one plus group. | |
| **Khunti** (2008)[196]** | Any educational intervention for migrant South Asian populations | Five RCTs; 1004; 1997–2006 | Narrative synthesis | Suggestion of benefit for improved glycaemic control in the short term, less evidence of benefit longer term Some suggestion of improved BP outcomes Mixed findings for cholesterol, suggests some benefit Mixed findings for weight/BMI, inconclusive, No | Educational interventions for migrant South Asian populations improved glycaemic control in the short term, but not long-term. Also some suggestion of improved BP. |

| Reference and weighting Outcome | Focus | RCTs, n; Participants, n; Date range | Synthesis | Main results | Main conclusions (review author); *Important quality concerns (review author)* |
|---|---|---|---|---|---|
| | | | | difference between group and one to one | |
| **Nam** (2012)[197]*** | Culturally tailored diabetes education interventions | 12 RCTs; 1495; 1997–2009 | Meta-analysis | Overall reduction on HbA1ccompared with control (ES–0.29). No evidence of benefit long-term. | Culturally tailored interventions improve glycaemic control short term. Community-based interventions may have larger benefits than hospital or clinic based. |
| | | | Additional | Suggestion that community-based interventions may lead to larger benefits than hospital based interventions. Suggestion of marginally increased benefit in individual with lower baseline HbA1c. | |
| **Pérez-Escamilla** (2008)[198]* | Peer nutrition education and counselling - delivered to Latinos by community | Two RCTs; 214; 1997–2007 | Narrative synthesis | Inconclusive mixed effects community health workers associated with greater completion rates. | Peer nutrition education had inconclusive mixed effects. |
| **Additional reviews retrieved (QA completed by HIQA)** | | | | | |
| **Pal** (2014) (CR)[179]*** | Computer-based DM self-management interventions | 11 RCTs; 2637 participants | Meta-analysis | Computer-based diabetes self-management interventions to manage T2DM appear to have a small beneficial effect on blood glucose control and the effect was larger in the mobile phone subgroup. | There is no evidence to show benefits in other biological outcomes or any cognitive, behavioural or emotional outcomes.<br>An exploratory analysis which considered which techniques featured most in effective interventions, these included 'prompting self-monitoring of behavioural outcomes and providing feedback on performance.<br>Due to the limitations of the studies reviewed, the authors reported that the effectiveness of existing IT based interventions was unclear and difficult to attribute solely to the interventions. The review concluded that future research efforts needed to focus on methodological issues to produce valid, reliable and generalisable findings. |
| | | 16 RCTs; 3578 participants | Narrative | HRQoL: 5 studies reported this outcome, none showed statistically significant differences. | |
| | | | | Death from any cause: three died in two studies out of the 16 RCTs. | |
| | | | | Cognitions: 4four studies reported positive effects of the interventions on knowledge. | |
| | | | | Self-efficacy: both studies measuring self-efficacy suggested positive effects of interventions. | |
| | | | | Physical activity: There seemed to be difficulty in converting the positive effects on knowledge and self-efficacy into behavioural change such as physical activity: in only two | |

| Reference and weighting Outcome | Focus | RCTs, n; Participants, n; Date range | Synthesis | Main results | Main conclusions (review author); *Important quality concerns (review author)* |
|---|---|---|---|---|---|
| | | | | out of five studies did there appear to an increase in physical activity. The effects of interventions on physical activity were generally mixed. | |
| | | | | Diet: six studies looked at changes in diet and five reported statistically significant improvements. Clinical benefits and impact on health outcomes of these changes is unknown as the effects of interventions on weight or BMI, were not convincing with no statistically significant improvements in weight seen when the results from five studies were combined in a meta-analysis | |
| | | | | Blood pressure: The evidence for computer-based self-management interventions improving blood pressure was mixed. | |
| | | | | Cholesterol: Effects of interventions on cholesterol were mixed. | |
| | | | | Adverse events: 1one study reported a participant withdrawing due to anxiety related to the study. One study noted non-statistically significant increase in minor hypoglycaemic episodes in the intervention group but no difference in major or nocturnal hypoglycaemic episodes. One study specifically reported no adverse events. | |
| **Song** (2014)[182]** | Effect of motivational interviewing on self-management in patients with T2DM | 10 RCTs; 2957 participants | Meta-analysis | | MI was associated with improved self-management abilities among patients with T2DM, and short-term MI (≤6 months) effectively decreased the HbA1c level. The effect of long-term MI (>6 months) on the HbA1c level remains uncertain. Large-scale, higher-quality randomised controlled trials are needed to confirm the present findings. |
| **Antoine** (2014)[183]** | Improving the adherence of | 5 RCTs, 1 cluster RCT; 1025 | Narrative | Six publications were included. Two studies mainly examining educational interventions | Although pharmacist interventions might potentially improve adherence to T2DM |

| Reference and weighting Outcome | Focus | RCTs, n; Participants, n; Date range | Synthesis | Main results | Main conclusions (review author); *Important quality concerns (review author)* |
|---|---|---|---|---|---|
| | T2DM patients with pharmacy care | participants | | showed a significant improvement in adherence. The quality of the included studies was deficient. | medication, high-quality studies are needed to assess effectiveness.<br>A possible limitation is that pharmacists might differ in the way they provide their adherence intervention. |
| **Schellenberg** (2013)[184]*** | Lifestyle Interventions for Patients With and at Risk for T2DM | 2 RCTs; 5305 participants | Meta-analysis | For all-cause mortality, the pooled results showed no difference between the intervention and control groups at more than 10 years of follow-up. The strength of evidence was low for this outcome. | Limitations of this review include low- or insufficient strength evidence for most outcomes across the various interventions. These low grades were driven by high- or unclear risk of bias within individual studies (largely due to inability to blind patients in the treatment group), lack of direct evidence for patient-important outcomes, and lack of consistency and precision among studies. |
| | | 11 RCTs; Number of participants ranged from 72 to 5145 | Narrative | In patients who have T2DM, the evidence for benefit of comprehensive lifestyle interventions on patient-oriented outcomes is less clear. There is no evidence of benefit in all-cause mortality and insufficient evidence to suggest benefit on cardiovascular and microvascular outcomes. Improvement was seen for some secondary outcomes, but it generally did not persist beyond the intervention phase, and the clinical significance is unclear. | |
| **Attridge** (2014) (CR)[185]*** | Culturally appropriate health education for people in ethnic minority groups | 33 RCTs; 7453 participants | Meta-analysis | Glycaemic control (HbA1c) showed improvement following culturally appropriate health education at 3 months (MD -0.4%) and at 6 months (MD -0.5%) post intervention compared with control groups (usual care). Sustained to a lesser extent at 12 months (MD -0.2%). Neutral effects on HRQoL measures were noted and there was a general lack of reporting of adverse events in most studies. | Culturally appropriate health education has short- to medium-term effects on glycaemic control and on knowledge of diabetes and healthy lifestyles. None of the studies were long-term trials, and so clinically important long-term outcomes could not be studied. The heterogeneity of the studies made subgroup comparisons difficult to interpret with confidence. Long-term, standardised, multi-centre RCTs are needed to compare different types and intensities of culturally appropriate health education within defined ethnic minority groups, as the medium-term effects could lead to clinically important health outcomes, if sustained. |
| | | | Narrative | HRQoL: Neutral effects on HRQoL measures were noted and there was a general lack of reporting of adverse events in most studies - the other two primary outcomes for this review. | |

| Reference and weighting Outcome | Focus | RCTs, n; Participants, n; Date range | Synthesis | Main results | Main conclusions (review author); *Important quality concerns (review author)* |
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| | | | | Neutral effects on total cholesterol, low-density lipoprotein (LDL) cholesterol or high-density lipoprotein (HDL) cholesterol were reported at any follow-up point. | |
| | | | | Other outcome measures (blood pressure, body mass index, self-efficacy and empowerment) also showed neutral effects compared with control groups. | |
| | | | | Data on the secondary outcomes of diabetic complications, mortality and health economics were lacking or were insufficient. | |
| **Saffari** (2014)[180] ** | Health education via mobile phones | 10 RCTs; 960 participants | Meta-analysis | HbA1c: Statistically significant effect in favour of health education via mobile phones. Effect greater among studies which used both SMS and internet for health education (n=4RCTs). | The findings of this systematic review and meta-analysis support the hypothesis that health education through mobile text-messaging may help to improve glycemic control in patients with Type2 diabetes. The effect size was greater among studies that used both text-messaging and internet for health education. They noted that although significant in both age brackets, the effect size found in younger patients indicates a higher reduction in HbA1c than in patients over age 55 years. |
| **Cotter** (2014)[177]** | Internet interventions to support lifestyle modification | 8 RCTs (1 quasi-experimental) | Narrative review | Physical activity: 2/8 reported a statistical significant improvement. | Two studies demonstrated improvements in diet and/or physical activity and two studies demonstrated improvements in glycemic control comparing web-based intervention with control. Successful studies were theory-based, included interactive components with tracking and personalised feedback, and provided opportunities for peer support. |
| | | | | Dietary changes: 1/5 reported a statistical significant improvement. | |
| | | | | HbA1c: 2/7 reported a statistical significant improvement. | |
| | | | | BMI: 1/4 reported a statistical significant improvement in weight. | |
| | | | | Diabetes knowledge: | |

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| **Bolen** (2014)[176]*** | Patient activation interventions | 138 RCTs; 33,124 participants | Meta-analysis | A1c: WMD 0.37 %, CI 0.28–0.45 %, $I^2$ 83 %;<br>SBP: WMD 2.2 mmHg, CI 1.0–3.5 mmHg, $I^2$ 72 %;<br>Body weight: WMD 2.3 lbs, CI 1.3–3.2 lbs, $I^2$ 64 %;<br>LDLc: WMD 4.2 mg/dL, CI 1.5–6.9 mg/dL, $I^2$ 64 %]. | Patient activation interventions modestly improve A1c in adults with T2DM without increasing short-term mortality. The evidence was moderate for A1c, low/very low for other intermediate outcomes. Higher baseline A1c, pharmacist-led interventions, and longer follow-up were associated with larger A1c improvements. No intervention strategy outperformed any other in adjusted meta-regression. |
| **Huang** (2015)[178]*** | Telecare interventions | 18 RCTs; 3,798 participants | Meta-analysis | HbA1c: -0.54 95% CI -0.75 to -0.34; p<0.05<br>BMI: -0.59kg/$m^2$ 95% CI -1.52 to 0.34; p=0.21<br>Weight change: 1.01 pounds 95% CI -3.31 to 5.33; p=0.65. | Patients monitored by telecare showed significant improvement in glycemic control in Type 2 diabetes when compared with those monitored by routine follow-up. Subgroup analysis indicate that studies that observed greater reductions in HbA1c levels were associated with Asian populations, small sample size, baseline HbA1c greater than 8.0%, and human calls-based intervention. No effect was observed for automated calls interventions. |
| **Zhai** (2014)[181]*** | Telemedicine | 35 RCTs; 8,149 participants | Meta-analysis | HbA1c: MD -0.37 95% CI -0.49 to -0.25; p<0.001<br>HbA1c (telephone based): MD -0.53 95% CI -0.81 to -0.26; p<0.001<br>HbA1c (internet based): MD -0.62 95% CI -0.82 to -0.42; p<0.001 | Overall, pooled results from the studies revealed a small, but statistically significant, decrease in HbA1c following intervention, compared to conventional treatment.<br>Optimisation of telemedicine approaches could potentially allow for more effective self-management of disease in Type 2 diabetes patients, though evidence to-date is unconvincing. Furthermore, significant publication bias was detected, suggesting that the literature should be interpreted cautiously. |

***Key:** **CCM:** Chronic care model; **ED:** Emergency department; **HCP:** Healthcare professionals; **NNT:** Numbers needed to treat; **OR:** Odds ration; **PEFR:** Peak expiratory flow rate; **QoL:** Quality of life; **RCT:** Randomised controlled trial; **SMD:** Standardised mean difference; **T1DM:** Type 1 diabetes mellitus; **T2DM:** Type 2 diabetes mellitus; **WAPs:** Written action plans.

# Table A7.5 – Appraisal of study quality for included cost-effectiveness studies

| Study | Quality | Reasons for downgrading |
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| **Albisser (2001)** | Low | Longitudinal observation study reporting costs. |
| **Banister (2004)** | Low | Observational cohort study with historical comparison group that reported costs - risk of bias. |
| **Barnett (2007)** | Low | Unclear whether all relevant costs have been identified and included appropriately. Insufficient sensitivity analyses to determine effect of uncertainty. |
| **Biermann (2002)** | Low | Poorly described costing study. Insufficient information to determine perspective and if all relevant costs were included. |
| **Brown (2012)** | Low | Data derived from single trial involving 30 patients receiving the intervention. High-risk of bias. |
| **Brownson (2009)** | Low | It is unclear that discounting has been correctly applied. |
| **Dall (2011)** | Low | Poorly described costing study. Insufficient information to determine if all relevant costs were included. |
| **Farmer (2009)** | High | |
| **Fedder (2003)** | Low | Poorly described costing study. Insufficient information to determine if all relevant costs were included and appropriately interpreted. |
| **Fera (2009)** | Low | Poorly described costing study. No assessment of uncertainty. |
| **Fischer (2012)** | Low | Poorly described costing study. Unclear purpose and design. No assessment of uncertainty. |
| **Garrett (2005)** | Low | Analysis at risk of bias as it is based on pre-post analysis of medical claims data. |
| **Gillespie (2012)** | Moderate | Clinical effectiveness was not shown in the underlying trial. |
| **Gillespie (2014)** | Moderate | Unclear that sensitivity analysis was comprehensive. |
| **Gillett (2010)** | High | |
| **Gilmer (2005)** | Low | Costing study based on small sample with no sensitivity analysis. |
| **Gilmer (2007)** | Low | Figures reported by type of health insurance cover - unclear applicability to Irish setting. |
| **Gordon (2014)** | Low | The validity of the model is unclear as are the sources of the transition probabilities. |
| **Handley (2008)** | Moderate | Unclear that discounting has been appropriately applied. Lack of sensitivity analysis to determine effect of uncertainty. |
| **Ismail (2010)** | High | |
| **Jacobs-van der Bruggen (2009)** | High | |
| **Kesavadev (2012)** | Low | Costing study based retrospective cohort study. |
| **Kruger (2013)** | High | |
| **Kuo (2011)** | Low | The validity of the model is unclear. Inadequate assessment of impact of uncertainty. |
| **Letassy (2003)** | Low | Before and after comparison reporting estimated cost savings. Study design at high-risk of bias. |
| **Mason (2006)** | Low | Study poorly described with inadequate information to determine whether perspective and costs were appropriate. |
| **Molsted (2012)** | Low | Poorly described costing study. Inappropriate design. No assessment of uncertainty. |

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| **Moreno (2009)** | Low | Poorly described study with no analysis of uncertainty. |
| **O'Reilly (2007)** | Low | Model data sourced from single RCT of 401 patients. |
| **Palmas (2010)** | High | |
| **Petkova (2006)** | Low | Inappropriate study design. |
| **Ritzwoller (2011)** | High | |
| **Salzsieder (2011)** | Low | Not all relevant costs identified. Insufficient analysis of uncertainty. |
| **Schechter (2012)** | Low | Not all relevant costs included in the analysis. |
| **Shearer (2004)** | Low | Effectiveness data from single RCT with 169 patients. Inadequate analysis of the impact of uncertainty. |
| **Stock (2010)** | Low | Matched pair wise comparison using registry data and national drug and hospital costs. Design at risk of bias. |
| **Trento (2002)** | Low | Discounting not applied appropriately. No analysis of uncertainty. |
| **Wiegand (2008)** | Low | Presented as preliminary investigation. Poorly described with data sources not clearly listed. |

## Table A7.6 Cost effectiveness studies investigating SMS education programmes in diabetes mellitus

| Study | Intervention | Population | Analysis Details | Clinical & QALY Outcomes | Costs | Results |
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| **Albisser** (2001)[203] | Comparison of education alone, education with self management training and education with computer assisted self care in patients with diabetes | A total of 978 health plan members with diabetes within a mixed model HMO were included in the initiatives for improving blood glucose control. | Country: US<br>Study Type: Longitudinal observational study reporting costs | With the education alone initiative, A1c and body weight were unchanged. When education was supplemented with ongoing self-management training, A1c fell 1.1% ($p<0.01$) and body weight rose by 11 kg ($p<0.01$). When education was supplemented with ongoing computer-assisted self-care, A1c also dropped by 1.1% ($p<0.01$), body weight was unchanged ($p<0.4$) | With the education alone initiative, costs were unchanged. When education is supplemented with ongoing self-management training cost of care increased by $18 per member per month. When education is supplemented with ongoing computer-assisted self-care, cost of care was $1.31 per member per month.<br>(Cost year NR) | The authors concluded that in choosing a diabetes disease management programme, it would appear that costs should be the primary consideration and methodologies that control body weight should be a priority. |
| **Banister** (2004)[204] | Diabetes self-management involving a four hour training session, dietician consultations and monthly support meetings | 70 adults with Type 2 diabetes attending a diabetes self management community clinic in areas below the US federal poverty level. Mean age 49 years. | Country: US<br>Study Type: Observational cohort study with historical comparison group that reported costs | After 2 to 12 months of programme participation, mean A1C improved from 9.7±2.4% to 8.2±2.0% ($p<.001$) | The cost of community clinic DSMT was approximately $280 (€367) per person per year, $185 (€242) for each point reduction in A1C. | The authors concluded that community clinic DSMT can improve glycaemic control at a modest cost. |
| **Brown** (2012)[207] | Lifestyle modification programme led by community health workers | Hispanic adults aged 18 or older with Type 2 diabetes | Country: US<br>Model Type: Mathematical with continuous time<br>Perspective: Societal<br>Discount rate:3% on costs and benefits<br>Time Horizon: 20 years | The analysis used a previously validated mathematical model that projected changes in A1c levels on to future health outcomes and rate of diabetes complications. | Costs of medical treatment and staff costs were taken from the area in which the intervention was carried out (Laredo, Texas). | The ICER in the primary analysis was $33,319 (€30,671)/QALY. The intervention was more cost-effective in the subgroup of people with high glycaemic index (A1c level>9%). |

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| **Brownson** (2009)[208] | CDSM - self-management programmes in primary care settings (different programme in each of four sites) | Patients with Type 2 diabetes living in disadvantaged areas. | Country: US<br>Study Type: CEA using data from four sites (with UKPDS model assumptions)<br>Perspective: health systems perspective<br>Discount rate: 3% costs and benefits<br>Time horizon: diagnosis to age 95 | 14.36 QALYs for usual care, 14.65 QALYs for intervention | Costs: $866 (€999) per annum for intervention; $49,474 (€57,047) or usual care; $61,234 (€70,607) for intervention | The incremental cost-effectiveness ratio was $39,563 (€45,619 /QALY. |
| **Dall** (2011)[209] | Diabetes self management programme involving the posting out of educational materials and telephone counselling once a month | 37,370 people in a health insurance programme for military service personnel, retirees and their dependents in the United States. | Country: US<br>Study Type: Observational cohort study with historical comparison group that reported costs | Participants in the programme were reported to have reduced inpatient bed-days, fewer ED visits, more ambulatory care episodes and greater frequency of testing that historical controls | Total care costs for participants from 2007 and 2008 for hospital care, ED visits, ambulatory care and prescriptions were compared to predicted costs in the absence of the programme, based on historical data | Per-person total saving from participation in the programme were estimated to be $783 (€769), primarily as a result of fewer inpatient days and fewer prescriptions. |
| **Farmer** (2009)[210] | CDSM - Blood glucose self-monitoring with and without an educational component | Patients with non-insulin treated Type 2 diabetes, aged ≥ 25 years and with glycosylated haemoglobin (A1c) ≥ 6.2%. Mean age 65.7 years. | Country: UK<br>Study Type: CEA simulation<br>Perspective: NHS<br>Discount rate: 3.5% costs and benefits<br>Time horizon: lifetime horizon | Utilities at follow-up (and baseline): 0.772 (0.828) for intensive, and 0.761 (0.798) for standard self monitoring. | Intervention cost of £173 (€262) for intensive and £181 (€274) for standard self monitoring. Usual care (with no self monitoring) had an intervention cost of £89 (€135). | The mean estimates suggest that both forms of SMBG are more costly and less effective than standardised usual care, with relatively wide CIs around the point estimates. |
| **Garrett** (2005)[214] | CDSM - pharmacists supported patients through a structured series of visits that focused on knowledge, skills, and performance | Patients with diabetes covered by employers' health plans. Mean age 55 years. | Country: US<br>Study Type: Pre-post analysis of medical claims data<br>Perspective: payer<br>Discount rate: not applicable | Not applicable. | Baseline data: mean total healthcare cost per patient = $8,185.( €9,851)<br>Year one actual = $8,464. ( €10,187)<br>Year one projected = $9,382 (€11,292). | Projected costs for the study year were based on national market changes as agreed to by the pilot site implementation committee employers |

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| | | | Time horizon: mean 10 months after enrolment | | | and health benefit consultants. |
| **Gillespie** (2012)[215] | CDSM – peer support for patients with Type 2 diabetes | Patients with Type 2 diabetes in Irish general Practice. Mean age 64.6 years. | Country: Ireland<br>Study Type: Estimate from RCT data and UKPDS model<br>Perspective: societal provider<br>Discount rate: 3.5% costs and benefits<br>Time horizon: lifetime | Lifetime QALYs: 6.76 for intervention, 6.67 for usual care. | Intervention set-up was €246 (€291) per patient. | The intervention was more effective and less costly than routine care. The intervention is the most cost-effective option at a range of thresholds using both payer and societal perspectives. |
| **Gillespie** (2014)[216] | CDSM – group follow-up post DAFNE facilitated by trained educators using a structured curriculum compared to individual follow-up | Patients with a diagnosis of Type 1 diabetes and who completed the DAFNE programme. Mean age 40.8 years. | Country: Ireland<br>Study Type: trial based CEA<br>Perspective: healthcare provider<br>Discount rate: no discounting applied<br>Time horizon: 18 months | Utilities at 18 month follow-up (and baseline): 0.88 (0.87) for group, and 0.90 (0.88) for individual follow-up. | With respect to total healthcare costs at 18 months, the mean cost per patient was €4,337 (€4,999) for individual follow-up and €3,551 (€4,019) for group follow-up. | Group follow-up is less costly and less beneficial than individual follow-up. At thresholds of €20,000 and €45,000, individual follow-up is the most cost-effective option. At thresholds of €15,000 and less, group follow-up is most cost effective. |
| **Gillett** (2010)[217] | A six hour structured group education programme delivered in the community by two professional healthcare educators | Patients with newly diagnosed Type 2 diabetes in primary care trusts in the UK. Mean age 61 years | Country: UK<br>Model Type: Markov<br>Perspective: NHS<br>Discount rate:3.5% on costs and benefits<br>Time Horizon: 80 years | Estimates of the effect of the intervention were taken from a 12 month RCT carried out in the UK in 2004 (DESMOND trial). This found no significant difference in A1c levels. Long-term outcomes were then modelled using the Sheffield Type 2 diabetes model. | Intervention cost of £203 (€282) per patient. Intervention costs were calculated using data from the 2004 trial. A secondary analysis was carried out that included economy of scale saving associated with larger patient groups. | The ICER based on the DESMOND trial data was estimated to be £5,387 (€7,477)/QALY. In the secondary analysis that included projected savings associated with large scale rollout the ICER was £2,092 (€2,904) /QALY. |

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| **Gilmer** (2005)[218] | CDSM - a combined stepped-care diabetes nurse case management programme and culturally oriented peer-led self-empowerment training program | Uninsured adults with diabetes. Mean age 51.5 years. | Country: US<br>Study Type: pre-post analysis of medical claims data compared to historical controls<br>Perspective: payer<br>Discount rate: not applicable<br>Time horizon: 12 months | Project Dulce participants had reductions in A1c (0.8%), systolic and diastolic blood pressure, total cholesterol, and low-density-lipoprotein cholesterol. | Diabetes management = $507 (€635).<br>Total costs: intervention = $5,711 (€7,150); control = $4,365 (€5,465). | Project Dulce led to improved clinical outcomes for control of diabetes and related conditions in a medically indigent, culturally diverse population. |
| **Gilmer** (2007)[219] | CDSM - a culturally specific diabetes case management and self-management training programme (Project Dulce) | Low-income adults with diabetes. Mean age 51.2 years. | Country: US<br>Model Type: Markov<br>Perspective: Third party payer<br>Discount rate: 3% on costs and benefits<br>Time Horizon: Lifetime | Clinical outcomes were obtained from an observational study involving four cohorts defined by health insurance status, all of which had lower A1c scores following the implementation of the intervention. The intervention was expected to produce QALY gains of between 0.9 to 0.2 QALYs per patient. | Total costs were $1,383( €1,664) higher among participants during the first year of case management, including increased costs of visits to clinicians, participation in group classes, and administrative overheads, pharmaceuticals and supplies; and an offset by reduced hospital and emergency room expenditures. | Costs per QALY were reported by insurance status (increasing wealth): uninsured $10,141(€12,205); CMS $24,584 (€29,588); Medi-Cal $44,941 (€54,088); Commercial $69,587 (€83,750).<br><br>At a threshold of $50,000/QALY, only the commercial cohort has a probability less than 0.5 of being most cost-effective. |
| **Gordon** (2014)[220] | Telephone-linked care intervention for patients with Type 2 diabetes | Simulated cohort of patients with Type 2 diabetes. | Country: Australia<br>Model Type: Markov<br>Perspective: Health Service<br>Discount rate:5% on costs and benefits<br>Time Horizon: 5 years | QALY outcomes were obtained from an RCT that measured QoL using the SF-36. There was no statistically significant difference in SF-6D scores at the end of this study. | All costs were inflated to 2011 Australian dollars. Costs savings associated with the intervention were as a result of lower medication costs across a broad range of medication categories, some of which were unrelated to the intervention | The intervention dominated routine care in the primary analysis (cost saving and generated 0.004 QALYs per person), with a 55% chance of being cost-effective at a WTP threshold of $50,000 (€31,512)/QALY |

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| **Ismail** (2010)[222] | CDSM – motivational enhancement therapy (MET) and cognitive behaviour therapy (CBT) delivered by general nurses with additional training in these techniques | The study population was adults with a confirmed diagnosis of Type 1 diabetes for a minimum duration of 2 years and a current A1c value between 8.2% and 15%. Mean age 36.4 years. | Country: UK<br>Study Type: trial based CEA<br>Perspective: health and social care; and societal<br>Discount rate: not applied<br>Time horizon: 12 months | Mean for first year: MET = 0.77; MET + CBT = 0.782; usual care = 0.789 (all based on EQ-5D) | The unit cost for a 50-minute MET session was estimated at £49 (€74) and £48 (€73) per session including and excluding training, respectively. The respective estimates for a 50-minute session of CBT were £81(€123) and £73 (€111).<br>The average total cost of each treatment approach was approximately £195 (€296) for MET and £660 (€1,003) for MET + CBT. | Results here relate to EQ-5D.<br><br>MET vs. usual care: £48,636 (€73,919)/QALY (payer), £160,750 (€244,316) /QALY (societal).<br><br>MET+CBT vs. usual care: £311,970 (€474,147)/QALY (payer), £271,333 (€412,385)/QALY (societal).<br>MET dominates MET+CBT. |
| **Jacobs-van der Bruggen** (2009)[223] | Lifestyle modification interventions involving at least nutrition or exercise programmes for Type 2 diabetes (seven different interventions were modelled) | Simulated cohort of patients with Type 2 diabetes. | Country: The Netherlands<br>Model Type: Markov<br>Perspective: Health Service<br>Discount Rate: 4% on costs, 1.5% on benefits<br>Time Horizon: Lifetime | All 7 modelled programmes were expected to lead to QALY gains (from 0.1 to 0.14 QALYs per patients). However major uncertainty exists in relation to how long improvements are maintained. | | ICERs for each of the 7 interventions were considered cost-effective (ICERs ranged from €9,000 (€11,414) /QALY to €39,000 (€49,460)/QALY. The ICER for the intervention with the greatest utility gain was €10,000 (€12,682)/QALY. |
| **Kruger** (2013)[225] | Training in flexible intensive insulin therapy as provided in the DAFNE programme, compared with no training | Simulated cohort of adults with Type 1 diabetes. | Country: UK<br>Model Type: Markov<br>Perspective: NHS<br>Discount Rate: 3.5% on costs and benefits<br>Time Horizon: Lifetime | Training was associated with increased life expectancy (0.08 LYG per patient) and an average QALY gain of 0.03 QALYs per patient. | The cost of the intervention was obtained from the literature £359 (€432) per patient. | The ICER for the intervention was estimated to be £14,475 (€17,432)/QALY |

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| **Kuo** (2011)[226] | Chronic care model for diabetes management delivered through a diabetes outreach clinic (DOC) in a medical centre run by the US military compared to usual care based on matched cohort with no access to the DOC. | 9,405 diabetes patients aged 18 year or over. Adult patients (veterans) with a diagnosis of Type 2 diabetes. Mean age 50 years. | Country: US<br>Model Type: Markov<br>Perspective: Health Service and societal<br>Discount rate: 3% on costs and benefits<br>Time Horizon: 20 years | Outcome data was taken from a primary study carried out in the US military setting and from published literature. The base case assumed a 0.3% decrease in A1c. | Treatment costs were taken from the records of the military funded setting, and from published literature. The societal perspective included the cost of patient time and travel costs. | In the primary analysis the ICER from the perspective of the payer was $45,495 (€41,880)/QALY, and from a societal perspective it was $42,051 (€38,709). |
| **Molsted** (2012)[229] | CDSM - an empowerment-based structured diabetes self-management education programme patients with Type 2 diabetes | Patients with Type 2 diabetes, diagnosed at least 12 months before programme start. Mean age 61 years. | Country: Denmark<br>Study Type: costing study<br>Perspective: not reported (assume health system)<br>Discount rate: not applicable<br>Time horizon: 12 months before and after. | Not applicable. | Cost of programme estimated at €489 (€489) per patient. | The intervention can be implemented in a primary care setting and can improve glycaemic control and other metabolic parameters as well as change lifestyle in patients with T2DM. |
| **O'Reilly** (2007)[231] | Multidisciplinary diabetes care programme involving nurse liaison, patient education and the additional of a diabetes tracker component into the patients electronic medical record | Modelled cohort was based on 401 adults with Type 2 diabetes, with a mean age of 61 years. | Country: Canada<br>Model Type: Mathematical model using 18 months of trial data<br>Perspective: Health Service<br>Discount rate:3% on costs and benefits<br>Time Horizon: 40 years | Results of the primary study found that patients who participated in the programme had an average A1c reduction of 1.02%. The long-term implications of this were modelled, using an assumption that the treatment effect persisted for one year | Intervention and care costs were taken from the primary study and from national Canadian data sources (2001 Canadian dollars). | Cost per patient for the intervention was $664 (€525). The ICER for the intervention compared with routine care was estimated at $5,992 (€4,738)/QALY. |

