Health Information and Quality Authority

An tÚdarás Um Fhaisnéis agus Cáilíocht Sláinte

# Health technology assessment (HTA) of smoking cessation interventions

## Appendices

**22 March 2017**

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# List of abbreviations used in this report

| | |
|---|---|
| BIOCHEM | biochemically validated abstinence |
| CBT | cognitive behavioural therapy |
| CAR | continuous abstinence rate |
| COPD | chronic obstructive pulmonary disease |
| EAG | Expert Advisory Group |
| EMA | European Medicines Agency |
| ENDS | electronic nicotine delivery system |
| ENNDS | electronic non-nicotine delivery system |
| FDA | Food and Drugs Authority |
| FTND | Fagerstrom Test for Nicotine Dependence |
| HIQA | Health Information and Quality Authority |
| HPRA | Health Products Regulatory Authority |
| HR | hazard ratio |
| HSE | Health Service Executive |
| HTA | health technology assessment |
| ICER | incremental cost-effectiveness ratio |
| NICE | National Institute for Health and Care Excellence |
| NRPA | nicotine receptor partial agonist |
| NRT | nicotine replacement therapy |
| OR | odds ratio |
| PCRS | Primary Care Reimbursement Scheme |
| PP | point prevalence abstinence |
| PTSD | Post-traumatic stress disorder |
| QALY | quality-adjusted life year |
| RCT | randomised controlled trial |
| RR | relative risk |
| SR | self reported |
| TQD | target quit date |
| UK | United Kingdom |
| WHO | World Health Organization |

# Appendices

## Appendix 1 Search details for review of smoking cessation interventions among users of secondary mental health services

### Figure 1.1 Flow diagram of included studies from the updated search

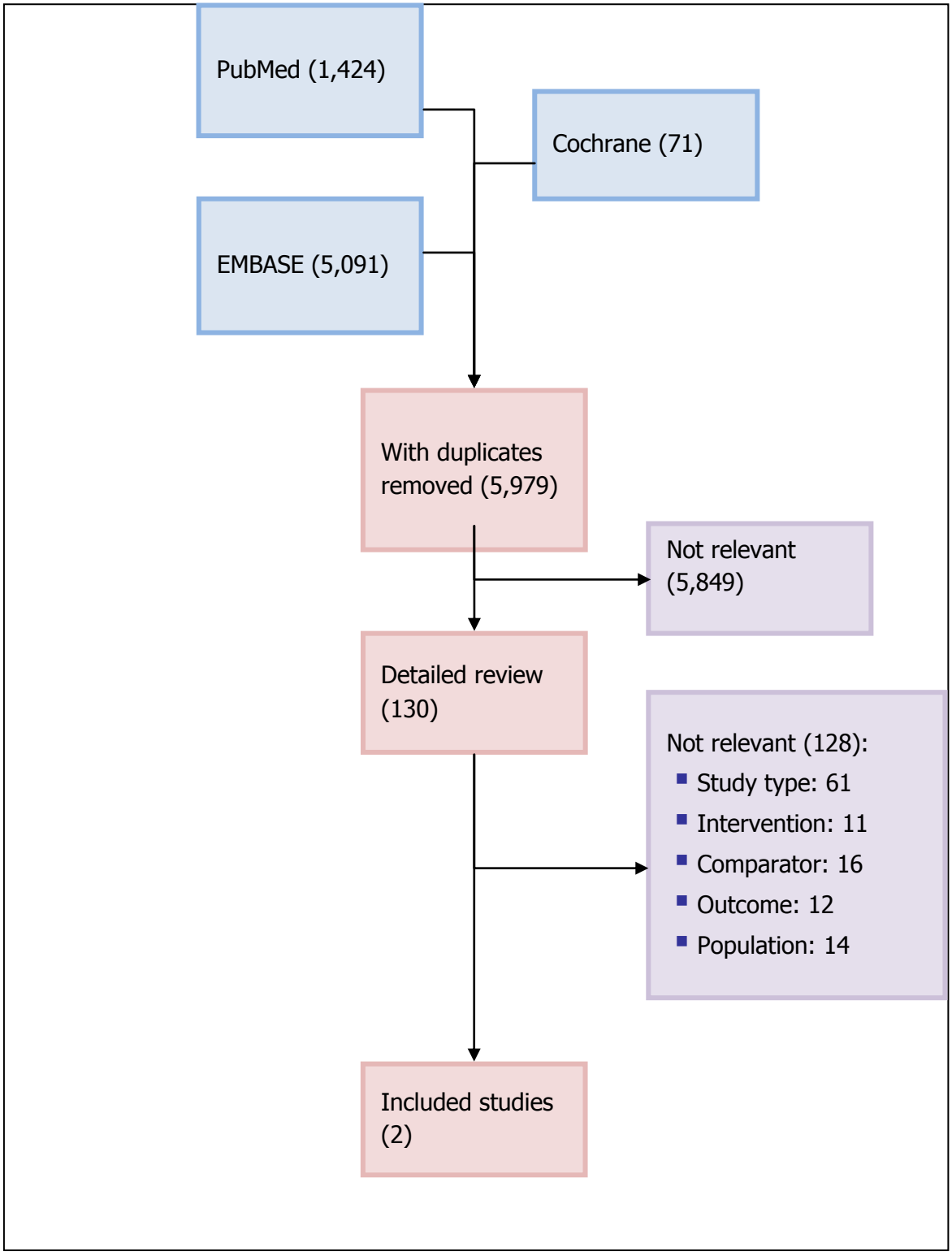


**Table 1.1 Search string used in PubMed**

| Search string | Results |
|---|---|
| (((((((((bipolar[Title/Abstract]) OR depress*[Title/Abstract]) OR schizophren*[Title/Abstract]) OR mental health[Title/Abstract]) OR mental illness*) OR mental disorder*[Title/Abstract]) OR "Mental Health Services"[Mesh]) OR "Mental Disorders"[Mesh]))<br>AND<br>((((("Tobacco Use Cessation products"[Mesh]) OR "Tobacco Use Cessation"[Mesh]) OR "Smoking"[Mesh]) OR ((((((abstinence[Title/Abstract]) OR cessat*[Title/Abstract]) OR quit*[Title/Abstract]) OR stop*[Title/Abstract])) AND (((cigarette*[Title/Abstract]) OR tobacco[Title/Abstract]) OR smok*[Title/Abstract])))<br>AND<br>((Clinical Trial[ptyp] OR Randomized Controlled Trial[ptyp] OR Clinical Trial, Phase I[ptyp] OR Clinical Trial, Phase II[ptyp] OR Clinical Trial, Phase III[ptyp] OR Clinical Trial, Phase IV[ptyp] OR systematic[sb] OR Review[ptyp])<br>AND<br>("2012/01/01"[PDat] : "2016/12/31"[PDat]) AND Humans[Mesh]) | 1,424 |

# Appendix 2 Included studies for those with a diagnosis of schizophrenia or schizoaffective disorder

## Table 2.1 Bupropion + behavioural intervention with/without NRT versus placebo + behavioural intervention with/without NRT

| Study | Country | Setting | Participants | Mean age | Female | Population | Intervention | Control | Support | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Evins 2001[1] | USA | Community volunteers | 19 | 44.1 | 42% | DSM-IV diagnosis of schizophrenia | Bupropion 150mg/day for 12 wks | Placebo for 12 wks | Both groups received brief advice and 9 wkly 1-hour sessions of group CBT | 6m (biochem, PP) | High |
| Evins 2005[2] | USA | Community volunteers | 57 | 45.7 | 31.6% | DSM-IV diagnosis of schizophrenia or schizoaffective disorder, depressed type | Bupropion 300mg/day for 12 wks (150mg/day for first wk) | Placebo for 12 wks | Both groups received 12 wkly 1-hour sessions of group CBT | 6m (biochem and self-reported, CAR, PP) | High |
| Evins 2007[3] | USA | Community volunteers | 51 | 44.2 | NR | DSM-IV diagnosis of schizophrenia | Bupropion SR 300mg/day for 12 wks. (150mg/day for first 7 days) | Placebo for 12 wks | Both received 1) 12 wkly 1-hour sessions of group CBT; (2) TNP (from wk 4) 21 mg/day for 4 wks, then 14 mg/day for 2 wks, 7 mg/day for 2 wks + up to 18 mg per day NG as required | 6m, 12m (biochem, PP) | Low |
| George 2002[4] | USA | Community volunteers | 32 | 43.2 | 43.8% | DSM-IV diagnosis of schizophrenia or schizoaffective disorder. 20 had | Bupropion 300mg/day for 10 wks (150mg/day for first 3 | Placebo for 10 wks | Both groups received 10 wkly 1-hour sessions of group therapy for motivational | 6m (biochem, CA) | Unclear |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | a diagnosis of schizophrenia | days) | | enhancement, psychoeducation and relapse prevention | | |
| George 2008[5] | USA | Community volunteers | 59 | 40.3 | 40.7% | DSM-IV diagnosis of schizophrenia or schizoaffective disorder. 32 had a diagnosis of schizophrenia | Bupropion 300mg/day for 10 wks (150mg/day for first 3 days) | Placebo for 10 wks | Both groups received 10 wkly 50-minute sessions of GBT and TNP (21mg per 24 hours) from day 15 to day 70 | 6m (PP, biochem CA) | Unclear |

## Table 2.2 Varenicline + behavioural intervention versus placebo + behavioural intervention

| Study | Country | Setting | Participants | Mean age | Female | Population | Intervention | Control | Support | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Williams 2012[6] | USA, Canada | Community volunteers | 128 | 41.1 | 23.4% | DSM-IV TR diagnosis of schizophrenia or schizoaffective disorder. 91 had schizophrenia. 109 pts on atypical antipsychotic | Varenicline (0.5mg daily for 3 days then twice daily for 4 days then 1mg twice daily) for 12 wks | Placebo for 12 wks | Both groups received wkly counselling (less than 30 minutes) | 6m (biochem, PP) | Unclear |

## Table 2.3 Individual counselling + NRT versus routine care

| Study | Country | Setting | Participants | Mean age | Female | Population | Intervention | Control | Additional support | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Baker 2006[7] | Australia | Community volunteers | 298 | 37.2 | 48% | ICD-10 diagnosis of psychotic disorder. 126 had a diagnosis of schizophrenia and 43 a diagnosis of schizoaffective disorder | Individually administered SC intervention (6 wkly sessions & 2 boosters at wks 8 and 10, 1 hour each): based on MI and CBT + TNP (21mg from wk 3 (quit date set) to 8; 14mg from week 9 to 10; 7mg from wk 11 to 12) | Routine care | Both groups received booklets on smoking cessation | 6m, 12m, 4yrs (CA, biochem, PP) | High |

## Table 2.4 High-intensity individual counselling + NRT versus lower-intensity individual counselling + NRT

| Study | Country | Setting | Participants | Mean age | Female | Population | Intervention | Control | Additional support | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Williams 2010[8] | USA | Community volunteers | 100 | 45.2 | 45% | DSM-IV diagnosis of schizophrenia or schizoaffective disorder | High intensity: TANS (treatment of nicotine addiction in schiz): 24 individual sessions of 45 minutes psychological intervention over 26 wks (MI, social skills training, use of NRT, relapse prevention technique) | Medication Management: 9 individual sessions of 20 minutes psychological intervention over 26 wks (medication compliance, education about NRT) | Both groups also received TNP for 16 wks after quit date (21mg for 12 wks then 14mg for remaining 4 wks) | 6, 12m (PP, biochem) | High |

## Table 2.5 Group behavioural intervention (generic) + NRT versus group behavioural intervention (tailored to schizophrenia) + NRT

| Study | Country | Setting | Participants | Mean age | Female | Population | Intervention | Control | Additional support | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|---|
| George 2000[9] | USA | Unclear | 45 | 39.7 | 33.3% | DSM-IV diagnosis of schizophrenia (n=19) or schizoaffective disorder | Specialised smoking cessation group therapy designed for pts with schizophrenia, wkly for 10 wks (60 minutes each session): first 3 wks motivational enhancement therapy + last 7 wks psycho-education, social skills training and relapse prevention strategy | American Lung Assoc. (ALA) programme wkly for 10 wks (60 minutes each session): first 7 wks behavioural group therapy + final 3 wks supportive group counselling | Both groups received nicotine patch (21mg/day for first 6 wks then 14mg/day for another 2 wks and 7mg/day for final 2 wks) | 6m (CA, biochem + SR) | High |

# Appendix 3 Included studies for those with a diagnosis of bipolar disorder

## Table 3.1 Varenicline + brief advice versus placebo + brief advice

| Study | Country | Setting | Participants | Mean age | Female | Population | Intervention | Control | Additional support | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Chengappa 2014[10] | USA | Outpatient clinics | 60 | 46 | 37% | DSM-IV bipolar disorder | Varenicline | Placebo | Smoking cessation counselling provided to all patients | 6m (PP, biochem at 12 weeks only) | Low |

# Appendix 4 Studies from the UK Centre for Tobacco Control Studies (UKCTCS) report that were excluded from this review

| | Study (year) | Reason | Reason for exclusion |
|---|---|---|---|
| 1 | Akbarpour 2010 | Outcome | Outcome not applicable (reduction in smoking - abstinence not defined or measured). |
| 2 | Axtmayer 2011 | Outcome | Outcome not applicable ('number of cigarettes smoked per day' - not smoking cessation). |
| 3 | Baker 2009 | Study design | Study design not applicable (uncontrolled before and after study). |
| 4 | Barnett 2008 | Intervention | Intervention not applicable (participants received $25 payment for each research assessment). |
| 5 | Bloch 2010 | Outcome | Outcome not applicable (reduction in smoking - abstinence not defined or measured). |
| 6 | Batra 2010 | Population | Current depression population - not clear if all attending secondary mental health services. |
| 7 | Brown 2003 | Population | Population not applicable (people aged less than 18 years old). |
| 8 | Brown 2007 | Population | Current depression population - not clear if all attending secondary mental health services. |
| 9 | Catley 2005 | Population | Current depression population - not clear if all attending secondary mental health services. |
| 10 | Chen 2002 | Short-term | Short-term only (7 day point prevalence quit rates at 4 and 8 weeks). No 6-month cessation data. |
| 11 | Chou 2004 | Short-term | Short-term only (cessation measured at 8 weeks only). |
| 12 | Cornelius 1997 | Intervention | Intervention not applicable (fluoxetine). |
| 13 | Culhane 2008 | Short-term | Short-term only (12 weeks only). |
| 14 | Currie 2008 | Study design | Study design not applicable (not random assignment). |
| 15 | Dalack 1999 | Outcome | Outcome not applicable (reduction in smoking, abstinence not defined or measured). |
| 16 | de Leon 2005b | Intervention | Intervention not applicable (clozapine). |
| 17 | Dixon 2009 | Study design | Patients not randomised. |
| 18 | Dutra 2012 | Comparator | No comparison group. Uncontrolled before-and-after study. |
| 19 | Fatemi 2005 | Outcome | Outcome not applicable (reduction in smoking, abstinence not defined or measured). |
| 20 | Gallagher 2007 | Intervention | Intervention not applicable (includes contingency payments). |
| 21 | Hall 2006 | Population | Current depression population - not clear if all attending secondary mental health services. |
| 22 | Hartman 1991 | Outcome | Outcome not applicable (reduction in smoking, abstinence not defined or measured). |
| 23 | Hertzberg 2001 | Population | Population not applicable (PTSD in male combat veterans). |
| 24 | Hill 2007 | Short-term | Non-randomised pilot study, outcomes measured at 3 months only. |

| | | | |
|---|---|---|---|
| 25 | Kelly 2008 | Intervention | Intervention not applicable (galantamine). |
| 26 | Kinnunen 2008 | Population | Current depression population - not clear if all attending secondary mental health services. |
| 27 | Kisely 2003 | Study design | Study design not applicable, non-randomised cross-over study. |
| 28 | Levine 2010 | Population | Current depression, but not clear if all attending secondary mental health services. |
| 29 | Li 2009 | Short-term | Short-term only, cessation measured at 1, 2, 4 and 8 weeks. |
| 30 | McEvoy 2005 | Intervention | Intervention not applicable (clozapine). |
| 31 | McFall 2005 | Population | Population not applicable, (PTSD in veterans). |
| 32 | McFall 2010 | Population | Population not applicable, (PTSD). |
| 33 | Morris 2011 | Outcome | Outcomes not applicable (50% reduction and not cessation). |
| 34 | Panchas 2012 | Study design | Study design not applicable - before-and-after study without randomisation. |
| 35 | Rabius 2007a | Population | Current depression population - not clear if all attending secondary mental health services. |
| 36 | Rabius 2007b | Population | Current depression population - not clear if all attending secondary mental health services. |
| 37 | Roll 1998 | Intervention | Intervention not applicable (contingency payments). |
| 38 | Saxon 2003 | Population | Population and intervention not applicable: veterans in treatment for alcohol or drug dependency. |
| 39 | Smith 2009 | Short-term | Short-term follow-up (9 weeks only). |
| 40 | Steinberg 2003 | Outcome | Outcome not applicable (reduction in smoking, abstinence not defined or measured). |
| 41 | Szombathyne 2010 | Outcome | Outcome (abstinence not defined or measured) and intervention (altrexone) not applicable. |
| 42 | Thorsteinsson 2001 | Short-term | Short-term follow-up period (29 days). |
| 43 | Tidey 2002 | Intervention | Intervention not applicable (contingency payments). |
| 44 | Tidey 2011 | Outcome | Outcome not applicable (reduction in smoking, abstinence not defined or measured). |
| 45 | Van der Meer 2010 | Population | Current depression population - not clear if all attending secondary mental health services. |
| 46 | Weinberger 2008a | Study design | Study design not applicable (pilot study of 5 people). |
| 47 | Weiner 2001 | Comparator | No comparison group. |
| 48 | Weiner 2011 a | Short-term | Short-term only (cessation measured at 4 and 12 weeks only). |
| 49 | Weiner 2011 b | Short-term | Short-term only (cessation measured at 12 weeks only). |
| 50 | Williams 2007 | Short-term | Short-term only (cessation measured at 8 weeks only). |
| 51 | Wotjna 2009 | Study design | Study design (lack of randomisation). |