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| **Ritzwoller** (2011)[234] | CDSM – a culturally adapted lifestyle change programme | Latinas with Type 2 diabetes. | Country: US<br>Model Type: trial based costing study<br>Perspective: societal<br>Discount rate: not applicable<br>Time horizon: six months | Not applicable. | Per participant cost of $4,634 (€4,720)<br>Per unit reduction in A1c = $7,723 (€7,866) | Given the benefits of Viva Bien, cost reductions are recommended to enhance its efficiency, adoption, and long-term maintenance without diluting its effectiveness. |
| **Shearer** (2004)[237] | A structured treatment and teaching programme (STTP) combining dietary freedom with insulin adjustment for Type 1 diabetes. | Simulated cohort of patients with Type 1 diabetes | Country: UK<br>Model Type: Markov<br>Perspective: NHS<br>Discount rate:6% on costs and 1.5% on benefits<br>Time Horizon: 10 years | The net survival gain accruing after 10 years is 5.31 life-years per 100 patients (5.16 discounted life-years), which is equivalent to an expected increase in longevity of 19 days per patient. | National UK costs estimates were used, but no year was reported. Discounted over 10 years, STTPs save £2,200 per patient and break even at approximately four years post intervention. | The intervention was the dominant strategy, yielding immediate effectiveness gains and saving money in the long-term. |
| **Stock** (2010)[238] | Incentivised national chronic disease self management programme for diabetes patients. | 19,882 matched pairs from national insurance records | Country: Germany<br>Study Type: Match pair wise comparison using registry data and national drug and hospital costs | The study found a mortality rate of 2.3% in the treatment group, compared to 4.7% in the control group. | Drug and hospital costs, length of hospital stay and average number of hospitalisations were lower from patients participating in the programme. | The mean difference in cost per patient before and after the introduction of the programme was $1,444, (€1,147) compared with $1,890 (€1,501) in the control group. |
| **Trento** (2002)[239] | Lifestyle intervention by group care | Patients with non-insulin-treated Type 2 diabetes (n=56) | Country: Italy<br>Study Design: randomised controlled clinical trial<br>Perspective: Healthcare system and patient<br>Discount Rate: N/A<br>Time Horizon: 4 year | The HR-QOL scores improved with group care but worsened among the control patients. An average of 8.4 patients attended the 12 sessions monitored, resulting in 12.4 min per patient-session or 196 min spent by INHS staff per patient over the study. Seeing | In total, each patient on group care cost US $756.54 (€1,120) and each control US $665.77 (€985), with a difference of US $90.77 (€134) per patient treatment over the observation period. Taking the differential DQOL/Mod score as a proxy outcome, each incremental | Group care by systemic education is feasible in an ordinary diabetes clinic and cost-effective in preventing the deterioration of metabolic control and quality of life in Type 2 diabetes without increasing pharmacological |

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| | | | | patients individually 12.0 minutes per patient, or 150 minutes of INHS staff per patient over the study. | improvement in QoL on group care was obtained with an expenditure of only US $ 2.12 (€3.14). | treatment. |
| **Wiegand** (2008)[240] | CDSM - a behaviour change intervention to enhance medication adherence | Patients aged over 16 years with Type 2 diabetes. | Country: US<br>Study design: theoretical model<br>Perspective: payer<br>Discount rate: not reported<br>Time horizon: 16 years | Not reported. | Annual cost per patient of $29. Assuming 100% medication adherence, potential cost savings of $22,954.<br>(US $ cost year NR) | It appears that the cost to implement this behavioural intervention is reasonable and permits further evaluation in other chronic conditions with notoriously poor adherence levels. |

***KEY: CI**: Confidence Interval; **ICER**: Incremental cost-effectiveness ratio; **NR**: Not reported **QALY**: Quality adjusted life year; **RCT**: Randomised Control trial; **SMS**: Self-management support; **T1DM**: Type I Diabetes Mellitus; **T2DM**: Type II Diabetes Mellitus, **CDSM** – Chronic Disease Self Management; **CBT** – Cognitive behavioural therapy; **WTP** – Willingness to pay; QoL – Quality of life

## Table A7.7 Cost effectiveness studies investigating telemedicine programmes in diabetes mellitus

| Study | Intervention | Population | Analysis Details | Clinical & QALY Outcomes | Costs | Results |
|---|---|---|---|---|---|---|
| **Barnett** (2007)[205] | Telemedicine (home messaging device to monitor veterans with diabetes) | Veterans with diabetes; two or more VA hospitalisations or VA ED visits in the 12 months before enrolment; multiple (>10) medication prescriptions; access to a working telephone line; and were not institutionalised. Mean age 68.2 years. | Country: US<br>Study Type: CEA using data from retrospective cohort<br>Perspective: direct costs to the Department of Veterans Affairs<br>Discount rate: not specified<br>Time horizon: 12 months | Not clearly reported | Not clearly reported | The overall mean ICER for the full sample was $60,941 |
| **Biermann** (2002)[206] | Telemedicine – automated uploading of blood glucose monitor data to a diabetes centre | Patients with diabetes mellitus on intensified insulin therapy. Mean age 30.3 years. | Country: Germany<br>Study Type: trial-based costing study<br>Perspective: not reported<br>Discount rate: not applicable<br>Time horizon: maximum 8 months | Not applicable. | No costs reported. | Not applicable. |
| **Fedder** (2003)[211] | Telemedicine – Community Health Worker Outreach (CHW) programme combining in-home visits and phone calls | Medicaid enrollees with DM. Mean age 57.4 years. | Country: US<br>Study Type: retrospective costing study<br>Perspective: payer<br>Discount rate: not applicable<br>Time horizon: 12 months before and after | Not applicable. | Expenditure per enrolled patient decreased from $8,266 to $6,020. No comparator data provided.<br><br>US $ Cost year NR | The CHW programme resulted in an average savings of $2,245 per patient per year, and a total savings of $262,080 for 117 patients, with improved quality of life (QOL) indicating cost effectiveness. |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Fischer** (2012)[213] | Nurse-Run, Telephone-Based Outreach program | Adults with diabetes at a federally funded community health centre (aged >17 years) (n=762) | Country: US<br>Study Design: Prospective RCT.<br>Perspective: Healthcare system<br>Discount Rate: N/A<br>Time Horizon: 20 months | The intervention group performed significantly better than the usual-care group on our primary outcome, the percent of patients with an LDL less than 100 mg/dL in the preceding year (increased from 52.0% to 58.5% vs. decreased from 55.6% to 46.7%. No change was report in glycaemic control. | Incorporating programme costs, the average cost per patient to the healthcare system was €$6,600 (€7,019) whereas the average cost per patient for those with diabetes not enrolled in the programme was $9,033 (€9,607). The difference in average per patient cost between these two groups was $2,433 (€2,588). | Nurses can improve lipid control in patients with diabetes in a primarily indigent population through telephone care using moderately complex algorithms, but a more targeted approach is warranted. Telephone-based outreach may decrease resource utilisation, but more study is needed. |
| **Handley** (2008)[221] | Telephone self-management support intervention with nurse care management for patients with Type 2 diabetes | 226 primary care patients with Type 2 diabetes with a mean age of 56 years. | Country: US<br>Study Design: RCT<br>Perspective: Health Service<br>Discount Rate: Not reported<br>Time Horizon: 12 month study period | QoL scores for patients in the intervention and control arm were recorded using the SF-36 | Per patients start up costs were $394 (€436) and annual running costs were $388 (€429). All costs were in 2005 USD. | The ICER for the intervention (including start-up costs) compared with routine care was $65,167 (€72,097)/QALY. |
| **Kesavadev** (2012)[224] | Telemedicine - blood glucose self-monitoring supported by the Diabetes Tele-Management System | T2DM patients enrolled in DTMS-based management, 30-75 years old, eligible for a glycosylated haemoglobin (A1c) target <6.5% and actively participating in various components of DTMS | Country: India<br>Model Type: retrospective cohort study<br>Perspective: NR<br>Discount rate: NR<br>Time horizon: 6 months | The mean ± SD A1c value was 8.5 ± 1.4% at the initial visit and was reduced to 6.3 ± 0.6% at 6 months | The recurring extra cost to patient for DTMS, not considering cost of oral drugs and insulin, was equivalent to 9.66 US dollars/month | The intervention appears to be safe and cost-effective in the intensive treatment of T2DM without serious co-morbidities. |

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|---|---|---|---|---|---|---|
| **Mason** (2006)[228] | Telemedicine (via telephone) to support glycaemic control in patients with Type 2 diabetes | 591 patients with Type 2 diabetes, with a mean age of 67 years | Country: UK<br>Study Design: CEA alongside RCT<br>Perspective: NHS<br>Discount Rate: 5% on costs and benefits | Treated patients achieved an average reduction in A1c of 0.31%, giving a number needed to treat to achieve a 1% reduction in A1c of 10 | Annual cost of running the call centre was £93,690 (€148,680).<br>Cost per patient: £1,088 (€1,727) (trial caseload), £714 (€1,133) (routine caseload) | The cost for a 1% reduction in A1c was estimated to be between £1,600 (€2,539) and £3,500 (€5,554), with a corresponding cost per QALY of between £33,700 (€53,480) and £43,400 (€68,873). Based on trial and routine-use estimates, the probability of cost-effectiveness at £30,000 (€47,608)/QALY was 0.10 and 0.29, respectively. |
| **Moreno** (2009)[230] | Diabetes Education and Telemedicine (IDEATel) Home Telemedicine Demonstration | Eligible Medicare beneficiaries with Type 2 diabetes. (n=2169) | Country: US<br>Study Design: RCT<br>Perspective: N/A<br>Discount Rate: N/A<br>Time Horizon: 6 years | N/A | Total intervention costs were $8,924 and $8,437 per person per year for phases I and II, respectively. The savings in total Medicare expenditures in any site or cohort were either nonexistent or too small to offset the high costs of the intervention. | For IDEATel to be cost-effective, the intervention-related costs would have to be drastically reduced, while maintaining clinical impacts. |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Palmas** (2010)[232] | Telemedicine - case management with usual care | Older, ethnically diverse, medically underserved participants with diabetes mellitus in urban and rural settings. Mean age 70.8 years. | Country: US<br>Study Type: trial-based costing study<br>Perspective: payer<br>Discount rate: not applicable<br>Time horizon: 5 years | Not applicable. | Project intervention costs were estimated at $622 (€662) per participant per month of intervention delivered.<br><br>Mean annual payments were estimated as $9,040(€9,615) and $9,669 (€10,284) for the usual care and telemedicine groups, respectively. | In conclusion, telemedicine case management did not reduce Medicare claims for clinical services in the medically underserved older adult population enrolled in the IDEATel project. To be viable and adopted in clinical settings, less costly technology will be required, most likely incorporating mobile phone technology and computers that are owned and maintained by participants. |
| **Salzsieder** (2011)[235] | Telemedicine-based eHealth programs using personalised decision support (PDS) | Adult diabetes patients (n=538) | Country: Germany<br>Study Design: RCT<br>Perspective: Insurer<br>Discount Rate: N/A<br>Time Horizon: 2 years | Significant reductions were found in A1c (7.1% to 6.7%). In contrast, in the group of patients whose physicians denied KADIS-based PDS, the A1c values increased significantly by 0.5% (6.8% to 7.3%). | The cost of the intervention was €2,908 (€2,908). The insurance company revealed an annual cost reduction of about €918 (€918) per participant in the programme. There was an increase in the costs of medication and of costs for financing the telemedicine supported healthcare services, including PDS, provided by the Diabetiva | KADIS-based PDS in combination with telemedicine has high potential to improve the outcome of routine outpatient diabetes care. |

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|---|---|---|---|---|---|---|
| | | | | | programme. These enhanced costs, however, were completely compensated by the reduction in both the number of diabetes- | |
| **Schechter** (2012)[236] | A telephonic behavioural intervention to promote glycaemic control | Adults with Type 2 diabetes | Country: US<br>Model Type: Mathematical<br>Perspective: Health service<br>Discount rate: 0%<br>Time Horizon: 1 year | Results from a previous study involving this intervention showing a 0.36% decrease in A1c were applied. | Staff costs were obtained for 2009 from the US Department of Labour. Telephone charges were also included. | The total cost of the intervention for the telephone group was $180.61 (€172) per person, or $490.58 (€467) per percentage improvement in A1c. |

*__KEY: ICER__: Incremental cost-effectiveness ratio; __NR__: Not reported __QALY__: Quality adjusted life year; __RCT__: Randomised Control trial; __SMS__: Self-management support, __DTMS__: Diabetes Tele Management System; __USD__- US Dollars; __VA__: Veterans Association; __ED__: Emergency Department

## Table A7.8 Cost-effectiveness studies investigating pharmacist programmes in diabetes mellitus

| Study | Intervention | Population | Analysis Details | Clinical & QALY Outcomes | Costs | Results |
|---|---|---|---|---|---|---|
| **Fera** (2009)[212] | Pharmacist - the Diabetes Ten City Challenge (DTCC), a multisite community pharmacy health management programme for patients with diabetes | Patients with diabetes who had baseline and year one medical and pharmacy claims and two or more documented visits with pharmacists. Mean age 57 years. | Country: US<br>Study Type: Pre-post analysis of medical claims data<br>Perspective: payer<br>Discount rate: not applicable<br>Time horizon: 12 months before and after | Not applicable. | Baseline data: mean total healthcare cost per patient = $13,131 (€13,966).<br>Year one actual = $13,829 (€14,708).<br>Year one projected = $14,909 (€15,857). | Positive clinical and economic outcomes were identified for 573 patients who participated in the programme for at least one year, compared with baseline data. |
| **Letassy** (2003)[227] | Pharmacist-led diabetes education programme | 136 patients with Type 2 diabetes, with a mean age of 55 years | Country: US<br>Study Design: Before and after comparison reporting estimated cost savings | After one year the average reduction in A1c was 3.1% | Estimates of the average saving from a sustained 1% A1c reduction were obtained from the literature ($685(€698) per patient per year, 2001 dollars) | The overall cost implications of the intervention were crudely estimated as $244,500 (€320,475) for a cohort of 600 patients |
| **Petkova** (2006)[233] | Five month diabetes educational programme delivered by pharmacists | 24 patients with Type 2 diabetes, with a mean age of 64 years | Country: Bulgaria<br>Study Design: Case series reporting cost data | After six months blood glucose levels had decreased and quality of life scores had increased, compared to the baseline results. | The total cost of the six month programme was €5.95 (€7.28) per person (costs in 2004 Euro) | Total cost of the programme for all 24 patients was €142.80 (€175). The cost per a one mmol/l decrease in blood glucose levels was €7.50 (€9.17). |

## Table A7.9 Cost-effectiveness studies investigating other self-management support programmes in diabetes mellitus

| Study | Intervention | Population | Analysis Details | Clinical & QALY Outcomes | Costs | Results |
|---|---|---|---|---|---|---|
| **Ismail** (2010)[222] | CDSM – motivational enhancement therapy (MET) and cognitive behaviour therapy (CBT) delivered by general nurses with additional training in these techniques | The study population was adults with a confirmed diagnosis of Type 1 diabetes for a minimum duration of two years and a current A1c value between 8.2% and 15%. Mean age 36.4 years. | Country: UK<br>Study Type: trial based CEA<br>Perspective: health and social care; and societal<br>Discount rate: not applied<br>Time horizon: 12 months | Mean for first year: MET = 0.77; MET + CBT = 0.782; usual care = 0.789 (all based on EQ-5D) | The unit cost for a 50-minute MET session was estimated at £49 (€74) and £48 (€73) per session including and excluding training, respectively. The respective estimates for a 50-minute session of CBT were £81(€123) and £73 (€111).<br>The average total cost of each treatment approach was approximately £195 (€296) for MET and £660 (€1,003) for MET + CBT. | Results here relate to EQ-5D.<br><br>MET vs. usual care: £48,636 (€73,919)/QALY (payer), £160,750 (€244,316) /QALY (societal).<br><br>MET+CBT vs. usual care: £311,970 (€474,147)/QALY (payer), £271,333 (€412,385)/QALY (societal).<br>MET dominates MET+CBT. |

*__KEY__: __QALY__: Quality adjusted life year;

# Appendix A8 - Stroke

## Table A8.1 Stroke — results of meta-analyses from PRISMS review and the systematic reviews from the updated search. Table adapted from the PRISMS review

| Reference and weighting outcome | Intervention and comparator | Outcome | Time (from initiation of intervention) | Sample size | Significance [9] | ES (95% CI) |
|---|---|---|---|---|---|---|
| **Aziz** (2008)[265]** | Rehabilitation therapy 1 year post stroke | 1o ADL | 3-12 months | 5 RCTs; 487 participants | 0 | - |
| | | Extended ADL | | | 0 | - |
| | | QoL | | | 0 | - |
| | | 2o Mood | | | 0 | - |
| | | Poor outcome(s) or death | | | + | 0.32 95% CI (0.14 to 0.71) p= 0.03 |
| **Legg** (2006)[267]*** | OT rehabilitation | 1o ADL | 3-12 months | 9 RCTs (8 relevant); 1,258 participants | ++ | Increased ADL scores (SMD 0.18, 95% CI 0.04 to 0.32; p= 0.01). |
| | | Extended ADL | | | + | Increased extended ADL scores (SMD 0.21, 95% CI 0.03 to 0.39; p= 0.02). |
| | | QoL | | | 0 | - |
| | | 2o Mood | | | 0 | - |
| | | Poor outcome(s) or death | | | + | Reduction in odds of poor outcome or death (OR 0.67, 95% CI 0.51 to 0.87; p = 0.003). Reduction in odds of deterioration or death (OR 0.60, 95% CI 0.39 to 0.91; p = 0.02). |
| **OST** (2003)[268]*** | Rehabilitation therapy for cognitive impairment | 1o ADL | 3-12 months | 14 RCTs (11 relevant); 1,617 participants | + | Increased ADL scores (SMD 0.14, 95% CI 0.02 to 0.25; p= 0.02). |
| | | Extended ADL | | | ++ | Increased extended ADL scores (SMD 0.17, 95% CI 0.04 to 0.30; p= 0.01). |
| | | QoL | | | 0 | - |
| | | 2o Mood | | | 0 | - |
| | | Service use | | | 0 | - |
| | | Poor outcome(s) or death | | | ++ | Reduction in odds of a poor outcome or death (OR 0.72, 95% CI 0.57 to 0.92; p = 0.009) |
| **Steultjens** | OT rehabilitation | Comprehensive OT: | NR | 18 RCTs (6 | + | Small but significant ES on ADL (SMD 0.31, 95% CI |

[9] Significance 0 p > 0.05, no evidence of effect; +/– 0.05 ≥ p > 0.01, some evidence of effect in favour of intervention/control; ++/– – 0.01 ≥ p > 0.001, strong evidence of effect in favour of intervention/control; +++/– – – p ≤ 0.001, very strong evidence of effect in favour of intervention/control.

| Reference and weighting outcome | Intervention and comparator | Outcome | Time (from initiation of intervention) | Sample size | Significance [9] | ES (95% CI) |
|---|---|---|---|---|---|---|
| (2003)*** | | 1o ADL | | relevant); 1,825 participants | | 0.03 to 0.60). |
| | | Extended ADL | | | 0 | - |
| | | Community reintegration | | | 0 | - |
| | | Cognitive function: 1o ADL | | | | - |
| | | Training of skills: | | | 0 | - |
| | | 1o ADL | | | + | Significant effect on ADL in one study (SMD 0.46, 95% CI 0.05 to 0.87) |
| **Walker** (2004)[271]*** | OT rehabilitation | 1o ADL | End of intervention 1.25–6months. End of trial 4.5–12 months | 8 RCTs; 1,143 participants | + | Positive effect on ADL (OR 0.71, 95% CI 0.52 to 0.98) at intervention end |
| | | Extended ADL | | | + | Positive effect on extended ADL (WMD 1.30 points, 95% CI 0.47 to 2.13 points) |
| | | Community reintegration | | | + | (WMD 1.51 points, 95% CI 0.24 to 2.79 points) at trial end |
| | | 2o Mood | | | 0 | |
| | | Poor outcome(s) or death | | | 0 | |
| | | OT emphasising ADL: | | | | |
| | | 1o Extended ADL | | | + | Improved extended ADL (WMD 1.61 points, 95% CI 0.72 to 2.49 points). |
| | | Community reintegration | | | 0 | |
| | | OT emphasising leisure: | | | | |
| | | 1o Extended ADL | | | 0 | |
| | | Community reintegration | | | + | Improved community reintegration (WMD 1.96 points, 95% CI 0.27 to 3.66 points) |
| **Ellis** (2010)[274]*** | Stroke liaison | 1o ADL | NR | 16 RCTs; 4,759 participants | 0 | |
| | | Extended ADL | | | 0 | |
| | | Community reintegration | | | 0 | |
| | | QoL | | | 0 | |
| | | 2o Mood | | | 0 | |
| | | Poor outcome(s) or death | | | 0 | |
| | | Education and | | | + | Positive subgroup result for QoL (SMD –0.24, 95% CI – |

| Reference and weighting outcome | Intervention and comparator | Outcome | Time (from initiation of intervention) | Sample size | Significance [9] | ES (95% CI) |
|---|---|---|---|---|---|---|
| | | information emphasis: 1o QoL | | | | 0.44 to –0.04; p = 0.02) |
| | | Barthel Index 15–19: 2o Poor outcome(s) or death | | | ++ | (mild to moderate disability): significant reduction in dependence (OR 0.62, 95% CI 0.44 to 0.87; p= 0.006), death or dependence (OR 0.55, 95% CI 0.38 to 0.81; p= 0.002). Significant subgroup heterogeneity found for Barthel Index 15–19 group (χ2 p < 0.05) |
| **Smith** (2008)[273]*** | Information provision | 1o ADL | 1 week–1 year | 17 RCTs (9 relevant); 2,831 participants | 0 | |
| | | Community reintegration | | | 0 | |
| | | QoL | | | 0 | |
| | | 2o Mood | | | ++ | Clinically small evidence of benefit of information provision on depression scores (WMD –0.52, 95% CI –0.10 to 0.93; p= 0.01, for continuous data outcomes). Active information vs. passive information: active information significantly more effective than passive for patient depression (p < 0.02 for trials reporting dichotomous or continuous data), and anxiety (p < 0.05 dichotomous data, p < 0.01 continuous data) |
| | | Service use | | | 0 | |
| | | Compliance | | | 0 | |
| | | Poor outcome(s) or death | | | 0 | |
| HIQA studies | | | | | | |
| **Cheng** (2014)[259]** | Psychosocial interventions for stroke family caregivers and stroke survivors | Psychosocial wellbeing: effects on caregivers burden | Immediately post-intervention – 4 months | 2 RCTs, 1 quasi-RCT; 167 participants | 0 | SMD: 0.18, 95% CI: -0.13 to 0.48, p = 0.25 |
| | | Psychosocial wellbeing: caregiving competency | | 2 RCTs; 260 participants | 0 | SMD: -0.09, 95% CI: -0.49 to 0.31, p = 0.66 |
| | | Psychosocial wellbeing: depression | | 2 RCTs, 1 quasi-RCT; 178 participants | 0 | SMD: 0.19, 95% CI: -0.11 to 0.48, p = 0.22 |
| | | Family functioning | | 2 RCTs; 186 | + | SMD: -0.12, 95% CI: -0.23 to -0.01, p = 0.03 |

| Reference and weighting outcome | Intervention and comparator | Outcome | Time (from initiation of intervention) | Sample size | Significance [9] | ES (95% CI) |
|---|---|---|---|---|---|---|
| | | | | participants | | |
| **Forster** (2012)[258]*** | Information provision (update to Smith's CR above) | Patient knowledge | 1 week to 1 year (NR in 4 RCTs) | 6 RCTs, 536 participants | ++ | SMD 0.29, 95% CI 0.12 to 0.46, P < 0.001 |
| | | Patient knowledge: Passive v active | | 4 RCTs (passive), 2 RCTs (active) | 0 | SMD 0.26, 95% CI 0.04 to 0.48, active: SMD 0. 34, 95% CI 0.07 to 0.61, test for subgroup differences P = 0.65) |
| | | Anxiety (dichotomised data) | | 6 RCTs, 681 participants | 0 | OR 0.89, 95% CI 0.57 to 1.38, P = 0.60 |
| | | Anxiety (continuous data) | | 7 RCTs, 720 participants | 0 | MD-0.34, 95% CI -1.17 to 0.50, P = 0.43 |
| | | Depression (dichotomised data) | | 8 RCTs, 956 participants | 0 | OR 0.90, 95% CI 0.61 to 1.32, P = 0.59 |
| | | Depression (continuous data) | | 7 RCTs, 720 participants | + | MD -0.52, 95% CI -0.93 to -0.10, P = 0.015 |
| | | Patient satisfaction with information about causes and nature of the stroke | | 5 RCTs, 541 participants | ++ | OR 2.07, 95% CI 1.33 to 3.23, P = 0.001 |
| | | Patient satisfaction with information about allowances and services | | 4 RCTs, 452 participants | 0 | OR 1.18, 95%CI 0.76 to 1.83, P = 0.46 |
| | | Patient satisfaction with information (causes and nature of stroke): Passive v active | | 5 RCTs, 541 participants | 0 | passive: OR 1.86, 95% CI 0.81 to 4.27; active: OR 2.16, 95% CI 1.28 to 3.67, test for subgroup differences P > 0.2 |
| | | Death | | 9 RCTs, 1553 participants | 0 | OR 0.86 95% CI 0.59 to 1.25, P = 0.43 |
| | | Carer knowledge | | 4 RCTs, 336 participants | + | SMD 0.74, 95% CI 0.06 to 1.43, P = 0.03 |
| | | Carer emotional outcome: Psychological distress (dichotomised data) | | 4 RCTs, 498 participants | 0 | OR 1.13, 95% CI 0.65 to 1.97, P = 0.65 |
| | | Carer satisfaction with information about recovery and rehabilitation | | 2 RCTs, 165 participants | 0 | OR 1.78, 95% CI 0.88 to 3.60, P = 0.11 |
| | | Carer satisfaction with | | 3 RCTs, 214 | 0 | OR 1.30, 95% CI 0.71 to 2.37, P = 0.39 |

| Reference and weighting outcome | Intervention and comparator | Outcome | Time (from initiation of intervention) | Sample size | Significance [9] | ES (95% CI) |
|---|---|---|---|---|---|---|
| | | information about allowances and services | | participants | | |
| **Laver** (2013)[251]** | Telerehabilitation (comparator: inperson rehabilitation (usual care) or no rehabilitation) | Independence in ADL | 1-6 months | 2 RCTs, 661 participants | 0 | Case management after discharge -telephone calls and home visits: SMD 0.00, 95% CI -0.15 to 0.15, p=0.99 |
| | | Upper limb function | | 2 RCTs, 46 participants | 0 | Computer software programme to retrain upper limb function: MD 3.65, 95% CI -0.26 to 7.57, p=0.067 |
| **Laver** (2015)[253]*** | Virtual reality rehabilitation (comparator: conventional therapy) | ADL outcome | | 8 RCTs; 253 participants | +++ | SMD: 0.43, 95% CI: 0.18 to 0.69, p=0.00086. (Grade: very low) |
| | | Upper limb function | | 12 RCTs; 397 participants | + | SMD: 0.29, 95% CI: 0.09 to 0.49, p=0.0048 (Grade: low) |
| | | Grip strength | | 2 RCTs; 44 participants | 0 | MD: 3.55, 95% CI -0.20 to 7.30, p=0.063 |
| | | Gait speed | | 3 RCTs; 58 participants | 0 | MD: 0.07, 95% CI: -0.09 to 0.23, p=0.38 (Grade: very low) |
| | | Global motor function | | 2 RCTs; 27 participants | 0 | SMD: 0.14 95% CI: -0.63 to 0.9, p= 0.73. (Grade: very low) |
| **Lennon** (2013)[260]** | Lifestyle interventions for secondary disease prevention | Mortality | | 8 RCTs; 2,478 participants | 0 | RR: 1.13 95% CI: 0.85–1.52, p=0.40 |
| | | CVD events | | 4 RCTs; 1,013 participants | 0 | RR:1.16 95% CI: 0.80–1.71, p=0.43 |
| | | Physical activity participation | | 5 RCTs; 657 participants | ++ | SMD: 0.24 95% CI: 0.08– 0.41, p=0.004 |
| **Zhang** (2013)[250]*** | Stroke rehabilitation in China | Functional outcome (changes in ADL: functional recovery expressed as a change in BI, Barthel Index) | | 31 RCTs; 5,220 participants | +++ | SMD BI: 1.04 (95% CI: 0.88–1.21, P ≤0.001; ($I^2$ = 85.9%; P < 0.001). WMD: 20.6 points (95% CI: 18.7–23.0, P < 0.001). It is noted that a 20-point improvement constitutes an improvement of 1/5th of the potential BI scale. |
| | | Change in impairment (Fugl-Meyer Score, FMS) | | 27 RCTs; 4,501 participants. | +++ | SMD: 1.10 (95% CI, 0.82–1.38, P < 0.001. ($I^2$ = 94.3%; P < 0.001). WMD: 17.2 points (95%CI: 13.5–20.9, P <0.001), with high heterogeneity ($I^2$ = 95.1%; P <0.001). |

**Key: 1o:** Primary; **2o:** Secondary; **ADL:** Activities of Daily Living; **BI:** Barthel Index; **CI:** Confidence Interval; **MD:** Mean Difference; **NR:** Not reported; **OR:** Odds Ratio; **RCT:** Randomised Controlled Trial; **SMD:** Standard Mean Difference; **WMD:** Weighted Mean Difference.

## Table A8.2 Stroke — summary of results from systematic reviews, Table extracted from PRISMS review and systematic reviews from updated search

| Reference and weighting outcome | Focus | Synthesis | RCTs, n; Participants, n; date range | Main results | Main conclusions (review author) |
|---|---|---|---|---|---|
| **Aziz** (2008)[265]** | Rehabilitation therapy one year post stroke | Meta-analysis | 5 RCTs; 487 participants | **Poor outcome(s) or death:** The only positive finding is based on a single study: 0.32 95% CI (0.14 to 0.71) p= 0.03. | Inconclusive evidence whether or not therapy-based rehabilitation intervention one year post-stroke was able to influence any relevant patient outcome |
| **Hoffman** (2010)[266]** | OT rehabilitation for cognitive impairment | Narrative review | 1 RCT (0 relevant); 33 participants | **ADL:** No significant findings to report. | There is a paucity of RCTs evaluating cognitive rehabilitation in stroke survivors as only one RCT was identified |
| **Legg** (2006)[267]*** | OT rehabilitation | Meta-analysis | 9 RCTs (8 relevant); 1,258 participants | **ADL:** Increased scores (SMD 0.18, 95% CI 0.04 to 0.32; p= 0.01). **Extended ADL:** Increased scores (SMD 0.21, 95% CI 0.03 to 0.39; p= 0.02). **Poor outcome or death:** Reduction in odds (OR 0.67, 95% CI 0.51 to 0.87; p = 0.003). **Deterioration or death:** Reduction in odds (OR 0.60, 95% CI 0.39 to 0.91; p = 0.02) | OT rehabilitation has positive outcomes on Extended ADL + personal ADL. |
| **OST** (2003)[268]*** | Rehabilitation therapy for cognitive impairment | Meta-analysis | 14 RCTs (11 relevant); 1,617 participants | **ADL:** Increased scores (SMD 0.14, 95% CI 0.02 to 0.25; p= 0.02). **Extended ADL:** Increased scores (SMD 0.17, 95% CI 0.04 to 0.30; p= 0.01). **Poor outcome or death:** Reduction in odds (OR 0.72, 95% CI 0.57 to 0.92; p = 0.009) | Both positive outcomes indicate therapy-based rehabilitation to have a positive effect on personal ADL. |
| **Poulin** (2012)[269]** | Rehabilitation therapy for cognitive impairment | Narrative review | 3 RCTs (1 relevant); 109 participants | **ADL:** Positive effect on cognitive failures in daily living (ES=0.80; p=0.005). **Extended ADL:** Positive effect (p<0.01). More improvement in problem-solving self-efficacy for face-to-face training vs. intervention delivered via computer assisted training, or online though video conferencing (F=6.45; p=0.003). Positive effect on compliance in activities achieved (z=2.953, p=0.003) | All findings are based on a single study so are taken with caution. Strategy training is the only intervention which meets our definition of self-management support. The review offers some support for the effectiveness of strategy training on improving extended ADL. All RCTs involved individuals in the chronic phase of recovery, highlighting need for research into cognitive rehabilitation at early stages |
| **Steultjens** (2003)[270]*** | OT rehabilitation | Meta-analysis | 18 RCTs (6 relevant); 1,825 | **ADL:** Comprehensive OT subgroup: small but significant ESs on ADL (SMD 0.31, 95% CI 0.03 to | Comprehensive OT (only subgroup we define as self-management support) positively affected more |

| Reference and weighting outcome | Focus | Synthesis | RCTs, n; Participants, n; date range | Main results | Main conclusions (review author) |
|---|---|---|---|---|---|
| | | | participants | 0.60). | outcomes than any other subgroup. Outcomes reported for comprehensive OT are composite of six RCTs. Isolated OT elements were less effective than comprehensive OT; only training of skills found any beneficial effects based on single study so must be taken with caution. No RCTs explored education of family/caregivers by OT. Education provision is an important role of OT, but is unlikely to be done in isolation. This may explain the paucity of RCTs in this area. |
| | | Narrative review | | **ADL:** Training of skills subgroup: significant effect on ADL in one study (SMD 0.46, 95% CI 0.05 to 0.87)<br>**Extended ADL:** Significant effect on extended ADL in another study (SMD 2.29, 95% CI 1.26 to 3.32). | |
| **Walker** (2004)[271]*** | OT rehabilitation | Meta-analysis | 8 RCTs; 1,143 participants | **ADL:** Positive effect on ADL (OR 0.71, 95% CI 0.52 to 0.98) at intervention end.<br>**Extended ADL:** Positive effect on extended ADL (WMD 1.30 points, 95% CI 0.47 to 2.13 points)<br>**Community reintegration:** (WMD 1.51 points, 95% CI 0.24 to 2.79 points) at trial end.<br>**Extended ADL:** OT emphasising ADL subgroup: improved extended ADL (WMD 1.61 points, 95% CI 0.72 to 2.49 points).<br>**Community reintegration:** OT emphasising leisure subgroup: improved reintegration (WMD 1.96 points, 95% CI 0.27 to 3.66 points) | Effect of ADL-based intervention on extended ADL varied by patient age; older patients appeared to benefit more than younger ones (interaction term between age and intervention; p = 0.01). Patients with lower levels of dependency appeared to benefit more in leisure scores (WMD 2.86 points, 95% CI 0.70 to 5.02 points). Duration and intensity of intervention did not appear to mediate effect on primary outcome (data not shown). Review provides support for OT rehab, showing positive effects on extended ADL and leisure scores. Subgroup analysis highlights lack of applicability between OT interventions targeting ADL or leisure |
| **Ellis** (2010)[274]*** | Stroke liaison | Meta-analysis | 16 RCTs; 4759 participants | | No positive overall effects were demonstrated for stroke liaison. Post-hoc analysis found positive effects for those individuals with mild to moderate disability. |
| **Ko** (2010)** | Patient-held medical records | N/A | 0 RCTs; 0 participants | No RCTs were identified which studied the use of patient-held medical records in stroke survivors. This highlights an area of potential stroke self-management where more primary research is required. | |
| **Korpershoek** (2011)[272]* | Self-efficacy enhancing | Narrative review | 4 RCTs (2 relevant); 630 participants | **HRQoL:** Significant positive effect on HRQoL outcomes, including mobility ($p < 0.01$), self-care ($p < 0.001$), thinking ($p < 0.01$) and social roles ($p< 0.001$).<br>Computer generated tailored information: Anxiety scores changed significantly in favour of control (95% CI 0.2 to 2.8; p= 0.03) | Results must be taken with caution: each subgroup represents a single study. From descriptions provided by the review authors we can only be confident of chronic disease self-management course meeting our definition of self-management support. We reject information provision intervention as self-management support because it |

| Reference and weighting outcome | Focus | Synthesis | RCTs, n; Participants, n; date range | Main results | Main conclusions (review author) |
|---|---|---|---|---|---|
| | | | | | was a relatively passive intervention. The chronic disease self-management course shows positive results on a range of HRQoL outcomes, but results from one RCT must be interpreted with caution |
| **Lui** (2005)[275]** | Caregiver problem-solving | Narrative review | 6 RCTs; 1679 participants | **Community reintegration:** Better patient adjustment at 12 months after stroke ($p < 0.01$). Improvement of social outcome in patients with mild disability at 6 months ($p = 0.03$) | Inconclusive evidence. The reported positive results represent only one study each. There is a paucity of evidence exploring caregiver problem-solving that report outcomes on stroke survivors (only three of six RCTs reported outcomes for stroke survivors) |
| **Rae-Grant** (2011)* | Self-management programmes | N/A | 0 RCTs; 0 participants | No RCTs were identified. There is an absence of RCTs explicitly. | |
| **Smith** (2008)[273]*** | Information provision | Meta-analysis | 17 RCTs (9 relevant); 2831 participants | **Depression:** Clinically small evidence of benefit of information provision on depression scores (WMD –0.52, 95% CI –0.10 to 0.93; p= 0.01, for continuous data outcomes)<br>Active information significantly more effective than passive for patient depression ($p < 0.02$ for trials reporting dichotomous or continuous data), and anxiety ($p < 0.05$ dichotomous data, $p < 0.01$ continuous data) | We take active, but not passive, information provision to be self-management support. This review provides evidence that active information has a positive impact on anxiety and depression in stroke survivors |
| | | | | | |
| **Cheng** (2014)[259]** | Psychosocial interventions for stroke family caregivers and stroke survivors | Meta-analysis | 18 RCTs; 3,559 participants | **Family functioning:** Pooled analysis of 2 individual psychoeducation programs showed a small effect on improving family functioning. | Evidence on effects of psychosocial interventions limited. More RCTs of multifaceted psychoeducation programs needed to further examine the optimal dose and format.<br>Caregivers receiving psychoeducation that aimed at equipping caregivers with the skills of problem-solving, caregiving, and stress-coping appeared to have a more positive influence on the caregivers' psychosocial wellbeing and a reduced use of healthcare resources by stroke survivors. |
| | | Narrative review | | **Hospital readmissions:** Stroke survivors in social support group had significantly fewer hospital readmissions (66%) than control group ($p < 0.01$). | |
| | | | | **ED visits:** Fewer stroke survivors in social support group visited ED within 12-months of intervention ($p < 0.01$). | |
| | | | | **Physician visits:** Significantly fewer stroke survivors in psychoeducation group visited physicians at 3-months post-intervention ($p < 0.01$) | |
| | | | | **Placements in residential / nursing home:** | |

| Reference and weighting outcome | Focus | Synthesis | RCTs, n; Participants, n; date range | Main results | Main conclusions (review author) |
|---|---|---|---|---|---|
| | | | | Stroke survivors in individual psychoeducation group had significantly fewer placements in a residential or nursing care home (p = 0.03) at 11- months post-intervention. | |
| | | | | **Remaining at home:** More stroke survivors in psychoeducation group remained at home compared with control group (p = 0.04) at 2-years post-intervention. | |
| **Cheng** (2015)[262]** | Motivational interviewing (MI) | Narrative review | 1 RCT, 411 participants | **ADL, death rate, mood:** No significant differences between groups receiving MI or usual stroke care for participants who were not dependent on others for ADL, nor on the death rate after 3- and 12-month follow-up, but participants receiving MI more likely to have normal mood than those who received usual care at 3- and 12-months follow-up. | There is insufficient evidence to support the use of MI for improving ADL after stroke. Further well designed RCTs are needed. |
| **Dorstyn** (2014)[263]* | Leisure therapy in community based stroke rehab | Narrative review | 8 RCTs; 610 participants | **QoL (SA-SIP):** Treatment gains noted for psychological measures relating to QoL (difference = 2.10, 95% CI 0.84 - 3.37)) immediately post intervention. Medium effect. | The findings of this systematic review are promising and show that leisure therapy helps to optimise the short-term psychological and leisure outcomes of adults who have sustained a stroke. Only 1 RCT assessed effect in longer term (6 months) with no effect. |
| | | | | **Mood – depression:** Depression (Centre for Epidemiological Studies Depression Scale) produced a medium effect (difference = 0.54) in 1 RCT (95% CI 0.05 - 1.03). Medium effect. | |
| | | | | **Leisure activity:** difference range, 0.81 to 1.23) following 2 individually delivered leisure programmes | |
| | | | | **Mobility & independence:** difference = −0.51, 95% CI −0.95 −0.07. Negative effect. | |
| | | | | **Longer-term effects of leisure therapy:** non-significant treatment effects (difference range, −0.07 to 0.13) across individual measures of mood and physical functioning at 6 months following an active leisure rehabilitation program. Large effect. | |
| **Fens** (2013)[264]** | Multidisciplinary care delivered to stroke patients | Narrative review | 14 RCTs; 2,389 participants | **ADL:** None of the studies found an effect of the intervention on daily activities. | The definition of usual care differed considerably between studies, such as outpatient rehabilitation at a day clinic, inpatient case management, care |
| | | | | **QoL:** 2 RCTs reported favourable effects of the | |

| Reference and weighting outcome | Focus | Synthesis | RCTs, n; Participants, n; date range | Main results | Main conclusions (review author) |
|---|---|---|---|---|---|
| | living in the community | | | intervention on QoL.<br>SA-SIP30: Experimental group: 0.8 (SD –), Control:0.71 (SD –) (Significant difference)<br>EQ-5D: Experimental group: 0.71 (IQR 0.59–0.81, Control: 0.54 (IQR 0.26–0.73) (Significant difference). | from a GP, home care services with non-professional support or a service information pack. Little evidence for effectiveness of multidisciplinary care for stroke patients being discharged home. Additional research should provide more insight into potentially effective multidisciplinary care for community living stroke patients. |
| **Forster** (2012)[258]*** | Information provision | Meta-analysis | 21 RCTs; 3,579 participants (2,289 patient; 1,290 carers) | **Patient knowledge, carer knowledge, patient satisfaction, patient depression:** Meta-analyses showed a significant effect in favour of intervention on patient knowledge, carer knowledge, one aspect of patient satisfaction, and patient depression scores. There was no significant effect (P > 0.05) on number of cases of anxiety or depression in patients, carer mood or satisfaction, or death. | There is evidence that information improves patient and carer knowledge of stroke, aspects of patient satisfaction, and reduces patient depression scores. However, the reduction in depression scores was small and may not be clinically significant. Although the best way to provide information is still unclear there is some evidence that strategies that actively involve patients and carers and include planned follow-up for clarification and reinforcement have a greater effect on patient mood. |
| | | Narrative review | | Qualitative analyses found no strong evidence of an effect on other outcomes. | |
| **Laver** (2013)[251]** | Telerehabilitation (comparator: in-person rehabilitation (usual care) or no rehabilitation) | Meta-analysis | 10 RCTs; 933 participants | **ADL:** no statistically significant results for independence in ADL (2 studies, 661 participants) were noted when a case management intervention was evaluated.<br>**Upper limb function:** No statistically significant results (2 studies, 46 participants) were observed when a computer programme was used to remotely retrain upper limb function. **HRQoL / patient satisfaction:** Evidence was insufficient to draw conclusions on effects of intervention on mobility, HRQoL or participant satisfaction with the intervention. | We found insufficient evidence to reach conclusions about the effectiveness of telerehabilitation after stroke. Which intervention approaches are most appropriately adapted to a telerehabilitation approach remain unclear, as does the best way to utilise this approach. |
| | | Narrative | | **Participant satisfaction:** No significant differences between intervention and control groups. | |
| | | | | **Self-reported HRQoL:** 1 study reported that people in the intervention group were more likely to respond to one or more of the outcomes within the SF-36 subscales (OR: 1.41, 95% CI 1.11 to 1.79). | |

| Reference and weighting outcome | Focus | Synthesis | RCTs, n; Participants, n; date range | Main results | Main conclusions (review author) |
|---|---|---|---|---|---|
| **Laver** (2015)[253]*** | Virtual reality rehabilitation (comparator: conventional therapy) | Meta-analysis | 37 RCT; 1,019 participants | **Upper limb function:** Results were statistically significant for upper limb function.<br>**Grip strength, gait speed, global motor function:** There were no statistically significant effects for grip strength, gait speed or global motor function.<br>**ADL:** Results were statistically significant for ADL. | We found evidence that the use of virtual reality and interactive video gaming may be beneficial in improving upper limb function and ADL function when used as an adjunct to usual care (to increase overall therapy time) or when compared with the same dose of conventional therapy. There was insufficient evidence to reach conclusions about the effect of virtual reality and interactive video gaming on grip strength, gait speed or global motor function. It is unclear at present which characteristics of virtual reality are most important and it is unknown whether effects are sustained in the longer term.<br>There were few adverse events reported across studies and those reported were relatively mild. |
| **Lennon** (2013)[249]** | Self-management programmes | Narrative review | 9 RCTs; 1,191 participants | Statistically significant improvement over the control group in measures of: disability and confidence in recovery (n=1 RCT); the stroke-specific QoL sub-scales of family roles ($p < 0.010$) and fine motor tasks ($p < 0.05$) (n=1); stroke knowledge (n=1); the physical component summary of the HRQoL and the Modified Rankin (n=1). | Significant treatment effects in favour of the self-management intervention were found in 6/9 RCTs in this review. However, 2 of these were based on the CCM with no reference to SMS and 2 were not compared to 'usual care'.<br>Randomised controlled studies in this review rated from poor to moderate quality. |
| **Lennon** (2013)[260]** | Lifestyle interventions for secondary disease prevention | Meta-analysis | 17 RCTS; 7,742 participants | **Physical activity participation:**<br>SMD: 0.24 95% CI: 0.08– 0.41, p=0.004.<br>**Mortality, CVD events, physical activity participation:** No significant difference | There is currently insufficient high quality research to support lifestyle interventions post-stroke or TIA on mortality, CVD event rates and cardio-metabolic risk factor profiles. Promising blood pressure reductions were noted in multimodal interventions which addressed lifestyle. |
| **Vallury** (2015)[261]*** | Family-oriented interventions reduce post-stroke depression | Narrative review | 22 RCTs; >3,739 participants | **Depression:** Only five of 22 RCTs reported statistically significant reductions in post-stroke depression among stroke survivors. | Family-oriented models of care can be effective in reducing depression in patients and their caregivers post-stroke. Four reported improved PSD outcomes in stroke survivors only and one had positive impacts on depression for both stroke survivors and their family caregivers. |
| **Warner** (2015)[257]** | SM Programmes | Narrative review | 6 RCTs; only results included | No significant differences in 2 RCTs. Statistically significant difference between intervention (based on | Conclusions are based on a range of study types so are not included here. |

| Reference and weighting outcome | Focus | Synthesis | RCTs, n; Participants, n; date range | Main results | Main conclusions (review author) |
|---|---|---|---|---|---|
| | | | for 3 RCTs in addition to Lennon (2013) above. | Orem) and control in function (FIM) from baseline to 6-month assessment. Also significant differences in global assessment of health, adherence, and psychosocial symptoms. | |
| **Zhang** (2013)[250]*** | Stroke rehabilitation in China | Meta-analysis | 37 RCTs; 5,916 participants | **Functional outcome:** SMD BI: 1.04 (95% CI: 0.88–1.21, P ≤0.001; ($I^2$ = 85.9%; P < 0.001). WMD: 20.6 points (95% CI: 18.7–23.0, P < 0.001). It is noted that a 20-point improvement constitutes an improvement of 1/5th of the potential BI scale. **Change in impairment:** SMD: 1.10 (95% CI, 0.82–1.38, P < 0.001. ($I^2$ = 94.3%; P < 0.001). WMD: 17.2 points (95%CI: 13.5–20.9, P <0.001), with high heterogeneity ($I^2$ = 95·1%; P <0.001). | Data provide some evidence that rehabilitation post-stroke is more effective than no rehabilitation, improving ADL and reducing disability. Although results are limited by low reporting quality and study heterogeneity, conducting research in countries in which rehabilitation is not standard care provides an opportunity to advance our understanding and should be encouraged. There were insufficient data reported on adverse events, deaths, or institutionalisation to allow separate analyses of these variables. The rehabilitation interventions in the Chinese RCTs were often not well described. Many of the trials included also incorporated traditional Chinese therapies such as acupuncture as part of the rehabilitation package. |

**Key 1o:** Primary; **2o:** Secondary; **ADL:** Activities of Daily Living; **BI:** Barthel Index; **CI:** Confidence Interval; **MD:** Mean Difference; **NR:** Not reported; **OR:** Odds Ratio; **RCT:** Randomised Controlled Trial; **SMD:** Standard Mean Difference; **WMD:** Weighted Mean Difference;

## Table A8.3. CEA Studies investigating exercise-based programmes

| Study | Study design | Intervention | Comparators | Population | Findings |
|---|---|---|---|---|---|
| **Huijbregts (2008)**[276] | Non-randomised trial-based costing study with 6 months follow-up (n=30). | Self-management programme with land and water exercise. | Standard education programme. | Stroke survivors at least 3 months post stroke, had completed all active stroke rehabilitation. Mean age 68 years. | The intervention group showed significant improvements in balance. Differences between intervention and control were not significant.<br><br>The intervention cost $384 (€313) per person while routine care cost $105 (€86) per person. |
| **Harrington (2010)**[277] | RCT-based costing study with 12 months follow-up (n=243). | Exercise and education programme. | Routine care. | Stroke survivors at least 50 years old at time of stroke and had returned to living in the community for at least 3 months. Mean age 70 years. | Significant differences between groups on SIPSO scale.<br><br>The intervention cost £250 (€371) per person while routine care cost £99 (€174) per person.<br><br>Participants in the intervention group cost on average £746 (€1,108) (95% CI – £432 to £924) more to care for than those in the control group. |

**Abbreviations**: **RCT**, randomised controlled trial; **SIPSO**, Subjective Index of Physical and Social Outcome.

## Table A8.4 CEA Studies investigating computer-based rehabilitation therapy

| Study | Study design | Intervention | Comparators | Population | Findings |
|---|---|---|---|---|---|
| **Latimer (2013)**[278] | Decision analytic model based on RCT data with 8 months follow-up (n=28). | Self-managed computer therapy. | Routine care (general language stimulation). | Stroke survivors with long-standing aphasia experiencing word-finding difficulties. Mean age 68 years. | The QALYS were 3.07 for controls and 3.22 for intervention, which resulted in an incremental QALY increase of 0.14.<br><br>The total cost was £18,687 (€25,036) for controls and £19,124 (€25,621) for intervention participants.<br><br>The intervention had an ICER of £3,058 (€4,097) compared with usual care. The likelihood of the intervention being cost-effective was 75.8 percent at a cost-effectiveness threshold of £20,000 per QALY gained. |
| **Llorens (2015)**[279] | RCT-based costing study with 3 months follow-up (n=30). | Home-based virtual reality telerehabilitation. | Clinic-based virtual reality telerehabilitation. | Stroke survivors with residual hemiparesis aged 40 to 75 years and at least 6 months post-stroke. Mean age 56 years. | Both intervention and control groups showed significant improvements in balance. No significant differences were found between the groups.<br><br>The mean cost per participant was $836 (€820) for the intervention, and $1,490 (€1,461) for controls.<br><br>Home-based virtual reality telerehabilitation may be less costly and as effective as a clinic-based programme. |

**Abbreviations**: **RCT**, randomised controlled trial; **QALY**, quality-adjusted life year.

# Appendix A9 – Ischaemic heart disease

## Table A9.1 Ischaemic heart disease: results of meta-analyses

| Reference and weighting outcome | Intervention and comparator | Outcome | Time (from initiation of intervention) | Sample size | Significance | ES (95% CI) |
|---|---|---|---|---|---|---|
| **Barth** (2015)[293]*** | Psychosocial interventions for smoking cessation | Abstinence from smoking | 6 to 12 months | 37 RCTs; n=7,682 | +++ | RR 1.22 (95% CI: 1.13 to 1.32) [result with outliers removed] |
| | | | | 31 RCTs, n=4,968 | +++ | More intense interventions: RR 1.28 (95% CI: 1.17 to 1.40) |
| | | | | 5 RCTs, n=2,693 | 0 | Brief interventions: RR 1.01 (95% CI: 0.91 to 1.12) |
| **Brown** (2011)[292]*** | Patient information was the primary intention of the intervention, with a minimum follow-up of 6 months. | Mortality | 6 to 60 months; median 18 months | 6 RCTs; n=2,330 | 0 | RR 0.79 (95% CI: 0.55 to 1.13) |
| | | Myocardial infarction | | 2 RCTs, n=209 | 0 | RR 0.63 (95% CI: 0.26 to 1.48) |
| | | Revascularisation | | 2 RCTs, n=209 | 0 | RR 0.58 (95% CI: 0.26 to 1.48) |
| | | Hospitalisation | | 4 RCTs; n=12,905 | 0 | RR 0.83 (95% CI: 0.65 to 1.07) |
| | | Drop-out | | 8 RCTs; n=2,862 | 0 | RR 1.03 (95% CI: 0.83 to 1.27) |
| **Clark** (2010)[298]** | Home-based (HB) interventions, relating to prevention, rehabilitation and support services. Comparators: usual care (UC), cardiac rehabilitation (CR). | All-cause mortality | 1 to 14 months | 4 RCTs, n=2,510 | 0 | HB vs UC, RR 1.22 (95% CI: 0.83 to 1.80) |
| | | | | 6 RCTs, n=1,548 | 0 | HB vs CR, RR 1.08 (95% CI: 0.73 to 1.60) |
| | | Cardiovascular events | | 5 RCTs, n=2,078 | 0 | HB vs UC, RR 0.91 (95% CI: 0.78 to 1.05) |
| | | | | 3 RCTs, n=778 | 0 | HB vs CR, RR 0.90 (95% CI: 0.33 to 2.43) |
| | | Quality of life | | 5 RCTs, n=644 | + | HB vs UC, WMD 0.23 (95% CI: 0.02 to 0.45) |
| | | | | 5 RCTs, n=1,070 | 0 | HB vs CR, WMD 0.13 (95% CI: -0.03 to 0.30) |
| **Heran** (2011)[296]*** | Exercise-based cardiac rehabilitation: either exercise alone or in combination with | Overall mortality | ≥ 12 months | 16 RCTs, n=5,790 | + | RR 0.87 (95% CI: 0.75 to 0.99) |
| | | Cardiovascular mortality | ≥ 12 months | 12 RCTs, n=4,757 | +++ | RR 0.74 (95% CI: 0.63 to 0.87) |

| Reference and weighting outcome | Intervention and comparator | Outcome | Time (from initiation of intervention) | Sample size | Significance | ES (95% CI) |
|---|---|---|---|---|---|---|
| | psychosocial or educational interventions. Usual care could include standard medical care, such as drug therapy, but did not receive any form of structured exercise training or advice. | Hospital admissions | <12 months | 4 RCTs, n=463 | + | RR 0.69 (95% CI: 0.51 to 0.93) |
| **Huang** (2014)[300]** | Telehealth delivered cardiac rehabilitation | All-cause mortality | 2 to 24 months; one study with six year follow-up | 10 RCTs, n=1,303 | 0 | RR 1.15 (95% CI: 0.61 to 2.19) |
| | | Blood pressure (systolic) | | 6 RCTs, n=903 | 0 | MD -1.27 (95% CI: -3.67 to +1.13) |
| | | Blood pressure (diastolic) | | 5 RCTs, n=777 | 0 | MD 1.00 (95% CI: -0.42 to 2.43) |
| | | Weight | | 5 RCTs, n=532 | 0 | SMD -0.13 (95% CI: -0.30 to 0.05) |
| | | Smoking prevalence | | 5 RCTs, n=856 | 0 | RR 1.03 (95% CI: 0.78 to 1.38) |
| | | Exercise capacity | | 11 RCTs, n=1,269 | 0 | SMD -0.01 (95% CI: -0.12 to 0.10) |
| **Kotb** (2014)[301]** | Telephone support | All-cause mortality | 1.25 to 48 months | 11 RCTs, n=2,937 | 0 | OR 1.12 (95% CI: 0.71 to 1.77) |
| | | Hospitalisation | | 4 RCTs, n=706 | + | OR 0.62 (95% CI: 0.40 to 0.97) |
| | | Smoking cessation | | 6 RCTs, n=1,727 | ++ | OR 1.32 (95% CI: 1.07 to 1.62) |
| | | Depression | | 5 RCTs, n=1,491 | + | SMD -0.10 (95% CI: -0.21 to -0.00) |
| **McGillion** (2014)[294]** | Self-management | Frequency of angina symptoms | Up to 6 months | 7 RCTs, n=732 | +++ | SMD 0.30 (95% CI: 0.14 to 0.47) |
| | | Reduction in SL Nitrate use | | 2 RCTs, n=195 | +++ | SMD -0.49 (95%CI -0.77 to -0.20) |
| | | Physical limitation (SAQ) | | 4 RCTs, n=606 | +++ | SMD 0.38 (95%CI 0.20 to 0.55) |

| Reference and weighting outcome | Intervention and comparator | Outcome | Time (from initiation of intervention) | Sample size | Significance | ES (95% CI) |
|---|---|---|---|---|---|---|
| | | Depression score | | 3 RCTs, n=478 | + | SMD -1.38 (95%CI -2.46 to -0.30) |
| **Neubeck** (2009)[302]** | Telehealth intervention | All-cause mortality | 3 to 48 months | 8 RCTs, n=2,918 | 0 | RR 0.70 (95% CI: 0.45 to 1.10) |
| | | Total cholesterol | | 8 RCTs, n=2,501 | +++ | WMD -0.37 mmmol/L (95% CI: -0.56 to -0.19) |
| | | Blood pressure (systolic) | | 5 RCTs, n=1,728 | +++ | WMD -4.69 mmHg (95% CI: -6.47 to -2.91) |
| | | Smoking prevalence | | 7 RCTs, n=296 | + | RR 0.83 (95% CI: 0.70 to 0.99) |
| **Taylor** (2010)[299]*** | Home-based cardiac rehabilitation programme | Exercise capacity | ≥ 12 months | 3 RCTs, n=1,074 | 0 | SMD 0.11 (95% CI: -0.01 to 0.23) |
| | | Blood pressure (systolic) | < 12 months | 8 RCTs, n=1,053 | 0 | MD 0.58 (95% CI: -3.29 to 4.44) |
| | | Total cholesterol | < 12 months | 7 RCTs, n=1,019 | 0 | MD -0.13 (95% CI: -0.31 to 0.05) |
| | | Smoking prevalence | < 12 months | 5 RCTs, n=922 | 0 | RR 1.00 (95% CI: 0.71 to 1.41) |
| | | Mortality | | 4 RCTs, n=909 | 0 | RR 1.31 (95% CI: 0.65 to 2.66) |
| **Whalley** (2014)[295]** | Psychological interventions in which treatment was delivered directly to patient | All-cause mortality | 6 to 69 months | 17 RCTs, n=6,852 | 0 | RR 0.89 (95% CI: 0.75 to 1.05) |
| | | Cardiac mortality | | 5 RCTs, n=3,893 | + | RR 0.80 (95% CI: 0.64 to 1.00) |
| | | Revascularisation | | 12 RCTs, n=6,670 | 0 | RR 0.95 (95% CI: 0.80 to 1.13) |
| | | Non-fatal MI | | 11 RCTs, n=7,535 | 0 | RR 0.87 (95% CI: 0.67 to 1.13) |
| | | Depression | | 12 RCTs, n=5,041 | ++ | SMD -0.21 (95% CI: -0.35 to -0.08) |
| | | Anxiety | | 8 RCTs, n=2,771 | + | SMD -0.25 (95% CI: -0.48 to -0.03) |
| **Cole** (2011)[303]** | A combination of dietary changes, exercise, education, psychological or | All-cause mortality | 3-5 years | 6 RCTs n=7,053 | ++ | RR 0.75 (95% CI: 0.65 to 0.87) |
| | | Cardiovascular mortality | 2-5 years | 8 RCTs n= 7,188 | ++ | RR 0.63 (95% CI: 0.47 to 0.84) |

| Reference and weighting outcome | Intervention and comparator | Outcome | Time (from initiation of intervention) | Sample size | Significance | ES (95% CI) |
|---|---|---|---|---|---|---|
| | organisational changes. | Non-fatal cardiac events (MI/PCI/CABG/coronary angioplasty) | 1-5 years | 9 RCTs n=13,349 | ++ | RR 0.68 (95% CI: 0.55 to 0.84) |
| **Lawler** (2011)[297]** | Exercise-based cardiac rehabilitation | All-cause mortality | 3 to 120 months | 15 RCTs n=2,547 | + | OR 0.74 (95% CI: 0.58 to 0.95) |
| | | Cardiac mortality | | 18 RCTs n=2,200 | ++ | OR 0.64 (95% CI: 0.46 to 0.88) |
| | | Reinfarction | | 27 RCTs n=4,812 | +++ | OR 0.54 (95% CI: 0.38 to 0.76) |
| **Schadewaldt** (2011)[401]* | Nurse led clinics | Blood pressure (systolic) | 6 to 8 months | 2 RCTs n=260 | 0 | MD -6.59 (95% CI: -18.11 to 4.94) |
| | | Blood pressure (diastolic) | | 2 RCTs n=260 | 0 | MD -6.99 (95% CI: -18.79 to 4.80) |
| | | Total cholesterol | | 2 RCTs n=162 | 0 | MD -0.30 (95% CI: -0.63 to 0.03) |
| | | Smoking cessation | 1 to 3 months | 2 RCTs n=125 | 0 | OR 0.92 (95% CI: 0.72 to 1.17) |

**Key**: **RCT** = randomised controlled trial; **RR** = relative risk; **SMD** = standardised means difference; **WMD** = weighted mean difference.