# Appendix 5 Studies from the Cochrane review of smoking cessation in schizophrenia that were excluded from this review

| | Study (year) | Reason | Reason for exclusion |
|---|---|---|---|
| 1 | Akbarpour 2010 | Outcome | Outcome is reduction in smoking; abstinence not defined or measured. |
| 2 | Bloch 2010 | Outcome | Outcome is reduction in smoking; abstinence not defined or measured. |
| 3 | Brown 2003 | Population | Population less than 18 years old. |
| 4 | Chen 2012 | Short-term | Abstinence reported at 8 weeks only. |
| 5 | Dalack 1999 | Outcome | Outcome is reduction in smoking; abstinence not defined or measured. |
| 6 | de Leon 2005b | Intervention | Use of Clozapine. |
| 7 | Dutra 2012 | Comparator | No comparison group. Uncontrolled before-and-after study. |
| 8 | Fatemi 2005 | Outcome | Outcome is reduction in smoking, abstinence not defined or measured. |
| 9 | Gallagher 2007 | Intervention | Includes contingency payments. |
| 10 | Gelkopf 2012 | Outcome | Outcome is reduction in smoking; abstinence not defined or measured. |
| 11 | Hartman 1991 | Outcome | Outcome is reduction in smoking; abstinence not defined or measured. |
| 12 | Hong 2011 | Outcome | Effect of varenicline on neurobiological and cognitive biomarkers in schizophrenia. Abstinence not defined or measured. |
| 13 | Horst 2005 | Outcome | Relapse prevention after smoking cessation. Abstinence not defined or measured. |
| 14 | Kelly 2008 | Intervention | Use of Galantamine. |
| 15 | Li 2009 | Short-term | Cessation measured at 1, 2, 4 and 8 weeks only. |
| 16 | McEvoy 1995 | Intervention | Use of Clozapine. |
| 17 | McEvoy 1999 | Intervention | Use of Clozapine. |
| 18 | Meszaros 2012 | Outcome | Effect of varenicline on alcohol dependence (as primary outcome according to protocol). Abstinence not defined or measured. |
| 19 | Pachas 2012 | Study design | Before and after study without randomisation. |
| 20 | Roll 1998 | Intervention | Contingency payments. |
| 21 | Sacco 2009 | Intervention | Use of Atomoxetine. |
| 22 | Shim 2012 | Outcome | Outcome is reduction in smoking; abstinence not defined or measured. |

| | | | |
|---|---|---|---|
| 23 | Steinberg 2003 | Outcome | Outcome is reduction in smoking; abstinence not defined or measured. |
| 24 | Szombathyne 2010 | Outcome<br>Intervention | Outcome is reduction in smoking; abstinence not defined or measured.<br>Use of Naltrexone. |
| 25 | Tidey 2002 | Intervention | Contingency payments. |
| 26 | Tidey 2011 | Outcome | Outcome is reduction in smoking; abstinence not defined or measured. |
| 27 | Weinberger 2008 | Intervention | Use of Topiramate. |
| 28 | Weiner 2001 | Comparator | No comparison group. |
| 29 | Weiner 2011 a (var) | Short-term | Cessation measured at 4 and 12 weeks only. |
| 30 | Weiner 2012 | Short-term | Cessation measured at 12 weeks only. |
| 31 | Williams 2007 | Short-term | Cessation measured at 8 weeks only. |
| 32 | Wing 2012 | Intervention | Active Repetitive Trancranial Magnetic Stimulation (rTMS) - bilateral to dorsolateral prefrontal cortex v Sham rTMS. |

# Appendix 6 Studies from the Cochrane review of smoking cessation in current and past depression that were excluded from this review

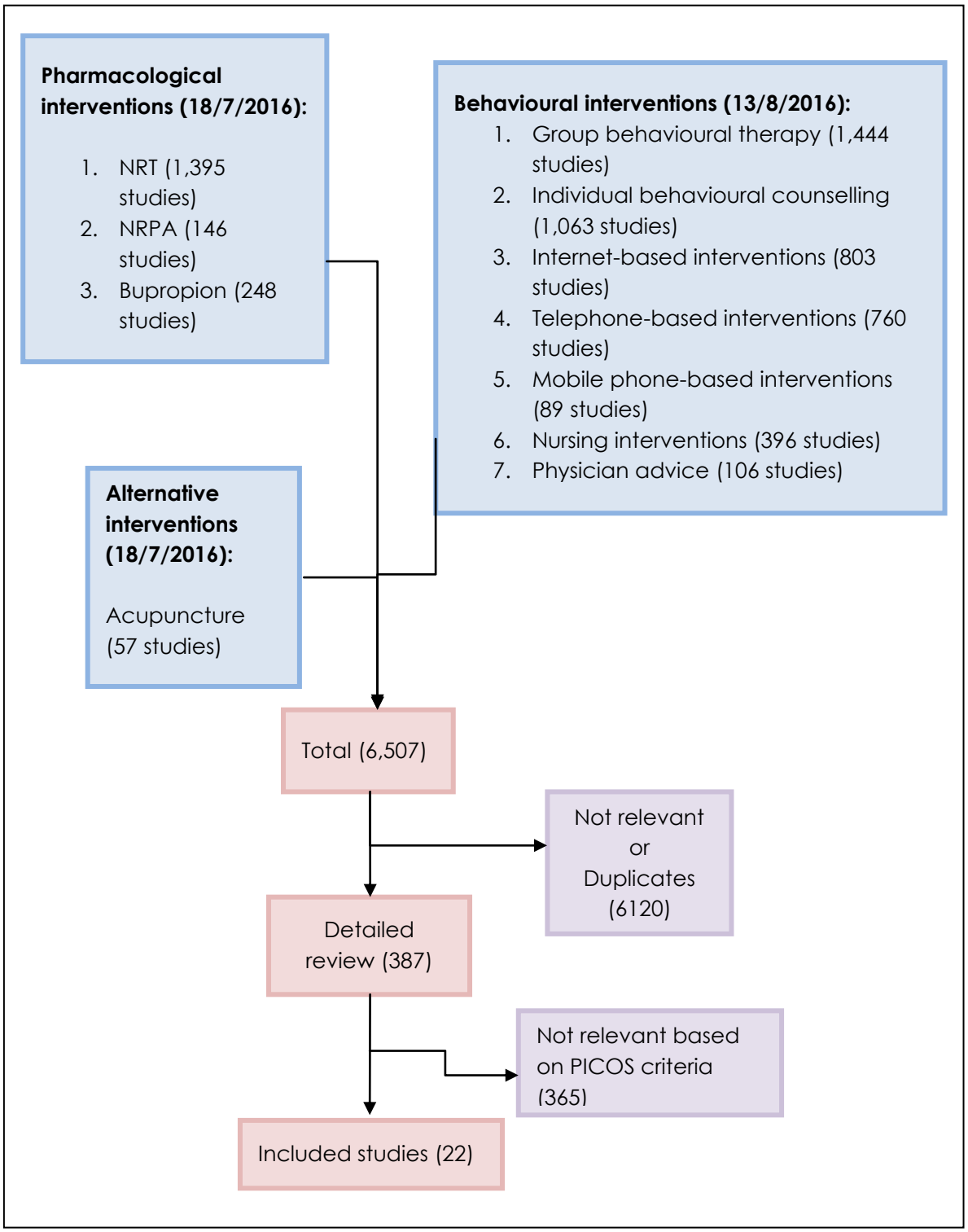
| | Study (year) | Reason | Reason for exclusion |
|---|---|---|---|
| 1 | Batra 2010 | Population | Current depression population; not clear if all attending secondary mental health services. |
| 2 | Blondal 1999 | Intervention | Use of Fluoxetine. |
| 3 | Brown 2001 | Population | Past depression. |
| 4 | Brown 2007 | Population | Current depression population; not clear if all attending secondary mental health services. |
| 5 | Carmody 2008 | Intervention | Includes hypnosis. |
| 6 | Catley 2003 | Intervention | Culturally-sensitive self-help materials. |
| 7 | Catley 2005 | Population | Current depression population; not clear if all attending secondary mental health services. |
| 8 | Cinciripini 2010 | Population | Pregnant smokers. |
| 9 | Covey 1999 | Intervention | Use of Naltrexone. |
| 10 | Covey 2002 | Intervention | Use of Sertraline. |
| 11 | Duffy 2006 | Population | Smokers with head and neck cancer. |
| 12 | Hall 1994 | Population | Past depression. |
| 13 | Hall 1996 | Population | Subgroup of past depression only. |
| 14 | Hall 1998 | Population | Past depression. |
| 15 | Hall 2002 | Population | Past depression. Only information available which compared nortriptyline versus bupropion (CR). |
| 16 | Hall 2006 | Population | Current depression population; not clear if all attending secondary mental health services. |
| 17 | Hall 2009 | Population | Subgroup of past depression only. |
| 18 | Hayes 2010 | Population | Medically ill smokers using home healthcare nursing services with current depressive symptoms. |
| 19 | Hayford 1999 | Population | Past depression. |
| 20 | Kahler 2008 | Population | Heavy drinking and smoking adults. |
| 21 | Killen 2000 | Intervention | Use of Paroxetine. |
| 22 | Killen 2008 | Population | Current depression population; not clear if all attending secondary mental health services. |
| 23 | Kinnunen 2008 | Population | Current depression population; not clear if all attending secondary mental health services. |

| | | | |
|---|---|---|---|
| 24 | Kodl 2008 | Population | Adult alcohol-dependent smokers. |
| 25 | Levine 2003 | Population | Current depression population; not clear if all attending secondary mental health services. |
| 26 | Levine 2010 | Population | Current depression population; not clear if all attending secondary mental health services. |
| 27 | MacPherson 2010 | Population | Mildly elevated depressive symptoms (BDIII ≥ 10). Recruited through community and University, so not clear if attending secondary health. Intervention=BATS. |
| 28 | McAlister 2004 | Population | Mild depression: depression according to a single self-report question: 'Have you felt sad or blue every day for the last two weeks?' Recruited through community and quitline so not clear if attending secondary mental health. |
| 29 | McFall 2010 | Population | PTSD related to military service. |
| 30 | Muñoz 1997 | Intervention | Quit smoking guide (Spanish: Guía) + mood management. |
| 31 | Muñoz 2006a | Intervention | Guía + Individually Timed Educational Messages + mood management course versus Guía + Individually Timed Educational Messages. |
| 32 | Muñoz 2006b | Intervention | Guía + Individually Timed Educational Messages + mood management course versus Guía + Individually Timed Educational Messages. |
| 33 | Muñoz 2009 | Intervention | Guía + Individually Timed Educational Messages + mood management course versus Guía + Individually Timed Educational Messages versus Guía + Individually Timed Educational Messages + mood management course + virtual group versus Guía alone. |
| 34 | Patten 1998 | Population | Abstinent alcoholics. |
| 35 | Piper 2009 | Population | Not clear if attending secondary mental health services. |
| 36 | Rabius 2007a | Population | Current depression population; not clear if all attending secondary mental health services. |
| 37 | Rabius 2007b | Population | Current depression population; not clear if all attending secondary mental health services. |
| 38 | Rabius 2008 | Intervention | Tailored interactive site versus control (minimally interactive) site. |
| 39 | Sauls 2004 | Intervention | Use of Fluoxetine. |
| 40 | Schnoll 2010 | Population | Cancer and depressive symptoms. |
| 41 | Smith 2003 | Population | Subgroup of past depression only. |
| 42 | Spring 2007 | Intervention | Use of Fluoxetine. |
| 43 | Swan 2010 | Population | Not clear if attending secondary mental health services. |
| 44 | Thorndike 2008 | Population | Acute cardiovascular disease. |
| 45 | Van der Meer | Population | Current depression population; not clear if all attending secondary mental health services. |

| | | | |
|---|---|---|---|
| | 2010 | | |
| 46 | Vickers 2009 | Intervention | Exercise counselling. |
| 47 | Walsh 2008 | Intervention | Use of Naltrexone. |
| 48 | Weinberger 2010b | Intervention | Use of Selegiline hydrochloride (antidepressant). |
| 49 | Wewers 2009 | Population | Primary care and women's health clinics that served a socio-economically diverse population and reported >200 Pap smears per month were invited to participate in the study. Not clear if attending secondary mental health. |

# Appendix 7 Search details for review of smoking cessation interventions among unselected adults

## Figure 7.1 Flow diagram of included studies from the updated search



## Table 7.1 Sample search strategy: Updated review for NRT (Medline)

| Pubmed 18/07/2016 | | Search strings | Results |
|---|---|---|---|
| Searches | #1 | (("Smoking Cessation"[Mesh]) OR ("Tobacco Use Cessation"[Mesh]) OR (Stop* smoking) OR (Quit* smoking)) | 31023 |
| | #2 | (((((((((NRT) OR (nicotine AND patch*)) OR (nicotine AND gum)) OR (nicotine AND nasal AND spray)) OR (nicotine AND lozenge*)) OR (nicotine AND tablet*)) OR (nicotine AND sublingual)) OR (nicotine AND inhal*)) OR (nicotine AND replacement)) OR (nicotine AND therap*) | 10421 |
| | #3 | #1 AND #2 | 4353 |
| | #4 | #3 AND Filters:<br>• From 2012/05/01 to 2016/07/18<br>• Clinical Trial; Randomized Controlled Trial; Review; Systematic Reviews; Meta-Analysis<br>• Humans | 451 |

Search string: *((((((((((NRT) OR (nicotine AND patch*)) OR (nicotine AND gum)) OR (nicotine AND nasal AND spray)) OR (nicotine AND lozenge*)) OR (nicotine AND tablet*)) OR (nicotine AND sublingual)) OR (nicotine AND inhal*)) OR (nicotine AND replacement)) OR (nicotine AND therap*))) AND ((("Smoking Cessation"[Mesh]) OR ("Tobacco Use Cessation"[Mesh]) OR (Stop* smoking) OR (Quit* smoking)))*

# Appendix 8 Included studies: Unselected adults

## Table 8.1 Included studies from systematic review: nicotine gum versus placebo

| Study | Country | Setting | Participants | Mean age | Female | Intervention | Control | Support | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|
| Ahluwalia 2006[11] | USA | Community volunteers | 755 | 45 | 67% | Nicotine gum (2mg), recommended use tailored to cpd. Highest 10/day for 4 wks, tapering for 4 wks | Placebo gum, 8 wks | 3 in-person visits at randomisation, wk 1, wk 8, and phone contact at wk 3, wk 6, wk 16, content based on either motivational interviewing or health education principles | 6m (biochem, pp) | Low |
| Areechon 1988[12] | Thailand | Community volunteers | 200 | 39 | 6% | Gum (2mg) x 8 boxes | Placebo gum x 8 boxes | Weekly visits with physician | 6m (biochem, pp) | High |
| Blondal 1989[13] | Iceland | Community volunteers | 182 | 42 | 57% | Gum (4mg) for at least 1 month | Placebo gum (containing pepper) for 1m or more | Group therapy, 5x1hr sessions, TQD at session 1 | 12m (biochem, car) | Unclear |
| Campbell 1987[14] | UK | Primary care | 836 | 39 | 61% | Nicotine gum (2mg) x 6 boxes | Placebo gum x 6 boxes | No further face-to-face contact, 2/3rds received a letter after 1m | 12m (biochem, car) | Unclear |
| Campbell 1991[15] | UK | Hospital inpatients | 212 | 53% 50+ | 44% | Gum 2-4mg (3m) | Placebo gum | Support at 2, 3, 5 wks, 3m, 6m | 12m (biochem, sustained) | Unclear |
| Clavel 1985[16] | France | Community volunteers | 427 | 34 | 51% | Nicotine gum (2mg) x 1 box | Control group (time lock controlled cigarette case) | 3x1hr group therapy sessions in first month | 13m (biochem, car) | High |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Clavel-Chapelon 1992[17] | France | Community volunteers | 996 | 34 | 45% | Nicotine gum (2mg) for up to 6m, max 30/day | Placebo gum (contained 1mg unbuffered nicotine) | 3 acupuncture session at 0, 7, 28 days | 13m (self, NR) | High |
| Cooper 2005[18] | USA | Community volunteers | 439 | 38 | 100% | Nicotine gum (2mg), 10-12 pieces/day recommended, for 9 wks, weaning last 3 wks | Placebo gum | 13x1hr weekly cognitive behavioural group sessions. Reduction prior to TQD wk 5 | 12m (biochem, pp) | Unclear |
| Fagerstrom 1982[19] | Sweden | Smoking cessation clinic | 100 | NS | 59% | Nicotine gum (2mg) for at least 4 wks | Placebo gum for at least 4 wks | Individual counselling, average 7.7 sessions | 6m (biochem, pp) | Unclear |
| Fagerstrom 1984[20] | Sweden | Primary care | 145 | 40 | 56% | Nicotine gum (2 or 4mg) + long or short follow-up | Advice + long or short follow-up | Low | 12m (self, car) | High |
| Fee 1982[21] | UK | Smoking cessation clinic | 352 | NS | NS | Gum (2mg) given for 5 wks | Placebo gum given for 5 wks | 10 group therapy sessions | 12m (biochem, pp) | Unclear |
| Fortmann 1995[22] | USA | Community volunteers | 1044 | 40 | 42% | Nicotine gum (2mg, 1 per hr, at least 10/day and not more than 30/day) | Incentive alone | Low | 12m (biochem, pp) | Unclear |
| Garcia 1989[23] | Spain | Primary care | 106 | 36 | 65% | Gum (2mg) for 3-4m | Placebo gum for 3-4m | | 6m (biochem, car) | Unclear |
| Garvey 2000[24] | USA | Community volunteers | 608 | NS | 51% | 4mg nicotine gum (recommended 9-15 pieces), | Placebo gum | Brief counselling (5-10 mins) at each study visit (1, 7, 14, 30 days, 2, 3, | 12m (biochem, car) | High |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | weaning from 2m; 2mg nicotine gum, use as 1 | | 6, 9, 12m) | | |
| Gilbert 1989[25] | Canada | Primary care | 223 | NR | NS | Support from physician plus offer of nicotine gum prescription (2mg) | Support from physician (no placebo) | Enrolment, quit day, offer of 4 support visits, 2 in wk 1, 1m, 2m | 12m (biochem, car) | High |
| Gross 1995[26] | USA | Community volunteers | 177 | 42 | 51% | Nicotine gum (2mg), tapered from wk 12. Active gum groups further randomised to chew 7, 15 or 30 pieces of gum | No gum | 1 pre-quit group counselling session, 14 clinic visits in 10 wks | 6m (biochem, car) | High |
| Hall 1985[27] | USA | Community volunteers + physician referrals | 120 | 38 | 47% | Combined - 2mg nicotine gum (period of use not specified) and intensive behavioural treatment | Intensive behavioural treatment (14 group sessions over an 8 wk period) | High | 12m (biochem, NR) | High |
| Hall 1987[28] | USA | Community volunteers | 139 | 39 | 47% | Nicotine gum (2mg) up to 12m | Placebo gum up to 12m | Both group-based, 14x75 min sessions, or 5x60 min sessions | 12m (biochem, pp) | Unclear |
| Hall 1996[29] | USA | Community volunteers | 207 | 40 | 52% | Nicotine gum (2mg) for 8 wks, 1 piece/hr for 12 hrs/day | Placebo gum, same schedule | Group-based, 10 sessions over 8 wks, TQD session 3 | 12m (biochem, car) | Unclear |

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| Harackiewicz 1988[30] | USA | Primary care | 197 | 36 | 63% | Nicotine gum (2mg, 6 wks initial supply, suggested tapering after 3m, available for 6m) plus self-help manual | Self-help manual; Control (booklet) | Single appointment with doctor or nurse, length not specified | 12m (biochem, car) | High |
| Herrera 1995[31] | Venezuela | Community volunteers | 322 | 38 | 43% | 2mg nicotine gum (low dependence) | Placebo gum (low dependence) | 12 group sessions over 6 wks + 6 weekly maintenance sessions | 24m (biochem, car) | Unclear |
| Hjalmarson 1984[32] | Sweden | Smoking cessation clinic | 206 | 42 | 56% | Nicotine gum (2mg) (no restrictions on amount or duration of use) | Placebo gum | 6 group sessions in 6 wks | 12m (biochem, car) | Unclear |
| Huber 1988[33] | Germany | Community volunteers | 225 | NS | NS | Nicotine gum (no details of dose) and behaviour therapy | Behaviour therapy, 5 weekly group meetings | High | 12m (self, NR) | Unclear |
| Hughes 1989[34] | USA | Primary care | 315 | 37 | 56% | Nicotine gum (2mg for 3-4m) | Placebo gum | 29-35 min at first visit including nurse & physician advice, and materials, follow-up appointment 1-2 wks later | 12m (biochem, car) | Low |
| Hughes 1990[35] | USA | Community volunteers | 78 | 40 | 54% | Nicotine gum - 1mg/2mg/4mg | Placebo gum | 29-35 min at 1st visit including nurse and physician advice, and | 6m (self, car) | Unclear |