## Table A9.2 Ischemic heart disease: summary of results from quantitative systematic reviews

| Reference and weighting outcome | Focus | Synthesis | RCTs, n; participants, n; date range | Main results | Main conclusions (review author); important quality concerns (review author) |
|---|---|---|---|---|---|
| **Barth** (2015)[293]*** | Psychosocial interventions for smoking cessation | Meta-analysis | 40 RCTs; n=7,682; 1974-2012 | Positive effect on abstinence after 6 to 12 months (RR 1.22, 95% CI (1.13 to 1.32), I2 54%, Abstinence rate treatment group 46%, Control group 37.4%, Heterogeneity reported as substantial; RR across different intervention strategies were similar (Behavioural, telephone support or self-help); More intense interventions showed increased quit rates (RR 1.28, 95% CI 1.17 to 1.40, I2 58%) compared to brief interventions, which were not effective (RR 1.01, 95% CI 0.91 to 1.12, I2 0%). Long-term follow-up did not show any benefits. | Psychosocial smoking cessation interventions are effective in promoting abstinence up to one year, provided they are of sufficient duration. Favourable effects were reported after one year. |
| **Brown** (2011)[292]*** | Patient information was the primary intention of the intervention, with a minimum follow-up of 6 months. | Meta-analysis | 13 RCTs; n=68,556; 1991-2009 | Mortality (6 Studies): RR 0.79, (95% CI 0.55, 1.13), I2 16%; Myocardial infarction (2 Studies): RR 0.63 (95% CI 0.26, 1.48) I2 0%; Revascularisation (2 Studies): RR 0.58 (95% CI 0.26, 1.48) I2 0%; Hospitalisation (4 Studies) RR 0.83 (95% CI 0.65, 1.07) I2 32%; Drop out (8 Studies) RR 1.03 (95% CI 0.83, 1.27) I2 34%. Heterogeneity reported in outcome measures and reporting methods: Over 60 months, 14 scores were significantly in favour of exercise and 67 scores showed no difference between exercise and control. No studies showed HQRoL scores that favoured the control group. | There was no strong evidence to support the hypothesis that education improves all-cause mortality or cardiac morbidity, at a median of 18 months follow-up, in patients with CHD compared to usual care. The study found that HQRoL scores improved with educational interventions, which may reduce downstream healthcare utilisation and costs. |
| **Clark** (2010)[298]** | Home-based (HB) interventions, relating to prevention, rehabilitation and support services. Comparators: usual care (UC), cardiac | Meta-analysis | 36 RCTs; n=8,297; 1983-2007 | All-cause mortality: HB vs UC (n=2510): RR 1.22 (95%CI 0.83-1.80) I2 = 0%; HB vs CR (n=1548): RR 1.08 (95% CI 0.73-1.60) I2 = 0%; Cardiovascular events: HB vs UC (n=2078): RR 0.91 (95%CI 0.78-1.05) I2 = 0%; HB vs CR (n=778): RR 0.90 (95%CI 0.33-2.43) I2 = 90%; QoL: HB vs UC (n=644) | Home-based interventions for the secondary prevention of CHD showed a number of benefits on the QoL and CHD risk factors when compared to usual care. |

| Reference and weighting outcome | Focus | Synthesis | RCTs, n; participants, n; date range | Main results | Main conclusions (review author); important quality concerns (review author) |
|---|---|---|---|---|---|
| | rehabilitation (CR). | | | 0.23 (95%CI 0.02-0.45), with more significant improvements in short-term effects; HB vs CR (n=1070): RR 0.13 (95%CI -0.03-0.30) not significant. Significant benefits were also noted in resting systolic blood pressure, cholesterol levels, smoking cessation rates and depression scores for home-based interventions over usual care, but not cardiac rehabilitation. | |
| **Cole** (2011)[303]** | Lifestyle and /or behavioural interventions in the primary or community care setting for the secondary prevention of CHD including dietary, exercise, psychological. Educational, multifactorial, organisational interventions vs usual care. | Systematic review | 21 RCTs N=10,799 1993-2010 | All cause mortality RR: 0.75 (95%CI 0.65-0.87) (significant effect observed in 4 of 6 RCTs); Cardiovascular mortality RR: 0.63 (95%CI 0.47-0.84) (significant effect observed in 3 of 8 RCTs); Non-fatal cardiac events RR: 0.68 (95%CI 0.55-0.84) (significant effect observed in 5 of 9 RCTs); | *The effectiveness of lifestyle interventions within secondary prevention of CHD remains unclear. The overall results for modifiable risk factors suggested improvement in dietary and exercise outcomes, but no overall effect on smoking outcomes. The heterogeneity between trials and generally poor quality trials make any concrete conclusions difficult, however the beneficial effects observed are encouraging.* |
| **Heran** (2011)[296]*** | Exercise-based cardiac rehabilitation: either exercise alone or in combination with psychosocial or educational interventions. | Meta-analysis | 47 RCTs; n=10,794; 1975-2008 | Exercise-based cardiac rehabilitation reduced overall and cardiovascular mortality in medium to longer term studies (≥ 12 months follow-up) [RR 0.87 (95% CI 0.75 to 0.99) and 0.74 (95% CI 0.63 to 0.87), respectively]. In the shorter term (< 12 months follow-up), hospital admissions were reduced [RR 0.69 ((5% CI 0.51 to 0.93)]. Cardiac rehabilitation did not reduce the risk of MI, CABG or PTCA. In most trials, HRQoL scores were significantly higher in exercise-based cardiac rehabilitation compared with usual care. | Exercise-based cardiac rehabilitation is effective in reducing hospital admissions in the short term and in reducing total and cardiovascular mortality in the longer term. Population characteristics were predominantly low risk, middle aged males; more representative RCTs in CHD patients required. |

| Reference and weighting outcome | Focus | Synthesis | RCTs, n; participants, n; date range | Main results | Main conclusions (review author); important quality concerns (review author) |
|---|---|---|---|---|---|
| **Huang** (2014)[300]** | Telehealth delivered cardiac rehabilitation | Meta-analysis | 9 RCTs; n=1,546; 1984-2011 | No significant differences were reported between telehealth or centre delivered cardiac rehabilitation: All-cause mortality: RR 1.15 (95% CI 0.61 to 2.19); Blood pressure (Systolic: MD 1.27 (95% CI -3.67 to +1.13; Diastolic: MD 1.00 (95% CI -0.42 to 2.43); Weight SMD -0.13 (95% CI -0.30 to 0.05); Smoking: RR 1.03 (95% CI 0.78 to 1.38); Exercise Capacity SMD -0.01 (95% CI -0.12 to 0.10); lipid profile, quality of life and psychological state. | Telehealth intervention delivered cardiac rehabilitation has similar outcomes to centre-based supervised programmes in low to moderate risk CAD patients. |
| **Kotb** (2014)[301]** | Telephone support | Meta-analysis | 26 RCTs; n=4,081; 1985-2011 | No difference observed for mortality OR 1.12 (95% CI 0.71 to 1.77); Fewer hospitalisations were recorded for intervention group OR 0.62 (95% CI 0.40 to 0.97); Smoking cessation favoured the intervention group: OR 1.32 (95% CI 1.07 to 1.62); Intervention favoured lowering of systolic BP WMD -0.22 (95%CI -0.24 to -0.04); No difference was reported for LDL cholesterol WMD -0.10 (95% CI -0.23 to +0.03). | Regular telephone support and monitoring can reduce certain risk factors in CAD patients; reducing depression, improved control over cardiac risk factors and fewer hospitalisations; thereby potentially reducing some of the burden on the healthcare system. |
| **Lawler** (2011)[297]** | Exercise-based cardiac rehabilitation among post MI patients | Meta-analysis | 34 RCTs N=6,111 1979-2009 | Patients randomised to exercise-based cardiac rehabilitation had a lower risk of all-cause mortality (OR 0.74, 95%CI 0.58-0.95); cardiac mortality (OR 0.64, 95%CI 0.46-0.88); and re-infarction (OR 0.53, 95%CI 0.38-0.76); | *Exercise-based cardiac rehabilitation is associated with reductions in mortality and re-infarction post-MI. Secondary analyses suggest that even shorter CR programmes (1-3 months) may translate into improved long-term outcomes, although these results need to be confirmed in an RCT.* Of note, 89% of included patients were men with mean age 54.7 years - *additional studies are required among women and older patients.* |
| **McGillion** (2014)[294]** | Self-management interventions | Meta-analysis | 9 RCTs; n=1,282; 1994-2012 | Significant improvements were reported for: Frequency of angina symptoms: SMD 0.30 (95% CI 0.14 to 0.47); Reduction in sub- | SM interventions significantly improve angina frequency and physical limitation, reduce sub-lingual nitrate use and improve |

| Reference and weighting outcome | Focus | Synthesis | RCTs, n; participants, n; date range | Main results | Main conclusions (review author); important quality concerns (review author) |
|---|---|---|---|---|---|
| | | | | lingual nitrate use: SMD -0.49 (95%CI -0.77 to -0.20); Physical limitation (SAQ): SMD 0.38 (95%CI 0.20 to 0.55) and Depression scores: SMD -1.38 (95%CI -2.46 to -0.30). No differences were reported between groups on HRQoL dimensions of angina stability, disease perception and treatment satisfaction. | depression scores. |
| **Neubeck** (2009)[302]** | Telehealth Intervention | Meta-analysis | 11 RCTs; n=3,145; 1994-2007 | Intervention was associated with non-significant reduction in all-cause mortality: RR 0.70 (95% CI 0.45 to 1.10); Significant reduction in total cholesterol: WMD 0.37 mmol/L (95% CI 0.19 to 0.56), Systolic BP WMD 4.69 mmHg (95% CI 2.91 to 6.47), fewer smokers RR 0.84 (95% CI 0.65 to 0.98). Favourable changes were also found in HDL and LDL levels. | Effective risk factor reduction was observed with the use of telehealth interventions. Optimal frequency or duration of interventions to improve cardiovascular risk profiles was not established. The improvement in survival observed, although non-significant, would benefit from larger trial to improve statistical power to establish effect. |
| **Schadewaldt** (2011)[401]* | Nurse-led clinics for patients with coronary heart disease (adults admitted to a hospital or general practice with newly diagnosed or existing CHD) comprising health education, counselling behaviour change and promotion of a healthy lifestyle vs. usual care | Systematic review and meta-analysis | 7 RCTs N=3,246 1998-2007 | No pooling of data was possible for short-term BP results up to 6-mo f/u ;<br>No difference in BP at 6-8mo f/u (systolic p=0.26, diastolic p=0.25);<br>No improvements in long term BP outcomes, in total cholesterol, or HDL levels; No difference in smoking cessation in short term; or in body weight in short or long term; equivocal results for improvements in medication compliance reported in individual studies (n=2) variable results for improvements in quality of life (SF36) with improvements noted in four of eight domains up to one year. | *The results indicated that care was equivalent to non-nurse managed clinics, and there was no greater risk of poorer outcomes in the nurse-led clinics. The effectiveness of the clinics may depend on the intensity of nursing support. The combination of counselling and regular assessment of risk factors and health status delivered at nurse-led clinics is supported by the available research, and given equivalent outcomes with non-nurse led clinic. Further research should investigate the cost-effectiveness of the different models of care.*<br>Although conclusions compared nurse-led clinics with other clinics, standard of care described in the included RCTs was 'no clinic'. |

| Reference and weighting outcome | Focus | Synthesis | RCTs, n; participants, n; date range | Main results | Main conclusions (review author); important quality concerns (review author) |
|---|---|---|---|---|---|
| **Taylor** (2010)[299]*** | Home-based cardiac rehabilitation programme | Meta-analysis | 12 RCTs; n=1,938; 1984-2007 | No differences in outcomes of home versus centre-based cardiac rehabilitation programmes were reported with respect to mortality risk, cardiac events, exercise capacity or in modifiable risk factors (systolic BP, diastolic BP, total cholesterol, HDL and LDL cholesterol, in the proportion of smokers at follow up or in HRQoL scores. No consistent difference in healthcare costs was observed. | Home and centre-based cardiac rehabilitation appear to be equally effective in improving clinical and HRQoL outcomes in acute MI and revascularisation patients. Home based cardiac-rehabilitation would support greater choice for patients' preferences, which may improve cardiac rehabilitation uptake. |
| **Whalley** (2014)[295]** | Psychological interventions in which treatment was delivered directly to patient | Meta-analysis | 26 RCTs; n=9,296; 1984-2008 | There was no evidence of significant effect on all-cause mortality: RR 0.89 (95% CI 0.75 to 1.05). There was some evidence of reduced cardiac mortality: RR 0.80 (95% CI 0.64 to 1.00). There was no evidence of significant effect on revascularisation or non-fatal MI. A significant reduction in depression was observed: SMD -0.21 (95% CI -0.35 to -0.08); and anxiety: SMD -0.25 (95%CI -0.48 to -0.03). | Psychological interventions appear effective in treating psychological symptoms of CAD patients. There is uncertainty about differential benefit with respect to patient subgroups and the most successful intervention characteristics. |

**Key**: **BP** = blood pressure; **CABG** = coronary artery bypass graft; **CAD** = coronary artery disease; **CHD** = coronary heart disease; **CR** = Cochrane review; **HDL** = high-density lipoprotein; **HRQoL** = health-related quality of life; **LDL** = low-density lipoprotein; **MI** = myocardial infarction; **PTCA** = percutaneous transluminal coronary angioplasty; **QoL** = quality of life; **RCT** = randomised controlled trial; **RR** = relative risk; **SM** = self-management; **SMD** = standardised means difference; **WMD** = weighted mean difference.

## Table A9.3 Summary of cost-effectiveness studies for cardiac rehabilitation

| Study | Intervention | Population | Analysis details | Clinical and QALY Outcomes | Costs | Authors' conclusions |
|---|---|---|---|---|---|---|
| **Ballegaard** (2004)[304] | Integrated rehabilitation (IR) (Acupuncture, self care programme, stress management and lifestyle adjustments) | 168 patients with severe angina pectoris (no high risk patients were included) | Country: Data from US but adopted to Danish population<br>Study Design: Retrospective cohort study Perspective: health care<br>Discount rate: NA<br>Time horizon: 13.5 year<br>Costs: 1999 Danish Krone | The three year accumulated risk of death was 2.0% for patients requiring invasive treatment compared to 6.4% in the general Danish population. After the 3 year follow up the IR group had a reduction of 96% in hospitalisations, 88% reduction in family doctor visits, 84% reduction in heart failure specialist visits and medication expenditure fell by 78%. | Cost savings for the IR group were US$12,000 (€10,518) and US$7,500 (€6,574) yearly per patient, respectively for patients who did and did not proceed to surgery. Cost savings over 3 years were US$36,000 (€31,555) for surgical and US$22,000 (€19,284) for non-surgical patients. | IR reduced the risk of dying and the need for invasive treatment among patients with severe angina pectoris. |
| **Briffa** (2005)[307] | 18 sessions of Cardiac rehabilitation (CR) versus conventional care | 113 CAD patients aged 41–75 years who experienced an acute coronary syndrome, were self-caring and literate in English. | Country: Australia<br>Study Design: RCT<br>Perspective: health system<br>Discount rate: NA<br>Time horizon: 1 year<br>Costs: 1998 AUSD | At 6 months, the mean incremental improvement in health utility was 0.012 for conventional care and 0.016 for rehabilitation care, respectively. At 12 months, there was a non-significant improvement from baseline of 0.010 in conventional care and a significant improvement of 0.026 in rehabilitation care. | Estimated base-case incremental cost per QALY saved for CR was AUS$42,535 (€43,589), when modelling included treatment effect on survival. This increased to AUS$70,580 (€72,330) per QALY saved if survival effect not included. | The findings of the study strengthen the case for rehabilitation services to be made available and routinely offered to all survivors of acute coronary syndromes. The advantages in QOL were mostly non-significant, but the cost of delivering rehabilitation was low. |
| **Dendale** (2008)[308] | Cardiac rehabilitation | Patients post percutaneous coronary intervention (PCI) | Country: Belgium<br>Study Design: CBA<br>Perspective: Health care provider<br>Discount rate: NR<br>Time horizon: 4.5 year<br>Costs: 2005 euro | CR resulted in a significant reduction in hospitalisations for angina (75% vs 45%) and coronary revascularisations (17% vs 7%); however a significant increase in MI was reported (2.5% vs 7.5%). Overall, reported incidence of cardiac events were IG 0.93 events/patient and CG 1.52 events/patient. | Cost of one CR session was €23.25 (€27) per patient. The total health care cost (including cost of CR) at 4.5 years was €4,862 (€5655)/patient in IG compared with €5,498 (€6395)/patient in CG. | CR following PCI significantly reduces the number of cardiac events and results in costs savings for the health payer. |

| Study | Intervention | Population | Analysis details | Clinical and QALY Outcomes | Costs | Authors' conclusions |
|---|---|---|---|---|---|---|
| **Jolly** (2007)[311] | Home-based programme of cardiac rehabilitation using the Heart Manual, compared with centre-based programmes. | Patients who experienced an MI or coronary revascularisation within the previous 12 weeks from four hospitals in predominantly inner-city, multi-ethnic, socio-economically deprived areas | Country: UK<br>Study Design: RCT<br>Perspective: Societal<br>Discount rate: NR<br>Time horizon: 24 month<br>Costs: 2001 GBP | At all three follow-up points no clinically or statistically significant differences were found in any of the primary outcome measures between the home- and centre-based groups or in any of the secondary outcomes. QALYS reported after 24 months for home based and centre based were .731 and .753 a difference of 0.022 | The mean cost per patient referred to CR in the home-based arm was £198 (€337), approximately 25% above that of the hospital arm of £157 (€267). From an NHS perspective, the home-based arm was more costly than the hospital-based arm. From a societal perspective, however, the inclusion of patient travel costs and travel time increased the mean cost of the hospital-based arm to £181 (€308). | For low- to moderate-risk patients following CAD event, a home-based cardiac rehabilitation programme does not produce inferior outcomes compared with the traditional centre-based programmes. With the level of home visiting in this trial, the home-based programme was more costly to the health service, but with the difference in costs borne by patients attending centre-based programmes. |
| **Marchionni** (2003)[402] | Cardiac rehab (exercise program)<br><br>1)hospital-based CR (Hosp-CR)<br><br>2)home-based CR (Home-CR)<br><br>3) no CR | 270 post myocardial infraction patients without cardiac failure, dementia, disability, or contraindications to exercise | Country: Italy<br>Study design: RCT<br>Perspective: Healthcare<br>Discount rate: N/A<br>Time horizon: 14 month<br><br>Costs: USD 2000 | TWC improved in the Hosp-CR and Home-CR groups but not in controls, with no significant difference between Hosp-CR and Home- CR. In middle-aged and old patients, HRQL improved significantly over the entire study duration regardless of treatment assignment, whereas in very old patients, HRQL improved significantly with either active treatment but not with no CR | Direct costs, calculated as the sum of CR programme and healthcare utilisation costs over the study duration, amounted to $21,298 (€26.234) ($8,841±$12,457) for Hosp- CR, $13,246 (€16,316) ($1,650±$11,596) for Home-CR, and $12,433 (€15,315) (healthcare utilisation costs only) for no CR. Fewer medical visits (6.5±0.5 versus 7.1±0.6 versus 9.2±0.9, *P*=0.018) and rehospitalisations (0.33±0.07 versus 0.46±0.10 versus 0.49±0.10, *P*=0.492) in Home-CR compared with Hosp-CR and no-CR patients | Post-MI Hosp-CR and Home-CR are similarly effective in the short term and improve TWC and HRQL in each age group. However, with lower costs and more prolonged positive effects, Home-CR may be the treatment of choice in low-risk older patients. |

| Study | Intervention | Population | Analysis details | Clinical and QALY Outcomes | Costs | Authors' conclusions |
|---|---|---|---|---|---|---|
| | | | | | contributed, at least in part, to produce the differences. | |
| **Reid** (2005)[313] | Cardiac rehabilitation (CR) (standard (33 sessions for 3 months) versus distributed (33 sessions for 12 months) | 392 patients with severe CAD | Country: Canada<br>Study Design: RCT<br>Perspective: Health system<br>Discount rate: 5%<br>Time horizon: 24 month<br>Costs: 2004 USD | There were no clinically meaningful or statistically significant between group differences for outcomes at 12 or 24 months. Both groups showed improvements over time in cardio respiratory fitness, daily physical activity, low-density lipoprotein cholesterol, generic and heart disease HRQL, and depressive symptoms. | At 2 years, the total direct costs of DCR were $5,267 (€6,073)<br>($759 [€875] for programme delivery + $4508 [€5198] for cardiac health care costs) versus $5132 (€5,918 ) for SCR ($681 [€785] for programme delivery + $4451 [€5,132] for cardiac health care costs) | Our data indicate that there are no clinically meaningful or statistically significant differences between a standard 3-month, 33-session programme of CR and one that has the same number of contacts distributed over a 12-month period. |
| **Taylor** (2007)[315] | Home-based versus hospital-based rehabilitation | 104 patients with an uncomplicated acute myocardial infarction and without major co morbidity | Country: UK<br>Study Design: CEA<br>Perspective: Health service<br>Discount rate: NA<br>Time horizon: 9 month<br>Costs: 2002 GBP | Mean utility values for the home and hospital groups were comparable at baseline (0.76 vs. 0.74), and 9 months (0.74 vs 0.78). Although there was a small mean QALY gain from baseline to nine months for the hospital-based group and a small QALY loss for the home based group, no significant difference was seen between the groups (−0.06) | The mean cost of cardiac rehabilitation was lower by £30 (€51) per patient for the home-based group than the hospital-based group. This difference was primarily the result of reduced personnel costs. the overall healthcare costs of the home-based and hospital-based groups did not differ significantly | Although the mean QALY and healthcare cost favoured the hospital group, the difference in QALYs and costs between groups was small and was highly variable. Individual simulations included all four-quadrants of the cost effectiveness plane and ranged from a small QALY gain and lower cost in favour of hospital to a small QALY gain and lower cost in favour of home. Results were similar for each group. |

## Table A9.4 Summary of cost-effectiveness studies for telemedicine

| Study | Intervention | Population | Analysis details | Clinical and QALY Outcomes | Costs | Authors' conclusions |
|---|---|---|---|---|---|---|
| **Berndt** (2015)[306] | Smoking cessation counselling delivered via usual care (UC) (n=245), vs. telephone counselling (TC) (n=223) or face-to-face counselling (FC)(n=157). TC and FC arms included access to nicotine replacement therapy | Patients over 18 recently hospitalised and who smoked on average >5 cigarettes per day prior to admission or quit smoking < 4 weeks prior to admission | Country: Netherlands<br>Study Design: RCT with 6months follow-up<br>Perspective: Societal<br>Discount rate: NA<br>Time horizon: 6 month<br>Costs: 2011 Euro | Compared with UC, a significantly higher proportion of patients in the TC and FC groups achieved continued abstinence (37.9%, 54.1%, 51.6%, respectively) and 7-day abstinence (41.5, 57.1, 54.9, respectively). Reported QALYS for UC TC AND FC were 0.489, 0.491 and 0.487, respectively. | Societal costs over the 6-month follow-up period were lowest in the TC group at €8,124 (€8,293), compared to €8,988 (€9,175) in the FC group and €9,181 (€9,372) in the UC group. | TC dominated (more effective and less costly) UC and FC. FC was dominated by UC, since FC was more costly and reached somewhat lower effects in QALYs gained compared to UC. Assuming a willingness-to-pay of €20,000/ abstinent patient, telephone counselling would be a highly cost-effective smoking cessation intervention assisting cardiac patients to quit. |
| **Turkstra** (2013)[316] | Telephone delivered CHD secondary prevention programme (ProActive Heart [HC]) | 430 adult myocardial infarction patients | Country: Australia<br>Study Design: RCT<br>Perspective: Health care<br>Discount rate: NA<br>Time horizon: 12 month<br>Costs: 2008 AUSD | Incremental health status after 12 months was 0.132 for HC and 0.120 for usual care. The incremental effectiveness was 0.012 QALYs | Higher hospitalisation ($6,841 vs. $4,984 [€4,893 vs. €3,565]) and total treatment cost ($10,574 versus $8,534 [€7,563 versus €6,104]) were observed for patients randomised to receive HC versus usual care. The incremental cost was $2,040 (€1,459). The cost of the health coaching sessions was $37 (€26) per session. | The incremental cost-effectiveness ratio (ICER) of HC vs. usual care for patients with a recent MI was $85,423 (€61,102)/QALY. ProActive Heart, was not a cost-effective intervention in the short-term compared to UC. There was no significant improvement in utility and it resulted in significantly increased costs. |

## Table A9.5 Summary of cost-effectiveness studies for case management

| Study | Intervention | Population | Analysis details | Clinical and QALY outcomes | Costs | Authors' conclusions |
|---|---|---|---|---|---|---|
| **Seidl** (2014)[314] | Nurse-based case management | Elderly (≥65 years) patients with myocardial infarction | Country: Germany<br>Study Design: RCT<br>Perspective: Societal<br>Discount rate: NA<br>Time horizon: 12 month<br>Costs: 2010 Euro | The mean QALY difference, adjusted for gender, age in groups and number of co morbidities, between the intervention and control groups was -0.0163. Utility scores from EQ-5D-3L were significantly increased in the intervention group at month 3 (0.077) and month 6 (0.0509), but returned towards baseline levels in month 12. | Cost of the intervention was €130(€145)/patient. Total costs for the intervention and control groups were €8,289 and €8,880 (€9223 and €9881). The adjusted overall cost difference was estimated at €17.61 (€20). The ICER was calculated to be €1,080 (€1202)/QALY, representing the savings per additional QALY lost. | In conclusion, the KORINNA study failed to show that the case management intervention was an effective and cost effective alternative to usual care within a time horizon of one year. |
| **Barley** (2014)[305] | UPBEAT Nurse-Delivered Personalised Care (PC) Intervention (standardised, face to face, bio-psychosocial assessment) with telephone follow-up | Adults with symptomatic CHD, reporting depression symptoms were eligible | Country: UK<br>Study Design: RCT<br>Perspective: Healthcare<br>Discount rate: NA<br>Time horizon: 12 month<br>Costs: 2010 GBP | The average EQ-5D utility scores at baseline were slightly higher for the PC group, although the difference between groups was not statistically significant In terms of QALYs, the control group showed an incremental QALY gain of 0.038 compared to personalised care over the 12-month treatment period. | (Total cost PC vs control, mean: baseline £1,773 vs £3,604[€2,322 vs €4,721]; 6 months £832 vs £1,191[€1,090 vs €1,560]; 12 months £1,088 vs £2,014[€1,425 vs €2,638]) Hospital services were used more intensively by the control group than the PC group at all time points, and as a result recorded higher inpatient costs. For the PC group, the intervention itself accounted only for 6.7% of total costs. | Cost-utility results yielded an incremental cost-effectiveness ratio (ICER) of £29,921 (€39,193) per additional QALY. The point estimate of the incremental cost-effectiveness ratio falls in the south-western (SW) quadrant, representing the situation where the PC group has reduced costs and worse outcomes. |

## Table A9.6 Summary of cost-effectiveness studies for other self-management support interventions

| Study | Intervention | Population | Analysis details | Clinical and QALY outcomes | Costs | Authors' conclusions |
|---|---|---|---|---|---|---|
| **Furze** (2012)[309] | Lay-facilitated angina management programme (LAMP) vs routine care | Participants with new stable angina (n=142) | Country: UK<br>Study Design: RCT<br>Perspective: NHS<br>Discount rate: NA<br>Time horizon: 6 Month<br>Costs: 2008 GBP | There was no important difference in angina frequency at 6 months. The LAMP group had significantly higher quality of life as measured by EQ-5D index scores, at both 3 months = 0.82 vs. 0.70 and at 6 months = 0.82 vs. 0.68. There was a statistically significant difference in average QALY per patient of 0.045. | A total of six lay facilitators were recruited in the LAMP trial and each cost £179 (€248) for training. The average cost per patient in the control group was £1,259 (€1743) whilst in the intervention group it was £1,496 (€2071). the average incremental net benefit of LAMP over control was positive (£354.60 [€490.60]). | The intervention was found to be cost-effective and at a willingness-to-pay (WTP) threshold of £20,000 (€27,680) the probability of LAMP being cost-effective is 80%, increasing to 90% at a threshold of £30,000 (€41,521) /QALY |
| **Ito** (2012)[310] | The study evaluated mailed education, disease management, polypill use, and combinations of these interventions | Hypothetical cohort of patients' post-myocardial infarction. | Country: USA<br>Study Design: Markov<br>Perspective: Societal<br>Discount rate: 3%<br>Time horizon: Lifetime<br>Costs: 2010 USD | All interventions had a higher total QALY gain than usual care which had a QALY of 4.4756 while the interventions ranged from 4.4848 to 4.5235. | The calculated cost per QALY gained were mailed education plus disease management $74,600 (€68,672), disease management $69,200 (€63,701), polypill use $133,000 (€122,431), polypill use plus mailed education $113,000 (€104,020), polypill plus disease management $142,900 (€131,544). Mailed education was the only intervention with an ICER <$100,000 (€92,053) per QALY. | Mailed education and a polypill, once available, may be cost-saving strategies for improving post-MI medication adherence. |
| **Ladapo** (2011)[312] | Nurse-led smoking cessation counselling plus post-discharge follow-up | Hypothetical US cohort of 327,600 smokers hospitalised with AMI. | Country: US<br>Study Design: Monte Carlo model<br>Perspective: Societal<br>Discount rate: 3% | Both patients in both groups experienced a decrease in QALYs however there was 32,950 additional patients who resulted in a QALY loss | The intervention was estimated to cost US$27.3 (€27) per patient per year; however, the intervention resulted in a decrease in | Nurse-led smoking cessation counselling with post-discharge follow-up has the potential to be cost-effective relative to |

| Study | Intervention | Population | Analysis details | Clinical and QALY outcomes | Costs | Authors' conclusions |
|---|---|---|---|---|---|---|
| | | | Time horizon: 10 year<br><br>Costs: 2008 USD | in the control group (154,700 vs 121,700). The control group also had higher numbers of death, AMI episodes, more continued to smoke and there was greater number of patients with life years lost. | total health costs of $894 (€878). The programme would cost $540 (€530) per quitter and $19,800 (€19,447) per AMI avoided (considering only intervention costs), and the cost-effectiveness would be $4,350 (€4,272) per life-year and $5,050 (€4,960) per QALY (considering all health care costs). | the standard of care and may lead to significant reductions in the incidence of smoking and its associated adverse health events and social costs. |
| **Raftery** (2005)[317] | Nurse led secondary prevention clinics for coronary heart disease | 1343 patients (673 in intervention group and 670 in control group) aged under 80 years with a diagnosis of coronary heart disease but without terminal illness or dementia and not housebound. | Country: UK<br>Study Design: CEA alongside RCT<br>Perspective: Societal<br>Discount rate: 3.5%<br>Time horizon: 4.7 years RCT follow up<br>Costs: 1999 GBP | Overall, 28 fewer deaths occurred in the intervention group leading to a gain in mean life years per patient of 0.110 and of 0.124 QALYs. | The cost of the intervention (clinics and drugs) was £136 (€251) per patient higher in the intervention group, but the difference in other NHS costs, although lower for the intervention group, was not statistically significant. The incremental cost per life year saved was £1236 (€2,282) and that per QALY was £1097 (€2,025). | Nurse led clinics for the secondary prevention of coronary heart disease in primary care seem to be cost effective compared with most interventions in health care, with the main gains in life years saved. |