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| | | | | | | | | materials, follow-up appointment 1-2 wks later | | |
| Jamrozik 1984[36] | UK | Primary care | 200 | NS | NS | Nicotine gum (2mg) for 3m+ | Placebo gum | Follow-up visits at 2, 4, 12 wks for data collection | 6m (biochem, pp) | Unclear |
| Jarvis 1982[37] | UK | Smoking cessation clinic | 116 | 40 | 55% | Nicotine gum (2mg) unrestricted amount for at least 3m | Placebo gum (1mg unbuffered nicotine) | Group therapy 6x1hr weekly | 12m (biochem, car) | High |
| Jensen 1991[38] | Denmark | Smoking cessation clinic | 293 | 42 | 54% | Nicotine gum (2mg for 3m) | Standard chewing gum | 9 group meetings over a year, weekly to wk 4 | 12m (biochem, car) | High |
| Killen 1984[39] | USA | Community volunteers | 64 | 44 | 72% | Nicotine gum (2mg) for 7 wks; Skills training plus nicotine gum | Skills training | Group therapy | 10.5m (biochem, car) | High |
| Killen 1990[40] | USA | Community volunteers | 1218 | 43 | 52% | Nicotine gum (2mg, 8 wks) ad lib dosing; Nicotine gum on a fixed dose | Placebo gum; No gum | Randomised to 1 of 3 psychological interventions | 12m (biochem, pp) | Unclear |
| Llivina 1988[41] | Spain | Smoking cessation clinic | 216 | NR | NR | Nicotine gum (dose not stated) for 1m | Placebo gum | Group support | 12m (biochem, car) | Unclear |
| Malcolm 1980[42] | UK | Community volunteers | 194 | 45 | 41% | Nicotine gum (2mg) at least 10/day for at least 3m | Placebo gum; Control | Weekly individual counselling for 1m | 6m (biochem, car) | Unclear |
| McGovern 1992[43] | USA | Community volunteers | 293 | NS | NS | American Lung Assoc. Freedom from Smoking clinic | ALA Freedom from Smoking clinic programme | Group support | 12m (biochem, pp) | Unclear |

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| | | | | | | programme plus nicotine gum (2mg for 3m) | alone (no placebo gum) | | | |
| Mori 1992[44] | Japan | Hospital | 364 | NR | NR | Nicotine gum 2mg for 3m | Placebo gum | | 6m (NR, biochem) | Unclear |
| Nakamura 1990[45] | Japan | Community volunteers | 60 | NS | NS | Nicotine gum (2mg for 2m or longer) | Non-placebo control group received counselling | High | 6m (biochem, car) | High |
| Nebot 1992[46] | Spain | Primary care | 425 | NS | NS | Physician counselling plus nicotine gum | Brief counselling from physician; health education from nurse | Low | 12m (biochem, pp) | High |
| Niaura 1994[47] | USA | Outpatients | 173 | 42 | 50% | Nicotine gum 2mg, ad lib for up to 4m (participants given prescription for gum, not free) | No gum | 4 individual counselling sessions and ALA self-help treatment manuals | 12m (biochem, car) | Unclear |
| Niaura 1999[48] | USA | Community volunteers | 62 | 28 | 50% | Intensive cognitive behavioral relapse prevention (CBRP) with cue exposure + nicotine gum | Intensive CBRP with cue exposure | 5 group sessions within 3 wks of TQD | 12m (biochem, car) | Unclear |
| Ockene 1991[49] | USA | Primary care | 1223 | 35 | 57% | Patient-centred counselling | Patient-centred counselling | Mixed | 12m (self, car) | Unclear |

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| | | | | | | and offer of nicotine gum(2mg) plus minimal or intensive follow-up by telephone | | | | |
| Page 1986[50] | Canada | Primary care | 275 | NS | NS | Advice to quit plus offer of nicotine chewing gum prescription (2mg) | No advice; Advice to quit | Low | 6m (self, car) | High |
| Pirie 1992[51] | USA | Community volunteers | 417 | NS | 100% | Group therapy plus nicotine gum; Group therapy plus weight control programme and nicotine gum | Group therapy; Group therapy plus weight control programme | High | 12m (biochem, car) | Unclear |
| Puska 1979[52] | Finland | Community volunteers | 229 | NS | NS | Nicotine gum (4mg) for 3 wks | Placebo gum for 3 wks | Group therapy | 6m (self, pp) | Unclear |
| Richmond 1993[53] | Australia | Primary care | 450 | NS | NS | Smokescreen programme plus nicotine gum, dose and duration not stated | Smokescreen programme alone | 5 visits during first 3m | 12m (biochem, car) | High |
| Roto 1987[54] | Finland | Primary care | 121 | NS | 43% | Nicotine gum (2mg and 4mg), + advice | Advice only (no placebo) | Low | 6m (NR, NR) | Unclear |
| Russell 1983[55] | UK | Primary care | 2106 | NS | NS | As group 2, plus offer of | No intervention; | Low | 12m (biochem, | High |

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| | | | | | | nicotine gum prescription, Individual therapy, Single visit 1 minimal content, 1 more intensive content, untrained therapist | Advised to stop smoking plus provided with a 'give up smoking' booklet | | car) | |
| Schneider 1985A[56] | USA | Community volunteers | 60 | 38 | 60% | Nicotine gum, (2mg duration not stated) | Placebo gum | Individual support at multiple clinic assessment visits, daily during week 1, weekly to wk 5 | 12m (biochem, car) | Unclear |
| Schneider 1985B[56] | USA | Community volunteers | 36 | NS | NS | Nicotine gum, (2mg duration not stated) | Placebo gum | Weekly laboratory visits for 5 wks but no support provided | 12m (biochem, car) | Unclear |
| Segnan 1991[57] | Italy | Primary care | 923 | NS | NS | Repeated counselling plus prescription for nicotine gum unless contraindicated, dose not stated, up to 3m | Advice and leaflet; Repeated counselling (follow-up at 1, 3, 6, 9m); Repeated counselling plus spirometry | High | 12m (biochem, car) | Low |
| Shiffman 2009 (2mg)[58] | USA | Community volunteers | 1636 | 42 | 64% | Nicotine gum 2mg. Instructed to gradually reduce smoking while increasing gum | Placebo gum, same schedule as above | Designed to simulate over the counter (OTC) setting | 6m (biochem, car) | Unclear |

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| | | | | | | use for up to 8 wks. Post-quit; instructed to use 1 piece every 1-2hrs for first 6 wks; 1 every 2-4hrs for next 3 wks; 1 every 4-8hrs for final 3 wks | | | | |
| Shiffman 2009 (4mg)[58] | USA | Community volunteers | 1661 | 46 | 50% | Nicotine gum 4mg. Instructed to gradually reduce smoking while increasing gum use for up to 8 wks. Post-quit; instructed to use 1 piece every 1-2hrs for first 6 wks; 1 every 2-4hrs for next 3 wks; 1 every 4-8hrs for final 3 wks | Placebo gum, same schedule as above | Designed to simulate OTC setting | 6m (biochem, car) | Unclear |
| Tonnesen 1988[59] | Denmark | Primary care | 113 | 45 | 56%/ 58% | Nicotine Gum (2mg) for 16 wks | Placebo | Informal group support, 6 sessions | 12m (biochem, car) | Unclear |
| Villa 1999[60] | Spain | Worksite volunteers | 47 | 36 | 72% | Nicotine gum (2mg) | No gum | 8 weekly group sessions, 5 before TQD. Reduction prior to quitting | 12m (self, NR) | Unclear |
| Zelman 1992[61] | USA | Community volunteers | 116 | 32 | 54% | Nicotine gum 2mg, average | Rapid smoking + support | 6x60-75 min group sessions over 2 | 12m (self, car) | High |

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| | | | | | | 10 pieces/day, duration not stated + skills training; Nicotine gum + support counselling | counselling; Rapid smoking + skills training | wks, starting on quit day | | |

## Table 8.2 Included studies from systematic review: NRT patches versus placebo

| Study | Country | Setting | Participants | Mean age | Female | Intervention | Control | Support | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|
| Abelin 1989[62] | Switzerland | Primary care | 199 | 41 | 40% | Nicotine patch, 24hr, 12 wks with weaning; 21mg smokers of >20 cpd, 14mg for <20 cpd | Placebo patch | Unclear | 12m (biochem, car) | High |
| Buchkremer 1988[63] | Germany | Community volunteers | 131 | 35 | 50% | Nicotine patch (24hr/day, 8 wks, 15cm with weaning) + behavioural therapy | Placebo patch + behavioural therapy; Behavioural therapy alone | 9 weekly group sessions | 12m (self, NR) | Unclear |
| Campbell 1996[10] | UK | Hospital inpatients and outpatients | 234 | 49 | 54% | Patch (21mg, 24hr, 12 wks with dose tapering) | Placebo patch | Counselling at 2, 4, 8,12 wks | 12m (biochem, continuous) | Unclear |
| CEASE 1999[64] | Europe | Community volunteers | 3575 | 41 | 48% | Nicotine patch 15/25mg (16hr), duration of active treatment 12/28 wks (incl 4 wk | Placebo | Brief advice & self-help brochure, visits at enrolment, TQD, wk 1, 2, | 12m (biochem, car) | Low |

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| | | | | | | fading) | | 4, 8, 12, 22, 26 | | |
| Daughton 1991[65] | USA | Community volunteers | 158 | 42 | 53% | Nicotine patch (15cm², 4 wks) worn for 16 or 24hr/day | Placebo patch, 4 wks | Unclear & differed between sites | 6m (self, car) | Unclear |
| Daughton 1998[66] | USA | Community volunteers | 158 | 42 | 53% | Nicotine patch (21mg, 16hr, 10 wks with weaning) | Placebo patch | Nicoderm Committed Quitters Programme support booklet + follow-up visit 1 wk after quit day | 12m (biochem, car) | Low |
| Davidson 1998[67] | USA | Community volunteers | 802 | 39 | 54% | Nicotine patch (22mg, 24hr, for up to 6 wks) | Placebo patch | Self-help book provided. Participants visited mall weekly to obtain patches. CO levels were monitored | 6m (self, car) | Low |
| Ehrsam 1991[68] | Switzerland | Primary care | 112 | 26 | NS | Nicotine patch (21 or 14mg/24hr, 9 wks, tapered) | Placebo patch | High (no counselling)? | 12m (biochem, car) | Unclear |
| Fiore 1994A[69] | USA | Community volunteers | 88 | NS | NS | Nicotine patch (22mg/24hr, 8 wks, no weaning) | Placebo patch | Intensive group counselling | 6m (biochem, pp) | Low |
| Fiore 1994B[69] | USA | Community volunteers | 112 | NS | NS | Nicotine patch (22mg/24hr, 6 wks incl weaning) | Placebo patch | 8 weekly 10-20 min individual counselling | 6m (biochem, pp) | Unclear |
| Glavas 2003a[70] | Croatia | NS | 112 | 34 | 66% | Nicotine patch, 24hr, 25mg/15 mg/8mg starting dose depending on baseline cpd 3 wks | Placebo patch | Visits to pick up patch at 7, 14, 21 days, no details about advice given | 12m (biochem, car) | Unclear |

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| Glavas 2003b[71] | Croatia | Community volunteers | 160 | NS | NS | Nicotine patch, 24hr, 25mg/15mg/8mg starting dose depending on baseline cpd. 6 wks; Nicotine patch, 24hr, 25mg/15mg starting dose depending on baseline cpd 3 wks | Placebo patch. 6 wks; Placebo patch 3 wks | | 6m (biochem, NR) | Unclear |
| Hand 2002[72] | UK | Hospital inpatient/outpatient | 245 | NR | 54% | Nicotine patch (initially 30 or 20mg based on smoking rate) and inhaler for 3 wks including patch tapering. Same counselling as control | Individual counselling, 4 sessions in 4 wks. No placebo | | 12m (biochem, sustained) | High |
| Hays 1999[73] | USA | Community volunteers | 958 | 44 | 50% | Nicotine patches (22mg, 24hr for 6 wks) purchased by participants, open label; Nicotine patches (22mg, 24hr for 6 wks) provided, double blind | Placebo patches provided | No advice, counselling or interaction with medical personnel | 6m (biochem, pp) | Low |
| Hughes 1999[74] | USA & Australia | Community volunteers | 1039 | 43 | 50% | 42mg nicotine patch (24hr, 6 wks + 10 wks tapering); 35mg nicotine patch; 21mg nicotine patch | Placebo patch | Group behaviour therapy for 7 wks, brief individual counselling at 5-dose tapering meetings. Self- | 6m (biochem, car) | High |

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| | | | | | | | | help booklet | | |
| Hughes 2003[75] | US | Community volunteers | 115 | NR | 32% | Nicotine patch (21mg, 24hr, 6 wks + 4 wks tapering + 2 wks placebo) | Placebo patch 12 wks | Group behaviour therapy x 6, brief individual counselling x 3 | 6m (biochem, sustained) | Unclear |
| Hurt 1990[76] | USA | Community volunteers | 62 | 39 | 53% | Nicotine patch (30mg 24hrs, 6 wks + option of further 12 wks +/- tapering) | Placebo patch (continuing smokers at 6 wks were offered active patch) | Brief advice from nurse co-ordinator at 6 weekly visits | 12m (biochem, car) | Unclear |
| Hurt 1994[77] | USA | Community volunteers | 240 | 43 | 53% | Nicotine patch (22mg/24hr, 8 wks, no tapering) | Placebo patch | Nurse counselling at 8 weekly visits, weekly phone calls to wk 12 | 12m (biochem, car) | Unclear |
| ICRF 1994[78] | UK | Primary care | 1686 | 43 | 55% | Nicotine patch (21mg/24hr, 12 wks incl tapering) | Placebo patch | Brief advice from nurse at 4 study visits | 12m (biochem, car) | Low |
| Jorenby 1999[79] | USA | Community volunteers | 893 | 43 | 52% | Nicotine patch and placebo tablets | Placebo patch and placebo tablets | <15min individual counselling session at each weekly assessment. One phone call 3 days after quit day | 12m (biochem, car) | Unclear |
| Joseph 1996[3] | US | VA medical centres | 584 | 60 | ~100% | Nicotine patch, (21mg/24hr for 6 wks, 14mg for 2 wks, 7mg for 2 wks) | Placebo patch | Self-help pamphlets and brief behavioural counselling on | 12m (biochem, pp) | Unclear |

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| | | | | | | | | 3 occasions | | |
| Killen 1997[80] | USA | Community volunteers | 424 | 45 | 50% | Nicotine patch (21mg/24hr) for 8 wks, 14mg for 4 wks, 7mg for 4 wks; Nicotine patch and video | Placebo patch; Placebo patch and video | All treatment groups received a self-help treatment manual designed to develop self-regulatory skills | 12m (biochem, car) | Unclear |
| Kornitzer 1995[81] | Belgium | Worksite volunteers | 374 | 40 | 39% | Nicotine patch (12 wks 15mg/16hr, 6 wks 10mg, 6 wks 5mg) and placebo gum | Placebo patch and placebo gum | Nurse counselling | 12m (biochem, car) | Low |
| Lewis 1998[4] | US | Hospital in-patients | 185 | 44 | 46% | Nicotine patch (22mg/ 24hrs for 3 wks, tapered to 11mg for 3 wks) | Placebo patch. | Nurse provided brief telephone counselling at 1, 3, 6 and 24 wks | 6m (biochem, PP) | Low |
| Molyneux 2003[5] | UK | Hospital | 274 | 60 | 40% | Choice of NRT products (15mg 16hr patch/2mg or 4mg gum, 10mg inhalator/2mg sublingual tablet, 0.5mg spray) | Brief counselling only; Usual Care, no smoking advice | | 12m (biochem, car) | Unclear |
| Oncken 2007[82] | USA | Community volunteers | 152 | 55 | 100% | Nicotine patch (21mg for 13 wks incl 4 wks tapering) | Placebo patch | 7 visits incl 4 x 2hr group counselling, 1 pre-TQD | 16m (biochem, pp) | Unclear |
| Paoletti 1996[83] | Italy | Community volunteers | 297 | 43 | 40% | Nicotine patch (15mg/16hr, 18 wks incl taper); Nicotine patch 25 mg | Placebo patch | Low | 12m (biochem, pp) | Unclear |
| Perng | Taiwan | Outpatient | 62 | 62 | 6% | Nicotine patch | Placebo | Weekly visit to | 12m (NR) | Unclear |

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| 1998[84] | | chest clinics | | | | (24mg/24 hr for 6 wks, no weaning) | patch | outpatient department for assessment | | |
| Piper 2009[85] | USA | Community volunteers | 1504 | 45 | 58% | Nicotine patch (24hr, 21, 14, and 7mg titrated down over 8 wk period post quit) | Placebo (5 groups matched to above 5 interventions) | 7 one-to-one 10-20min counselling sessions | 6m (biochem, pp) | Unclear |
| Richmond 1994[86] | Australia | Community volunteers | 315 | NS | NS | Nicotine patch (24 hr, 22mg/24 hr, 10 wks incl tapering) | Placebo patch | Group therapy | 12m (biochem, car) | Low |
| Sachs 1993[87] | USA | Community volunteers | 220 | NS | NS | Nicotine patch (15mg/16hr, 12 wks + 6 wks tapering) | Placebo patch | Physician advice, 8 visits during treatment period | 12m (biochem, car) | Unclear |
| Sonderskov 1997[88] | Denmark | Pharmacy customers | 522 | 39 | 50% | Nicotine patch (24 hr). >20/day smokers used 21mg for 4 wks, 14mg for 4 wks, 7mg for 4 wks. Smokers of <20/day used 14mg for first 8 wks, 7mg for 4 wks | Placebo patches | Brief instructions on patch use at baseline, visit to collect further patches at 4 and 8 wks, no behavioural support | 6m (self, pp) | Low |
| Stapleton 1995[89] | UK | Primary care | 1200 | NS | NS | Nicotine patch standard dose (15mg/16hr for 18 wks); Nicotine patch with dose increase to 25mg at 1 wk, if required | Placebo patch group | Physician advice & brief support at 1, 3, 6, 12 wks | 12m (biochem, car) | Low |
| TNSG 1991[90] | USA | Community volunteers | 808 | 43 | 60% | Nicotine patch (21mg /24 hr, 6 wks+); Nicotine | Placebo patch | Group therapy, 6+ sessions | 6m (biochem, car) | Unclear |

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| | | | | | | patch 14mg | | | | |
| Tonnesen 1991[91] | Denmark | Community volunteers | 289 | 45 | 70% | Nicotine patch (15mg/16hr for 12 wks with tapering) | Placebo patch | 7 clinic visits including a few minutes of advice | 12m (biochem, car) | Low |
| Tonnesen 2000[92] | Denmark | Lung clinic referrals | 446 | 49 | 52% | 15mg (16hr) nicotine patch for 12 wks (up to 9m on request) | 5mg nicotine patch (placebo) | Physician advice at baseline, brief (15min) nurse counselling at 2, 6 wks | 12m (biochem, sustained) | Unclear |
| Westman 1993[93] | USA | Community volunteers | 158 | 41 | 57% | Nicotine patch (25mg/24hr, 6 wks incl weaning) | Placebo patches | Brief counsellor support at 3 clinic visits, 4 telephone counselling sessions, self-help materials | 6m (biochem, car) | Unclear |
| Otero 2006[94] | Brazil | Community volunteers | 1199 | 42 | 63% | Nicotine patch (21mg, 14mg for FTND<5) 8 wks incl tapering + behavioural support | Cognitive behavioural support only | Mixed (Low=single 20 min session. High= 1, 2, 3 or 4 weekly 1hr sessions. Maintenance or recycling sessions provided at 3, 6, 12 months) | 12m (self, pp) | High |
| Cinciripini 1996[95] | USA | Community volunteers | 64 | NR | 70% | Nicotine patch (21mg, 12 wks incl weaning) | Behaviour therapy only (no placebo) | Group therapy weekly for 9 wks | 12m (biochem, car) | Unclear |
| Prapavessis 2007[96] | New Zealand | Community volunteers | 121 | NR | 100% | Nicotine patch (21mg/24hr for 10 wks, no weaning) | No patch | 36x45 min session over 12 wks of group | 12m (biochem, car) | Unclear |