# Appendix A10 - Hypertension

## Table A10.1 Results of meta-analyses from PRISMS review and the systematic reviews from the updated search. Table adapted from the PRISMS review

| Reference and weighting outcome | Intervention and comparator | Outcome | Time (from initiation of intervention) | Sample size | Significance‡ | ES (95% CI) |
|---|---|---|---|---|---|---|
| **PRISMS retrieved reviews** | | | | | | |
| **Chodosh** (2005)[187]*** | Self-management programmes for hypertension | SBP change | NR | NR | + | –0.39 (–0.51 to –0.28) |
| | | DBP change | NR | NR | + | –0.51 (–0.73 to –0.30) |
| **Dickinson** (2006)[347]** | Lifestyle interventions Combinations of interventions (improved diet, exercise, alcohol restriction, sodium restriction) | Mean SBP change | NR | 6 RCTs; 374 participants | +++ | –5.5 (–8.8 to –2.3) |
| | | Mean DBP change | NR | 6 RCTs; 374 participants | +++ | –4.5 (–6.9 to –2.0) |
| **Ebrahim** (1998)[343]** | Methods for improving adherence and control | Home monitoring (included effects of family monitoring): Mean DBP change | NR | NR | 0 | –0.5 (–0.7 to 0.7) |
| | | Self-monitoring: Mean DBP change | NR | NR | + | –1.5 (–2.7 to –0.3) |
| | | Patient education: Mean SBP change | NR | NR | +++ | –7.6 (–8.5 to –6.7) |
| | | Patient education: Mean DBP change | NR | NR | +++ | –4.2 (–4.6 to –3.8) |
| | | Patient education without Hypertension Detection and Follow-up Programme: Mean SBP change | NR | NR | 0 | –0.7 (–2.8 to 1.4) |
| | | Patient education without Hypertension Detection and Follow-up Programme: Mean DBP change | NR | NR | 0 | –0.6 (–1.6 to 0.4) |
| | | Education of Professionals: Mean DBP change | NR | NR | + | –1.9 (–3.3 to –0.5) |

| Reference and weighting outcome | Intervention and comparator | Outcome | Time (from initiation of intervention) | Sample size | Significance‡ | ES (95% CI) |
|---|---|---|---|---|---|---|
| **Glynn** (2010)[337]*** | Model of care that improves BP control or follow-up care of patients | Self-monitoring: Mean SBP change | NR | 12 RCTs | ++ | –2.5 (–3.7 to –1.3) |
| | | Mean DBP change | NR | 14 RCTs | ++ | –1.8 (–2.4 to –1.2) |
| | | BP control achieved | NR | 6 RCTs | 0 | OR 0.97 (0.81 to 1.16) |
| | | Educational interventions directed at patient: BP control achieved | NR | 8 RCTs | + | OR 0.83 (95% CI 0.75 to 0.91) |
| | | Educational interventions directed to physician: Mean SBP change | NR | NR | 0 | –0.4 (–1.1 to 0.2) |
| | | Mean DBP change | NR | NR | 0 | –0.4 (–1.1 to 0.3) |
| | | Appointment reminder systems: BP control achieved | NR | 2 RCTs | + | OR 0.54 (0.41 to 0.73) |
| **Takiya** (2004)[349]** | Adherence tools and methods to improve adherence | Behavioural interventions Adherence (different measures converted to ES) | NR | NR | 0 | 0.04 (–0.01 to 0.09) |
| **Verberk** (2011)[345]** | Telecare for the management of hypertension | Telecare intervention vs. control Mean SBP change | NR | NR | +++ | –5.2 (p < 0.001) |
| | | Mean DBP change | NR | NR | ++ | –2.1 (p < 0.01) |
| | | Percentage meeting BP targets | NR | NR | 0 | 2.7% (p = 0.6) |
| | | Intervention but without antihypertensive drug modification vs. control Mean SBP change | NR | NR | 0 | –8.6 (no p-value provided) |
| | | Mean DBP change | NR | NR | 0 | –3.6 (no p-value provided) |
| | | Intervention with antihypertensive drug modification based on measured BP values vs. control Mean SBP change | NR | NR | 0 | –5.1 (p = 0.07) Mean DBP change NR NR 0 –2.2 (p = 0.22) |

| Reference and weighting outcome | Intervention and comparator | Outcome | Time (from initiation of intervention) | Sample size | Significance‡ | ES (95% CI) |
|---|---|---|---|---|---|---|
| **Reviews retrieved in updated search** | | | | | | |
| **Cheema** (2014)[340]** | Community pharmacist interventions (meta-analysis included: patient education on hypertension, identification of drug-related problems and lifestyle advice) | Effects on SBP | 3 to 13 months | 11 RCTs; 2,240 participants | +++ | −6.13 (−8.44, −3.81) p < 0.00001; $I^2$ = 36% |
| | | Effects on DBP | | 11 RCTs; 2,246 participants | +++ | −2.51 (−3.46, −1.55) p < 0.00001; $I^2$ = 0% |
| | | Effects on SBP on hypertension without cardiovascular problems | | 5 RCTs; 1,082 participants | ++ | −7.2 (95% CI −3.6 to −10.8, p = 0.004) $I^2$ = 32% |
| | | Effects on DBP on hypertension without cardiovascular problems | | 5 RCTs; 1,078 participants | +++ | −3.4 (95% CI −1.9 to −5.0, p< 0.00001) $I^2$ = 0% |
| | | Effects on SBP on hypertension with cardiovascular problems | | 6 RCTs; 1,158 participants | +++ | −5.3 (95% CI −1.7 to −8.9, P < 0.0001) $I^2$ = 46% |
| | | Effects on SBP on hypertension with cardiovascular problems | | 6 RCTs; 1,168 participants | + | −1.9 (95% CI −0.7 to −3.1, *P* = 0.002) $I^2$ = 0% |
| | | Medication adherence | | 6 RCTs; 290 | +++ | OR 12.1, 95% CI 4.2–34.6; *P* < 0.001 |
| **Fletcher** (2015)[338]*** | SMBP (includes some telemonitoring studies) | Adherence to antihypertensive medication | 2 weeks to 12 months (median 6 months) | 13 RCTs; 1,809 | ++ | SMD 0.21, 95% CI 0.08, 0.34 ($I^2$ = 43%) |
| | | Adherence to antihypertensive medication – assessed by electronic monitoring | | 2 RCTs; | + | SMD 0.45, 95% CI 0.10 to 0.79 ($I^2$ = 59%) |
| | | Adherence to antihypertensive medication – pill counts | | 5 RCTs; | + | SMD 0.30, 95% CI 0.10 to 0.59 ($I^2$ = 42%) |
| | | Adherence to antihypertensive medication – pharmacy fill data | | 2 RCTs; | 0 | SMD 0.12, 95% CI -0.05 to 0.29 ($I^2$ = 0%) |
| | | Adherence to antihypertensive medication – self-report | | 4 RCTs; | 0 | SMD 0.05, 95% CI -0.13 to 0.22 ($I^2$ = 0%) |
| | | DBP | 6 months | 11 RCTs; 1,798 | +++ | WMD −2.02, 95% CI −2.93 to −1.11, ($I^2$ = 0%). |

| Reference and weighting outcome | Intervention and comparator | Outcome | Time (from initiation of intervention) | Sample size | Significance‡ | ES (95% CI) |
|---|---|---|---|---|---|---|
| **Omboni**[1] (2013)[(334)]*** | SMBP - telemonitoring | Office SBP | Median 24 weeks (range 8–240 weeks) | 17 RCTs; 6,389 participants | +++ | WMD: −4.71(95% CI: -6.18, -3.24; $I^2$=52.2% |
| | | Office DBP | | 15 RCTs; 5,496 participants | +++ | WMD: −2.45 (-3.33, -1.57) $I^2$=40.4%. |
| | | Ambulatory BP | | 5 RCTs; 935 participants | +++/0 | SBP: -3.48mmHg (95% CI: -5.31 to -1.64) DBP: -1.43mmHg (95% CI: -2.86 to +0.00) |
| | | BP normalisation | | 10 RCTs; 3,596 participants | +++ | Improved by: RR: 1.16 (1.04, 1.29); P<0.001; $I^2$=69%. |
| | | Medication management: Number of medications | | 8 RCTs; 2,444 participants | +++ | HBPT had larger prescription of antihypertensives: WMD: 0.40 (0.17, 0.62) $I^2$=84.2%. |
| | | Medication management: Number of office visits | | 7 RCTs; 2,716 participants | 0 | WMD: -0.18 (-0.37, 0.00), $I^2$=32.7%. |
| | | Quality of life (PCS) | | 4 RCTs; 1,104 participants | +++ | WMD: 2.78 (1.15, 4.41) $I^2$=0%. |
| | | Quality of life (MCS) | | 4 RCTs; 1,104 participants | 0 | WMD: -0.11 (-1.65, 1.43) $I^2$=0%. |
| | | Adverse events | 48 weeks | 4 RCTs; 2,883 participants | 0 | WMD: 1.22 (0.86, 1.71), $I^2$=13.8%. |
| **Uhlig** (2013)[(339)]*** | SMBP (n=52) | SBP (SMBP alone versus usual care) | 6 months | 9 RCTs; 2,080 participants | +++ | WMD: -3.9mmHg. $I^2$=33%. |
| | | DBP (SMBP alone versus usual care) | | | +++ | WMD: -2.4 mmHg. $I^2$=44%. |
| | | SBP (SMBP alone versus usual care) | 12 months | 8 RCTs; 2,290 participants | 0 | WMD: -1.5mmHg. $I^2$=51%. |
| | | DBP (SMBP alone versus usual care) | | | 0 | WMD: -0.8 mmHg. $I^2$=77%. |

| Reference and weighting outcome | Intervention and comparator | Outcome | Time (from initiation of intervention) | Sample size | Significance‡ | ES (95% CI) |
|---|---|---|---|---|---|---|
| **Xu** (2014)[341]*** | Health education - China | SBP | 1 month to 2 years | 14 RCTs; 2,475 participants | +++ | WMD: −19.03, 95% CI (−23.26, −14.80), P < 0.001 |
| | | DBP | | 14 RCTs; 2,475 participants | +++ | WMD = −10.33, 95% CI (−13.40, −7.26), P < 0.001) |

**Key: BP** = blood pressure; **DBP** = diastolic blood pressure; **MCS =** mental component summary; **NR** = not reported; **OR** = odds ration; **PCS =** physical component summary; **QoL** = quality of life; **RCT** = randomised controlled trial; **SBP** = systolic blood pressure; **SMBP** = self-monitoring of blood pressure; **SMD** = standardised mean difference; **WMD** = weighted mean difference.

[1] Numbers of participants adjusted for double-counting.

Significance 0 $p > 0.05$, no evidence of effect; +/− $0.05 \geq p > 0.01$, some evidence of effect in favour of intervention/control; ++/− − $0.01 \geq p > 0.001$, strong evidence of effect in favour of intervention/control; +++/− − − $p \leq 0.001$, very strong evidence of effect in favour of intervention/control.

## Table A10.2 Summary of results from systematic reviews. Table extracted from PRISMS review and systematic reviews from updated search

| Reference and weighting outcome | Focus | Synthesis | RCTs, n; Participants, n; | Main results | Main conclusions (review author); *Important quality concerns (review author)* |
|---|---|---|---|---|---|
| **PRISMS reviews retrieved** | | | | | |
| **Bosch-Capblanch** (2007)[346]** | Contracts between practitioners and patients | Narrative | 4 RCTs; 382 participants | **BP changes:** 2/4 trials exploring contracts between health-care providers and patients reported on BP changes. One found no difference between groups at 1-year follow-up, and the other reporting statistically significant improvement in DBP measured over four visits. **Adherence outcomes:** 2/4 trials reported adherence outcomes. In one study the group with contracts performed worse in terms of adherence on relaxation practices. In the other study, fewer people in the contracts group discontinued treatment, compared with controls | There is not enough evidence to recommend the widespread introduction of patient contracts into health services. |
| **Chodosh** (2005) [187]*** | Self management programmes for hypertension | Meta-analysis | 13 RCTs, 1,557 participants | **SBP/DBP:** Programmes associated with a significant reduction in both SBP and DBP. | Overall pooled results from 13 studies show a statistically and clinically significant reduction in SBP and DBP. Unaccounted for heterogeneity, may be due to publication bias, pooled results must be viewed with caution. |
| **Dickinson** (2006)[347]** | Lifestyle interventions | Meta-analysis | 6 RCTs; 413 participants | **SBP/DBP:** Combined lifestyle interventions were found to be associated with a significant reduction in SBP and a significant reduction in DBP | Despite the likelihood of achieving only a small reduction in BP, some patients with mild hypertension may wish to change their lifestyle in an effort to delay or prevent starting antihypertensive drug therapy. In people with more severe hypertension, lifestyle changes may complement the BP lowering effect of drugs and thereby reduce the number of medications needed to control BP. |
| **Ebrahim** (1998)[343]** | Methods for improving adherence | Meta-analysis | 46 RCTs; >32,000 participants | **BP:** Home monitoring: No significant reduction in BP. **DBP:** SMBP: Statistically significant reduction in | Evidence is lacking to support any specific approaches to improving patient adherence with antihypertensive drugs or lifestyle changes. |

| Reference and weighting outcome | Focus | Synthesis | RCTs, n; Participants, n; | Main results | Main conclusions (review author); *Important quality concerns (review author)* |
|---|---|---|---|---|---|
| | and control | | | DBP.<br>**SBP/DBP:** Patient education: Significant reductions in SBP and DBP.<br>**BP:** Patient education without the Hypertension Detection and Follow-up Programme (RCT): No significant reductions in BP.<br>**DBP:** Professional education: Significant reductions in DBP. | Evidence to support nurse-led care compared with doctor-led care as a better option in achieving BP control is very sparse |
| | | Narrative synthesis | | No single approach to improve adherence can be recommended on the basis of the evidence reviewed.<br>Complex interventions may improve adherence and control in difficult patients.<br>Worksite, nurse-led, protocol-guided care may have advantages over usual care in younger men<br>Educational interventions are unlikely to be effective on their own<br>Changes in the location of care (e.g. worksite to home care) without use of guidelines to improve professional adherence are unlikely to yield benefits<br>Simpler drug regimens are likely to improve adherence<br>Simple reminder packaging does not improve adherence or control<br>SMBP at home appears to have a small but significant effect on BP control. However, the pooled estimates for home monitoring included family monitoring, which was associated with a net rise in BP in one study, and thereby an insignificant reduction of BP. These studies were all conducted prior to the widespread use of ambulatory monitoring but suggest that simpler techniques of self-monitoring may be effective. The evidence base to support SMBP is small.<br>Patient education produced the largest reductions in BP, but this is explained by the Hypertension | |

| Reference and weighting outcome | Focus | Synthesis | RCTs, n; Participants, n; | Main results | Main conclusions (review author); *Important quality concerns (review author)* |
|---|---|---|---|---|---|
| | | | | Detection and Follow-up Program, which achieved major reductions in BP due to a comprehensive stepped care approach involving several elements (i.e. education, free care, specialist clinics and protocols). Consequently, it is likely that the small and statistically insignificant effects of patient education found in the remaining trials are more typical of what might be achieved without attention to other aspects of hypertensive patient care.<br>Professional education achieved a small but statistically significant pooled effect in lowering BP. Most likely due to increased use of drug therapy in intervention groups rather than to the greater use of other non-pharmacological approaches to BP control or better adherence to treatment.<br>Nurse-led clinics were directly compared with doctor-led care in only 1 trial, which found substantially worse BP control, (small sample size, no p-value). Another trial also compared nurse-led with doctor-led care, and this provided stronger evidence to support nurse-led clinics.<br>The evidence to support free preventative health care comes only from the Rand Health Insurance Trial, finding that methods of financing of health care, particularly for poorer people and those with risk factors that require a preventative approach, have an impact on control. | |
| **Glynn** (2010)[337]*** | Models of care that improve BP control or follow-up care of patients | Meta-analysis | 72 RCTs; >87,000 participants | **SBP/DBP:** SMBP: associated with significant reductions in both SBP and DBP. No significant difference in the odds of achieving BP control targets.<br>**BP control:** Educational interventions directed to patients: Significant increase in odds of achieving BP control.<br>Educational interventions directed to physicians: No significant reduction in BP. | Effective delivery of hypertension care in the community requires a rigorous approach in terms of identification, follow-up and treatment with antihypertensive drugs. This systematic review shows that such an approach is likely to translate into reductions in cardiovascular mortality and morbidity.<br>Supplementary and alternative models of care, including self-monitoring of BP by patients, BP |

| Reference and weighting outcome | Focus | Synthesis | RCTs, n; Participants, n; | Main results | Main conclusions (review author); *Important quality concerns (review author)* |
|---|---|---|---|---|---|
| | | | | Appointment reminder systems: Significant increase in odds of achieving BP control. | management by allied HCPs and computer-based clinical decision support systems require further development and evaluation. Educational interventions directed to either patients or health professionals alone are unlikely to produce clinically important reductions in either SBP or DBP. |
| | | Additional narrative synthesis | | Educational interventions directed to patient: MD in SBP ranged from –15.7mmHg to +1.3 mmHg, and MD in DBP ranged from –8.7mmHg to +7.1mmHg<br>Educational interventions directed to physicians: Control of BP produced heterogeneous results (OR ranged from 0.8 to 1.0).<br>Health professional (nurse or pharmacist)-led care (12 RCTs) may be a promising way of delivering care, with the majority of RCTs associated with improved BP control. MD in SBP was reported in 10 RCTs with a range of difference in mean SBP from –13 mmHg to 0 mmHg.<br>MD in DBP was reported in 11 RCTs, ranging from –8mmHg to 0 mmHg. Control of BP was reported in six RCTs and produced heterogeneous results (OR ranged from 0.1 to 0.9)<br>Organisational interventions that aimed to improve the delivery of care (nine RCTs). The largest RCT, the Hypertension Detection and Follow-Up Programme produced substantial reductions in SBP and DBP. At 5-year follow-up, these reductions in BP were associated with a significant reduction in all-cause mortality (6.4% vs. 7.8%; risk difference 1.4%)<br>Appointment reminder systems (eight RCTs). Pooled data from two small RCTs, gave heterogeneous results in terms of SBP and DBP | |
| **Ogedegbe** (2006)[344]** | Effects of home BP monitoring on adherence | Narrative synthesis | 11 RCTs; 1,550 participants | **Medication adherence:** Home BP monitoring reported to be associated with statistically significant improvement in medication adherence in 6 of 11 RCTs. Five of these were complex interventions which involved home BP monitoring plus additional components such as patient counselling, provision of advice and reinforcement | The data on the effects of home BP monitoring on patients' medication-taking behaviour are mixed, given that only a little over half of the studies reviewed reported a statistically significant improvement in medication adherence between intervention and control. The reported improvement in adherence was |

| Reference and weighting outcome | Focus | Synthesis | RCTs, n; Participants, n; | Main results | Main conclusions (review author); *Important quality concerns (review author)* |
|---|---|---|---|---|---|
| | | | | of positive behaviour. All five reported similar ES. Only one of the RCTs to report positive results looked at home BP monitoring in isolation. All three RCTs conducted in primary care settings reported negative findings. Only 4 of 11 RCTs reported statistically significant improvements in both medication adherence and BP control. | greater in the trials that tested home BP monitoring along with other adherence-enhancing strategies such as patient counselling, patient reminders and the use of nurse case managers. Home BP monitoring could be considered a useful adherence-enhancing strategy in combination with other strategies such as patient counselling |
| **Saksena** (2010)[336]** | Effectiveness of computer-based interventions | Narrative synthesis | 4 RCTs; 1,319 participants | **BP control:** Computer-based education: (n=1 RCT) No significant improvements compared with usual care.<br>Pharmacist assistance in creating a management plan in addition to computer-based education: Significant improvement in BP control compared with either usual care or computer-based education alone. | Computer-based interventions in isolation were insufficient to change health behaviours. There is promising evidence that computer-based interventions with additional pharmacist care can improve BP control |
| **Schroeder** (2004)[348]*** | Interventions designed to enhance medication adherence | Narrative synthesis | 38 RCTs; 15,519 participants | Of all the interventions for improving adherence to treatment, 19 reported an improvement in adherence alone (13 of which reported on BP outcome). 7 RCTs found an improvement in adherence combined with a reduction in BP, and in 7 a reduction in BP occurred without an increase in adherence.<br>Patient education seemed largely unsuccessful. Only 1/6 RCTs improved adherence with no reported effect on BP.<br>Simplification of dosing regimens improved adherence in 7/9 RCTs.<br>Patient motivation, support and reminders were successful in 10 / 24 RCTs, with mostly small increases in adherence. Effective interventions included daily drug reminder charts, training on self-determination, reminders and packaging, social support, nurse telephone calls, family member support, electronic medication aid cap and telephone-linked computer counselling. | Findings suggest that introducing simpler dosing regimens can be effective in improving adherence, but the effect on subsequent BP reduction has not been established and may not be clinically important. The results of various motivational and more complex interventions are promising, although there is insufficient evidence to suggest a single approach<br><br>The results of this review should be interpreted with caution due to the poor methodological quality and heterogeneity of trials included. |

| Reference and weighting outcome | Focus | Synthesis | RCTs, n; Participants, n; | Main results | Main conclusions (review author); *Important quality concerns (review author)* |
|---|---|---|---|---|---|
| | | | | Complex health and organisational interventions including interventions in combination increased adherence in 8 / 18 RCTs. Interventions were mainly complex combined interventions or structured hypertension management.<br>Worksite care through specially trained nurses improved adherence and showed very strong evidence of a reduction in DBP compared with control. A combination of home visits, education and special dosing devices improved adherence.<br>A strategy involving an educational leaflet, a telephone reminder, a mailed reminder and an educational newsletter was successful in both previously treated hypertensive patients and those who were newly diagnosed. There is weak evidence of an effect of a patient-centred pharmaceutical care model in which pharmacists either used a structured, brief questioning protocol to identify patients' medication-related problems and their information needs relating to hypertension and its treatment, or a combination of structured brief questioning protocol with advice, information and referral to the family practitioner | |
| **Takiya** (2004)[349]** | Adherence tools and methods to improve adherence | Meta-analysis | 16 RCTs; 2446 participants | **Medication adherence:** Behavioural interventions were found not to be associated with any significant increase in medication adherence.<br>No synthesised results reported for combined or educational interventions | There is no single intervention that improves adherence to antihypertensives over others; therefore a patient-specific approach should be modelled. |
| **Verberk** (2011)[345]** | Telecare for the management of hypertension | Meta-analysis | 9 RCTs; 2501 participants | Very strong and strong evidence to support significant reduction in SBP and DBP, respectively, using telecare compared with control. No significant increase in the odds of meeting BP targets using telecare compared with control.<br>No evidence to suggest a significant reduction in BP between those RCTs in which treatment was not adjusted during the study compared with usual | Telecare leads to a greater decrease in SBP and DBP than is obtained with usual care.<br>Telecare may be particularly useful for increasing patients' awareness, which may lead to improved adherence to treatment and lifestyle advice |

| Reference and weighting outcome | Focus | Synthesis | RCTs, n; Participants, n; | Main results | Main conclusions (review author); *Important quality concerns (review author)* |
|---|---|---|---|---|---|
| | | | | care.<br>No evidence to suggest a significant reduction in BP in those studies where drug modification was based on measured BP values compared with usual care | |
| **Reviews retrieved in updated search** | | | | | |
| **Chandak** (2014)[342]* | Technology-enabled interventions | Narrative | 12 RCTs; | Results reported for 3 telemonitoring studies, only 1 is a unique RCT to this overview: It showed a significant reduction in SBP for the intervention group and a significant reduction in mean DBP. | More longitudinal studies are needed where technology can be utilised to implement multifaceted interventions based on comprehensive JNC-7 guidelines. Interventions to improve BP control for SM of hypertension should be aimed at physicians and patients. |
| **Cheema** (2014)[340]** | Community pharmacist interventions | Meta-analysis | 16 RCTs; 3,032 participants | Pharmacist-led interventions were patient education on hypertension, management of prescribing and safety problems associated with medication, and advice on lifestyle. These interventions were associated with significant reductions in SBP and DBP. | Community pharmacist-led interventions can significantly reduce SBP and DBP. These interventions could be useful for improving clinical management of hypertension. |
| **Fletcher** (2015)[338]*** | SMBP effect on medication adherence and lifestyle factors | Meta-analysis | 28 RCTs; 7,021 participants | Pooled analysis of adherence measures demonstrated a small but significant overall effect of SMBP. | SMBP may contribute to improvements in medication adherence in hypertensives. However, evidence for the effect of SMBP on lifestyle change and medication persistence is scarce, of poor quality, and suggests little clinically relevant benefit. |
| | | Narrative review | | Meta-analysis was not completed for lifestyle factor outcomes due to insufficient data.<br>Dietary outcomes (8 RCTs) 1/8 showed a significant improvement in overall diet quality, 1/8 showed significant improvement in average number of fruit and vegetables consumed.<br>Physical activity (6 RCTs): 1/6 showed an increase in mean energy expenditure. | |
| **Omboni** (2013)[334]*** | Home blood pressure telemonitoring | Meta-analysis | 23 RCTs; 7,037 participants | HBPT resulted in statistically significant improvements in office SBP and DBP, ambulatory BP and BP normalisation. A significantly larger use of antihypertensive medications was observed in the HBPT than in the control group at the study end. Results for QoL were mixed. | Patients randomised to HBPT received a more intensive treatment. This might reasonably be one of the most plausible causes of the enhanced BP control achieved in the intervention group, as adherence to hypertension medications and number of office |

| Reference and weighting outcome | Focus | Synthesis | RCTs, n; Participants, n; | Main results | Main conclusions (review author); *Important quality concerns (review author)* |
|---|---|---|---|---|---|
| | | | | | visits were both comparable between the two study arms.<br>Given the high level of heterogeneity of studies published so far, future well designed, large-scale, prospective, controlled trials are needed to understand the long-term benefit of such technologies. |
| **Uhlig** (2013)[339]*** | SMBP | Meta-analysis | SMBP (n=52, 5 include telemonitoring or telecounsellin g); 5,400 participants | SBP (SMBP alone versus usual care): SMBP was associated with statistically significant net changes in both SBP and DBP at 6 months but were no longer statistically significant at 12-months. | SMBP with or without additional support lowers BP compared with usual care, but the BP effect beyond 12 months and long-term benefits remain uncertain.<br>Additional support enhances the BP-lowering effect.<br><br>*The evidence base has several limitations. Many studies were quality C and were likely underpowered, even for BP outcomes. Duration of follow-up in most instances was less than 12 months. Data on clinical outcomes were lacking. Given the clinical heterogeneity stemming from the variation in the populations, interventions, outcomes, and time points examined, often only 1 or 2 studies were available for specific comparisons.* |
| | | Narrative | 25 RCTs; | SMBP plus additional support versus usual care: At 12 months: 5/25 RCTs reporting a mean net reduction in SBP or DBP. Results were mixed at 18 months. 2/25 studies found statistically significant net reductions in SBP and DBP at 24 to 60 months. | |
| **Xu** (2014)[341]*** | Health education - China | Meta-analysis | 14 RCTs; 2,475 participants | | The effect of health education fell off as patients were followed up over a longer period. Health education plays an important role in blood pressure control in hypertensive patients, potentially reducing blood pressure by one level. |

**Key: BP** = blood pressure; **DBP** = diastolic blood pressure; **HBPT** = home blood pressure telemonitoring; **OR** = odds ration; **QoL** = quality of life; **RCT** = randomised controlled trial; **SBP** = systolic blood pressure; **SMBP** = self-monitoring of blood pressure; **SMD** = standardised mean difference; **WMD** = weighted mean difference.

## Table A10.3 CEA Studies investigating self-monitoring of blood pressure

| Study | Intervention | Population | Analysis details | Clinical and QALY outcomes | Costs | Results |
|---|---|---|---|---|---|---|
| **Arrieta** (2014)[353] | Home blood pressure telemonitoring compared with usual care (clinic-based monitoring) | Employee plan members aged 20 to 44 and 45 to 64 years, and for Medicare Advantage plan members aged ≥65 years. | Country: US<br>Study design: cost-benefit simulation model<br>Perspective: payer<br>Discount rate: 3%<br>Time horizon: 10 years | None reported. | Depending on the insurance plan and age group, estimated net savings of home monitoring ranged from $33 to $166 per member in the first year, and from $415 to $1,364 over 10 years. | Estimated net saving of home monitoring ranged from $33 (€27) to $166 (€136) per member in the first year, and the return on investment ranged from $0.85 (€0.70) to $3.75 (€3.08) per dollar invested. |
| **Madsen** (2011)[358] | Home blood pressure telemonitoring compared with conventional office-based monitoring. | Patients (n=223) age 20-80 years with uncontrolled hypertension (>150/95mmHg or systolic BP >150mmHg and diastolic BP <90mmHg). Mean age 57 years. | Country: Denmark<br>Study design: RCT-based costing study<br>Perspective: payer<br>Discount rate: NA<br>Time horizon: 6 months | After 6 months, daytime ambulatory blood pressure was reduced by 11.9/6.2 mmHg in the intervention group and 9.6/5.4 mmHg in the control group with no significant differences between the groups. | Consultation and medication costs were lowered in the intervention group. Average intervention cost was DKK 1,343 (€166) per patient. | For systolic ambulatory blood pressure, the ICER was 256 DKK (€32) /mmHg (95% UI: -860 to 4,544).<br>For diastolic ambulatory blood pressure, the ICER was 655 DKK (€81) /mmHg (95% UI: -674 to 69,315). |
| **McManus** (2005)[359] | Blood pressure self-monitoring at GP practice compared with usual care. | Patients (n=400) aged 35-75 receiving treatment for hypertension with BP in the range 140/85 mm Hg to 200/100 mm Hg. Mean age 62.6 years. | Country: UK<br>Study design: RCT-based costing study<br>Perspective: payer<br>Discount rate: 3.5% (capital costs)<br>Time horizon: 12 months | Systolic blood pressure significantly lower in the intervention group at 6 months (mean difference in change 4.3 mm Hg (95% CI: 0.8 to 7.9 mm Hg); but not at 1 year (−1.6 mm Hg (95% CI: − 5.3 to 2.2 mm Hg). No significant effect on diastolic blood pressure. | Mean cost of delivering intervention = £27 (€42) per patient. | The mean incremental cost effectiveness ratio (£/mm Hg) was 5.10 (€7.94) (95% CI: -7.2 to 19.1).<br>Blood pressure can be controlled to the same degree with either practice based self monitoring or usual care. Self monitoring has negligible costs, reduces practice consulting rates, is acceptable to (and preferred by) patients and does not increase anxiety. |

| Study | Intervention | Population | Analysis details | Clinical and QALY outcomes | Costs | Results |
|---|---|---|---|---|---|---|
| **Parati** (2009)[360] | Home blood pressure telemonitoring compared with office-based monitoring. | Patients (n=298) with uncontrolled hypertension (systolic blood pressure>=140mm Hg or diastolic blood pressure>=90mm Hg), aged between 18 and 75 years. Mean age 57.5 years. | Country: Italy<br>Study design: RCT-based costing study<br>Perspective: payer<br>Discount rate: NA<br>Time horizon: 6 months | Percentage patients with daytime blood pressure normalisation was higher in the intervention (62%) then in controls (50%) (P<0.05).<br>Treatment changes were less frequent in the intervention group (9% vs. 14%, P<0.05). | The overall cost of management per patient was €123 for intervention and €125 for controls. | Home blood pressure teletransmission led to a better control of ambulatory blood pressure than with usual care. There was no difference in costs. |
| **Staessen** (2004)[363] | Blood pressure measurement at home compared with in the physician's office. | Patients (n=400) with hypertension and a minimum age of 18 years were eligible if they were either untreated or being treated with maximum 2 different antihypertensive agents. | Country: Belgium & Ireland<br>Study design: RCT-based costing study<br>Perspective: payer<br>Discount rate: NA<br>Time horizon: 12 months | After controlling for baseline differences, the final differences between the 2 arms ranged from 4.8 to 6.8 mm Hg for systolic BP and from 2.9 to 3.5 mm Hg for diastolic BP. More intervention than control patients could permanently stop drug treatment. | The intervention cost €333 (€408) per 100 patients treated for 1 month.<br><br>The total cost per 100 patients treated for 1 month was €3,522 (€4,317) for intervention and €3,875 (€4,750) for controls. | Home BP instead of office blood pressure led to less intensive drug treatment and marginally lower medical costs but also to less long-term blood pressure control with no differences in general well-being and electrocardiographic or echocardiographic left ventricular mass. |
| **Stoddart** (2013)[364] | Home blood pressure telemonitoring compared with usual care. | Participants (n=401) with daytime ambulatory blood pressure averaged ≥135/85 and <210/135 mm Hg. Mean age 60.7 years. | Country: UK<br>Study design: RCT-based CEA<br>Perspective: payer<br>Discount rate: NA<br>Time horizon: 6 months | Mean daytime systolic ambulatory BP fell from 146.20 to 140.15 mm Hg for intervention and 146.22 to 144.50 mm Hg in control arm. The difference in mean daytime systolic ambulatory BP at 6 months was 4.51 mm Hg (95% CI 2.49 to 6.61; p<0.001) | The intervention cost £70.77 (€92) per patient in equipment, training and staff costs. | The ICER was £25.60 (€33) /mm Hg (95% CI £16.05 to £46.69). The intervention was significantly more effective than usual care but also significantly more costly on average lowering systolic ambulatory blood pressure by 4.51 mm Hg and raising the total cost by £115.32 (€149). |

| Study | Intervention | Population | Analysis details | Clinical and QALY outcomes | Costs | Results |
|---|---|---|---|---|---|---|
| **Verberk** (2007)[366] | Self-measurement of blood pressure compared with office-based measurement. | Patients (n=430) aged 18+ years with SBP >139 mm Hg and/or DBP >89 mm Hg. Mean age 55 years. | Country: Netherlands<br>Study design: RCT-based costing study<br>Perspective: payer<br>Discount rate: NA<br>Time horizon: 12 months | 24-hour ambulatory blood pressure values at the end of the trial were higher in the intervention than in the control group: 125.9 versus 123.8 mm Hg (P 0.05) for SBP and 77.2 versus 76.1 mm Hg (P 0.05) for DBP. The self-pressure group used less medication than the OP group (1.47 versus 2.48 drug steps; P<0.001). | The BP device cost $490 (€434) for 100 patients for 1 month.<br><br>The intervention group lower costs than the control group ($3,222 [€2,854] versus $4,420 [€3,915] per 100 patients per month; P 0.001). | The findings support the use of self-monitoring in addition to office-based monitoring in regular clinical care to improve overall BP control and to prevent unnecessary treatment prescriptions with associated healthcare costs. |

**Abbreviations**: **RCT** = randomised controlled trial; **ICER** = incremental cost-effectiveness ratio; **CI** = confidence interval; **UI** = uncertainty interval.

## Table A10.4 CEA Studies investigating other self-management support interventions

| Study | Intervention | Population | Analysis details | Clinical and QALY outcomes | Costs | Results |
|---|---|---|---|---|---|---|
| **Datta** (2010)[354] | Behavioural intervention providing tailored information bimonthly for 2 years via telephone, compared with usual care. | Patients (n=588) with a hypertension diagnosis and had a hypertensive medication prescription filled within the last year (mean age 63 years). | Country: US<br>Study design: RCT-based simulation study<br>Perspective: payer<br>Discount rate: 3% (costs only)<br>Time horizon: life expectancy | The mean life expectancy was between 0.03 and 0.07 years greater in the intervention group, depending and patient sex and BMI. | The average annual cost per patient depended on the caseload of the nurse, and ranged between $112 and $224.<br><br>The average incremental cost ranged between $2,614 and $2,972 depending on the patient sex and BMI. | The ICER ranged between $42,457 and $87,300 per life year saved, depending on patient sex and BMI. If the conventional $50,000 per life-year saved is used, the intervention can be considered cost-effective for the overweight male cohorts and normal-weight female cohorts and moderately cost-effective for the normal-weight male and overweight female cohorts.<br><br>Note: only costs were discounted so the findings are not reliable. Population 98% male. |
| **Fishman** (2013)[355] | Home blood pressure monitoring (with and without pharmacist care) compared with usual care (including information resources and a website to facilitate communication with healthcare providers). | Individuals with mean diastolic blood pressure between 90 and 109 mmHg or mean systolic blood pressure between 140 and 199 mmHg (mean age approx 60 years). | Country: US<br>Study design: unclear<br>Perspective: payer<br>Discount rate: 3/5/7%<br>Time horizon: 12 months follow-up, life expectancy | Controlled hypertension increased life expectancy by between 3.4 and 6.2 years for men, and between 1.6 and 4.9 years for women. | Mean cost of care per patient:<br>usual care = $10.56<br>blood pressure monitoring = $67.36<br>blood pressure monitoring with pharmacist support (e-BPM) = $400.36 | Blood pressure monitoring was dominated for all but decrease in systolic blood pressure ($23.76/mmHg drop).<br>Cost per life year saved for e-BPM was $1,850 for men and $2,220 for women.<br><br>Note: the intervention was introduced to an already well-developed infrastructure. Usual care may not be applicable to Ireland. |

| Study | Intervention | Population | Analysis details | Clinical and QALY outcomes | Costs | Results |
|---|---|---|---|---|---|---|
| **Kaambwa** (2013)[356] | Self-monitoring with self-titration of antihypertensives and telemonitoring of blood pressure measurements compared with usual care. | Data from trial of 527 patients aged 35-85 years with uncontrolled hypertension (>140/90 mmHg) and in receipt of treatment. Modelled from age 66 years. | Country: UK<br>Study design: simulation model<br>Perspective: payer<br>Discount rate: 3.5%<br>Time horizon: 35 years | Self-management was more effective by 0.24 and 0.12 quality QALYs gained per patient for men and women, respectively. | The mean total cost per patient of the intervention was £7,090 (€9,197) for men and £7,296 (€9,464) for women.<br>The mean total cost per patient of usual care was £6,707 (€8,700) for men and £6,720 (€8,717) for women. | The ICER for self-management was £1,624 (€2,107) per QALY for men and £4,923 (€6,386) per QALY for women. |
| **Maciejewski** (2014)[357] | Three nurse-led telephone-based self-management programmes compared with usual care. | Patients (n=591) with hypertension, using antihypertensives, and with inadequate BP control (>140/90 mmHg for all patients). Mean age 64 years. | Country: US<br>Study design: RCT-based model<br>Perspective: payer<br>Discount rate: not reported<br>Time horizon: 18 months | Eighteen months after trial completion, compared with usual care the increased proportion patients with adequate BP control was statistically significant for all three interventions (ranging from 17.1% to 20.4%). | There was no statistically significant difference in costs compared with usual care. | Behavioural and medication management can generate systolic blood pressure improvements that are sustained 18 months after trial completion. Utilisation and expenditure trends were similar for patients in all 4 arms.<br><br>Note: the study population was 92% male and unlikely to be applicable to the Irish setting. |
| **Perman** (2011)[361] | A multidisciplinary antihypertensive programme for middle-class elderly patients compared with usual care. | Patients (n=500) aged 65 years and over with hypertension. Mean age 72.5 years. | Country: Argentina<br>Study design: simulation model using observational data<br>Perspective: payer<br>Discount rate: 5%<br>Time horizon: life expectancy | The mean life years gained was 10.78 for controls and 10.96 for the intervention arm. | Programme cost of the intervention was $14.70 (€13) per patient. | The ICER for the intervention was $1,124 (€1,003) per life year gained. The programme was considered highly cost-effective. |

| Study | Intervention | Population | Analysis details | Clinical and QALY outcomes | Costs | Results |
|---|---|---|---|---|---|---|
| **Reed** (2010)[362] | Telephonic behavioural lifestyle intervention, patient self-monitoring, and both interventions combined compared with usual care. | Patients with (n=636) hypertension and using anti-hypertension medication. Mean age 60.5 years. | Country: US<br>Study design: RCT-based study<br>Perspective: societal<br>Discount rate: 3% on costs<br>Time horizon: 24 months | At 24 months, compared with the usual care group, mean systolic blood pressure decreased by 0.6 mm Hg (P = .69) in the home monitoring arm, increased by 0.6 mm Hg (P = .67) in the behavioural intervention arm, and decreased by 3.9 mm Hg (P = .01) in the combined intervention. | Intervention cost:<br>home monitoring: $90 (€81);<br>behavioural: $345 (€312);<br>combined: $416 (€376);<br>usual care: NA | The incremental 2-year cost per 1-point reduction in systolic blood pressure was $107 (€97) in direct medical costs and $297 (€268) when including patient time costs. The combined intervention improved blood pressure. However, it is more expensive than usual care. |
| **Trogdon** (2012)[365] | Collaborative hypertension intervention (including home BP monitoring, education) compared to no intervention (i.e. do nothing). | High-risk patients with uncontrolled hypertension (systolic blood pressure>=140 mm Hg or diastolic blood pressure>= 90 mm Hg). | Country: US<br>Study design: simulation model<br>Perspective: payer<br>Discount rate: 3%<br>Time horizon: 12 months and 10 years | Number of cases brought under control = 151 of 534.<br>Adverse events avoided: 0.29 after 1 year, 3.92 after 10 years.<br>Life years gained: 2.77 after 1 year, 20.51 after 10 years. | Total cost of programme delivered to 534 members was $122,403 (€114,821).<br><br>Incremental cost of intervention was $116,154 (€108,959) after 1 year and $38,098 (€35,735) after 10 years. | ICERs at 1 year: $767 (€719) per person brought under control, $404,705 (€379,635) per event avoided, or $41,927 (€39,330) per LYG.<br><br>ICERs at 10 years: $9,720 per event avoided and $1,857 per LYG. |

**Abbreviations**: **RCT** = randomised controlled trial; **ICER** = incremental cost-effectiveness ratio; **QALY** = quality-adjusted life year; **LYG** = life years gained; **BMI** = body mass index.

# Appendix A11 – Heart failure

## Table A11.1 Results of meta-analyses

| Reference and weighting outcome | Intervention and comparator | Outcome | Time (from initiation of intervention) | Sample size | Significance | ES (95% CI) |
|---|---|---|---|---|---|---|
| **Feltner** 2014[374] | Patient education | All cause readmission | 3-6 months | 200 | 0 | RR 1.14 (0.84–1.54) |
| | | HF-related readmission | | 223 | +++ | RR 0.53 (0.31–0.90) |
| | | Mortality | | 423 | 0 | RR 1.20 (0.52–2.76) |
| | Home-visiting programmes | All-cause readmission | 3-6 months | 1563 | +++ | RR 0.75 (0.68–0.86) |
| | | HF-specific readmission | | 282 | +++ | RR 0.51 (0.31–0.82) |
| | | Mortality | | 1693 | ++ | RR 0.77 (0.60–0.997) |
| | | All-cause readmission | 30 days | 418 | +++ | High-intensity (1 study): RR 0.34 (0.19–0.62) |
| | | | | | 0 | Medium-intensity (1 study): RR 0.89 (0.43–1.85) |
| | | Mortality | | 239 | 0 | RR 1.03 (0.15–7.16) |
| | Telemonitoring | All-cause readmission | 30 days | 168 | 0 | RR 1.02 (0.64–1.63) |
| | | All-cause readmission | 3-6 months | 434 | 0 | RR 1.11 (0.87–1.42) |
| | | HF-specific readmission | | 182 | 0 | RR 1.70 (0.82–3.51) |
| | | Mortality | | 564 | 0 | RR 0.93 (0.25–3.48) |
| | Structured Telephone Support | All-cause readmission | 30 days | 134 | 0 | RR 0.80 (0.38–1.65) |
| | | HF-specific readmission | | 134 | 0 | RR 0.63 (0.24–1.87) |
| | | All-cause readmission | 3-6 months | 2166 | 0 | RR 0.92 (0.77–1.10) |
| | | HF-specific readmission | | 1790 | ++ | RR 0.74 (0.61–0.90) |
| | | Mortality | | 2011 | ++ | RR 0.74 (0.56–0.97) |
| **Wakefield** 2013[375] | Patient educational interventions versus usual care | Mortality | Mean 204 days (SD 135) | N/A | ++ | OR 0.79 (0.69-0.92)** |
| | | Readmissions | | N/A | ++ | SMD 0.157 (0.071-0.244) |
| | | HF-specific QoL | | N/A | ++ | SMD 0.231 (0.064-0.399) |
| | | Generic QoL | | N/A | ++ | SMD 0.283 (-0.093-0.659) |

| Reference and weighting outcome | Intervention and comparator | Outcome | Time (from initiation of intervention) | Sample size | Significance | ES (95% CI) |
|---|---|---|---|---|---|---|
| | | ED Visits | | N/A | ++ | SMD 0.123 (-0.089-0.335) |
| **Taylor** 2014 | Exercise-based interventions with six months' follow-up or longer compared with a no exercise control that could include usual medical care | All-cause mortality | Up to 12 months | 1871 | 0 | RR 0.93 [0.69, 1.27] |
| | | Hospital admission | | 1328 | +++ | RR 0.75 [0.62, 0.92] |
| | | All-cause mortality | More than 12 months | 2845 | 0 | RR 0.88 [0.75, 1.02] |
| | | Hospital admission | | 2722 | 0 | RR 0.92 [0.66, 1.29] |
| | | HF-Admissions | N/A | 1036 | +++ | RR 0.61 [0.46, 0.80] |
| | | HRQoL | | 3240 | _ _ | SMD -0.46 [-0.66, -0.26] |
| **Kotb** 2015[386] | Structured telephone support | All-cause mortality | N/A | N/A | ++ | OR 0.80 (0.66, 0.96) |
| | Telemonitoring | | | | +++ | OR 0.53 (0.36, 0.80) |
| | Telemonitoring and telephone support | | | | 0 | OR 0.77 (0.58, 2.35) |
| | Video monitoring | | | | 0 | OR 1.18 (0.58, 2.35) |
| | ECG monitoring | | | | 0 | OR 0.78 (0.57, 1.06) |
| **Conway** 2014[387] | Structured telephone support | All-cause mortality | 3-18 months | 5511 | 0 | RR 0.87 (0.75, 1.01) |
| | | HF - Hospitalisations | | 4269 | +++ | RR 0.77 (0.68, 0.87) |
| | Telemonitoring | All-cause mortality | 3-15 months | 2222 | +++ | RR 0.62 (0.50, 0.77) |
| | | HF - Hospitalisations | | 1215 | ++ | RR 0.75 (0.63, 0.91) |
| **Inglis** 2010[392] | Structured telephone support | All-cause mortality | 3-18 months | 5563 | 0 | RR 0.88 [0.76, 1.01] |
| | | All-cause hospitalisations | | 4295 | ++ | RR 0.92 [0.85, 0.99] |
| | | HF hospitalisations | | 4269 | +++ | RR 0.77 [0.68, 0.87] |
| | | All-cause mortality | >6 months | 4292 | 0 | RR 0.87 [0.74, 1.02] |
| | | All-cause hospitalisations | | 2343 | ++ | RR 0.91 [0.83, 0.99] |
| | | HF hospitalisations | | 2948 | +++ | RR 0.76 [0.65, 0.89] |
| | Telemonitoring | All-cause mortality | 3-18 months | 2710 | +++ | RR 0.66 [0.54, 0.81] |
| | | All-cause hospitalisations | | 2343 | ++ | RR 0.91 [0.84, 0.99] |
| | | HF hospitalisations | | 4674 | +++ | RR 0.77 [0.68, 0.87] |
| | | All-cause mortality | >6 months | 1994 | +++ | RR 0.69 [0.55, 0.86] |
| | | All-cause hospitalisations | | 1748 | ++ | RR 0.87 [0.80, 0.95] |

| Reference and weighting outcome | Intervention and comparator | Outcome | Time (from initiation of intervention) | Sample size | Significance | ES (95% CI) |
|---|---|---|---|---|---|---|
| | | HF hospitalisations | | 1570 | ++ | RR 0.79 [0.67, 0.94] |
| **Pandor** 2013[389] | Structured telephone support – Human to machine | All-cause mortality | N/A | N/A | 0 | HR 1.35 (0.78, 2.36) |
| | | All-cause hospitalisations | | | 0 | HR 0.87 (0.54,1.29) |
| | | HF hospitalisations | | | 0 | HR 0.69 (0.34, 1.43) |
| | Structured telephone support – Human to human | All-cause mortality | | | 0 | HR 0.87 (0.69, 1.14) |
| | | All-cause hospitalisations | | | 0 | HR 0.86 (0.62, 1.17) |
| | | HF hospitalisations | | | 0 | HR 0.67 (0.37, 1.05) |
| | Home telemonitoring – Office hours | All-cause mortality | | | 0 | HR 0.85 (0.59, 1.20) |
| | | All-cause hospitalisations | | | 0 | HR 1.17 (0.89, 1.59) |
| | | HF hospitalisations | | | 0 | HR 0.70 (0.34, 1.50) |
| | Home telemonitoring – 24/7 | All-cause mortality | | | 0 | HR 0.85 (0.58, 1.27) |
| | | All-cause hospitalisations | | | 0 | HR 0.84 (0.54, 1.15) |
| | | HF hospitalisations | | | 0 | HR 0.64 (0.34, 1.14) |
| **Nakamura** 2013[388] | Remote patient monitoring interventions in congestive heart failure patients | All-cause mortality | N/A | 3347 | ++ | RR 0.76 (0.62, 0.93) |
| **Clarke** 2011 | Telemonitoring of patients with congestive heart failure | All-cause mortality | 3-15 months | 2171 | ++ | RR 0.77 (0.61, 0.97) |
| | | All-cause hospital admissions | | 1951 | 0 | RR 0.99 (0.88, 1.11) |
| | | CHF hospital admissions | | 1772 | +++ | RR 0.73 (0.62, 0.87) |
| | | All-cause emergency visits | | 907 | 0 | RR 1.04 (0.86, 1.26) |

**RR**- Relative risk; **OR** = odds ratio; **HR** = hazard rate; **N/A** = not available; **HF** = heart failure; **CHF** = congestive heart failure; **ES** = effect size; **CI** = confidence interval; **HRQoL** = health related quality of life.

**Correspondence with the author indicates that what was reported as mortality was actually survival, so the value included in the above table is the reciprocal of the result reported in the article.

## Table A11.2 Summary of results from systematic reviews

| Review | Focus | Synthesis | RCTs, n; Participants, n; date range | Main results | Main conclusions (review author); important quality concerns (review author) |
|---|---|---|---|---|---|
| **Barnason** 2012[380] | Cognitive–behavioural interventions | Narrative summary | RCTs 19; Patients 3166; Dates 2000-2010 | Cognitive–behavioural intervention mechanisms were most frequently used to improve patient's heart failure self-care. In the majority of the studies, the interventions demonstrated efficacy by improving heart failure patients' self-care maintenance and management behaviours. Intervention group subjects, in the majority of studies, had significantly higher levels of knowledge pertaining to heart failure and heart failure related self-care. | Based on these findings, there are improved patient outcomes when standard patient education for heart failure is augmented using cognitive–behavioural strategies that include additional evidence-based education and counselling. |
| **Boren** 2009[378] | Heart failure self-management education programs | Narrative summary | RCTs: 35, Patients: 7413, Dates: 1998-2007 | A total of 113 unique outcomes in nine categories (satisfaction, learning, behaviour, medications, clinical status, social functioning, mortality, medical resource utilisation and cost) were measured in the studies. Sixty (53%) of the outcomes showed significant improvement in at least one study. | Educational interventions should be based on scientifically sound research evidence. The education topic list developed in this review can be used by patients and clinicians to prioritise and personalise education. |
| **Boyde** 2011[376] | Educational interventions defined as a prespecified learning activity | Narrative summary | RCTs: 19, Patients: 2686, Dates: 1998-2008 | Studies used a variety of outcome measures to evaluate their effectiveness. Of the studies reviewed, 15 demonstrated a significant effect from their intervention in at least one of their outcome measures. | It was difficult to establish the most effective educational strategy as the educational interventions varied considerably in delivery methods and duration as well as the outcome measures that were used for the evaluation. |
| **Clarke** 2011[391] | Telemonitoring on patients with congestive heart failure | Meta-analysis | RCTs: 13, Patients: 3480, Dates: 2003-2009 | Pooled estimate results showed that there was an overall reduction in all-cause mortality (P = 0.02). There was no overall reduction in all-cause hospital admission (P = 0.84), although there was a reduction in CHF hospital admission (P = 0.0004). There was no reduction in all-cause emergency admission (P = 0.67). There was no significant difference in length of stay in hospital, medication adherence or cost. | Telemonitoring in conjunction with nurse home visiting and specialist unit support can be effective in the clinical management of patients with CHF and help to improve their quality of life. |
| **Conway** 2014[387] | Non-invasive remote monitoring for heart failure | Meta-analysis | RCTs: 25, Patients: >4000, Dates: 1998-2008 | Only structured telephone calls and telemonitoring were effective in reducing the risk of all-cause mortality (relative risk [RR] = 0.87; 95% confidence interval [CI], 0.75–1.01; p = 0.06; and RR = 0.62; 95% CI, 0.50–0.77; p < 0.0001, respectively) and heart failure–related hospitalisations (RR = 0.77; 95% CI, 0.68–0.87; p < 0.001; and RR = 0.75; 95% CI, 0.63–0.91; p = 0.003, respectively). | Structured telephone calls and telemonitoring, in which physiological data are automatically transmitted, reduced the relative risk of all-cause mortality and hospitalisations when results were combined in the meta-analyses. More research data are required to evaluate the effectiveness of videophone and interactive voice response |

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|---|---|---|---|---|---|
| | | | | | technologies. |
| **Ditewig** 2010[377] | Interventions containing a self-management principle and/or an education component | Meta-analysis | RCTs: 19, Patients: 4162, Dates: 1996-2009 | The effectiveness of heart failure management programmes initiating self-management interventions in patients with chronic heart failure indicate a positive effect, although not always significant, on reduction of numbers of all-cause hospital readmitted patients and due to chronic heart failure, decrease in mortality and increasing quality of life. | Current available published studies show methodological shortcomings impairing validation of the effectiveness of self-management interventions on mortality, all-cause hospital readmissions, chronic heart failure hospitalisation rate and quality of life in patients with chronic heart failure. |
| **Feltner** 2014[374] | Education, home-visiting programmes and remote monitoring | Meta-analysis | RCTs: 47, Patients: >1,000, Dates: 1990-2013 | At 30 days, a high intensity home-visiting programme reduced all-cause readmission and the composite end point (all-cause readmission or death; low size of effect [SOE]). Over 3 to 6 months, home-visiting programmes and multidisciplinary heart failure (MDS-HF) clinic interventions reduced all-cause readmission (high SOE). Home-visiting programmes reduced HF-specific readmission and the composite end point (moderate SOE). Structured telephone support (STS) interventions reduced HF-specific readmission (high SOE) but not all-cause readmissions (moderate SOE). Home-visiting programs, MDS-HF clinics, and STS interventions produced a mortality benefit. Neither telemonitoring nor primarily educational interventions reduced readmission or mortality rates. | Home-visiting programmes and MDS-HF clinics reduced all-cause readmission and mortality; STS reduced HF-specific readmission and mortality. These interventions should receive the greatest consideration by systems or providers seeking to implement transitional care interventions for persons with HF |
| **Giamouzis** 2012[390] | Telemonitoring interventions in chronic HF patients | Narrative summary | RCTs: 12, Patients: 3877, Dates: 2007-2011 | Three studies reported reduced hospitalisation rates in telemonitoring groups that reached statistical significance, and another four studies also found reductions in hospitalisation rates in favour of telemonitoring without reaching statistical significance. In four studies there were more rehospitalisations in telemonitoring groups compared to usual care groups, but statistical significance was either not reported or was not important. With regard to all-cause mortality, three studies reported statistically significant results that favoured the telemonitoring group. In two of these studies, mean age was relatively low. | Currently available trial results may seem rather ambiguous and confusing. Nevertheless, it appears that the above presented randomised controlled trials tend to be in favour of telemonitoring. |
| **Gorthi** 2014[385] | Structured telephone support, telemonitoring interventions and home | Narrative summary | RCTs: 52, Patients: 19467, Dates: 1995-2012 | Structured telephone support follow-up has been shown to significantly reduce HF readmissions, but does not significantly reduce all-cause mortality or all-cause hospitalisation. A meta-analysis of 11 non-invasive telemonitoring studies demonstrated significant reductions in all-cause mortality and HF hospitalisations. Invasive telemonitoring is a potentially | Our data suggest that one approach applied to a broad spectrum of different patient types may produce an erratic impact on readmissions and clinical outcomes. HF disease management plans should include the flexibility to meet the individualised needs of specific patients. |

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| | visits | | | effective means of reducing HF hospitalisations, but only one study using pulmonary artery pressure monitoring was able to demonstrate a reduction in HF hospitalisations. Other studies using invasive hemodynamic monitoring have failed to demonstrate changes in rates of readmission or mortality. The efficacy of HF DMPs is associated with inconsistent results. | |
| **Hwang** 2009[384] | Centre-based exercise training, home-based exercise training or concurrent centre and home-based exercise training | Meta-analysis | RCTs: 19, Patients: 1069, Dates: 1992-2007 | The mean improvement in peak oxygen consumption was 2.86 ml/kg per min [95% confidence interval (CI): 1.43–4.29]. Exercise duration increased by 1.94 min (95% CI: 0.89–2.98) and distance on the six-minute walk test was increased by 30.41m (95% CI: 6.13–54.68). Other reported benefits of home-based programmes include increased quality of life and lowered hospital admission rates. | Home-based exercise programmes have been shown to benefit people with heart failure in the short term. Further research is required to investigate the long-term effects of home exercise and to determine the optimal strategies for improving exercise adherence in patients with heart failure. |
| **Inglis** 2010[392] | Structured telephone support or telemonitoring programmes for patients with chronic heart failure | Meta-analysis | RCTs: 25, Patients: 8323, Dates: 2006-2008 | Of the 25 full peer-reviewed studies meta-analysed, 16 evaluated structured telephone support (5613 participants), 11 evaluated telemonitoring (2710 participants), and two tested both interventions (included in counts). Telemonitoring reduced all-cause mortality (RR 0.66, 95%CI 0.54 to 0.81, P < 0.0001) with structured telephone support demonstrating a non-significant positive effect (RR 0.88, 95% CI 0.76 to 1.01, P = 0.08). Both structured telephone support (RR 0.77, 95% CI 0.68 to 0.87, P < 0.0001) and telemonitoring (RR 0.79, 95% CI 0.67 to 0.94, P = 0.008) reduced CHF-related hospitalisations. For both interventions, several studies improved quality of life, reduced healthcare costs and were acceptable to patients. Improvements in prescribing, patient knowledge and self-care, and New York Heart Association (NYHA) functional class were observed. | Structured telephone support and telemonitoring are effective in reducing the risk of all-cause mortality and CHF-related hospitalisations in patients with CHF; they improve quality of life, reduce costs, and evidence-based prescribing. |
| **Kotb** 2015[386] | Telemedicine interventions in adult heart failure patients | Network Meta-analysis | RCTs: 30, Patients: 10193, Dates: 1998-2012 | Compared to usual care, structured telephone support was found to reduce the odds of mortality (Odds Ratio 0.80; 95% Credible Intervals [0.66 to 0.96]) and hospitalisations due to heart failure (0.69; [0.56 to 0.85]). Telemonitoring was also found to reduce the odds of mortality( 0.53; [0.36 to 0.80]) and reduce hospitalisations related to heart failure (0.64; [0.39 to 0.95]) compared to usual post-discharge care. Interventions that involved ECG monitoring also reduced the odds of hospitalisation due to heart failure (0.71; [0.52 to 0.98]). | Compared to usual care, structured telephone support and telemonitoring significantly reduced the odds of deaths and hospitalisation due to heart failure. Despite being the most widely studied forms of telemedicine, little has been done to directly compare these two interventions against one another. Further research into their comparative cost-effectiveness is also warranted. |

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| **Nakamura** 2013[388] | Remote patient monitoring interventions in congestive heart failure patients | Meta-analysis | RCTs: 13, Patients: 3337, Dates: 2003-2013 | Remote patient monitoring resulted in a significantly lower mortality (risk ratio 0.76; 95% confidence interval 0.62 to 0.93) compared to usual care. | Remote patient monitoring is effective in chronic heart failure and rapid intervention was the most important factor in the remote patient monitoring model. |
| **Pandor** 2013[389] | Home telemonitoring or structured telephone support programmes after recent discharge in patients with heart failure | Network Meta-analysis | RCTs: 21, Patients: >1000, Dates: 2008-2012 | Compared with usual care, remote monitoring (RM) was beneficial in reducing all-cause mortality for human to human structured telephone support (STS HH) [hazard ratio (HR) 0.77, 95% credible interval (CrI) 0.55 to 1.08], Telemedicine (TM) during office hours (HR 0.76, 95% CrI 0.49 to 1.18) and TM 24/7 (HR 0.49, 95% CrI 0.20 to 1.18); however, these results were statistically inconclusive. The results for TM 24/7 should be treated with caution because of the poor methodological quality of the only included study in this network. No favourable effect on mortality was observed with human to machine structured telephone support (STS HM). Similar reductions were observed in all-cause hospitalisations for TM interventions, whereas STS interventions had no major effect. | Despite wide variation in usual care and RM strategies, cost-effectiveness analyses suggest that TM during office hours was an optimal strategy (in most costing scenarios). However, clarity was lacking among descriptions of the components of RM packages and usual care and there was a lack of robust estimation of costs. |
| **Pare** 2010[393] | Home telemonitoring in heart failure patients | Narrative summary | RCTs: 17, Patients: >1000, Dates: 1996-2008 | Due to the equivocal nature of current findings of home telemonitoring involving patients with heart failure, larger trials are still needed to confirm the clinical effects of this technology for these patients. | Although home telemonitoring appears to be a promising approach to patient management, designers of future studies should consider ways to make this technology more effective as well as controlling possible mediating variables. |
| **Rajati** 2014[381] | Exercise self-efficacy interventions designed to increase any type of physical activity | Narrative summary | RCTs: 10, Patients: 800, Dates: 2004 to 2013 | Limited published data exist evaluating the self-efficacy strategies to improve exercise in HF. Dominant strategies to improve patients' self-efficacy were performance accomplishments, vicarious experience, verbal persuasion, emotional arousal. | Findings of this study suggest that a positive relationship exists between self-efficacy and initiating and maintaining exercise in HF, especially in the short-term period. |
| **Samartizis** 2013[379] | Structured non-pharmacologic intervention conducted by health professionals | Meta-analysis | RCTs: 16, Patients: 2180, Dates: 1995-2010 | Psychosocial interventions improved quality of life (QoL) of CHF patients (standardized mean difference 0.46, confidence interval [CI] 0.19-0.72; P<.001). Face-to-face interventions showed greater QoL improvement compared with telephone interventions. Interventions that included caregivers did not appear to be significantly more effective. A trend was found for multidisciplinary team approaches being more effective | A significant overall QoL improvement emerged after conducting psychosocial interventions with CHF patients. Interventions based on a face-to-face approach showed greater benefit for patients' QoL compared with telephone-based approaches. |

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| | focused on improving the psychological and/or social aspects of a patient's health | | | compared with non-multidisciplinary approaches. | |
| **Taylor** 2014[382] | Exercise-based interventions with six months' follow-up or longer compared with a no exercise control that could include usual medical care | Meta-analysis | RCTs: 33, Patients: 4740, Dates: 2008-2013 | There was no difference in outcomes of home- versus centre-based cardiac rehabilitation in mortality risk ratio (RR) was1.31 (95% confidence interval (CI) 0.65 to 2.66), cardiac events, exercise capacity standardised mean difference (SMD) -0.11 (95%CI -0.35 to 0.13), as well as in modifiable risk factors (systolic blood pressure; diastolic blood pressure; total cholesterol; HDL-cholesterol; LDL-cholesterol) or proportion of smokers at follow-up or health-related quality of life. There was no consistent difference in the healthcare costs of the two forms of cardiac rehabilitation. | Home- and centre-based cardiac rehabilitation appear to be equally effective in improving the clinical and health-related quality of life outcomes in acute MI and revascularisation patients. |
| **Tierney** 2012[383] | Specific strategies/interventions to promote or improve exercise/physical activity adherence | Narrative summary | RCTs: 9, Patients: 3231, Dates: 2003-2010 | Positive outcomes occurred in the short-term from interventions using approaches such as exercise prescriptions, goal setting, feedback and problem-solving. However, longer-term maintenance of exercise was less successful. There was some support for interventions underpinned by theoretical frameworks, but more research is required to make clearer recommendations. | Motivational strategies such as goal setting, feedback and problem solving might be effective in the short-term, but how to sustain physical activity amongst those with HF remains unclear. |
| **Wakefield** 2013[375] | Patient educational interventions | Meta-analysis | RCTs: 35, Patients: 8071, Dates: 1995-2008 | The most commonly used interventions were patient education, symptom monitoring by study staff, symptom monitoring by patients, and medication adherence strategies. Most programmes had a teaching component with a mean (SD) of 6.4 (3.9) individual topics covered; frequent teaching topics were symptom recognition and management, medication review, and self-monitoring. Fewer than half of the 35 studies reviewed reported adequate data to be included in the meta-analysis. Some outcomes were infrequently reported, limiting statistical power to detect treatment effects. | The contribution of the individual interventions included in the multicomponent programme on patient outcomes remains unclear. |

**Key**: **CHF** = congestive heart failure; **CR** = Cochrane Review; **HDL** = high-density lipoprotein; **HRQoL** = health-related quality of life; **SD** = standard deviation; **HF** = heart failure; **SMD** = standardised mean difference.