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| | | | | | | | | CBT or supervised vigorous exercise, starting 6 wks before TQD | | |
| Wong 1999[97] | USA | Community volunteers | 100 | 42 | 53% | Nicotine patch: 21mg (24hr) for 8 wks, tapering to 14mg for 4 wks | Naltrexone: 50mg/day for 12 wks | Iindividual counselling, 15-20 mins at 8 study visits | 6m (biochem, car) | High |
| EAGLES 2016[98] | International | Community volunteers | 4028 | 46 | 66% | Patch, 21mg x 7 weeks, 14mg x 2 wks, 7mg x 2 weeks (11 weeks) | Placebo | All participants received counselling (up to 10 mins) at all contacts. Participants monitored at weeks 1-6, 8, 12, 13, 16, 20, 24; contacts were up to 15 face-to-face visits and 11 telephone visits | Abstinence at 6 months (biochem, car) | Low |

## Table 8.3 Included studies from systematic review: NRT inhaler versus placebo

| Study | Country | Setting | Participants | Mean age | Female | Intervention | Control | Support | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|
| Hjalmarson 1997[99] | Sweden | Smoking cessation clinic | 247 | 48 | 64% | Nicotine inhaler (recommended minimum 4/day, tapering after 3m, use permitted to 6m) | Placebo inhaler | 8 group meetings over 6 wks | 12m (biochem, car) | Low |

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| Leischow 1996[100] | USA | Community volunteers | 222 | 44 | 55% | Nicotine inhaler (10mg). Advised to use 4-20 cartridges/day for 3m. After this tapering was encouraged until 6m | Placebo inhaler | Brief individual smoking cessation support at each study visit, 10 in all | 12m (biochem, car) | Unclear |
| Schneider 1996[101] | USA | Community volunteers | 223 | 44 | 37% | Nicotine inhaler (4-20 inhalers per day) for up to 6m, with weaning from 3m | Placebo inhaler | Repeated clinic visits for assessment | 12m (biochem, car) | Low |
| Tonnesen 1993[102] | Denmark | Community volunteers | 286 | 39 | 60% | Nicotine inhaler (2-10/day) up to 6m | Placebo inhaler | Brief advice at 8 clinic visits, 0, 1, 2, 3, 6,12, 24, 52 wks | 12m (biochem, car) | Low |

## Table 8.4 Included studies from systematic review: NRT intranasal spray versus placebo

| Study | Country | Setting | Partici pants | Mean age | Female | Intervention | Control | Support | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|
| Blondal 1997[103] | Iceland | Community volunteers | 159 | 42 | 44% | Nicotine nasal spray (NNS) ad lib use. Each dose (2 squirts) delivered 1mg nicotine. Maximum dose 5mg/hr and 40mg/day. Recommended duration of use 3m | Placebo nasal spray containing piperine to mimic sensory effect of nicotine | Group therapy 6x1hr sessions | 12m (biochem, car) | Unclear |
| Hjalmarson 1994[104] | Sweden | Smoking cessation clinic | 248 | 45 | 57% | Nicotine nasal spray (0.5mg/spray) used as required up to 40mg/day for up to | Placebo spray | 8x45-60min group sessions over 6 wks with | 12m (biochem, car) | Unclear |

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| | | | | | | 1yr | | clinical psychologist | | |
| Schneider 1995[105] | USA | Community volunteers | 255 | NS | NS | Nicotine nasal spray (0.5mg of nicotine per spray) | Placebo spray | Repeated clinic visits for assessment | 12m (biochem, car) | Unclear |
| Sutherland 1992[106] | UK | Smoking cessation clinic | 227 | NS | NS | Nicotine nasal spray, maximum 40mg/day | Placebo spray | 4 wks group support | 12m (biochem, car) | Unclear |

## Table 8.5 Included studies from systematic review: NRT lozenge or tablet versus placebo

| Study | Country | Setting | Participants | Mean age | Female | Intervention | Control | Support | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|
| Dautzenberg 2001[107] | France | Community volunteers | 433 | 39 | 52% | Nicotine lozenge (1mg, 8-24/day, 6 wks + 6 wks weaning for quitters) | Placebo lozenge | Not stated | 6m (biochem, pp) | Unclear |
| Piper 2009[85] | USA | Community volunteers | 1504 | 45 | 58% | Nicotine lozenge 2 or 4mg for 12 wks (based on dose-for-dependence level as per instructions) | Placebo; 5 groups matched to above 5 interventions | 7 one-to-one 10-20min counselling sessions | 6m (biochem, pp) | Unclear |
| Shiffman 2002 (2mg)[108] | USA & UK | Community volunteers | 917 | 41 | 58% | Nicotine lozenge, 2mg. Recommended dose 1 every 1-2hrs, min 9, max 20/day for 6 wks, decreasing 7-12 wks, available as needed 13-24 wks | Placebo lozenge, same schedule | Brief advice at 4 visits in 4 wks from enrolment | 12m (biochem, car) | Unclear |
| Shiffman 2002 (4mg)[108] | USA & UK | Community volunteers | 901 | 44 | 55% | Nicotine lozenge, 4mg. Recommended dose 1 every 1-2hrs, min 9, max 20/day for 6 wks, | Placebo lozenge, same schedule | Brief advice at 4 visits in 4 wks from enrolment | 12m (biochem, car) | Unclear |

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| | | | | | | decreasing 7-12 wks, available as needed 13-24 wks | | | | |
| Glover 2002[109] | USA | Community volunteers | 241 | 42 | 54% | Nicotine sublingual tablet (2mg). Recommended dosage 1 tab/hr for smokers with FTND<7, 2 tabs/hr for scores 7. After 3m treatment, tapering period of 3m if necessary | Placebo tablet | Brief counselling at all visits 1, 2, 3, 6 wks, 3, 6,12m | 12m (biochem, car) | Low |
| Wallstrom 2000[110] | Sweden | Community volunteers | 247 | 45 | 59% | Nicotine sublingual tablet. Recommended dosage 1 tab/hr for smokers with FTND<7, 2 tabs/hr for scores 7. After 3m treatment, tapering period of 3m if necessary | Placebo tablet | Brief 5 mins counselling at study visits (0, 1, 2, 3, 6 wks, 3, 6m) | 12m (biochem, car) | Unclear |

## Table 8.6 Included studies from systematic review: NRT intranasal spray versus placebo

| Study | Country | Setting | Participants | Mean age | Female | Intervention | Control | Support | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|
| Tonnesen 2012[111] | Germany/ Denmark | Community volunteers | 479 | 47 | 56% | 1mg/spray oral nicotine spray (in development, name not provided) Active: wks 1-6: 1-2 sprays when participants would normally have smoked a cigarette or experienced a craving, up to 4 sprays/hr and 64 | Placebo on same schedule | General written and oral advice (less than 10min) at study start and less than 3mins at subsequent | 12m (biochem, car) | Low |

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|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | sprays/day. Tapered down wks 7-12 (end of wk 9 instructed to be using half as much as in wks 1-6, reducing to max 4 sprays/ day by wk 12). Occasional use (max 4 sprays/day) permitted wks 13-24 | | visits up to and including wk 24 (9 visits total) | | |

## Table 8.7 Included studies from systematic review: choice of NRT versus placebo

| Study | Country | Setting | Participants | Mean age | Female | Intervention | Control | Support | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|
| Kralikova 2002[112, 113] | Czech Republic | Community volunteers | 314 | 46 | 58% | Choice of 4mg nicotine gum (up to 24/day) or 10mg inhaler (6-12 daily) for up to 6m with further 3m tapering | Placebo gum or inhaler | Brief behavioural support at clinic visits (9 scheduled) | 12m (biochem, car) | Unclear |
| Wittchen 2011[114] | Germany | Primary care | 467 | 43 | 52% | CBT + NRT for 9-12 wks, patient's choice of patch (7mg-52.5mg), gum (2 or 4mg) or spray (10mg/ml) | No NRT | CBT, 4-5 one on one counselling sessions for 20-30min | 12m (self, NR) | High |

## Table 8.8 Included studies from systematic review: Combination NRT versus placebo

| Study | Country | Setting | Participants | Mean age | Female | Intervention | Control | Support | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|
| Piper 2009[85] | USA | Community volunteers | 1504 | 45 | 58% | Lozenge + patch (duration and dosage as above) | Placebo; 5 groups matched to above 5 | 7 one-to-one 10-20min counselling sessions | 6m (biochem, pp) | Unclear |

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|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | interventions | | | |
| Tonnesen 2000[2] | Denmark | Lung clinic referrals | 446 | 49 | 52% | 15mg (16hr) nicotine patch for 12 wks (up to 9m on request) plus nicotine inhaler | 5mg nicotine patch (placebo) | Physician advice at baseline, brief (15min) nurse counselling at 2, 6 wks, 3, 6, 9, 12m | 12m (sustained, biochem) | Unclear |
| Kornitzer 1995[81] | Belgium | Worksite volunteers | 374 | 40 | 39% | Nicotine patch (12 wks 15mg/16hr, 6 wks 10mg, 6 wks 5mg) and placebo gum | Placebo patch and placebo gum | Nurse counselling | 12m (sustained, biochem) | Low |

## Table 8.9 Included studies from systematic review: NRT plus bupropion versus placebo

| Study | Country | Setting | Participants | Mean age | Female | Intervention | Control | Support | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|
| Jorenby 1999[79] | USA | Community volunteers | 893 | 43 | 52% | Nicotine patch (21mg/24hr for 6 wks, tapered for 2 wks) and sustained release bupropion 300mg for 9 wks from 1 wk before quit day | Placebo patch and placebo tablets | <15min individual counselling session at each weekly assessment. One phone call 3 days after quit day | 12m (biochem, car) | Unclear |
| Piper 2009[85] | USA | Community volunteers | 1504 | 45 | 58% | Bupropion + lozenge (duration and dosage as above) | Placebo; 5 groups matched to above 5 interventions | 7 one-to-one 10-20min counselling sessions | 6m (biochem, pp) | Unclear |
| Piper 2007[115] | US | Community volunteers | 608 | 42 | 58% | Nicotine gum (4mg, 8 wks) and bupropion (300mg, 9 wks) | Placebo gum and bupropion | | 12m (biochem, pp) | Unclear |

## Table 8.10 Included studies from systematic review: NRT versus bupropion

| Study | Country | Setting | Participants | Mean age | Female | Intervention | Control | Support | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|
| Patch | | | | | | | | | | |
| Gariti 2009 (116) | USA | Community volunteers | 260 | 54 | 57% | Patch (for participants>10 cpd: 21mg/day for wks1-4, 14mg/day wks 5-6, 7mg/day wks 7-8; participants 10cpd: 14mg/day for 6 wks, 7mg/day for wks 7-8) + 9 wks placebo bupropion + 10 wks individualised counselling sessions; Patch (dose as above) for 8 wks + 9 wks placebo bupropion + four 5-10min counselling sessions | Placebo patch for 8 wks + 9 wks bupropion SR + 10 wks individualised counselling sessions; Placebo patch for 8 wks + 9 wks bupropion SR + 4x5-10min counselling sessions | High level of support via individual counselling sessions | 12m (biochem, pp) | Low |
| Jorenby 1999[79] | USA | Community volunteers | 893 | 43 | 52% | Nicotine patch and placebo tablets | Bupropion 300mg and placebo patch | <15min individual counselling session at eachweekly assessment. One phone call 3 days after quit day | 12m (biochem, car) | Unclear |
| Piper 2009[85] | USA | Community volunteers | 1504 | 45 | 58% | Nicotine patch (24hr, 21, 14, and 7mg titrated down over 8 wk period post quit) | Bupropion SR (150mg bid, 1 wk pre-quit, 8 | 7 one-to-one 10-20min | 6m (biochem, pp) | Unclear |

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|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | wks post quit) | counselling sessions | | |
| Smith 2009[117] | USA | Primary care | 1346 | 44 | 56% | Nicotine patch only (21mg post quit wk 1-4; 14mg wk 5-6; 7mg wk 7-8) | Bupropion only (up-titrated during wk pre-quitting, 150mg bid for 8 wks post quit) | Behavioural support optional | 6m (self, pp) | High |
| EAGLES 2016[98] | International | Community volunteers | 4028 | 46 | 66% | Nicotine patch, 21mg x 7 weeks, 14mg x 2 wks, 7mg x 2 weeks (11 weeks) | Bupropion SR, 150mg x 2/day (titrated for 3 days, then full dose for 11 weeks) | All participants received counselling (up to 10 mins) at all contacts. Participants were monitored at weeks 1 - 6, 8, 12, 13, 16, 20, 24; contacts were up to 15 face-to-face visits and 11 telephone visits | 6m (biochem, car) | Low |

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|---|---|---|---|---|---|---|---|---|---|---|
| Lozenge | | | | | | | | | | |
| Piper 2009[85] | USA | Community volunteers | 1504 | 45 | 58% | Nicotine lozenge 2 or 4mg for 12 wks (based on dose-for-dependence level as per instructions) | Bupropion SR (150mg bid, 1 wk pre-quit, 8 wks post quit) | 7 one-to-one 10-20min counselling sessions | 6m (biochem, pp) | Unclear |
| Smith 2009[117] | USA | Primary care | 1346 | 44 | 56% | Nicotine lozenge only (4mg lozenge if first cig of day smoked >30 min after waking, 2mg otherwise. 1 lozenge every 1-2hrs post-quit wk 1-6; 1 lozenge every 2-4hrs wk 7-9; 1 lozenge every 4-8hrs wk 10-12) | Bupropion only (up-titrated during wk pre-quitting, 150mg bid for 8 wks post quit) | Behavioural support optional | 6m (self, pp) | High |
| Choice of NRT | | | | | | | | | | |
| Wittchen 2011[114] | Germany | Primary care | 467 | 43 | 52% | CBT + NRT for 9-12 wks, patient's choice of patch (7mg-52.5mg), gum (2 or 4mg) or spray (10mg/ml) | CBT + bupropion SR (9-12 wks, 150mg;1/d for first 6d; 2/d thereafter) | 4-5 one-on-one counselling sessions for 20-30min | 12m (self, NR) | High |

## Table 8.11 Included studies from systematic review: NRT versus NRT

| Study | Country | Setting | Participants | Mean age | Female | Intervention | Control | Support | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|
| Komitzer 1995[81] | Belgium | Worksite volunteers | 374 | 40 | 39% | Nicotine patch + gum | Patch | Nurse counselling | 12m (biochem, car) | Low |
| Puska 1995[118] | Finland | Community volunteers | 300 | 20-65 | NS | Nicotine patch + gum | Gum | Advice from nurses | 12m (biochem, car) | Unclear |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Blondal 1999[119] | Iceland | Community volunteers | 237 | 42 | 67% | Nasal spray + patch | Patch | 4 support group meetings | 12m (biochem, car) | Low |
| Caldwell, 2014[120] | New Zealand | | 1423 | 45 | 54% | Nicotine patch + spray | Nicotine Patch + Placebo Spray | Physician advice and telephone calls to all participants | 12 month (7-day PP, Biochem) | Low |
| Cooney 2009[1] | US | Community volunteers + substance abuse clinic referrals | 96 | 45 | 25% | Nicotine patch (titrated, 21mg/d for 8 wks, 14mg/d for 2 wks, 7mg/d for 2 wks) + nicotine gum (2mg for 24 wks, ad lib but advised 6-20/day) | Nicotine patch + placebo gum (doses as above) | 16 individual 1hr weekly outpatient sessions of behavioural alcohol and smoking treatment over 6m | 12 month (continuous, Biochem) | Low |
| Croghan 2003[121] | USA | Community volunteers | 1384 | 42 | 58% | Nasal spray + nicotine patch | Spray or patch | Advice at each visit, 30-45 mins total | 6m (biochem, pp) | High |
| Bohadana 2000[122] | France | Community volunteers | 400 | NS | 51% | Nicotine patch + inhaler | Inhaler | Brief counselling and support from investigator at each visit | 12m (biochem, car) | Unclear |
| Piper 2009[85] | USA | Community volunteers | 1504 | 45 | 58% | Nicotine patch + lozenge | Patch or lozenge | 7 one-to-one 10-20min counselling sessions | 6m (biochem, pp) | Unclear |
| Smith 2009[117] | USA | Primary care | 1346 | 44 | 56% | Nicotine patch + lozenge | Patch or lozenge | Behavioural support optional | 6m (self, pp) | High |
| Croghan 2003[121] | USA | Community volunteers | 1384 | 42 | 58% | Nasal spray | Patch | Advice at each visit, 30-45 mins total | 6m (biochem, pp) | High |
| Lerman 2004[123] | USA | Community volunteers | 350 | 46 | 54% | Nasal spray | Patch | 7x90 min behavioural group | 6m (biochem, pp) | Low |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | counselling sessions. TQD in wk 3 | | |
| Piper 2009[85] | USA | Community volunteers | 1504 | 45 | 58% | Lozenge | Patch | 7 one-to-one 10-20min counselling sessions | 6m (biochem, pp) | Unclear |
| Schnoll 2010b[124] | USA | Community volunteers | 642 | 45 | 57% | Lozenge | Patch | 5 individual counselling sessions | 6m (biochem, car) | High |
| Smith 2009[117] | USA | Primary care | 1346 | 44 | 56% | Lozenge | Ppatch | Behavioural support optional | 6m (self, pp) | High |

## Table 8.12 Included studies from systematic review: e-cigarette versus placebo

| Study | Setting | Mean age | Ethnicity | Female | Participants | Intervention | Control | Behavioural support | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|
| Bullen 2013[125] | New Zealand | 42 | 33% Maori | 62% | 657 | E-cig 16mg for 13 weeks | Placebo | Referred to quitline and received an invitation to access phone or text-based support. | Abstinence at 6m (biochem, car) | Low |
| Caponnetto 2013[126] | Italy | 44 | NS | 36% | 300 | E-cig 7.2mg for 12 wks or 7.2 for 6 wks + 5.4mg for 6 wks | Placebo | Baseline visit and up to 7 follow-up visits to receive more cartridges, hand in diaries, measure CO and vital signs | Abstinence at 12m (self, car) | Low |

## Table 8.13 Included studies from systematic review: e-cigarette versus nicotine patch

| Study | Setting | Mean age | Ethnicity | Female | Participants | Intervention | Control | Behavioural support | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|
| Bullen 2013[125] | New Zealand | 42 | 33% Maori | 62% | 657 | E-cig 16mg for 13 weeks | Patch 21mg/24-hour, for 13 weeks | Referred to quitline and received an invitation to access phone- or text-based support. | Abstinence at 6m (biochem, car) | Low |

## Table 8.14 Included studies from systematic review: bupropion versus placebo

| Study | Setting | Mean age | Ethnicity | Female | Participants | Intervention | Control | Behavioural support | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|
| Ahluwalia 2002[127] | USA | 44 | African American | 70% | 600 | Bupropion 300mg for 7 weeks | Placebo | 8 sessions of in-person or telephone counselling and self-help guide | Abstinence at 6m (biochem. car) | Low |
| Aubin 2004[128] | France | 41 | NS | 56% | 504 | Bupropion 300mg for 7 weeks | Placebo | Motivational support at clinic visits at baseline, w3, w7, w12 & 3 phone calls TQD, 2-3 days later, w5, w18 | Abstinence at 6m (biochem, car) | Low |
| Brown 2007[129] | USA | 44 | NS | 48% | 524 | Bupropion 300mg/day for 12 weeks | Placebo | 12 x 90 min groups twice weekly/ weekly/ monthly for 12w | Abstinence at 12m (biochem, car) | Unclear |
| Cinciripini 2013[130] | USA | 44 | NS | 39% | 294 | Bupropion 150mg/d days 1-3, 300mg/d thereafter for 12 weeks | Placebo | 10 individual counselling sessions (6 in person, 4 via phone, 240mins total) | Abstinence at 6m (biochem, car) | Unclear |
| Collins 2004[131] | USA | 46 | NS | 57% | 555 | Bupropion 300mg/day for 10 weeks | Placebo | 7 sessions of group behavioural therapy | Abstinence at 6m (biochem, | Low |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | begun 2 weeks before TQD | | | car) | |
| Cox 2012[132] | USA | 47 | African American | 66% | 540 | Bupropion 300mg for 7 weeks | Placebo | Up to 6 one-to-one 15-20 minute individual counselling sessions, self-help guide at start | Abstinence at 6m (biochem, pp) | Unclear |
| Dalsgard 2004[133] | Denmark | 43 | NS | 75% | 335 | Bupropion 300mg for 7 weeks | Placebo | Motivational support around TQD, at w3 & 7, and at 12w follow up | Abstinence at 6m (biochem, car) | Low |
| Fossati 2007[134] | Italy | 49 | NS | 40% | 593 | Bupropion 300mg for 7 weeks | Placebo | GP visits at enrolment & 4, 7, 26 & 52w, phone calls 1 day pre TQD, 3 days post TQD, 10w post enrolment. Classified as low intensity | Abstinence at 12m (biochem, car) | Unclear |
| Gonzales 2001[135] | USA | 45 | NS | 52% | 450 | Bupropion 300mg for 12 weeks, begun 7 days pre-TQD | Placebo | Brief individual counselling at visits w1-7, 9, 12, + telephone counselling at 4 and 5m | Abstinence at 12m (biochem, car) | Unclear |
| Gonzales 2006[136] | USA | 42 | NS | 46% | 1025 | Bupropion 300mg for 12 weeks, begun 7 days pre-TQD | Placebo | Brief (<10 min) standardised individual counselling at 12 weekly visits during drug phase and 11 clinic/phone visits during follow up, problem solving and relapse prevention | Abstinence at 12m (biochem, car) | Low |
| Haggstram 2006[137] | Brazil | 44 | NS | 59% | 156 | Bupropion 300mg for 60 days, TQD during week 2 | Placebo | 6x 15-min individual CBT, weekly then bi-weekly | Abstinence at 6m (biochem, car) | Unclear |
| Hall 2002[138] | USA | 40 | NS | 44% | 220 | Bupropion 300mg/day for 12 weeks | Placebo | Medical management or psychological intervention | Abstinence at 12m (biochem, car) | High |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Holt 2005[139] | New Zealand | 40 | Maori | 72% | 134 | Bupropion 300mg for 7 weeks | Placebo | Counselling at 3 clinic visits during medication and 3 monthly follow ups, motivational phone call 1 day before & 2 days after TQD | Abstinence at 12m (biochem, car) | High |
| Hurt 1997[140] | USA | 44 | NS | 55% | 615 | Bupropion 300mg for 7 weeks | Placebo | Physician advice, self-help materials, and brief individual counselling by study assistant at each visit | Abstinence at 12m (biochem, car) | Unclear |
| Jorenby 1999[79] | USA | 43 | NS | 52% | 893 | Bupropion 300mg for 9w from 1w before quit day | Placebo | Brief (< 15 min) individual counselling session at each weekly assessment. One telephone call 3 days after quit day | Abstinence at 12m (biochem, car) | Unclear |
| Jorenby 2006[141] | USA | 42 | NS | 41% | 1027 | Bupropion 300mg for 12 weeks | Placebo | Brief (< 10 min) individual counselling at each weekly assessment for 12w & 5 follow-up visits. One telephone call 3 days after quit day | Abstinence at 12m (biochem, car) | Low |
| Levine 2010[142] | USA | 42 | NS | 100% | 349 | Bupropion SR for 26 weeks. 150mg/d for first 2 days and 300mg/d for remainder of treatment. | Placebo | 12, 90 minute group counselling sessions delivered over 3 months | Abstinence at 12m (biochem, car) | High |
| McCarthy 2008[143] | USA | 39 | NS | 50% | 463 | Bupropion SR 300mg for 8 weeks | Placebo | Counselling; 8 x10min session, 2 pre-quit, TQD, 5 over 4 wks or psycho-education about medication, support and encouragement. Same no. of sessions, 80mins less contact time | Abstinence at 12m (biochem, pp) | Low |
| Nides 2006[144] | USA | 41 | NS | 51% | 638 | Bupropion 300mg for 7 | Placebo | Up to 10 mins counselling at 7 weekly clinic visits, 12 & | Abstinence at 12m | Low |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | weeks | | 24w | (biochem, car) | |
| Piper 2007[115] | USA | 42 | NS | 58% | 608 | Bupropion 300mg for 9 weeks, starting 1wk before TQD | Placebo | 3x 10 min counselling over 3 weeks | Abstinence at 12m (biochem, pp) | Unclear |
| Piper 2009[85] | USA | 45 | NS | 58% | 1504 | Bupropion SR (150mg bid, 1 wk pre-quit, 8 wks postquit) | Placebo | 7 one-to-one 10-20min counselling sessions | Abstinence at 6m (biochem, pp) | Unclear |
| Rovina 2009[145] | Greece | 45 | NS | 40% | 205 | Bupriopion 300mg for 19 weeks | No treatment | Cognitive behavioral group therapy (CBGT), 1 hour weekly for 1 m, then every 3 wks until 19 wks | Abstinence at 12m (biochem, car) | High |
| Schmitz 2007[146] | USA | 48 | NS | 100% | 154 | Bupropion 300mg for 7 weeks | Placebo | Either CBT based on relapse prevention model, or group support therapy, both 7 weekly 60 min meetings, TQD morning of first session, 10 days after start of medications | Abstinence at 12m (biochem, pp) | Low |
| Selby 2003[147] | Canada | NR | NS | NS | 284 | Bupropion 300mg for 12 weeks | Placebo | Not described | Abstinence at 12m (biochem, pp) | Unclear |
| SMK20001[148] | USA | 42 | NS | 48% | 286 | Bupropion 300mg for 7 weeks | Placebo | Not described | Abstinence at 12m (biochem, car) | Unclear |
| Tonnesen 2003[149] | Europe, Australia, New Zealand | 42 | NS | 51% | 710 | Bupropion SR 300mg for 7 weeks | Placebo | Brief motivational support at weekly clinic visits and telephone support during follow up. 11 clinic visits and 10 phone calls scheduled. | Abstinence at 12m (biochem, car) | Low |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Uyar 2007[150] | Turkey | 36 | NS | 19% | 131 | Bupropion 300mg for 7 weeks | No treatment | Brief counselling on consequences of smoking with follow up for 24 weeks- more than low intensity | Abstinence at 6m (biochem, pp) | High |
| Zellweger 2005[151] | Europe | 40 | NS | 64% | 667 | Bupropion SR 300mg for 7 weeks | Placebo | Brief (10-15 min) motivational support at weekly clinic visits and telephone support one day before TQD, 3 days after TQD, monthly during follow up | Abstinence at 12m (biochem, car) | Unclear |
| Wittchen 2011[114] | Germany | 43 | NS | 48% | 467 | Bupriopion 300mg for 12 weeks | No treatment | CBT of 4-5 one-on-one counselling sessions for 20-30mins | Abstinence at 12m (self, car) | High |
| EAGLES 2016[98] | International | 46 | NS | 66% | 4028 | Bupropion SR, 150mg x 2/day (titrated for 3 days, then full dose for 11 weeks) | Varenicline 2mg/day for 12 weeks | All participants received counselling (up to 10 mins) at all contacts. Participants were monitored at weeks 1 - 6, 8, 12, 13, 16, 20, 24; contacts were up to 15 face-to-face visits and 11 telephone visits | Abstinence at 6m (biochem, car) | Low |

## Table 8.15 Included studies from systematic review: bupropion versus varenicline

| Study | Setting | Mean age | Ethnicity | Female | Participants | Bupropion | Varenicline | Behavioural support | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|
| Cinciripini 2013[130] | USA | 44 | NS | 39% | 294 | Bupropion 150mg/d days 1-3, 300mg/d thereafter for 12 weeks | Varenicline 0.5mg days 1-3, 1mg days 4-7, 2mg thereafter for | 10 individual counselling sessions (6 in person, 4 via phone, 240 mins total) | Abstinence at 6m (biochem, car) | Unclear |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | 12wks | | | |
| Gonzales 2006[136] | USA | 42 | NS | 46% | 1025 | Bupropion 300mg for 12 weeks, begun 7 days pre-TQD | Varenicline 2mg/day | Brief (<10 min) standardised individual counselling at 12 weekly visits during drug phase and 11 clinic/phone visits during follow up, problem solving and relapse prevention | Abstinence at 12m (biochem, car) | Low |
| Jorenby 2006[141] | USA | 42 | NS | 41% | 1027 | Bupropion 300mg for 12 weeks | Varenicline 2mg for 12 weeks | Brief (< 10 min) individual counselling at each weekly assessment for 12w & 5 follow-up visits. One telephone call 3 days after quit day | Abstinence at 12m (biochem, car) | Low |
| Nides 2006[144] | USA | 41 | NS | 51% | 638 | Bupropion 300mg for 7 weeks | Varenicline 2mg for 7 weeks | Up to 10 mins counselling at 7 weekly clinic visits, 12 & 24w | Abstinence at 12m (biochem, car) | Low |
| EAGLES 2016[98] | Internati onal | 46 | NS | 66% | 4028 | Bupropion SR, 150mg x 2/day (titrated for 3 days, then full dose for 11 weeks) | Varenicline 2mg/day for 12 weeks | All participants received counselling (up to 10 mins) at all contacts. Participants were monitored at weeks 1 - 6, 8, 12, 13, 16, 20, 24; contacts were up to 15 face-to-face visits and 11 telephone visits | Abstinence at 6m (biochem, car) | Low |

## Table 8.16 Included studies from systematic review: bupropion versus nicotine replacement therapy (NRT)

| Study | Setting | Mean age | Ethnicity | Female | Participants | Bupropion | NRT | Behavioural support | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|
| NRT patches | | | | | | | | | | |
| Gariti 2009[116] | USA | 54 | NS | 57% | 260 | Bupropion SR for 9 weeks | Nicotine patch for 8 weeks | 10 weeks of individual counselling sessions or four 5-10 minute counselling sessions | Abstinence at 12m (biochem, pp) | Low |
| Jorenby 1999[79] | USA | 43 | NS | 52% | 893 | Bupropion 300mg for 9w from 1w before quit day | Patch 24 hr, 21mg for 6 weeks, tapered for 2 weeks | Brief (< 15 min) individual counselling session at each weekly assessment. One telephone call 3 days after quit day | Abstinence at 12m (biochem, car) | Unclear |
| Piper 2009[85] | USA | 45 | NS | 58% | 1504 | Bupropion SR (150mg bid, 1 wk pre-quit, 8 wks postquit) | Patch 24 hr, 21, 14 and 7mg titrated down over 8 weeks | 7 one-to-one 10-20min counselling sessions | Abstinence at 6m (biochem, pp) | Unclear |
| Smith 2009[117] | USA | 44 | NS | 56% | 1346 | Bupropion SR (150mg bid, 1 wk pre-quit, 8 wks postquit) | Patch, 21, 14 and 7mg titrated down over 8 weeks | Quitline counselling - up to 4 calls + additional support if required | Abstinence at 6m (self, pp) | High |
| Uyar 2007[150] | Turkey | 36 | NS | 19% | 131 | Bupropion 300mg for 7 weeks | Patch 21mg for 6 weeks | Brief counselling on consequences of smoking with follow up for 24 weeks- more than low intensity | Abstinence at 6m (biochem, pp) | High |
| EAGLES 2016[98] | International | 46 | NS | 66% | 4028 | Bupropion SR, 150mg x 2/day (titrated for | Nicotine patch, 21mg x 7 weeks, 14mg x 2 | All participants received counselling (up to 10 mins) at all contacts. Participants were monitored at weeks 1 | Abstinence at 6m (biochem, car) | Low |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | 3 days, then full dose for 11 weeks) | wks, 7mg x 2 weeks (11 weeks) | - 6, 8, 12, 13, 16, 20, 24; contacts were up to 15 face-to-face visits and 11 telephone visits | | |
| NRT lozenges | | | | | | | | | | |
| Study | Setting | Mean age | Ethnicity | Female | Partici pants | Bupropion dose | NRT dose | Behavioural support | Outcome | Risk of bias |
| Piper 2009[85] | USA | 45 | NS | 58% | 1504 | Bupropion SR (150mg bid, 1 wk pre-quit, 8 wks postquit) | Lozenge 2 or 4mg for 12 weeks | 7 one-to-one 10-20min counselling sessions | Abstinence at 6m (biochem, pp) | Unclear |
| Smith 2009[117] | USA | 44 | NS | 56% | 1346 | Bupropion SR (150mg bid, 1 wk pre-quit, 8 wks postquit) | Lozenge 2 or 4mg for 12 weeks | Quitline counselling - up to 4 calls + additional support if required | Abstinence at 6m (self, pp) | High |
| NRT patch plus lozenge | | | | | | | | | | |
| Study | Setting | Mean age | Ethnicity | Female | Partici pants | Bupropion dose | NRT dose | Behavioural support | Outcome | Risk of bias |
| Piper 2009[85] | USA | 45 | NS | 58% | 1504 | Bupropion SR (150mg bid, 1 wk pre-quit, 8 wks postquit) | Lozenge 2 or 4mg for 12 weeks + 24 hr Patch, 21, 14 and 7mg titrated down over 8 weeks | 7 one-to-one 10-20min counselling sessions | Abstinence at 6m (biochem, pp) | Unclear |
| Smith 2009[117] | USA | 44 | NS | 56% | 1346 | Bupropion SR (150mg bid, 1 wk pre-quit, 8 wks postquit) | Lozenge 2 or 4mg for 12 weeks +Patch, 21, 14 and 7mg titrated | Quitline counselling - up to 4 calls + additional support if required | Abstinence at 6m (self, pp) | High |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | down over 8 weeks | | | |
| Any NRT | | | | | | | | | | |
| Study | Setting | Mean age | Ethnicity | Female | Partici pants | Bupropion dose | NRT dose | Behavioural support | Outcome | Risk of bias |
| Stapleton 2013[152] | UK | 41 | NS | 53% | 1071 | Bupropion 300mg for 8 weeks | Choice of patches, gums, lozenges, inhalator, nasal spray or microtab, for 12 weeks | 7 weekly behavioural support session, mainly in groups, lasting 60-90 mins each | Abstinence at 6m (biochem, car) | High |
| Wittchen 2011[114] | Germany | 43 | NS | 48% | 467 | Bupriopion 300mg for 12 weeks | Choice of patch (7-52.5mg), gum (2-4mg) or spray (10mg/ml) | CBT of 4-5 1on1 counselling sessions for 20-30mins | Abstinence at 12m (self, car) | High |

## Table 8.17 Included studies from systematic review: bupropion versus bupropion plus nicotine replacement therapy (NRT)

| Gum | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Study | Setting | Mean age | Ethnicity | Female | Partici pants | Bupropion | Bupropion+ NRT | Behavioural support | Outcome | Risk of bias |
| Piper 2007[115] | USA | 42 | NS | 58% | 608 | Bupropion 300mg for 9 weeks, starting 1wk | 4mg nicotine gum, 300mg bupropion | 3x 10 min counselling over 3 weeks | Abstinence at 12m (biochem, pp) | Unclear |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | before TQD | | | | |
| Lozenge | | | | | | | | | | |
| Study | Setting | Mean age | Ethnicity | Female | Partici pants | Bupropion | Bupropion+ NRT | Behavioural support | Outcome | Risk of bias |
| Piper 2009[85] | USA | 45 | NS | 58% | 1504 | Bupropion SR (150mg bid, 1 wk pre-quit, 8 wks postquit) | Bupropion SR (150mg bid, 1 wk pre-quit, 8 wks postquit)+Lozenge 2 or 4mg for 12 weeks | 7 one-to-one 10-20min counselling sessions | Abstinence at 6m (biochem, pp) | Unclear |
| Smith 2009[117] | USA | 44 | NS | 56% | 1346 | Bupropion SR (150mg bid, 1 wk pre-quit, 8 wks postquit) | Bupropion SR (150mg bid, 1 wk pre-quit, 8 wks postquit)+Lozenge 2 or 4mg for 12 weeks | Quitline counselling - up to 4 calls + additional support if required | Abstinence at 6m (self, pp) | High |
| Any NRT | | | | | | | | | | |
| Study | Setting | Mean age | Ethnicity | Female | Partici pants | Bupropion | Bupropion+ NRT | Behavioural support | Outcome | Risk of bias |
| Stapleton 2013[152] | UK | 41 | NS | 53% | 1071 | Bupropion 300mg for 8 weeks | Bupropion 300mg for 8 weeks + choice of patches, gums, lozenges, inhalator, nasal spray or microtab, for 12 weeks | 7 weekly behavioural support session, mainly in groups, lasting 60-90 mins each | Abstinence at 6m (biochem, car) | High |
| Patch | | | | | | | | | | |
| Study | Setting | Mean age | Ethnicity | Female | Partici pants | Bupropion | Bupropion+ NRT | Behavioural support | Outcome | Risk of bias |
| Jorenby | USA | 43 | NS | 52% | 893 | Bupropion | Bupropion | Brief (< 15 min) | Abstinence at | Unclear |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| 1999[79] | | | | | | 300mg for 9wk from 1wk before quit day | 300mg for 9w from 1w before quit day + Patch 24hr, 21mg for 6 weeks, tapered for 2 weeks | individual counselling session at each weekly assessment. One telephone call 3 days after quit day | 12m (biochem, car) | |

## Table 8.19 Included studies from systematic review: bupropion 300mg versus bupropion 150mg

| Study | Setting | Mean age | Ethnicity | Female | Participants | Bupropion dose | BupropiondDose | Behavioural support | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|
| Swan 2003[153] | USA | 45 | NS | 57% | 1524 | Bupropion 300mg | Bupropion 150mg | 4 telephone calls + quitline + self-help material or self-help + support line + 1 telephone call | Abstinence at 12m (biochem, pp) | High |
| Hurt 1997[140] | USA | 44 | NS | 55% | 615 | Bupropion 300mg for 7 weeks | Bupropion 150mg for 7 weeks | Physician advice, self-help materials, and brief individual counselling by study assistant at each visit | Abstinence at 12m (biochem, car) | Unclear |