## Table A11.3 Summary of cost-effectiveness studies for self-management support education programmes

| Study | Intervention | Population | Analysis details | Clinical and QALY outcomes | Costs | Authors' conclusions |
|---|---|---|---|---|---|---|
| **Agren** (2013)[403] | 1) nurse-led education & psychosocial support programme for patients with heart failure (HF) & their partners<br>2)usual care | Recently discharged HF patients and their partners | Country: Sweden<br>Study design: RCT economic evaluation<br>Perspective: Healthcare<br>Discount:<br>Time Horizon: 12 month<br>Costs calculated in Swedish Kronor and presented in Euros. | Patients in both the intervention group and the control group had a significantly improved QALY weight after 12 months compared with baseline. There was no significant difference between the two groups' mean improvements. The intervention, however, had positive effects on both the patient and the partner. | Total cost of the intervention including transportation was €15,825, or €223 per patient (€163 without transport). Patients in both groups had significantly improved QALY weights at 12 months. By analysing the QALY gained from the dyad, the cost gained per QALY was €16,159. | As there were no significant effects on QALY weights between the intervention group and the controls, the intervention was not found to be cost-effective for the patient alone, but was when dyad was included. |
| **Aguado** (2010)[404] | 1) A single home-based educational intervention. (Similar to medication adherence, how to fill medication boxes appropriately)<br><br>2) Usual care | 106 patients admitted with heart failure | Country: Spain<br>Study design: RCT<br>Perspective Healthcare<br>Discount:<br>Time Horizon: 24 month<br>2002 Spanish Euros | At 24 months of follow-up, there was a statistically significant reduction in the number hospitalisations in the intervention group. Mortality decreased by 9% in the intervention group. At 24 months, patient scores for both generic (SF-36) and specific (MLWHFQ) questionnaires, were significantly better than baseline in the intervention group. | The mean total cost per person was €671.56 (€898) for the intervention group and €2,154 (€2,879) for the control group, with a statistically significant difference of €1,482.68 (€1982) (P < .001). | For patients with systolic HF, a single educational home visit by a nursing staff member 1 week after hospital discharge reduces emergency visits and unplanned readmissions, lowers total healthcare costs, and shows a trend toward improvement in quality of life |
| **Koelling** (2005)[405] | One-on-one nurse-provided patient education at discharge (one hour) plus usual care compared with usual care | Patients admitted to hospital with a diagnosis of heart failure and documented left ventricular systolic dysfunction (ejection | Country: US<br>Study design: Costing study alongside RCT (n==223)<br>Perspective: Not stated (presume healthcare system)<br>Discount rate: N/A<br>Time horizon: 180 days | The number of days hospitalised or dead in the 180-day follow-up period, was lower (p=0.009) for the education group (1,554 days; mean ± SD, 14±36 days vs. 2,103 days; mean ± SD, 18±37 days). The intervention group had a lower risk of hospitalisation or death (RR | The intervention cost was estimated as $100 (€123) per subject (total2 hours of clinical nurse educator at $50 (€62)/hour). The overall cost of care (including the cost of the intervention) was lower in the education group by $2,823 (€3,477) (95%CI $202 (€249) to $5,644 (€6,952), p=0.035) | The authors concluded that addition of a one-hour, nurse educator–delivered teaching session at the time of hospital discharge resulted in improved clinical outcomes, increased self-care |

| Study | Intervention | Population | Analysis details | Clinical and QALY outcomes | Costs | Authors' conclusions |
|---|---|---|---|---|---|---|
| | | fraction ≤ 0.40) | Costs: USD 2003 | 0.65; 95%CI 0.45-0.93); a lower risk of rehospitalisation due to heart failure (0.49; 95%CI 0.27-0.88) and a longer time to first hospitalisation or death (p=0.012), but no difference in death rate (RR 0.94; 95%CI 0.34-2.6). The self-care measure score (sum of six self-care measures) was significantly higher for the intervention group at 30-day follow-up (p=0.001) | per subject in the 180-day follow-up period | measure adherence, and reduced cost of care in patients with systolic heart failure. |
| **Krumholz** (2002)[406] | Education and support intervention<br>2) Usual care | 88 HF patients 44 controls, 44 intervention, aged ≥50 | Country: US<br>Study Design: prospective, randomised trial<br>Perspective: Healthcare<br>Discount rate: NA<br>Time Horizon: 12 months<br><br>(US $ cost year NR) | Only 12 patients (27.3%) in the intervention group compared with 21 patients (47.7%) in the control group experienced more than one readmission. The number of patients experiencing HF or other CVD readmissions or death was 22 (50.0%) in the intervention group and 35 (79.6%) in the control group | The average total estimated cost was $530 per patient. Hospital readmission costs were higher in the control group by an average of $7,515 per patient ($21,935 in the control group and $14,420 in the intervention group, After taking into consideration the average cost of $530 per patient with intervention, the overall cost of care was $6,985 less per patient in the intervention group. | Results suggest that all patients with HF should be offered an education and support programme that extends beyond the hospitalisation. |
| **Lopez** (2006)[407] | Multi factorial educational intervention carried out by a pharmacist<br><br>2) Usual care | Heart failure patients (134 patients were included, with a mean age of 75 years and a low educational level.) | Country: Spain<br>Study Design: prospective RCT<br>Perspective: Healthcare<br>Discount rate:<br>Time Horizon: 12 month<br>(€ Spain cost year NR) | The patients in the intervention group were re-admitted less than those in the control group. One re admission a year would be prevented per every 6.5 patients with HF receiving the intervention. No significant differences between the two groups with regard to the | The cost of the intervention was €2,170. The global cost of the intervention amounted to €31 per patient. In terms of total costs the intervention resulted in savings of €30,995 (€100,815-€69,820) or €578 per patient. | In conclusion, this study demonstrates that a post discharge educational intervention in patients with heart failure, carried out by a pharmacist, in coordination with the rest of the staff, |

| Study | Intervention | Population | Analysis details | Clinical and QALY outcomes | Costs | Authors' conclusions |
|---|---|---|---|---|---|---|
| | | | | measurement of HRQoL throughout the follow-up, though satisfaction of care and the information received was greater in the patients of the intervention group | | reduces hospital re admissions and the total days of hospital stay, improving treatment compliance without increasing healthcare costs. |
| **Morcillo** (2005)[408] | 1) home-based educational intervention carried out by nursing staff<br>2) usual care | 70 Patients hospitalised with systolic HF | Country: Spain<br>Study Design: RCT<br>Perspective: Healthcare<br>Discount rate:<br>Time Horizon: 6 month<br><br>(Spain € 2003) | At 6 months of follow-up, the educational intervention had resulted in a marked, statistically significant reduction in the number of emergency visits and hospitalisations. At 6 months, the intervention group had a significantly higher physical and mental health summary patient score, whereas scores for the control patients remained stable | The total cost per person was €314.80 (€428) ±403.30 (€549) for the intervention group and €1505.60 (€2,048) ±1391.60 (€1,893) for the control group with a statistically significant difference of €1190.90 (€1,620) | To conclude the intervention is a cost-effective health management option that improves the quality of life of patients with systolic HF. |
| **Riegel** (2004)[409] | Peer support (We trained 9 persons with heart failure to mentor other heart failure patients) | 88 HF patients after recent exacerbation | Country: US<br>Study Design: RCT<br>Perspective: Healthcare<br>Discount rate:<br>Time Horizon: 3 month<br><br>(US $ cost year NR) | At 90 days, self-care management self-care self-confidence, and total SCHFI scores had risen significantly more in the intervention group than in the control group. The intervention group was 46% quicker to return to the hospital than the control group. | The intervention was estimated to cost $63 per patient in professional time required for training and oversight of the mentors. Over 90 days in patient HF costs were $1,899 and $2,201 for the intervention and UC respectively. All cause costs were $2,450 and $2,858. | The study concluded that this type of intervention is not universally appealing to hospitalised HF patients. In those who participated, it improved HF self-care and may have satisfied some social support needs, but the risk of increasing acute care resource use needs to be explored further. |

## Table A11.4 Summary of cost-effectiveness studies for telemedicine

| Study | Intervention | Population | Analysis details | Clinical and QALY outcomes | Cost | Authors' conclusions |
|---|---|---|---|---|---|---|
| **Berg** (2004)[410] | A telemedicine disease management programme<br><br>2)Usual care | Recent HF patients aged 65 and over (n=533) | Country: USA<br>Study Design: concurrent matched-cohort study.<br>Perspective: healthcare<br>Discount rate: N/A<br>Time Horizon: 1 year<br><br>(US$ 2000) | Intervention group had significantly lower rates of acute service utilisation vs. UC including 23% fewer hospitalisations, 26% fewer inpatient bed days, 22% fewer ED visits, 44% fewer HF hospitalisations, HF inpatient bed days (34% fewer), 70% fewer 30-day readmissions & 45% fewer SNF bed days. Intervention group had 4.5% more physician office visits, which was non-significant. There were no significant differences between the 2 groups for most recommended drug classes. | The average cost was $1,163 (€1,595) per intervention-group participant. Total cost in the intervention group, inclusive of programme fees, is $15,535 (€21,299), compared with $17,327 (€23,756) in the control group. Total intervention cost of $619,902 (€849,913) generated savings of $1,430,281 (€1,960,979), resulting in a return on investment of 2.31:1. | In summary, this community-based, concurrent trial of a commercial HF disease management intervention in the elderly demonstrated significant reductions in medical services, resulting in 10% lower cost of care. |
| **Boyne** (2013)[411] | Telemonitoring (TM)-supported education intervention versus usual care (UC) | 382 HF patients. Mean age was 71 yrs (range 32– 93), 59% were male. | Country: Netherlands<br>Study Design: CUA<br>Perspective: Healthcare<br>Discount rate: NA<br>Time Horizon: 12 months<br><br>(€2008, Dutch) | Utility scores improved by 0.07 points for the UC and 0.1 points for the TM group, but the difference between groups was not significant. This effect correlated with the QALY-score, which also showed no difference. The difference between the groups was -.0031 QALY with 95% CI of -0.0552 to 0.0578. | The total costs were €16,687 (€17,323) (CI 14,041–19,114) in the TM group and €16,561 (€17,192) (CI 13,635– 20,218) in the UC group. The difference between groups was €126 (€145) not a significant difference (CI -4,374–3,763). The ICER for TM versus UC amounted to €40,321 (€41,858) per QALY gained. | At a threshold of €50,000 (€57,481) the probability of TM being cost-effective is 48%. The overall incremental cost-effectiveness analysis showed a high level of decision uncertainty. Unambiguous conclusions about the whole group cannot therefore be drawn. |
| **Cui** (2013)[412] | 1)Standard treatment<br>2)health lines | 179 patients aged 40 and over with a diagnosis of CHF | Country: Canada<br>Study design: CUA<br>Perspective: health | Patients in the control group had more all-reasons hospital in-patient days than both intervention groups, but the | Mean per patient cost of intervention was $1,854 (€1,386) and $2,108 (€1,576) (HL, HLM) Compared to the | We estimated the ICER for HL compared to HLM by dividing these incremental |

| Study | Intervention | Population | Analysis details | Clinical and QALY outcomes | Cost | Authors' conclusions |
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| | 3) health lines plus in-house monitoring | levels II to IV | system<br>Discount: NA<br>Time Horizon: 12 months<br>(Can$ 2005) | differences were not significant (p=0.4865). Hospital in-patient days for CHF were significantly higher for the intervention groups relative to the control group (p<0.05). SF-6D utility scores were higher in the intervention groups at all measurements. Results reported QALYs for HLM and HL of .063 and 0.67 respectively. Difference of 0.04QALYs (95% CI: 0.01, 0.08 | control group, the total saving from averted healthcare utilisation costs through the interventions was $28,307 (€21,163) or $238 (€178) per capita. The total healthcare costs per patient, including intervention cost for the three study groups, were $7,151 (€5,346) (control group), $6,430 (€4,807) (HL) and $6,311 (€4,718) (HLM). The mean incremental cost of HL relative to HLM was $85 (€64) (95% CI: -$3,088 (-€2,309), $3,336 (€2,494)) taking into account savings from healthcare utilisation averted. | costs by incremental effectiveness. The HL was associated with an ICER of $2,975 (€2,224) in generating additional QALYs. HL can improve care and lower costs |
| **Dar** (2009)[413] | 1) Daily home telemonitoring of signs & symptoms (TM)<br>2) usual follow-up care available at each hospital from the cardiology service (UC) | 182 Patients with a recent HF hospital admission. | Country: UK<br>Study Design: a multi-centre randomised controlled<br>Perspective: NHS<br>Discount rate: N/A<br>Time Horizon: 6 month<br>(UK £ 2005) | During the 6 months of follow-up there was no difference in the median number of days alive and out of hospital in the two groups. There were significantly more emergency heart failure admissions in the UC group compared with the TM. There was no change in overall health-related quality-of-life as measured through the EQ5D over the 6 month follow-up period. | If mean direct NHS costs are considered, the incremental cost per patient for telemonitoring is statistically non-significantly higher by £1,600 (€2,290) per patient with a mean direct NHS cost for a telemonitored patient of £4,610 (€6,597) and £3,006 (€4,302) for usual care. The total median direct NHS costs per patient over the 6 month study period were £1,688 (€2,416) for the telemonitoring arm, and £1,498 (€2,144) for usual care. | Home telemonitoring in a typical elderly population of heart failure patients produces a similar outcome to 'usual' specialist care, but reduces clinic and emergency room visits and unplanned heart failure rehospitalisations at little additional cost. |
| **Dunagan** (2005)[414] | 1)Nurse-administered, telephone-based | patients hospitalised with heart failure | Country: US<br>Study Design: RCT | Intervention patients had longer time to encounter (HR 0.67; 95% CI 0.47–0.96; | The total overall hospital costs of the intervention were $1,323,166 (€1,814,120) and | A nurse-administered, telephone-based disease management |

| Study | Intervention | Population | Analysis details | Clinical and QALY outcomes | Cost | Authors' conclusions |
|---|---|---|---|---|---|---|
| | disease management programme<br>2) usual care as provided by their primary physician | n(=151) | Perspective: Healthcare<br>Discount rate: N/A<br>Time Horizon: 1 year<br>(US$ 2000) | P=.029), hospital readmission (HR 0.67; CI 0.46–0.99; P=.045) & heart failure–specific readmission (HR0.62; CI 0.38–1.03; P=.063). The number of admissions & hospital days were significantly lower during the first 6 months after intervention but not at 1 year. This was similar for physical functioning scores on both the SF-12 and the MLHF questionnaire at 6 months, but not at 12. | mean was $17,410 (€23,870). | programme delayed subsequent health care encounters, but had minimal impact on other outcomes. |
| **Giordano** (2009)[415] | 1)home based telemanagement (HBT)<br>2) Usual care | N=460 , 230 HBT, 230 UC, age 57 ±10 | Country: Italy<br>Study design: RCT<br>Perspective: healthcare<br>Discount rate: NA<br>Time horizon: 12 months<br>(Italian € cost year NR) | During one-year follow-up, all-cause hospital readmissions occurred in 67 patients in HBT group and 96 patients in UC group (RR=0.57, 95% [CI]: 0.39–0.84; p=0.03).Fifty five patients (24%) in HBT group and 83 patients (36%) in the UC group had at least one readmission due to cardiovascular reasons (RR=0.56, 95% [CI]: 0.38, 0.82; p=0.003). One-year total mortality was 9% HBT group and 14% in UC group. | The daily cost per patient of intervention in HBT group was €0.65. The mean annual cost per patient was € 185+/ −39. Mean cost for hospital readmission was significantly lower in HBT group (€ 843 +/−1733) than in UC group (€ 1298+/−2322), (−35%, p<001). According to estimated NNT the annual cost to prevent one readmission was € 638 (95% [CI]: 850–1913). | Telemedicine holds the promise of improving access to health care and of reducing costs; home telemanagement for cardiac chronic disease could be one of the most important applications |
| **Jerant** (2001)[416] | 1)Home telecare delivered via 2-way video-conference device with an integrated electronic | English-speaking patients 40 years of age and older with a primary hospital admission diagnosis of | Country: USA<br>Study Design: RCT<br>Perspective: Health system<br>Discount rate: N/A<br>Time Horizon: 6 | Both intervention groups had significantly fewer CHF-related ED visits (P = 0.0342) & charges (P = 0.0487) than the usual care group. Trends favouring both interventions were noted for | Mean total care charges were 68% lower in the home telecare group ($29,701) (€43,867) and 69% lower in the telephone group ($28,888) (€42,666) than in the usual care group ($93,686) | Substantial reductions in hospital readmissions, emergency visits, and cost of care for patients with CHF might be achieved by |

| Study | Intervention | Population | Analysis details | Clinical and QALY outcomes | Cost | Authors' conclusions |
|---|---|---|---|---|---|---|
| | stethoscope<br>2) nurse telephone calls<br>3) usual outpatient care | CHF. | months<br>(US $ 1998) | all other utilisation outcomes. | (€138,369) The difference was not statistically significant. | widespread deployment of distance technologies. Home telecare may not offer incremental benefit beyond telephone follow-up and is more expensive. |
| **Klersy** (2011)[417] | 1)multidisciplinary heart failure management remote patient monitoring (RPM)<br>2) usual care | Heart failure patients | Country: Italy<br>Study Design: CEA CUA review<br>Perspective: 3rd party payer<br>Discount rate:<br>Time Horizon: 1 year<br>(€ country not clear cost year NR) | RPM was associated with a significantly lower number of HF-related hospitalisations. The QALY gain due to reduction in mortality was 0.02, whereas the QALY gain due to reduced hospitalisations in surviving patients was 0.04, resulting in a total QALY gain of 0.06 for RPM. | The difference in costs between RPM and usual care ranged from about €300 to €1,000), RPM always being less costly than usual care. RPM is a 'dominant' approach over existing treatment as it is both cost saving and produces a positive QALY gain. | This novel cost-effectiveness data coupled with the demonstrated clinical efficacy of RPM compared with usual care, should encourage the acceptance of RPM amongst clinicians and consideration by third-party payers. |
| **Pandor** (2013)[389] | Home telemonitoring (TM) or structured telephone support (STS) Human to machine ( HM) or human to human (HH) | Adult patients recently discharged from acute care after a recent exacerbation of HF. | Country: UK<br>Study Design: Markov model<br>Perspective: NHS<br>Discount rate: 3.5%<br>Time Horizon: Lifetime<br>(GB £ 2011) | Both TM during office hours and STS HH are similar in terms of mean HRs for mortality. STS HH showing a higher QALY gain over usual care of 0.1059 compared with an additional 0.1038 QALYs gained with TM during office hours (equivalent to an additional 37.7 and 38.6 quality-adjusted days average gain for STS HH and TM respectively). | The total cost per patient for the STS HM intervention over 6 months was estimated to be £715 (€963), that is, a monthly cost of £119 (€160) per patient. The office hours TM intervention for 6 months was estimated to be £1051 (€1,416). That is, a monthly cost of £175 (€233) per patient. The total base-case cost per patient receiving the STS HH intervention for 6 months was estimated to be £1075 (€1448), that is, a monthly cost of £179 (€241) | Comparing STS HH with usual care, the incremental cost per QALY gained is<br>£1126 (€1,517)/0.1059 = £10,629 (€14,325), The ICER for TM during office hours compared with usual care is £992 (€1,336)/0.1038 = £9552 (€12,871). TM during office hours had an estimated |

| Study | Intervention | Population | Analysis details | Clinical and QALY outcomes | Cost | Authors' conclusions |
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| | | | | | per patient. The expected costs over a lifetime (30-year time horizon) differ for each strategy, with STS HH having the highest costs at £9604 (€12,938) followed by TM during office hours (£9470) (€12,757), STS HM (£9001) (€12,125) and usual care (£8478) (€11,421). | incremental cost effectiveness ratio (ICER) of £11,873 (€15,994.52) per QALY compared with usual care, whereas STS HH had an ICER of £228,035 (€307,194) per QALY compared with TM during office hours |
| **Riegel** (2002)[418] | Telephonic disease management | 130 Patients with recent HF hospitalisation | Country: USA<br>Study Design: RCT<br>Perspective: Healthcare<br>Discount rate: N/A<br>Time Horizon: 6 months<br>($ Cost year NR) | Heart failure hospitalisation rates at 3 months and 6 months were 45.7% and 47.8% lower in the intervention group than in the usual care control group respectively. Acute care utilisation was also lower. | The intervention was calculated to cost $443 per patient if the cost of training is included. The cost saving for acute care is about $1000 (usual care $2,186 vs intervention $1,192), usual care is almost double the cost of the intervention. | Intervention costs offset by savings from hospitalisations avoided. |
| **Scalvini** (2005)[419] | Home-based telecardiology (HBT consisted of trans-telephonic follow-up & ECG monitoring, followed by visits from the paramedical & medical team) compared with usual care | Chronic heart failure patients in stable condition. (n=426) mean age = 59 years | Country: Italy<br>Study Design: RCT<br>Perspective: Healthcare<br>Discount rate:<br>Time Horizon: 1 year<br>(€ cost year NR) | There was an increase in quality of life in the HBT group. The mean MLQ scores were 29 in the HBT group and 24 in the usual-care group; this difference was significant. There were significant reductions in hospitalisations and instability in the HBT group relative to the usual-care group. | The total costs of intervention were €75,426. There was a reduction of 24% in the total costs after one year in the group which underwent telecardiology. The total costs were lower in the HBT group (€107,494 and €140,874, respectively). | Results suggest that a telecardiology service can detect and prevent clinical instability, reduce rehospitalsation and lower the cost of managing CHF patients. |
| **Sohn** (2012)[420] | Telemedicine (nurse-calls to | Patients with Chronic Heart | Country: Germany<br>Study Design: | Participants of the "Telemedicine for the Heart" | Programme participants contributed about €2,633 less | Significant cost differences in favour |

| Study | Intervention | Population | Analysis details | Clinical and QALY outcomes | Cost | Authors' conclusions |
|---|---|---|---|---|---|---|
| | motivate patients to perform regular self-measurement) | Failure | retrospective matched-pairs analysis<br>Perspective: Health insurance<br>Discount rate:<br>Time Horizon: 1 year<br>(€ German cost year NR) | group exhibited significantly higher survival than participants of the control group. Regardless of the survival status, there were fewer hospital admissions in the programme group (1.02 vs. 1.30 per patient per year in the programme and control groups, respectively). | costs than the average patient in the control group. That corresponds to a 25.0% cost reduction | of the study group of up to 25% in relation to the total cost could be detected. This corresponds to an amount of about €1,500–€2,500 (€1,591- €2,651) total costs per patient per year. |
| **Soran** (2010)[421] | Computer based telephonic monitoring | 304 Recently hospitalised HF patients | Country: USA<br>Study Design: RCT<br>Perspective: Healthcare<br>Discount rate: N/A<br>Time Horizon: 6 months<br>(US $ cost year NR) | There were no significant statistical differences between the groups in regards to 6-month cardiac mortality, rehospitalisations for heart failure, or length of hospital stay. | The 6-month mean Medicare costs were estimated to be $17,837 and $13,886 for the intervention and the control groups, respectively. Mean cost of the interventions were $25 for standard care and $804 for HFMS. | Results suggest that enhanced patient education and follow-up is as successful and less costly than a sophisticated home monitoring device with an interactive programme in elderly patients. |
| **Wootton** (2009)[422] | Care coordination (including intervention telephone counselling, patient support and provision of facts sheets compared with usual care | Australian veterans with a diagnosis of congestive heart failure | Country: Australia<br>Study Design: RCT<br>Perspective: Healthcare<br>Discount rate:<br>Time Horizon:12 month<br>(AUS $ 2008) | There were no significant differences between the two groups in the change from baseline to follow-up for either group. | There were no significant differences in total costs of care between the intervention and control groups. | Results from the present RCT suggest that application of care coordination to veterans with CHF was successful, but did not have advantages over usual approaches to patient management. Statistically, there were no significant differences in costs of care or in QOL measurements. |

## Table A11.5 Summary of cost-effectiveness analyses for multidisciplinary care interventions

| Study | Intervention | Population | Analysis details | Clinical and QALY outcomes | Costs | Authors' conclusions |
|---|---|---|---|---|---|---|
| **Ledwidge** (2003)[423] | Multidisciplinary care (MDC) compared with routine care (RC) | 98 HF patients | Country: Ireland<br>Study Design: CBA RCT<br>Perspective: healthcare provider<br>Discount rate:<br>Time Horizon: 3 month<br>(€ Irish cost year NR) | The number of hospitalisations in the RC and MDC groups was 12 and 2, respectively, therefore there was an absolute reduction of 10 hospitalisations as a result of the intervention. | Dividing the absolute intervention cost by the absolute reduction in hospitalisations gives a service cost of €586 per hospitalisation prevented. The absolute cost-benefit of the programme ranges from €8,634 to €65,798. In addition, to the clinical benefits produced by the intervention, there was a net cost saving of €729 per patient treated. | MDC of HF remains cost-effective and cost-beneficial when combined with optimal medical care. The cost per HF hospitalisation prevented is €586. The service cost is €113 (95% CI: 185–244) per patient over 3 months and there is a net cost saving per patient treated of €729. |
| **Kasper** (2002)[424] | Multidisciplinary outpatient management programme compared with usual care | Two hundred patients hospitalised with CHF | Country: US<br>Study Design: prospective randomised trial<br>Perspective: Healthcare<br>Discount rate:<br>Time Horizon: 6 months<br>(US$ 1998) | There were fewer hospital admissions for any reason in the intervention group. Patients in the intervention group were more likely to report stable or improved symptoms, as compared with those in the non intervention group. Quality of life, measured by the Minnesota Living With Heart Failure Questionnaire improved in both groups, but patients in the intervention group improved more | The intervention, including salaries and supplies, cost $904 (€1,532) per patient. The mean outpatient pharmacy cost per patient was similar in both groups: $1,353 (€2,293) in the intervention group and $1,405 (€2,381) in the non intervention group. Mean inpatient costs for intervention group was $11,315 (€19,175) and $8,789 (€14,894) for the non-intervention group. | Our results indicate that a multidisciplinary approach to the management of high-risk outpatients with CHF improves quality of life, with a trend toward improvement in the primary end point of death and total number of CHF hospital admissions over a six-month intervention period. |
| **Stewart** (2002)[425] | Multidisciplinary home-based intervention (HBI) (comprising structure home visits by nurse ± pharmacist) | Patients aged 55 years hospitalised for HF and a history of ≥ 1 admission for acute HF. | Country: Australia<br>Study design: Costing study alongside RCT (n=297)<br>Perspective: Not stated (Presume healthcare payer) | During a median of 4.2 years follow-up, HBI was associated with fewer unplanned readmissions or death (0.21 vs. 0.37 per patient per month, p<0.01), longer event-free survival (7 vs. 3 months, p<0.01), | The median cost of readmissions was $A325 (€347) (IQR 21 (€22) to 831 (€888)) versus $A660 (€705) (IQR 74 (€79) to 1987 (€2,122)) per month per patient in the HBI and usual care groups, respectively (p<0.01). The total cost of these | The authors concluded that HBI is beneficial in reducing the frequency of unplanned readmissions for HF, that this persists in the long term and is associated with prolongation of survival, reduced levels of hospital |

| Study | Intervention | Population | Analysis details | Clinical and QALY outcomes | Costs | Authors' conclusions |
|---|---|---|---|---|---|---|
| | within 7-14 days of discharge) versus usual care | | Discount rate: None<br>Time horizon: 6 years<br>Costs: costs from 1995 to 2001 inflated and standardised to 2000/2001 AUSD | fewer deaths (56% vs. 65%, p=0.06), and a more prolonged survival (median 40 vs 22 months p<0.05). Overall, HBI patients accumulated 16% fewer unplanned readmissions (396 versus 475) and had a lower rate of unplanned readmission (mean of 0.17 versus 0.29 readmissions per patient per month, p<0.05). | clinic visits was $A165,579 (€176,866) versus $A241 552 (€258,018) for the HBI and usual care groups, respectively. The average cost of applying the HBI, taking into account both the cost of home visits and additional cardiology, primary care, and pharmacy consultations, was $A600 (€641)/patient. | activity and associated costs. |