## Table 8.20 Included studies from systematic review: varenicline versus placebo

| Study | Setting | Mean age | Ethnicity | Female | Participants | Varenicline | Control | Behavioural support | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|
| Cinciripini 2013[130] | USA | 44 | 66% White | 39% | 294 | 12 weeks varenicline 0.5mg/day days 1-3, 1.0mg/day days 4-7, 2.0mg/day | Placebo | 10 individual counselling sessions (6 in person, 4 via phone, 240mins total) | Abstinence at 6m (biochem, car) | Unclear |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | thereafter | | | | |
| Gonzales 2006[136] | USA | 42 | 79% White | 46% | 1025 | Varenicline 2mg/day for 12 weeks | Placebo | Brief (<10 min) standardised individual counselling at 12 weekly visits during drug phase and 11 clinic/phone visits during follow up, problem solving and relapse prevention | Abstinence at 12m (biochem, car) | Low |
| Jorenby 2006[141] | USA | 43 | 84% White | 42% | 1027 | Varenicline 2mg/day for 12 weeks | Placebo | Brief (< 10 min) individual counselling at each weekly assessment for 12w and 5 follow-up visits. One telephone call 3 days after quit day | Abstinence at 12m (biochem, car) | Low |
| Nides 2006[144] | USA | 42 | 87% White | 52% | 638 | Varenicline 2mg for 7 weeks | Placebo | Up to 10 mins counselling at 7 weekly clinic visits, 12 and 24w | Abstinence at 12m (biochem, car) | Low |
| Bolliger 2011[154] | Internatio nal | 44 | NS | 34% | 593 | Varenicline 2mg/day for 12 weeks | Placebo | All participants received 'You can quit smoking' self-help booklet at baseline, and brief counselling (≤10 mins) at each clinic or telephone contact, plus a phone call 3 days post-TQD | Abstinence at 6m (biochem, car) | Low |
| Nakamura 2007[155] | Japan | 40 | NS | 25% | 619 | Varenicline 2mg/day for 12 weeks | Placebo | All participants received a smoking cessation booklet 'Clearing the Air' at baseline, + brief counselling (≤10 mins) at each clinic visit. Weekly visits throughout treatment phase, plus a 5 min phone call at TQD | Abstinence at 12m (biochem, car) | Low |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | and +3 days post-TQD | | |
| Niaura 2008[156] | USA | 42 | 91% White | 48% | 320 | Varenicline 0.5 to 2mg/day for 12 weeks | Placebo | All participants received a smoking cessation booklet 'Clearing the Air' at baseline, + brief counselling (≤10 mins) at each clinic visit. Weekly visits throughout treatment phase | Abstinence at 12m (biochem, car) | Low |
| Oncken 2006[157] | USA | 43 | 80% White | 50% | 647 | Varenicline 2mg/day for 12 weeks | Placebo | All groups received self-help booklet at baseline, + brief (≤10mins) counselling at weekly clinic visits throughout treatment phase, and phone call 3d post-TQD. At each visit smoking status reported and CO-verified; vital signs, weight and adverse events. Urine, blood tests and ECGs at screening, baseline, wks 1, 2, 4, 7 and 12 | Abstinence at 12m (biochem, car) | Low |
| Rennard 2012[158] | International | 43 | 68% White | 40% | 659 | Varenicline 2mg/day for 12 weeks | Placebo | All participants received 'Clearing the Air: Quit smoking today' booklet at baseline, + brief counselling (≤10 mins) at each clinic visit. Weekly visits throughout treatment phase and in follow-up phase clinic visits at wks 13, 16, 20 and 24. Phone calls at wks 14, 18 and 22 | Abstinence at 6m (biochem, car) | Low |

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|---|---|---|---|---|---|---|---|---|---|---|
| Tsai 2007[159] | Taiwan and Korean | 40 | NS | 11% | 250 | Varenicline 2mg/day for 12 weeks | Placebo | All participants received a smoking cessation booklet 'Clearing the Air' at baseline, + brief counselling (≤10 mins) at each clinic visit. Clinic visits at baseline and at wks 1, 2, 3, 4, 6, 8, 10, 12, plus a 5 min phone call at +3 days post-TQD, and at wks 5, 7, 9, 11 | Abstinence at 6m (biochem, car) | Low |
| Wang 2009[160] | China, Singapore Thailand | 39 | NS | 3% | 333 | Varenicline 2mg/day for 12 weeks | Placebo | All participants received a smoking cessation booklet at baseline, + brief counselling (≤10 mins) at each clinic visit, except for wks 5 and 7, when counselling was conducted by phone | Abstinence at 6m (biochem, car) | Unclear |
| DeDios 2012[161] | USA | 42 | Latino | 53% | 32 | Varenicline for 12 weeks | Placebo | 30-minute face-to-face 'culturally informed' smoking cessation behavioural intervention, + a non-tailored self-help brochure, all available in both English and Spanish | Abstinence at 6m (biochem, pp) | Unclear |
| EAGLES 2016[98] | Internatio nal | 46 | NS | 66% | 4028 | Varenicline 2mg/day for 12 weeks | Placebo | All participants received counselling (up to 10 mins) at all contacts. Participants were monitored at weeks 1-6, 8, 12, 13, 16, 20, 24; contacts were up to 15 face-to-face visits and 11 telephone visits | Abstinence at 6m (biochem, car) | Low |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Gonzales 2014[162] | International | 48 | 93% White | 50% | 498 | Varenicline 12 wks, titrated in 1st wk, 1mg x 2/day | Placebo | Brief (< 10 mins) counselling at each contact. TQD set for wk 1 visit. Clinic visits at wks 1-4, 6, 8-13, 16, 24, 32, 40, 48, 52. Brief phone calls at wks 5, 7, 14, 20, 36, 44 | Abstinence at 12m (biochem, car) | Low |
| Heydari 2012[163] | Iran | 43 | NS | 41% | 272 | Varenicline 2mg/day for 8 weeks | No treatment | All received brief (5 mins) education and counselling at 4 x weekly sessions | Abstinence at 12m (biochem, pp) | High |
| Long-term use | | | | | | | | | | |
| Study | Setting | Mean age | Ethnicity | Female | Participants | Varenicline | Control | Behavioural support | Outcome | Risk of bias |
| Williams 2007[164] | USA, Australia | 47 | 89% White | 50% | 377 | Varenicline 2mg/day for 52 weeks | Placebo | Weekly visits throughout wks 1-8, then every 4 wks to wk 52, + wk 53 assessment | Abstinence at 12m (biochem, pp) | Unclear |
| Ebbert 2015[165] | International | 44 | NS | 44% | 1510 | Varenicline for 24 weeks | Placebo | All participants asked to reduce their smoking rate by 50% by wk 4, by 75%+ by wk 8, and 100% by wk 12. Individual 10-minute counselling at each visit (18 face-to-face and 10 phone calls), + a self-help book | Abstinence at 12m (biochem, car) | Low |
| NCT00828113[166] | USA | 43 | NS | 43% | 101 | 52-week varenicline therapy (2mg/day) | 13 weeks of varenicline therapy (2mg/day) | Individual smoking cessation counselling. Brief (<10 minutes) smoking cessation counselling delivered at clinic visits | Abstinence at 12m (biochem, pp) | High |

## Table 8.21 Included studies from systematic review: varenicline versus NRT

| Study | Setting | Mean age | Ethnicity | Female | Participants | Varenicline dose | Patch dose | Behavioural support | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|
| Aubin 2008[167] | Europe & USA | 43 | 93% White | 51% | 757 | Varenicline 2mg for 12 weeks | Patch 21mg week 2-6, 14mg weeks 7-9, 7mg weeks 10-11 | Self-help booklet at baseline, and brief counselling (≤ 10 mins) at each clinic visit or by phone. TQD was at wk 1 visit. Weekly visits throughout treatment phase, plus a phone call 3 days post-TQD | Abstinence at 6 months (biochem, car) | High |
| Baker 2016[168] | USA | 48 | 67% White | 52% | 1086 | Varenicline 2mg for 12 weeks | Patch 21mg wks 1-8, 14mg weeks 9-10, 7mg weeks 11-12 (11+ CPD): Patch 14mg wk 1-10, 7mg wks 11-12 (5-10 CPD) | All participants received counselling (20 mins at visits 1, 2 and 3, and 10 mins by phone and at visits 4, 5) at 1 week pre-TQD and at TQD, wks 1, 4, 12 post-TQD, plus phone call at wk 8. In follow-up phase, participants were contacted at wks 26 and 52 by phone | Abstinence at 6 months (biochem, car) | High |
| DeDios 2012[161] | USA | 42 | Latino | 53% | 32 | Varenicline for 12 weeks | Patch 12 wks: 4 wks @ 14mg, 8 wks @ 7mg | 30-minute face-to-face 'culturally informed' smoking cessation behavioural intervention, + a non-tailored self-help brochure, all available in both English and Spanish | Abstinence at 6m (biochem, pp) | Unclear |
| EAGLES 2016[98] | International | 46 | NS | 66% | 4028 | Varenicline 2mg/day for 12 weeks | Patch, 21mg x 7 weeks, 14mg x 2 wks, 7mg x 2 | All participants received counselling (up to 10 mins) at all contacts. Participants were | Abstinence at 6m (biochem, car) | Low |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | weeks (11 weeks) | monitored at weeks 1-6, 8, 12, 13, 16, 20, 24; contacts were up to 15 face-to-face visits and 11 telephone visits | | |
| Heydari 2012[163] | Iran | 43 | NS | 41% | 272 | Varenicline 2mg/day for 8 weeks | Patch: 8 wks of 15mg | All received brief (5 mins) education and counselling at 4 x weekly sessions | Abstinence at 6m (biochem, pp) | High |
| Tsukahara 2010[169] | Japan | 46 | NS | 25% | 32 | Varenicline 1.0mg x 2/day for 12 wks, following 1 wk titration | Patch for 8 wks (52.5mg/day for 4 wks, 35mg/day for 2 wks, 17.5mg/day for 2 wks) | Varenicline group received 8 clinic visits and nicotine group 5 visits over 12 wks, with 5 brief counselling sessions (≤ 10 mins) | Abstinence at 6m (self car) | High |
| NRT patch and lozenge | | | | | | | | | | |
| Study | Setting | Mean age | Ethnicity | Female | Participants | Varenicline | Patch + lozenge | Behavioural support | Outcome | Risk of bias |
| Baker 2016[168] | USA | 48 | 67% White | 52% | 1086 | Varenicline 2mg for 12 weeks | Patch (21mg week 1-8, 14mg weeks 9-10, 7mg weeks 11-12 (11+ CPD) : Patch 14mg week 1-10, 7mg weeks 11-12 (5-10 CPD)) + Lozenge (2mg or 4mg 5 id for 12 weeks) | All participants received counselling (20 mins at visits 1, 2 and 3, and 10 mins by phone and at visits 4, 5) at 1 week pre-TQD and at TQD, wks 1, 4, 12 post-TQD, plus phone call at wk 8. In follow-up phase, participants were contacted at wks 26 and 52 by phone | Abstinence at 6 months (biochem, car) | High |

## Table 8.22 Included studies from systematic review: varenicline versus bupropion

| Study | Setting | Mean age | Ethnicity | Female | Participants | Varenicline | Bupropion | Behavioural support | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|
| EAGLES 2016[98] | International | 46 | NS | 66% | 4028 | Varenicline 2mg/day for 12 weeks | Bupropion SR, 150mg x 2/day (titrated for 3 days, then full dose for 11 weeks) | All participants received counselling (up to 10 mins) at all contacts. Participants were monitored at weeks 1-6, 8, 12, 13, 16, 20, 24; contacts were up to 15 face-to-face visits and 11 telephone visits | Abstinence at 6m (biochem, car) | Low |
| Gonzales 2006[136] | USA | 42 | 79% White | 46% | 1025 | Varenicline 2mg/day for 12 weeks | Bupropion 150mg x 2/day for 12 weeks | Brief (<10 min) standardised individual counselling at 12 weekly visits during drug phase and 11 clinic/phone visits during follow up, problem solving and relapse prevention | Abstinence at 12m (biochem, car) | Low |
| Jorenby 2006[141] | USA | 42 | NS | 41% | 1027 | Varenicline 2mg for 12 weeks | Bupropion 300mg for 12 weeks | Brief (< 10 min) individual counselling at each weekly assessment for 12w & 5 follow-up visits. One telephone call 3 days after quit day | Abstinence at 12m (biochem, car) | Low |
| Nides 2006[144] | USA | 41 | NS | 51% | 638 | Varenicline 2mg for 7 weeks | Bupropion 300mg for 7 weeks | Up to 10 mins counselling at 7 weekly clinic visits, 12 & 24w | Abstinence at 12m (biochem, car) | Unclear |
| Cinciripini 2013[130] | USA | 44 | 66% White | 39% | 294 | Varenicline 0.5mg days 1-3, 1mg days 4-7, 2mg | Bupropion 150mg/d days 1-3, 300mg/d thereafter for | 10 individual counselling sessions (6 in person, 4 via phone, 240 mins total) | Abstinence at 6m (biochem, car) | Unclear |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | thereafter for 12 weeks | 12 weeks | | | |

## Table 8.23 Included studies from systematic review: cytisine versus placebo

| Study | Setting | Mean age | Ethnicity | Female | Participants | Cytisine | Control | Behavioural support | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|
| Scharfenberg 1971[170] | East Germany | NS | NS | 12% | 1214 | 20-day course. 1.5mg tabs: Days 1-3 6/day; days 4-12 5/day; days 13-16 4/day; days 17-20 3/day | Placebo | None | Abstinence at 24m (self reported pp) | Unclear |
| Vinnikov 2008[171] | Kyrgyzstan | 39 | NS | 3% | 197 | 25-day course. 1.5mg tabs: First 3 days: 6 tabs per day; reduce smoking by half. Days 4-12: 5 tabs per day; stop smoking completely. Days 13-16: 4 tabs per day. Days 17-20: 3 tabs per day. Days 21-22: 2 tabs per day. Days 23-25: 1 tab per day | Placebo | Behaviour counselling | Abstinence at 6m (biochem car) | Low |
| West 2011[172] | Poland | 48 | NS | 53% | 740 | 25-day course. 1.5mg tabs: First 3 days: 6 tabs per day. Days 4-12: 5 tabs per day. Days 13-16: 4 tabs per day. Days 17-20: 3 | Placebo | Quitting advice, randomisation and drugs dispensed at baseline visit; phone calls at TQD + 1 wk | Abstinence at 12m (biochem car) | Low |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | tabs per day. Days 21-22: 2 tabs per day. Days 23-25: 1 tab per day | | later (+ optional clinic visit). Clinic visit 4wks post-TQD, then phone calls at 6m and 12m, with visit to confirm abstinence if claimed. Behavioural support was minimal | | |

## Table 8.24 Included studies from systematic review: cytisine versus NRT

| Study | Setting | Mean age | Ethnicity | Female | Participants | Cytisine | NRT | Behavioural support | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|
| Walker 2014[173] | New Zealand | 38 | Maori | 57% | 1310 | Cytisine for 25 days + NRT vouchers if they needed them after 25 days | Choice of NRT (patch/gum/lozenge) for 8 weeks | Quitline support (3 10-15 minute calls over 8 weeks) | Abstinence at 6m (self reported, car) | High |

## Table 8.25 Included studies from systematic review: acupuncture versus sham acupuncture or no treatment

| Study | Setting | Participants | Mean age | Ethnicity | Female | Intervention dose | Control dose | Other support | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|
| Clavel 1992[17] | France | 515 | >18 | NS | NS | Facial acupuncture to two points (GB8 and Bitong) | Sham acupuncture (wrong | Both groups received placebo nicotine gum | Abstinence at 13m (self, car) | Unclear |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | points 2cm from the active sites) | | | |
| Clavel 1992 +NG[17] | France | 481 | >18 | NS | NS | Facial acupuncture to two points (GB8 and Bitong) | Sham acupuncture (wrong points 2cm from the active sites) | Both groups received active nicotine gum (2mg dose, up to 30 pieces/day, during first 6 months) | Abstinence at 13m (self, car) | Unclear |
| Cottraux 1983[174] | France | 558 | 18-50 | NS | NS | Facial acupuncture, 3 weekly sessions | Waiting list control (assessed at 12 months only) | NR | Abstinence at 12m (self, car) | High |
| Gillams 1984[175] | UK | 81 | NS | NS | NS | Indwelling needle in active auricular point ('Lung') for 4 weeks | Indwelling needle in inactive auricular point (as far from 'Lung' as possible) for 4 weeks | NR | Abstinence at 6m (self, car) | Low |
| He 1997[176] | Norway | 46 | NS | NS | NS | Combined body & auricular acupuncture. Genuine points described for smoking cessation: Body: LU6, LU7; Ear: Shenmen, mouth, lung; Ear sustained acupressure: Shenmen, mouth, | Sham points described for treating musculoskeletal conditions: Body: LI10,TE8; Ear: knees, lumbar | Both groups received combination of body electroacupuncture, ear acupuncture and ear acupressure. 6 treatments over 3 weeks | Abstinence at 8m (biochem, pp) | Low |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | lung, trachea, hunger, endocrine | vertebra, neck; Ear sustained acupressure: knees, lumbar vertebra, neck, shoulder, shoulder joint, buttock | | | |
| Lamontagne 1980[177] | Canada | 75 | 20-50 | NS | NS | Acupuncture to auricular points ('Zero' and 'Lung') | Self-monitor and report back | All subjects given 2 appointments 1 week apart. All smokers also given written advice on smoking cessation | Abstinence at 6m (self, pp) | Unclear |
| Leung 1991[178] | Hong Kong | 95 | NS | NS, Asian | NS | Indwelling needles in auricular points ('Shenmen' and 'Lung') checked every 7 days; Introductory information sessions followed by 8 attendances in total, for supervision of needles | Waiting list control | NR | Abstinence at 6m (self, pp) | High |
| Martin 1981a[179] | New Zealand | 126 | NS | NS | NS | Indwelling needles to 'effective' auricular points (lung and hunger) for 3 weeks | Indwelling needles to 'ineffective' auricular points (elbow and | NR | Abstinence at 6m (self, pp) | Unclear |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | eye) | | | |
| Martin 1981b[179] | New Zealand | 126 | NS | NS | NS | Combined body & auricular acupuncture indwelling needles to 'effective' auricular points (lung and hunger) for 3 weeks plus electroacupuncture for 20 minutes to LI4 in the hand and tongue point in the ear at the second attendance | Indwelling needles to 'ineffective' auricular points (elbow and eye) plus electroacupuncture for 20 minutes to LI4 in the hand and tongue point in the ear at the second attendance | NR | Abstinence at 6m (self, pp) | Unclear |
| Vandevenne 1985[180] | France | 200 | NR | NS | NS | Combined body & auricular acupuncture to 3 auricular and 2 body points | Sham acupuncture to nearby areas | Both interventions given on days 1, 4, 10 and 20 | Abstinence at 12m (self, pp) | Low |
| Waite 1998[181] | UK | 78 | >18 | NS | NS | Active group, lung point in ear | Control group, medial aspect of the patella, not on recognised acupuncture point | All smokers received structured counselling and written information before randomisation | Abstinence at 6m (biochem, pp) | Low |
| Wu 2007[182] | Taiwan | 131 | ≥18 | NS, Asian | NS | 'Real' points Shenmen, Lung, | 'Irrelevant' points eye, | NR | Abstinence at 6m (self, pp) | Low |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Mouth, Sympathetic (auricular and active states on pg 9) | elbow, shoulder, knee | | | |

## Table 8.26 Included studies from systematic review: Acupuncture versus NRT

| Study | Setting | Participants | Mean age | Ethnicity | Female | Intervention dose | NRT dose | Other support | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|
| Clavel 1992[17] | France | 515 | >18 | NS | NS | Facial acupuncture to two points (GB8 and Bitong) | 2mg nicotine gum | NR | Abstinence at 13m (self, car) | Unclear |
| Clavel 1985[16] | France | 651 | NS | NS | NS | Facial acupuncture using 2 points bilaterally, single session | 2mg nicotine gum | All groups also received 3 one-hour sessions of group therapy in first month | Abstinence at 13m (self, car) | Unclear |

## Table 8.27 Included studies from systematic review: Acupuncture versus counselling/psychological intervention

| Study | Setting | Participants | Mean age | Ethnicity | Female | Intervention | Control | Other support | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|
| Cottraux 1983[174] | France | 558 | 18-50 | NS | NS | Facial acupuncture, 3 weekly sessions | Behavioural therapy, 3 weekly sessions | NS | Abstinence at 12m (self, car) | High |
| Gillams 1984[175] | UK | 81 | NS | NS | NS | Indwelling needle in active auricular point ('Lung') for 4 weeks | Group therapy sessions, 1 hr/wk for 4 weeks | NS | Abstinence at 6m (self, car) | Low |
| Leung 1991[178] | Hong Kong | 95 | NS | Asian | NS | Indwelling needles in auricular points ('Shenmen' and 'Lung') | 10 daily sessions of behavioural therapy lasting 1.5 hours | NS | Abstinence at 6m (self, pp) | High |

## Table 8.28 Included studies from systematic review: group behavioural therapy (n=34)

| Study | Setting | Participants | Mean age | Ethnicity | Female | Intervention dose | Control dose | Other support | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|
| Bakkevig 2000[183] | Norway | 139 | 44 | NS | 67% | Group therapy; participants asked to attend 'Smokenders'. 7 weekly sessions + 1 follow up 4w later. Quit day after 5w. Multifaceted including cognitive therapies | Physician (GP) advice; participants instructed to visit their GP for support. GP told to offer NRT as appropriate and provide 1 follow-up visit | | Abstinence 1 yr post-quit date Biochem | Unclear |
| Batra 1994[184] | Germany | 232 | 41 | NS | 53% | Group therapy, 9 weekly 90 min sessions | Self-help materials | Both conditions received nicotine patch | Continuous abstinence at 12m SR | Unclear |
| Camarelles 2002[185] | Spain | 106 | 47 | NS | 54% | Group therapy, 7 x2hrs over 3w, TQD after w3 | Individual counselling, not matched for intensity, 2 sessions over 2w, with self-help materials | 72 participants eligible for nicotine patch, 53 used. | Sustained abstinence at 6m SR | Unclear |
| Cottraux 1983[174] | France | 558 (418 in arms of interest) | NS | NS | 24% | Behaviour therapy. Includes discussion, training in relaxation. 3 x 3 hr sessions over 2 weeks. Relaxation and stress-desensitisation audiotape for daily use | Placebo - lactose capsules for 2w. Met 2 x10min with a doctor | | Abstinence at 12m SR | Unclear |

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|---|---|---|---|---|---|---|---|---|---|---|
| *Cottraux 1983*[174] | France | 558 (418 in arms of interest) | NS | NS | 24% | Behaviour therapy. Includes discussion, training in relaxation. 3 x 3 hr sessions over 2 weeks. Relaxation and stress-desensitisation audiotape for daily use | 1 year waiting list control | | Abstinence at 12m SR | Unclear |
| Curry 1988[186] | USA | 139 | 41 | NS | 51% | Relapse prevention group. Focused on smoking as learned behaviour. Quit day at 3rd session. Additional elements included identifying high-risk situations, cognitive restructuring and role playing. AND 'Absolute Abstinence' (AA) group. Focused on addictive component of smoking. Quit day at 5th session. Additional elements included focused smoking, health education and contingency contract | Relapse prevention self help, workbook units absolute abstinence self help | | Abstinence from months 9 to 12 of follow up. Biochem | Unclear |

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|---|---|---|---|---|---|---|---|---|---|---|
| DePaul 1987[187] | USA | 233 | 43 | NS | 72% | Twice weekly 45 min group meetings for 3w | Self help alone | | Abstinence at 12m (multiple PP) SR | Unclear |
| DePaul 1989[188] | USA | 419 | 38 | NS | 63% in groups, 54% in S-H. | 6 x twice-weekly group meetings to coincide with the 3w television series, then monthly meetings for 1 yr. Abstinent smokers and 5 of their family and 5 co-workers entered for a lottery at the final group meeting and 12m follow up | Self-help manuals only | | Abstinence from end of programme to 12m Biochem | Unclear |
| DePaul 1994[189] | USA | 564 | 38 | NS | 58% | 6 group meetings over 3w followed by 14 booster meetings over 6m. Incentive payments. Handouts from same self-help manual. Maintenance manual (ALA A Lifetime of Freedom from Smoking) | Self-help manual and incentive payment of US$1 for each day abstinent up to US$175 | Worksite interventions were timed to coincide with a mass media intervention consisting of a week-long smoking cessation series on TV, and a complementary | Sustained abstinence at 12m Biochem | Unclear |

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|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | newspaper supplement | | |
| Garcia 1989[23] | Spain | 68 | 34 | NS | 41% | Group therapy, 7 sessions over 3m | Individual counselling in clinic, same schedule as groups | Both received NG 2mg | Sustained abstinence (quit at previous follow ups) at 6m Biochem | Unclear |
| Garcia 2000[190] | Spain | 162 | 32 | NS | 52% | 1. Multi-component programme, 10x 1hr sessions over 5w AND 2. Multi-component, 5x 1hr over 5w AND 3. As 2 plus self-help manual | 4. Self-help manual, 1 orientation session | | PP (7 day) abstinence at 12m Biochem | Unclear |
| Ginsberg 1992[191] | USA | 99 | 38 | NS | 54% | Nicotine gum and behavioural programme including skill training, 5 sessions over 4w AND Nicotine gum and behavioural programme and partner support programme, 8 sessions over 5w | Nicotine gum and educational materials, 2 sessions over 2 weeks | | Abstinence at 52w (not clear if abstinence required at prior assessment at weeks 4, 12, 26) 2&3v1 Biochem | Unclear |

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|---|---|---|---|---|---|---|---|---|---|---|
| Glasgow 1981[192] | USA | 88 (85 included in analysis) | NS | NS | NS | Therapist-administered programme based on either Danaher & Lichtenstein manual, Pomerleau & Pomerleau manual or I Quit Kit . 8 sessions over 8w | Self-administered using same 3 manuals | | Abstinence at 6m Biochem | Unclear |
| Gruder 1993[193] | USA | 1440 | NS | NS | NS | 1. Social Support. 3 x90 min group meetings and copy of 'Quitters Guide' for smokers, and 1 group meeting + Buddy Guide for buddies. Participants were instructed on how to get help from their buddies and others. Telephone calls to subjects and buddies at 1 and 2m AND<br>2. Discussion. Same schedule of meetings and phone calls as 1, but general information and review of self-help manual | 3. No-contact control | All participants sent 'ALA Freedom from Smoking in 20 days' manual and instructed to watch TV programme | Multiple point prevalence abstinence (post-intervention , 6m and 12m). 24m rates also given but substantial loss to follow up by this time so 12m rates used here. | Unclear |

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|---|---|---|---|---|---|---|---|---|---|---|
| Hill 1993[194] | USA | 82 | 50+ | NS | NS | 1. Behavioural training adapted from Lung Health Study programme. Included quit date setting, training with role play of coping responses. 12 x 90 min session over 3m | 2. Exercise and self-help pamphlet. This was a placebo control matched for contact time to 3. Therapist, who was blind to study hypothesis, encouraged smokers to quit at the exercise meetings | | 5 day abstinence at 12m. (Abstinence at previous follow ups not required) Biochem | Unclear |
| Hilleman 1993[195] | USA | 150 | 50 | NS | 67% | 1. Behaviour modification training, 12 x 1hr classes over 3m + transdermal clonidine 2. Same behaviour modification as 1, plus placebo patches | 3. Self-help printed material (I Quit Kit), transdermal clonidine AND 4. S-H printed material, placebo patches | | Cessation at 1 yr SR | Unclear |
| Hollis 1993[196] | USA | 2707 | NS | NS | NS | 3. Group referral. Cessation advice, CO assessment. Video encouraged use of intensive (9 meetings over 2m) group programme, and waiver of fee. Effort made to schedule attendance | 2. Self quit - cessation advice, CO assessment, 10 min video, stop smoking kit, and choice of self-help manuals. Encouraged to set quit date. 1 follow-up telephone call and mailings | Smokers who received provider (physician, physician assistant or nurse practitioner ) advice to quit | 1 yr 2-PP abstinence (7 days at 3 and 12m) Biochem | High |

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|---|---|---|---|---|---|---|---|---|---|---|
| Hollis 1993[196] | USA | 2707 | NS | NS | NS | 3. Group referral. Cessation advice, CO assessment. Video encouraged use of intensive (9 meetings over 2m) group programme, and waiver of fee. Effort made to schedule attendance | 1. Advice - In addition to provider advice, given brief pamphlet by health counsellor | Smokers who received provider (physician, physician assistant or nurse practitioner ) advice to quit | | |
| Jorenby 1995[197] | USA | 504 | 44 | NS | 53% | Group: Given self-help pamphlet at screening visit along with motivational message. Received 8x 1hr weekly group sessions. Skills training, problem-solving skills | Individual: Given self-help pamphlet at screening visit along with motivational message. Also met nurse counsellor x3 following quit date. Nurse helped generate problem-solving strategies and provided praise and encouragement | Compared 22mg vs 44mg nicotine patch and 3 types of adjuvant treatment. Patch groups collapsed. All participants had 8 weekly assessments by research staff | 7 day PP abstinence at 26w Biochem | Unclear |

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|---|---|---|---|---|---|---|---|---|---|---|
| Leung 1991[178] | Hong Kong | 95 (65 in relevant arms) | 37 | NS, Asian | 26% | Behavioural programme including self monitoring, management techniques, coping skills. 10 x 1½ hr sessions over 2w | Waiting list control | | Abstinence (not defined) at 6m SR | Unclear |
| McDowell 1985[198] | Canada | 366 | 36 | NS | 60% | Operation Kick-It programme. 9 sessions. Therapists: public health nurse or health educator and 3. Cognitive Behavior Modification programme. 9 sessions. Therapists: 1 of 2 M. Educational psychologists | Physician advice by one of 12 family physicians. 15 min counselling session with U.S. 'NCI Helping Smokers Quit Kit' and one postal follow up | | Abstinence (over 1w diary period) at 12m SR | Unclear |
| McDowell 1985[198] | Canada | 366 | 36 | NS | 60% | Operation Kick-It programme. 9 sessions. Therapists: public health nurse or health educator and 3. Cognitive Behavior Modification programme. 9 sessions. Therapists: 1 of 2 M. Educational psychologists | Self-monitoring control followed up at 2, 6 and 12m | | | |

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|---|---|---|---|---|---|---|---|---|---|---|
| Minthorn-Biggs 2000[199] | Canada | 75 | 41 | NS | 68% | 1. Canadian Lung Association Countdown programme. 7 weekly sessions and 2. Social interaction programme. 12 sessions over 6w + 4 weekly. Skills training | 3. No-treatment control | | Abstinence at 6m (12m rates only available for groups 1 and 2) SR | Unclear |
| Nevid 1997[200] | USA | 93 | 44 | Hispanic | 48% | Group therapy. 8 x 2 hrs. Included videos using culturally specific components. Motivation, nicotine fading, quitting techniques, RP, 'buddy' support. TQD 5th week | Self help with one group session for motivation and instructions and telephone contact. ALA Freedom from Smoking in 20 days in English and Spanish, also Guia para Dejar de Fumar | Both conditions received same maintenance programme ; ALA self-help manual 'A Lifetime of Freedom from Smoking' and 2 telephone calls a month for 6m | Abstinence at 12m (sustained from post-treatment). PP rates also reported. (excludes 56 people, 35 Gr, 21 S-H who were randomised but did not attend any session and were not included in further analysis); Biochem valid | Unclear |

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|---|---|---|---|---|---|---|---|---|---|---|
| Omenn 1988[201] | USA | 159 | 43 | NS | 44% | 1. Multiple component programme. 3 sessions over 3w. Didactic format and 2. relapse prevention programme. 8 sessions over 8w. Interactive format, choice of immediate or phased quit | 3. Minimal treatment programme. self-help materials only. ACS 22-page Quitter's Guide 7-day plan | | Abstinence at 12m (single PP) Biochem | Unclear |
| Otero 2006[94] | Brazil | 1199 (includes 254 non-attenders) | 42 | NS | 63% | 2. Cognitive behavioural, 1 or 2 weekly x1 hr sessions AND 3. As 2, with 3 or 4 weekly sessions | 1. Single 20 min session - classified as brief intervention control in meta-analysis | No patch in comparison 5 levels of behavioural support collapsed into 3 for analysis. Maintenance or recycling sessions provided to all groups at 3, 6, 12m | Abstinence at 12m (7 day PP) SR | Low |

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|---|---|---|---|---|---|---|---|---|---|---|
| Otero 2006[94] | Brazil | 1199 (includes 254 non-attenders) | 42 | NS | 63% | 2. Cognitive behavioural, 1 or 2 weekly x1 hr sessions AND 3. As 2, with 3 or 4 weekly sessions | 1. Single 20 min session- classified as brief intervention control in meta-analysis | Patch in comparison. Factorial design with NRT 21mg or 14mg patch for 8w incl tapering and 5 levels of behavioural support collapsed into 3 for analysis. Maintenance or recycling sessions provided to all groups at 3, 6, 12m | Abstinence at 12m (7 day PP) SR | Low |
| Pederson 1981[202] | USA | 40 | 39 | NS | 60% | 1. Pomerleau & Pomerleau manual, an introductory session, followed by 1 hr group meetings at 2 and 6w AND 2. Danaher & Lichtenstein manual and same schedule of meetings as 1 | 3. Waiting list control | | Abstinence at 6m for at least 3m SR | Unclear |

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|---|---|---|---|---|---|---|---|---|---|---|
| Pisinger 2005[203] | Denmark | 2408 | 46 | NS | 40% | 1. 'Low intensity': single 15-45 min session of individual lifestyle counselling using motivational interviewing | 2. 'High intensity': as 1 plus offer of participation in 6 session group course over 5m. Option to consider and be invited again in 3m | | PP abstinence at 5 yrs (follow up at 1 and 3 yrs also) Biochem | Unclear |
| Rabkin 1984[204] | Canada | 168 (67 in relevant arms) | 40 | NS | NS | Behaviour modification. Multi-component, 5 x 45-90 min meetings over 3w | Health Education. Single group meeting with didactic lectures by a health professional, film, discussion. Individual session with a therapist 1w later including a counselling element | | Self-reported abstinence via questionnaire at 6m follow up SR | |
| Romand 2005[205] | France | 228 | 42 | NS | 54% | Five Day Plan; 5 sessions on consecutive nights, and supplementary sessions 1-2w later | Control; 1hr of general information on tobacco-related health problems | | Abstinence at 12m, lapse-free (PP also reported) Biochem | Unclear |

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| Slovinec 2005[206] | Canada | 332 | 40 | NS | 100% | As control, plus Stress Management Training. 8 x 2 hr, 2 &1w before TQD, 1,2,3,4,5,7w after. CBT targeted smoking-specific and life stressors | 'Usual care' 3 x15 min physician visits, 2w before & 4 & 8w after TQD. Nicotine patch, S-H materials | | Abstinence at 12m (7 day PP) Biochem | Low |
| Zheng 2007[207] | China | 232 | 56 (int), 53 (control) | NS, Asian | 6% | Social cognitive group intervention, 5 x 2 hr twice weekly sessions | Waiting list control | | Sustained abstinence at 6m Biochem | High |

## Table 8.29 Included studies from systematic review: individual behavioural counselling

| Study | Setting | Partici pants | Mean age | Ethnicity | Female | Intervention | Control | Other support | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|
| Ahluwalia 2006[11] | USA | 755 | 45 | African American | 67% | Counselling using motivational interviewing approach. 3 in-person visits at randomisation, wk1, wk8, and phone contact at wk3, wk6, wk16, self-help materials | Counselling using health education approach. Same schedule & materials as intervention | | PP abstinence at 6m (7 day PP) Biochem | Low |
| Aleixandre 1998[208] | Spain | 48 | 36 | NS | 65% | 'Advanced', 4 x30 min over 4 wks, video, cognitive therapy, social influences, relapse prevention | 'Minimal' 3 min advice immediately after randomisation | | Abstinence at 12m, SR | Unclear |

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|---|---|---|---|---|---|---|---|---|---|---|
| Aveyard 2007[209] | UK | 925 | 43 | NS | 51% | Weekly support; as control, plus additional call at 10 days and visits at 14 and 21 days | Basic support; 1 visit (20-40 mins) before quit attempt, phone call on TQD, visits/ phone calls at 7-14 days & at 21-28 days (10-20 mins) | Both include 8 wks 16mg nicotine patch | Abstinence at 12m (sustained at 1, 4, 12, 26 wks) Biochem | Low |
| Bronson 1989[210] | USA | 155 | 42 | NS | 62% | Two 20 min counselling sessions during a periodic health examination (benefits of quitting, assessment of motivation, quit plan, high risk or problem solving) | Control (completed smoking behaviour questionnaire) | | Abstinence at 18m (sustained from 6-18m) Biochem | Unclear |
| Glasgow 2000[211] | USA | 1154 | 24 | NS | 100% | Video (9 min) targeted at young women. 12-15 min counselling session, personalised strategies, stage-targeted self-help materials. Offered telephone support call | Generic self-help materials | Both groups received 20sec provider advice | Abstinence at 6m (for 30 days) Biochem | Unclear |

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| Jorenby 1995[197] | USA | 504 | 44 | NS | NS | Individual – self-help at screening visit + motivational message. Met nurse counsellor x3 after TQD. Counsellor helped generate problem-solving strategies and provided praise and encouragement | Minimal - self-help materials from physician at screening visit for trial entry, instructed not to smoke while wearing patch. No further contact with counsellors | | 7 day PP abstinence at 26 wks Biochem | Unclear |

## Table 8.30 Included studies from systematic review: brief advice

| Study | Setting | Participants | Age | Ethnicity | Female | Intervention | Control | Outcome | Biochem | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|
| Betson 1997[212] | Hong Kong | 865 | >65 | NS | 8% | Arm 3. Physician advice (1min, based on 4As) AND Arm 4. Physician advice and booklet | Arm 1. No intervention and Arm 2. Written materials (Chinese translation of American Cancer Society booklet) | Abstinence at 1 yr (sustained from 3m) | N | Unclear |
| Butler 1999[213] | UK | 536 | NS | NS | 70% | Standardised brief advice (estimated time 2 minutes) | Structured motivational counselling (mean length 10mins) (based on stage of readiness to change) | PP at 6m (self-reported abstinence in the previous month) | N | Unclear |