## Table A11.6 Summary of cost-effectiveness analyses for disease management programmes

| Study | Intervention | Population | Analysis details | Clinical and QALY outcomes | Costs | Authors' conclusions |
|---|---|---|---|---|---|---|
| **Anderson** (2005) | Targeted inpatient education programme with comprehensive discharge planning & immediate outpatient reinforcement through a coordinated nurse-driven home health care programme compared with usual care | Heart failure patients over 50 years old. N=44 intervention group, n=77 UC | Country: US<br>Study design: RCT<br>Perspective: Healthcare<br>Discount:<br>Time Horizon: 6 month<br>(U$ 1997) | Intervention subjects had an 11.4% readmission rate within 6 months, compared with a 44.2% readmission rate in control subjects. Estimated that 14 readmissions were avoided in the intervention group | Hospital costs for programme implementation were $6960 (€10,608) for all 44 intervention subjects ($158 (€241) per subject).The average total 6-week cost savings for home health care for each subject in the intervention group was $1541 (€2,349). This cost saving was a direct result of decreased utilisation. The total cost saving for all 44 intervention subjects was $67,804 (€103,344). | These results suggest that all CHF patients should be offered comprehensive education and support that begins in the hospital and continues in the outpatient setting. |
| **Chen** (2010)[426] | Home-based heart failure centre management programme using nursing specialist-led telephone consultations (HFC group) compared with usual care | Chinese heart failure patients. (n=550) | Country: Taiwan<br>Study design: non concurrent, prospective design.<br>Perspective: Healthcare<br>Time Horizon: 6 months<br>Costs were converted from Taiwan dollars to us dollars in 2005 | The home-based intervention resulted in significantly lower all-cause admission rate/person (HFC 0.60 ± 0.77 times/person; UC 0.96 ± 0.85 times/person), shorter all-cause hospital stay (reduced by 8 days/person). | When considering all of the costs, despite having 58.9% higher out-patient care costs, the HFC home-based intervention still reduced the overall healthcare expenditure by 30.8% compared with the usual care programme. The total overall cost per month for UC and HFC were $1,454 (€1,609) and $1,006 (€1,113), respectively. | The 6-month, home-based intervention with nursing specialist-led telephone consultations may improve the clinical outcome and provide cost-savings for Chinese patients with heart failure. |
| **Discher** (2003)[427] | HF algorithm & clinical pathway incorporating AHCPR criteria for CHF, physician & nurse CHF education & patient educational materials compared with usual care | Patients admitted to hospital with CHF | Country: US<br>Study design: Before and after study<br>Perspective: Healthcare<br>Discount rate:<br>Time Horizon: 1 year | Managed patients had significantly lower length of stay (3.9±2.2 vs. 6.1±2.8 days; p<0.0001) vs. unmanaged. | The average cost per managed patient was lower than that for unmanaged patients ($4403.87±$1989.23 (€6,284±€2,838) vs. $6827.77±$3346.90 (€9,742±€4,776), respectively p<0.0001).Had all 593 patients | Disease management and clinical pathways may thus provide an acceptable and effective vehicle for both implementing and further updating the continually evolving |

| Study | Intervention | Population | Analysis details | Clinical and QALY outcomes | Costs | Authors' conclusions |
|---|---|---|---|---|---|---|
| | | | (US$ 1999) | | been enrolled in the CHF pathway, costs would have totalled (+) $437,693.30 ((+) 624,522) the potential loss, had all patients remained unmanaged, costs would have been $640,979.63 (€914,581) resulting in a total hospital saving of $1,078,672.93 (€1,539,104) for 1999. | diagnostic and therapeutic modalities for CHF, in service of further enhancing the quality and efficacy of patient care. |
| **Gregory** (2006)[428] | HF disease management (HFDM) programme delivered within a diverse provider network compared with usual care | Heart failure patients (n=200) | Country: US<br>Study Design: prospective randomised assessment<br>Perspective: Healthcare<br>Discount rate:<br>Time Horizon: 90 days<br>(US$ 2003) | Although not significant, the relative odds of at least one all-cause hospitalisation was 0.76 (95% CI 0.38-1.51) for the intervention compared with the control group. | The difference in hospitalisation cost between control & intervention groups was reduction in cost of $375 (€913)/patient. The net effect including the costs of the programme was an increase of $488 (€1,199)/patient for the intervention group vs. the control group. The programme would have been cost saving if HFDM costs had been 24% lower. | The intervention succeeded in reducing the rate of heart failure hospitalisations, although this effect was partially offset by an increase in non–heart failure hospitalisations. The resulting modest reduction in hospitalisation costs was exceeded by the cost of the intervention. |
| **Hebert** (2008)[429] | 1) nurse-led disease management intervention (face-to-face encounter with nurse & regular telephone follow-up)<br>2) usual care | 406 patients, 203 usual care, 203 nurse-led programme, mostly African American or Hispanic | Country: US<br>Study Design: CEA alongside RCT<br>Perspective: societal and payer<br>Discount rate:<br>Time Horizon:12 months<br>(US$ 2001) | Patients in the nurse-managed group maintained better physical functioning throughout the 12-month intervention than did patients who received usual care. In terms of QALYs the study reported 0.0497 QALY per person for the HUI3 and 0.0430 QALY per person for the EQ-5D. | Intervention costs totalled $2177 (€2,853) per patient. The 12-month incremental cost per QALY gained—the ICER—was $17 543 (€22,994) for the estimate of quality of life based on translation of the SF-12 to the EQ-5D and $15 169 (€19,883) for translation to HUI-3 From the perspective of a payer like Medicare, the incremental net cost over 12 months of implementing this programme was $158 (€207) per patient enrolled and $3673 | At less than $25 000 (€32,768) per QALY saved, this nurse-led disease management programme was reasonably cost-effective over 12 months, especially for patients with earlier stages of heart failure. Wider adoption of such programmes may be a sensible approach to reducing the burden of heart failure in ethnically |

| Study | Intervention | Population | Analysis details | Clinical and QALY outcomes | Costs | Authors' conclusions |
|---|---|---|---|---|---|---|
| | | | | | (€4,814) and $3176 (€4,163) per QALY for EQ-5D–derived and HUI-3-derived quality of life, respectively. | diverse, urban communities. |
| **Hendricks** 2014 [430] | Case management programme (CMP) compared with regular management | N=1202, 601 controls, 601 intervention | Country: Germany<br>Study design: Non concurrent control and intervention group<br>Perspective: Insurer<br>Discount rate: NR<br>Time horizon: 54months<br><br>(German € cost year NR) | The intervention group showed a lower rate of hospital admission/ readmission (6.2%/18.9% versus 16.6%/36.0%; p<0.0001 / p=0.041). Mortality rates did not differ significantly (5.0% versus 6.7%; p = 0.217). | Results show no significant difference in the mean cost per heart failure-related hospital stay, with a mean of €2841.59 (95% CI: 2627.51 to 3076.12) in the intervention group and €2651.71 [95% CI: 2476.87 to 2845.63] in the control group (p= 0.205). The annual heart failure-related hospitalisation costs per patient were €222.22 (95% CI: 145.10 to 307.77) in the intervention group versus €683.88 (95% CI: 522.33 to 850.70) in the control group (p<0.0001). For every case management programme participant, the health insurer therefore achieved a mean annual saving of €461.66 when compared to a patient receiving routine care | Fewer patients in the intervention group were admitted and readmitted to hospital, and lower inpatient treatment costs were identified. The physician contact rate was higher than in the control group. |
| **Inglis** (2006)[392] | Nurse-led, multidisciplinary, home-based intervention (HBI) compared with usual care | Elderly patients with HF. N=149 HBI, n=148 usual care | Country: Australia<br>Study Design: RCT<br>Perspective: Healthcare<br>Discount rate:<br>Time Horizon: 10 year<br><br>($AUS 2002) | Overall, statistically fewer patients in the HBI group compared with UC died during this period: 114 (77%) versus 132 (89%) overall, the HBI group accumulated more unplanned readmissions during follow-up. When we adjusted for the duration of follow-up, however, the rate of readmission was significantly lower in the HBI | The cost-benefit of HBI was estimated to be $1729 (€1,199) per additional life-year gained. The intervention cost $100,000 (€100,138). Total healthcare costs for the HBI and UC groups were $3,267,372 (€3,271,893) and $3,059,912 (€3,064,146) respectively, difference $207,460 (€207,747) | A simple cost- and time-effective nurse-led multidisciplinary intervention performed in the patient's home after hospitalisation relative to UC has the potential to extend the horizon of survival with CHF while cost-effectively reducing the frequency of recurrent |

| Study | Intervention | Population | Analysis details | Clinical and QALY outcomes | Costs | Authors' conclusions |
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| | | | | group: 3.66_7.62 versus 2.04_3.23 admissions per patient per year | | hospitalisation. |
| **Kwok** (2008)[431] | Community nurse-supported hospital discharge programme (home visits weekly x 4 then monthly; education; liaison support) versus usual care | Hospitalised patients aged ≥ 60 years with chronic heart failure and at least one admission for heart failure in the 12 months prior to the index admission | Country: Hong Kong<br>Study design: Costing study alongside RCT (n=105)<br>Perspective: Healthcare system / social care<br>Discount rate: N/A<br>Time horizon: 6 month<br><br>Costs: HKD 2000 (intervention 09/99-02/01) | At 6 months follow-up, there was no difference in re-admission rates or median number of readmissions for the intervention and control groups (46% vs. 57%, p=0.233 and 0 vs. 1 p=0.057, respectively). The intervention group had less handicap in independence (median change London Handicap Score 0 vs. 0.5, p=0.002), but there was no difference in six-minute walking distance (44m vs. 25m, p>0.05). | The median cost to the public health care system of the community nurse was HK$2,391 per subject (median visit cost =$385/subject). The median public health costs as a result of hospital stay and emergency care attendances were lower in the intervention group (HK$5,229 vs. HK$20,916, p=0.048), however the total public healthcare costs were not significantly different (HK$10,186 vs. $21,599, p>0.05). There was no difference in the median total personal costs (medical and social included) for the intervention and control groups (HK$1,457 versus HK$922, p=0.118). | The authors concluded that post-discharge visits by community nurses were not effective in reducing the change of readmission within six months, but were effective in preserving independence and were probably effective in reducing the number of unplanned admissions with no significant impact on public healthcare costs. |
| **Laramee** (2003)[432] | Case management (CM) (comprising early discharge planning and coordination of care, education of family and patient, 12-week telephone support and surveillance, optimisation of heart failure medication) versus usual care | Patients: admitted to hospital with primary or secondary diagnosis of CHF, LVEF <40% or radiological evidence of pulmonary oedema requiring diuresis; and who were at risk of early readmission (history of CHF or | Country: US<br>Study design: costing study alongside RCT (n=287)<br>Perspective: Not stated (? Healthcare provider)<br>Discount rate: N/A<br>Time horizon: 12 week<br><br>Costs: 2000 USD | There was no difference in 90-day readmission rates for the CM and usual care groups (37%). Patients in the CM group were more likely to be taking CHF medications at target doses (p>0.05), to be adherent with their treatment plan (p=0.40) and to be satisfied with their care (p<0.01). Subgroup analysis indicated a significant reduction in readmissions in patients initially admitted with | The intervention did not increase costs and there were no significant differences in outpatient and inpatient resource utilisation between the groups.<br>Based on an hourly cost of USD$34 (€48)/CM and an average time of 6.7hours/12 weeks, the average cost of the intervention was USD$228.52 (€321) per patient. Total inpatient and outpatient median costs were lower for the | The authors concluded that compared with usual care, case management did not reduce the 90-day readmission rate (possibly due to the heterogeneous population, varied access to care and lack of a coordinated system supports), but that it significantly improved treatment plan |

| Study | Intervention | Population | Analysis details | Clinical and QALY outcomes | Costs | Authors' conclusions |
|---|---|---|---|---|---|---|
| | | CHF-related admission or >4 admissions in previous 5 years or living alone or documented CHF knowledge deficits OR adherence issues). | | chronic renal failure or weight gain. | intervention group (USD$15,979 (€22,675) vs $18,662 (€26,188), p=0.14) | adherence and satisfaction in a cost-effective manner. |
| **Miller** (2009)[433] | Disease management programme vs. usual care<br><br>NB – modelled using data from Smith 2008 RCT | Community dwelling patients with systolic heart failure | Country: US<br>Study design: Markov model<br>Perspective: Health care system<br>Discount rate: 3 %<br>Time horizon: lifetime<br><br>Costs: 2003 USD | Baseline model results indicate that patients with systolic HF patients would live an average of 0.141 years (51 days) longer with disease management than those in the control group. The corresponding discounted QALY benefit was 0.111 per patient. | Discounted lifetime costs per patient averaged $74,025 (€91,182) and $78,875 (97,156) for the control and disease management groups, respectively. The average (undiscounted) per patient cost of the disease management programme was estimated at $8,586 (€10,576) ($246 (€303)/month for18-month DM programme or $107(€132)/month over average patient lifetime) | The net discounted disease management cost was $4,850 (€5,974) per patient resulting in an ICER of $43,650 (€53,767) per QALY saved. The authors concluded that that disease management of heart failure patients can be cost-effective in the long term, and that short terms results from a clinical trial might not reveal long term cost-effectiveness. |
| **Naylor** (2004)[434] | Transitional care planning by advanced nurse practitioners comprising discharge planning education, goal setting, use of evidence-based guidelines and home follow-up for 3 months compared with standard of care (which included site- | Patients aged 65 years and older hospitalised with a diagnosis of heart failure | Country: US<br>Study design: costing study alongside RCT (n=239)<br>Perspective: Not stated (Presume healthcare payer)<br>Discount rate: N/A<br>Time horizon: 52 week | Time to first readmission or death was longer in intervention patients (p=0.026). At 52 weeks, intervention group patients had lower rate of rehospitalisation or death (47.5% vs 61.2%, p=0.01), fewer readmissions (104 vs 162, p=0.047), and fewer hospital days (588 vs. 970, p=0.071). The proportion | Total and mean costs (reimbursements) per patient were lower in the intervention group than in the control group. Mean per patient 52-week total costs adjusted for unequal follow-up were significantly lower in the intervention groups were ($7,636 versus $12,481, p=0.002). The higher direct costs of the intervention | The authors concluded that a comprehensive transitional care intervention for elders hospitalised with heart failure increased the length of time between hospital discharge and readmission or death, reduced total number of rehospitalisations, and decreased healthcare |

| Study | Intervention | Population | Analysis details | Clinical and QALY outcomes | Costs | Authors' conclusions |
|---|---|---|---|---|---|---|
| | specific HF management, discharge planning and if necessary, referral to standard home care services) | | Cost year NR | patients remaining alive and with no hospital readmission was significantly lower in the control group at 30, 60, 90, 180 and 365 days post discharge.<br>Short term improvements in overall quality of life (12 weeks, p<0.05) and patient satisfaction (at 2 and 6 weeks, p<0.001) for the intervention group. | ($115,856 vs. $64,531) resulting from the increased number of home visits compared with usual care (13.2 vs 6.3), use of APN, and greater involvement of heart failure experts were offset by reductions in other home visits, acute care visits to physicians or the ED, and hospitalisations. | costs. |
| **Piepoli** (2006)[435] | multidisciplinary disease management programme<br>vs. Usual care | Patients recently hospitalised with heart failure | Country: Italy<br>Study Design: pre and post analysis<br>Perspective: Healthcare<br>Discount rate:<br>Time Horizon: 12 month<br>(Cost year unclear 2002-2004) | Compared with the 12 months before referral, the programme intervention was accompanied by a 56.8% reduction in the hospitalisation for all causes. Significant improvement in the global score was observed: from 2.61 to 2.10 (+19.4%). In fact 63.7% (324) of the patients improved NYHA functional class, | The total estimated saving in cost because of the hospitalisation for cardiovascular diseases was €300,305. The average estimated saving in hospital admission costs was €590 per patient. The total outpatient visits were €775, with an average of 1.5 per patient during the 12-month follow-up with an average cost of €68.5 per patient. | In summary, this prospective study has shown substantial effectiveness of our HF management programme developed with the contribution of health providers from both hospital and primary care settings. |
| **Pugh** (2001) | Case management by a nurse case manager (comprising enhanced discharge planning, post-discharge instruction and intensive post-hospital collaboration with their providers) versus usual care | Patients aged 65 years and older hospitalised for heart failure | Country: US<br>Study design: Costing study alongside a pilot RCT (n=58)<br>Perspective: Healthcare<br>Discount rate: N/A<br>Time horizon: 6 month<br>(Cost year not reported) | Compared with the control group, a positive effect was observed for the intervention in terms of SF-36 scores, functional status, and NYHA score; however these differences were not statistically significant. | The average monthly cost per patient was higher in the treatment group, but this difference was not significant ($1,379.96 [SD $1,596.35] vs. $1,038.31 [SD $1,263.05], p=0.51). | The authors concluded that the delivery model was no more expensive than usual care, and provided some positive effects on functional status and quality of life. |

| Study | Intervention | Population | Analysis details | Clinical and QALY outcomes | Costs | Authors' conclusions |
|---|---|---|---|---|---|---|
| **Postmus** (2011)[436] | Basic nurse-led disease management programme compared with intensive support by a nurse specialised in the management of patients with HF compared with care as usual (routine follow-up by a cardiologist) | 1023 Patients with HF | Country: The Netherlands<br>Study Design: RCT CEA COACH study<br>Perspective: Health service<br>Discount rate:<br>Time Horizon: 18 month<br>(Dutch €, 2009) | The mean quality-adjusted survival time was 287.6 days in the care-as-usual group, 296.1 days in the basic-support group, and 294.6 days in the intensive-support group. | In terms of cost per life-year, basic support dominated care as usual because it generated 0.048 additional life-years while saving €77(€79). When comparing the 2 disease management programs, intensive support was found to generate 0.0022 additional life-years at an excess cost of €1,178 (€1,211), yielding an ICER of €532,762 (€547,599) per life-year. In terms of cost per quality-adjusted life-year (QALY), basic support was found to dominate both care as usual and intensive support because it generated 0.023 and 0.004 excess QALYs while saving €77(€79) and €1,178 (€1,211), respectively. | To conclude the results provide a strong scientific case for a broader implementation of such programmes, provided that the intensity of the programme is tailored to the severity of the disease in individual patients<br>with HF. |
| **Roig** (2006)[437] | Specialised care programme that includes patient education on advanced heart failure, with day-care and home care elements, and involved intravenous drug administration when necessary. | 61 End stage heart failure patients | Country: Spain<br>Study Design: before and after Observational<br>Perspective: Healthcare<br>Discount rate:<br>Time Horizon: 1 year<br>(Spanish € cost year NR) | The mean number of hospital admissions required, the days spent in the hospital, and the number of visits to the emergency room per patient decreased very significantly after inclusion in the SCP, there were a total of 308 hospital admissions, a number that was reduced to 108 during the SCP. | The mean cost of health care per patient-year was €19 175. Total hospital costs were €17,585. Thus, the application of the SCP resulted in a savings of €1,590 per patient. When, under the SCP, home care replaced the day hospital, the cost was reduced to €14,675, resulting in an<br>even greater savings with respect to conventional car | Programmes of specialized care are of great utility in patients with end-stage HF; they reduce the numbers of readmissions and emergency room visits and, consequently, health care costs. |
| **Smith** (2008)[438] | Telephonic disease management (DM) compared with usual care | 1069 Community dwelling CHF patients | Country: USA<br>Study Design: RCT<br>Perspective: Health system | Disease management produced statistically significant survival advantages among all | Analyses of direct medical and intervention costs showed no cost savings associated with the intervention. For all patients | Telephonic DM did not reduce costs and was not cost-effective in this sample. However, when |

| Study | Intervention | Population | Analysis details | Clinical and QALY outcomes | Costs | Authors' conclusions |
|---|---|---|---|---|---|---|
| | | | Discount rate: N/A<br>Time Horizon: 18 months<br>(US $ 2003) | patients (17.4 days), among patients with NYHA class III/IV symptoms at baseline (47.7 days), among patients with SHF (24.2 days), and in the combined group | and considering all-cause medical care, the ICER was $146,870 (€176,762) per quality-adjusted life-year (QALY) gained, while for patients with NYHA class III/IV symptoms and patients with SHF, the ICERs were$67,784 (€81,580) and $95,721 (€115,203) per QALY gained, respectively. Costs per QALY gained were $101,120 (€121,700) for all patients, $72,501 (€87,257) for patients with SHF, and $41,348 (€49,764) for patients with NYHA class III/IV symptoms. the mean cost of DM services per patient per month was $246 (€296) | targeted properly, DM seems capable of producing life-span increases at costs that are less than $100,000 (€120,353) per QALY gained. |
| **Tsuyuki** (2004)[439] | Patient support programme (PSP) (education about HF, self-monitoring, adherence aids, newsletters, telephone hotline, & follow-up at 2 weeks, then monthly for 6 months after discharge) compared with usual care including frequent contact with study coordinators | 276 Hospitalised HF patients | Country: US<br>Study Design: RCT<br>Perspective: Health care service<br>Discount rate:<br>Time Horizon:6 month<br><br>(CAN$ 2000) | Although there were no differences in the number of all-cause physician visits, ER visits, or readmissions between treatment groups, there was a significant reduction in total length of hospital stay (627 days versus 1,082 days)and average length of hospital stay (6.6 days versus 11.0 days), between the patient support programme and usual care groups, respectively. | The total cost of care for CV-related events over the 6-month follow-up period of this study, was $CDN 4548 (€3,798) for usual care patients compared with $CDN 2017 (€1,684) for patient support programme patients, for a cost difference of $CDN 2531 (€2,113) per patient. For all-cause events, the cost difference per patient was $CDN 2463 (€2,057) ($CDN 6154 (€5,139) for usual care and $CDN 3691 (€3,082) for the patient support program). | A 6-month patient education and support programme for outpatients with HF had little impact on ACE inhibitor adherence however reduced utilisation of health care resources, resulting in a cost reduction of $CDN 2531 (€2,113) per patient for CV-related events. |

## Table A11.7 Summary of cost effectiveness analyses of other self-management support interventions

| Study | Intervention | Population | Analysis details | Clinical and QALY outcomes | Costs | Authors' conclusions |
|---|---|---|---|---|---|---|
| **Bruggink** (2007)[440] | Physician-and-nurse-directed heart failure clinic vs. usual care (UC) | 240 patients recently discharged HF patients with NYHA class III or IV. | Country: The Netherlands<br>Study design: RCT<br>Perspective: Healthcare<br>Discount:<br>Time Horizon: 12 months<br>Netherlands €, cost year NR) | The incidence rate of the composite end point for the intervention and UC groups were 20.7/ 100 and 42.2/100 patient years, respectively. At 12 months, LVEF had improved in the intervention group, but deteriorated in the UC group. After 3 and 12 months, the NYHA class had significantly improved in the intervention group compared with UC. Improvements in MLWHFQ scores were greater in the intervention group at 3 months than in the UC group with the difference persisted during the remaining 9 months. | The difference between the costs of hospitalisation in the intervention group €65,046 and in the usual care group €202,728 was €137,682. The total cost for the HF clinic programme (for the salary of the HF nurse, HF physician and the dietician, and for the extra lab and ECGs) was €50,246 As a result, the positive balance for the intervention group was €87,436 and the difference in the overall cost of care per patient was €741 | The intensive management programme substantially reduces hospitalisation for HF and/or all-cause mortality, while improving LVEF, NYHA class, quality of life and self-care behaviour, and achieving a reduction in costs. |
| **Mejia** (2014)[441] | Nurse facilitated, cognitive behavioural self-management programme compared with usual care | 260 Heart failure patients with mean age 70.60 | Country: UK<br>Study Design: RCT CEA<br>Perspective: NHS<br>Discount rate: N/A<br>Time Horizon: 12 months (UK £ 2008/09) | Both groups reported a similar frequency of contact with health care professionals. Patient reported length of stay was lower in the self-management group. Treatment was associated with a slight reduction in effectiveness of 0.02, but there was a large amount of uncertainty around this estimate, after using imputed data the figure changed to a reduction in QALY of 0.004 | The intervention would generate an additional cost of £313.3(€435). Based on the complete case data, the intervention cost approximately £321 (€446) more than usual care when imputed data was used this changed to £69.49 (€96). Using 2011/2012 costs, the intervention would be associated with an increase in costs of £92 (€128) and thus would be dominated by usual care using CBT manual alone. The probability that the intervention is cost | In conclusion, the addition of nurse facilitation to a cognitive-behavioural therapy for patients with heart failure is associated with no clear effect on costs or effectiveness as measured by QALY. |

| Study | Intervention | Population | Analysis details | Clinical and QALY outcomes | Costs | Authors' conclusions |
|---|---|---|---|---|---|---|
| | | | | | effective is around 45%. | |
| **Murray** (2007)[442] | Pharmacist intervention for improving medication adherence compared with usual care | 314 Low-income patients with heart failure. | Country: US<br>Study Design: RCT<br>Perspective: Payer<br>Discount rate:<br>Time Horizon: 12 month<br>(US $ 2003) | The intervention group had 19.4% fewer exacerbations on the combined end point of hospital admission or emergency department visit (incidence risk ratio, 0.82 (95% CI 0.73-0.93)). A significant improvement in adherence was observed in the 9-month intervention period, but dissipated in the 3-month post intervention follow-up. | The mean cost of the intervention was $205 (€247) per patient. The mean difference in the overall cost of health care was $3165 (€3,809) lower in the intervention group. Considering the costs of development and implementation, the intervention saved $2960 (€3,562) per patient. | In conclusion, we found that our pharmacy-based intervention for outpatients with heart failure improved adherence to cardiovascular medications and decreased health care use. |
| **Stauffer** (2011)[443] | Nurse-led transitional care programme compared with usual care | Heart failure patients 65 and older. | Country: US<br>Study Design: Prospective RCT<br>Perspective: budget holder and health care provider<br>Discount rate:<br>Time Horizon: 3 month | Adjusted 30-day readmission rate was 48% lower at BMCG after the intervention than before the intervention | Before the intervention, total 60-day direct cost for an HF index admission at BMCG was $1,251 less on average than the system average for BHCS. Although post intervention costs were less at BMCG, the difference between BMCG and the system narrowed during the intervention period owing to a significant reduction in total 60-day direct costs for BHCS facilities. | |

## Table A11.8 Summary of quality appraisal of cost-effectiveness studies

| Study | Quality | Notes |
|---|---|---|
| **Agren (2013)** | Moderate | |
| **Aguado (2010)** | Moderate | |
| **Anderson (2005)** | Poor | Poor quality reporting and study design. Cost data is poorly described. |
| **Berg (2004)** | Moderate | Potential bias due to study design. |
| **Boyne (2013)** | High | |
| **Bruggink (2007)** | Poor | Cost data is poorly described. |
| **Burri (2013)** | Poor | Intervention and condition not relevant |
| **Calo (2013)** | Poor | Intervention and condition not relevant |
| **Chen (2010)** | Poor | Relevance is questioned as the study focuses on Taiwan population |
| **Cui (2013)** | High | |
| **Dar (2009)** | Moderate | Short follow-up period of only 6 months. |
| **Discher (2003)** | Poor | Physician decided which patients entered the trial, strong chance of bias. |
| **Dunagan (2005)** | Moderate | Only mean hospital costs presented and no description of where costs come from. |
| **Gregory (2006)** | Moderate | Short follow-up of 90 days. Reports perspective as societal but does not examine all relevant costs. |
| **Giordano (2009)** | Moderate | Only hospital costs examined |
| **Hendricks (2014)** | Poor | Poor study design, control and intervention group not comparable, all important costs are not considered |
| **Hebert (2008)** | Moderate | Population focuses on urban African Americans which may not representative of this study's population |
| **Inglis (2006)** | High | |
| **Jerant (2001)** | Poor | Short follow-up, all important costs are not considered |
| **Kasper (2002)** | Moderate | Short follow-up |
| **Klersy (2011)** | Poor | Cost data poorly described |
| **Koelling (2005)** | Poor | Only hospital readmission costs examined |
| **Krumholz (2002)** | Moderate | Only hospital costs examined |
| **Ledwidge (2003)** | Moderate | Cost-benefit analysis, did not consider all outcomes. Not possible to determine how outcomes were valued |
| **Kwok (2008)** | Moderate | Short follow-up period of only 6 months. |
| **Laramee (2003)** | Moderate | Short follow-up period of only 12 weeks |

| | | |
|---|---|---|
| **Lopez (2006)** | Moderate | |
| **Maeng (2014)** | Poor | |
| **Mejia (2014)** | High | |
| **Miller (2009)** | Moderate | Costs not disaggregated; apportion intervention costs over lifetime of study, but unclear that this appropriate |
| **Morcillo (2005)** | Moderate | The study by Aguado et al. is an update of this study therefore findings should be taken from Aguado. |
| **Murray (2007)** | Moderate | Cost data is poorly described and reported. |
| **Naylor (2004)** | Moderate | Cost data presented in aggregate form only |
| **Pandor (2013)** | High | |
| **Piepoli (2006)** | Poor | Poor quality reporting and study design. Cost data is poorly described. |
| **Postmus (2011)** | Moderate | |
| **Pugh (2001)** | Poor | Costing study alongside pilot RCT (n=58) with 6-month follow-up. Cost data poorly described and reported and unclear whether all relevant costs are included. |
| **Riegel (2004)** | Poor | Poor quality reporting. Cost and outcome data are poorly described and it is unclear whether all relevant costs have been included. |
| **Riegel (2002)** | Poor | Poor quality reporting. Cost and outcome data are poorly described and it is unclear whether all relevant costs have been included. |
| **Roig (2006)** | Poor | Poor quality reporting. Cost and outcome data are poorly described and it is unclear whether all relevant costs have been included. |
| **Scalvini (2005)** | Poor | Poor quality reporting. Cost and outcome data are poorly described and it is unclear whether all relevant costs have been included. |
| **Smith (2008)** | Moderate | |
| **Sohn (2012)** | Moderate | Health insurance perspective may led to bias |
| **Soran (2010)** | Moderate | Poor quality reporting. Not possible to determine how clinical outcomes were measured or evaluated. It is unclear whether all relevant outcome data have been included |
| **Stauffer (2011)** | Poor | For profit, health insurer perspective taken |
| **Stewart (2002)** | Moderate | Community-based costs were not measured over the long term, |
| **Tsuyuki (2004)** | Moderate | Short follow-up with no incremental analysis |
| **Wootton (2009)** | Poor | Poor quality reporting. Cost and outcome data are poorly described and it is unclear whether all relevant costs have been included. |

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