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| Demers 1990[214] | USA | 519 | NS | NS | NS | 3 - 5 min smoking cessation counselling (and written materials) plus routine care | Routine care | Sustained at 12m (& 6m) | N | |
| Fagerström 1984[20] | Sweden | 145 (49 in relevant arms) | NS | NS | NS | Advice plus 2 appointments, phone call + letter (long follow up) | Advice plus 1 appointment (short follow up) | Sustained abstinence at 1, 6 and 12m | Y on random subset only | High |
| Haug 1994[215] | Norway | 274 | 18-34 | NS | 100% | Advice + leaflet + invitation to attend 4 follow-up visits | Normal care controls | Abstinence at 18m | Y at 12m only not at 18m | High |
| Higashi 1995[216] | Japan | 957 | NS | NS | NS | Brief advice plus leaflet, encouragement card at 1m and telephone card (incentivised) at 6m | No intervention | PP abstinence at 12m | N | Unclear |
| Jamrozik 1984[36] | UK | 2110 | NS | NS | NS | Brief advice to quit plus smoking cessation pamphlet | Normal care control group | PP abstinence at 12m | Y, random sample | High |
| Janz 1987[217] | USA | 250 | NS | NS | NS | Brief advice from physician and brief consultation from nurse | Normal care | PP abstinence at 6m | N | High |

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|---|---|---|---|---|---|---|---|---|---|---|
| Lang 2000[218] | France | 1095 | NS | NS | 17% | Intensive intervention; contract with quit date, phone call 7 days post-quit date, follow-up visit | Minimal advice; 5-10 min from occupational physician | Sustained abstinence (≥ 6m) at 12m, assessed at annual check up | Y for subsample | Low |
| Marshall 1985[219] | UK | 200 | NS | NS | NS | As control, plus offer of 4 follow-up visits over 3m | Advice plus nicotine gum | Sustained at 12m (from 6m) | Y | Low |
| McDowell 1985[198] | Canada | 366 (153 relevant to review) | NS | NS | NS | Brief physician advice | Control: self-monitoring of smoking | PP abstinence at 12m | N (but threatened to test them) | High |
| Meyer 2008[220] | Germany | 1499 (1011 in relevant conditions?) | 18-70 | NS | 48% | Brief advice from trained physician and selected self-help manuals | Control group (assessment only - 22-sided questionnaire administered in waiting room) | Abstinence at 24m (sustained for 6m) | N | High |

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| Morgan 1996[221] | USA | 659 | 50-74 | NS | NS | Physician advice, stage-based, tailored self-help guide. Follow-up letter from physician and call from project staff. Smokers in contemplation given prescription and free 1 wk supply of gum | Usual care (delayed intervention) | Abstinence at 6m (assume PP) | N | Unclear |
| Nebot 1989[222] | Spain | 424 | NS | NS | NS | Brief physician advice, 3-5 min, and self-help leaflet | Usual care | Abstinence at 12m (states definition unclear) | N incomplete | High |
| Ockene 1991[49] | USA | 1286 | NS | NS | NS | Patient-centred counselling, written materials, asked to schedule follow-up visit, follow-up letter | Advice only | PP abstinence at 6m (self-reported) | N | Unclear |
| Page 1986[50] | Canada | 289 | NS | NS | NS | Advice to quit | No advice | PP abstinence at 6m | N | High |
| Pieterse 2001[223] | Netherlands | 530 | NS | NS | NS | Advice or counselling tailored to stage of change, self-help manual, follow-up visit if quit date set. Approx 10 mins | Usual care | Sustained at 12m (from 6m) | N | Unclear |

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|---|---|---|---|---|---|---|---|---|---|---|
| Porter 1972[224] | UK | 191 | NS | NS | NS | 5 mins of advice delivered 'with conviction and vigour' plus anti-smoking leaflet | No advice | PP abstinence at 6m | N, validation: by family report/neighbour report | High |
| Richmond 1986[225] | Australia | 200 | NS | NS | NS | Six visits to the GP over 6m, including advice, spirometry demonstration and serum cotinine and written materials | Control group completed questionnaire and gave blood sample at single visit | Sustained abstinence 3 yrs (assessed at 6m & 3 yrs) | Y but not on all, some confirmation by relatives and or friends | High |
| Russell 1979[226] | UK | 2138 | NS | NS | NS | Advice to stop smoking. and 4. Advice to stop smoking plus leaflet plus a warning that the patient would be followed up | 1. No intervention and 2. Questionnaire only | Sustained abstinence at 12m (& 1m) | Y, sample only(n=23) | High |
| Russell 1983[55] | UK | 2106 (1377 in relevant arm) | NS | NS | NS | Advised to stop smoking plus provided with a 'give up smoking' booklet | No intervention | Sustained abstinence 12m (& 4m) | Y, 66% of quitters biochem val | High |
| Segnan 1991[57] | Italy | 923 | 20-60 | NS | NS | Repeated counselling (follow-up at 1,3,6,9m) or repeated counselling plus spirometry (conducted by specialist centre) | Advice and leaflet | Sustained abstinence at 12m (sustained for 3m by self report) | Y | Low |

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|---|---|---|---|---|---|---|---|---|---|---|
| Severson 1997[227] | USA | 1478 | New mothers | NS | 100% | As control, and extended support (counselling plus follow-up at 2, 4, and 5m visits) and materials (incl video tape, written materials) | Information pack including a letter from paediatrician on risks of passive smoking, provided by birth hospital | PP abstinence at 12m | N | Low |
| Slama 1990[228] | Australia | 311 | 18-64 , mean age NR | NS | NS | Advice plus leaflets (minimal intervention) | Control | Sustained abstinence at 12m (& 1m & 6m) | Y | Unclear |
| Thompson 1988[229] | USA | 1039 | NR | NS | NS | A. Structured physician advice (3 - 5 min talk);<br>C. Referral to group therapy | A. Structured physician advice (3 - 5 min talk) | PP abstinence at 9m | N | Unclear |
| Unrod 2007[230] | USA | 518 | NR | NS | NS | Physician & patient given 1-page tailored report based on computer-based assessment in waiting room. Physician trained to provide 5As-based brief counselling. Follow-up appointment could be arranged | No intervention (usual care) | PP abstinence at 6m | Y | High |

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|---|---|---|---|---|---|---|---|---|---|---|
| Wilson 1982[231] | Canada | 211 | NR | NS | NS | Brief advice plus follow-up appointments at 1, 3 and 6m | Brief advice (5 min counselling) | PP abstinence at 6m | N | Unclear |
| Wilson 1990[232] | Australia | 1238 | NR | NS | NS | Personalised advice plus leaflets and visual aids at single visit | Normal care control group (advice given if clinically indicated) | Sustained abstinence at 12m (and 6m) | N | Low |

## Table 8.31 Included studies from systematic review: nursing interventions

| Study | Setting | Participants | Mean age | Ethnicity | Female | Intervention | Control | Adjunct | Outcome | Biochem valid | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Aveyard 2003[233] | UK | 831 | NR | NS | NS | In addition to tailored self help, asked to make appointment to see practice nurse. Single postal reminder if no response. Up to 3 visits, at time of letters. Reinforced use of manual | Self-help manual based on Transtheoretical model, maximum of 3 letters generated by expert system. No face-to-face contact | | Abstinence at 12m, self-reported sustained for 6m | Y | Low |

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|---|---|---|---|---|---|---|---|---|---|---|---|
| Aveyard 2007[209] | UK | 925 | 43 | NS | NS | Basic support; 1 visit (20 - 40 mins) before quit attempt, phone call on TQD, visits/phone calls at 7 - 14 days and at 21 - 28 days (10 - 20 mins) | Weekly support; as 1. plus additional call at 10 days and visits at 14 and 21 days | Both interventions included 8 wks 16mg nicotine patch. Intensity high for both groups | Abstinence at 12m (sustained at 1, 4, 12, 26 wks) | Y | Low |
| Borrelli 2005[234] | USA | 278 | 57 | NS | 54% | Motivational enhancement. 3 x 20-30min sessions during nursing visits. 5min follow-up call | Standard care control based on 5As model, single 5-15min session with brief support at subsequent nursing visits, consistent with guidelines | | Abstinence at 12m (no smoking since 6m assessment) | Y but obtained for 60% only | Unclear |
| Janz 1987[217] | USA | NR? | NS | NS | NS | Physician discussed personal susceptibility, self efficacy and concern, trained nurse counselled on problems and strategies.<br>2. As 1, and self-help manual 'Step-by-Step Quit Kit' + 1 telephone call | Usual Care control (from physicians not involved in study) | | Abstinence at 6m (self report by telephone) | N | High |

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| Lancaster 1999[235] | UK | 497 | NS | NS | NS | As control, plus invitation to contact a trained practice nurse for more intensive tailored counselling. Up to 5 follow-up visits offered | Physician advice (face-to-face or in a letter) and a leaflet | Physician advice (face-to-face or in a letter) and a leaflet to both groups | Abstinence at 12m (sustained at 3m and 12m) | Y | Low |
| Sanz-Pozo 2006[236] | Spain | 125 | 40 | NS | 52% (intervention) 62% (control) | 1. Brief advice from doctor at recruitment, appointment with clinic nurse 7 days before TQD, on TQD, 1wk, 1m, 2m, 3m | 2. Brief advice only | | Sustained abstinence at 24m (from 12m) | Y | Unclear |

## Table 8.32 Included studies from systematic review: Internet interventions

| Study | Setting | Mean age | Ethnicity | Female | Participants | Intervention | Control | Adjunct | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|
| An 2008[237] | USA | 20 | NS | 75% | 517 | Interactive, tailored | Non-active | | 30w Abstinence (biochem, pp) | Low |
| Brendryen 2008a[238] | Norway | 29.5 | NS | 50% | 290 | Interactive, tailored, phone contact | Self-help book | | Abstinence at 6m (SR, PP), 12m (SR, car) | Low |
| Brendryen 2008b[239] | Norway | 36 | NS | 50% | 396 | Interactive, tailored, phone contact | Self-help book | NRT (both groups) | Abstinence at 6m (SR, PP), 12m (SR, car) | Low |
| Elfeddali 2012[240, 241] | Netherlands | 42 | NS | 62% | 2031 | Interactive, tailored (2 | Usual care | | Abstinence at 12m (SR, car) | High |

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|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | different types, combined for analysis) | | | | |
| McDonnell 2011[242] | USA | 35 | Korean-American | 12% | 1409 | Interactive, not tailored | Booklet of same content | | Abstinence at 6m (SR, car) | Low |
| Smit 2012[243] | Netherlands | 49.5 | NS | 52% | 1123 | Interactive, tailored | No Intervention | | Abstinence at 6m (SR, car) | High |

## Table 8.33 Included studies from systematic review: motivational interviewing(MI) versus routine care

| Study | Setting | Mean age | Ethnicity | Female | Participants | Intervention | Control | Adjunct | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|
| Bastian 2013[244] | USA | 47 | NS | 58% | 496 | 6 weekly MI telephone calls & control group Interventions | Self-directed materials | NRT (patches) to both groups | Abstinence at 6m (SR. PPA) | Unclear |
| Bock 2008[245] | USA | 47.7 | NS | 47% | 543 | 30 min MI counselling session, follow-up telephone calls | Usual care - referral sheet to smoking cessation resources | NRT (patches) to both groups | Abstinence at 6m (biochem. car) | Unclear |
| Bock 2014[246] | USA | 39.6 | NS | 69% | 846 | 45 min MI counselling, follow-up telephone call | Usual care - self-help guides | NRT (patches) to both groups | Abstinence at 6m, 12m (biochem (eCO2. PP) | Unclear |
| Borrelli 2005[234] | USA | 57.2 | NS | 54% | 278 | 3 x 20-30min MI counselling by nurse | 5-15min brief counselling (1 visit - nurse) | All received manual (clear horizons) | Abstinence at 6m, 12m (biochem (eCO2), car) | Unclear |
| Butler 1999[213] | UK | 41 | NS | 71% | 536 | MI counselling (mean 10 mins) by GP | Brief advice (2 mins) by GP | | Abstinence at 6m (SR. PPA) | Low |

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|---|---|---|---|---|---|---|---|---|---|---|
| Davis 2011[247] | USA | 37.6 | NS | 45% | 218 | MI counselling (nurse, mean 15min) | Prescriptive 15 min interview, nurse | No pharmaco therapy | Abstinence at 6m (SR. PPA) | Unclear |
| De Azevedo 2010[248] | Brazil | 47 | NS | 36% | 273 | MI counselling (counsellor) 30min Follow-up telephone call (x&, 10mins) | Low-intensity counselling (15min) by counsellor | No pharmaco therapy | Abstinence at 6m (SR. PPA) | High |
| Dornelas 2000[249] | USA | 54 | NS | 22% | 100 | MI counselling (psychologist, 20 mins, follow up phone calls) | Brief advice (10mins, psychologist) | | Abstinence at 6m (SR. car) | High |
| Ellerbeck 2009[240] | USA | 47.2 | NS | 59% | 726 | MI counselling calls (both medium and high-intensity groups), counsellors | Smoking cessation materials mailed | Both groups offered NRT +/- bupropion | Abstinence at 12m (biochem. PP) | Low |
| Glasgow 2000[211] | USA | 24 | NS | 100% | 1154 | MI counselling (12-15min, counsellor) | Brief advice + brochure | | Abstinence at 12m (biochem. PP) | Low |
| Hennrikus 2005[250] | USA | 47 | NS | 53% | 2095 | MI counselling (nurse, 20mins) and usual care. Follow-up telephone calls | Usual care | NRT / Bupropion encouraged but not provided | Abstinence at 12m (biochem. PP) | Unclear |
| Hollis 2007[251] | USA | 41 | NS | 60% | 4614 | MI counselling (40 mins MI counselling, follow-up call) | Usual care (brief counselling, 15 min call) | NRT in groups | Abstinence at 6m, 12m (SR. PPA) | Low |
| Lindqvist 2013[252] | Sweden | 48.6 | NS | 81% | 772 | MI counselling | Standard Swedish usual care | Pharmaco therapy received both groups | Abstinence at 12m (SR. PP) | High |
| McClure 2005[253] | USA | 33 | NS | 100% | 275 | MI counselling (15 min telephone calls, up to 4). Counsellor | Usual care | Pharmaco therapy to both | Abstinence at 12m (biochem. | Unclear |

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|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | groups | car) | |
| Rigotti 1997[254] | USA | 48 | NS | 46% | 650 | MI counselling (15 mins) + brief advice | Usual care | | Abstinence at 6m (biochem. PP) | High |
| Soria 2006[255] | Spain | 38 | NS | 53% | 200 | MI counselling (3x20 mins, GP) | Brief advice (GP) | Bupropion offered to highly dependent - both groups | Abstinence at 6m, 12m (biochem. PPA) | Low |
| Tevyaw 2009[256] | USA | 19.8 | NS | NR | 110 | MET (with MI principles) x3 sessions (60min, 30min, 30min) | Muscle relaxation (progressive muscle relaxation) to match intervention contact time | No pharmaco therapy | Abstinence at 6m (biochem. PP) | Unclear |

## Table 8.34 Included studies from systematic review: Motivational interviewing (MI) versus nothing

| Study | Setting | Mean age | Ethnicity | Female | Participants | Intervention | Control | Adjunct | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|
| Harris 2010[257] | USA | 19.5 | NS | 46% | 452 | MI counselling (smoking cessation) (20-30mins, 4 sessions) | MI counselling (healthy eating) (20-30mins, 4 sessions) | Pharmacotherapy to both (heavy smokers) | Abstinence at 6m (biochem. PP) | Unclear |

## Table 8.35 Included studies from systematic review: Mobile phone interventions

| Study | Setting | Mean age | Ethnicity | Female | Participants | Intervention | Control | Adjunct | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|
| Borland 2013[258] | Australia | 42.1 | NS | 60% | 3530 | Internet intervention: personalised tailored Internet-delivered | Minimal advice | No pharmacological | 7 months (6-month CAR), SR | Low |

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|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | (QuitCoach) | | adjunct | | |
| Borland 2013[258] | Australia | 42.1 | NS | 60% | 3530 | SMS intervention: interactive automated SMS programme (onQ) | Minimal advice | No Pharmaco logical adjunct | 7 months (6-month CAR), SR | Low |
| Borland 2013 | Australia | 42.1 | NS | 60% | 3530 | Combined Internet and SMS intervention | Minimal advice | No pharmaco logical adjunct | 7 months (6-month CAR), SR | Low |
| Ferguson 2015[259] | Australia | 42.1 | NS | 51% | 284 | SMS and self-help booklet | Self-help booklet | | Abstinence PP | Unclear |
| Haug 2013[260] | Switzerland | 18.2 | NS | 52% | 755 | SMS (3months) | Online health screen | | Abstinence at 6m (sr, pp) | Low |
| Naughton 2014[261] | UK | 41 | NS | 53% | 602 | SMS (90 days), counselling, pharmacotherapy | Counselling, pharmacotherapy - fairly intensive | | Abstinence at 6m (sr, car) | Low |
| Whittaker 2011[262] | New Zealand | 27 | 24% Maori | 47% | 226 | SMS and video message (6 months) | General health video message | | Abstinence at 6m (SR, car) | Low |

## Table 8.35 Included studies from systematic review: telephone interventions

| Study | Setting | Mean age | Ethnicity | Female | Participants | Intervention | Control | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|
| Abdullah 2005[263] | Hong Kong | NS; > 50% aged 36 - 45 | NS | 16% | 903 | Telephone intervention; smoker did not initiate contact | Self-help or minimal intervention | Abstinence at 6m (biochem, pp) | Unclear |
| An 2006[264] | USA | 57 | NS | 9% | 821 | Telephone intervention; smoker did not initiate contact | Self-help or minimal intervention | Abstinence at 12m (SR, CAR) | High |
| Aveyard 2003[233] | UK | 41 | NS | 54% | 2471 | Telephone intervention; smoker | Self-help or minimal intervention | Abstinence at 12m | Low |

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|---|---|---|---|---|---|---|---|---|---|
| | | | | | | did not initiate contact | | (biochem, car) | |
| Borland 2001[265] | Australia | NS; 37% aged 15 - 29, 26% aged 30 - 39 | NS | 52% | 998 | Additional proactive call(s) | Mailed material | Abstinence at 12m (SR, car) | High |
| Borland 2003[266] | Australia | NS; modal age 30 - 49 | NS | 54% | 1578 | Additional proactive call(s) | | Abstinence at 12m (SR, car) | High |
| Borland 2008[267] | Australia | 41 | NS | 55% | 1039 | Adjunct telephone intervention; smoker did not initiate contact | Brief intervention or counselling | Adjunct: pharmacotherapy to both groups | Abstinence at 12m (SR, car) | High |
| Boyle 2007[268] | USA | 47 | NS | 58% | 1329 | Adjunct telephone intervention to pharmacotherapy; smoker did not initiate contact | Pharmacotherapy | | Abstinence at 12m (SR, PP) | High |
| Brown 1992[269] | Australia | 40 | NS | 62% | 45 | Adjunct telephone intervention; smoker did not initiate contact | Brief intervention or counselling | | Abstinence at 12m (SR, PP) | Unclear |
| Curry 1995[270] | USA | 41 | NS | 52% | 1137 | Telephone intervention; smoker did NOT initiate contact | Self-help or minimal intervention | | Abstinence at 12m (biochem, car) | Unclear |
| Ebbert 2007[271] | USA | NS | NS | NS | 82 | Adjunct telephone intervention; smoker did not initiate contact | Brief intervention or counselling | | Abstinence at 6m (SR, pp) | High |
| Ellerbeck 2009[240] | USA | 47 | NS | 59% | 750 | Adjunct telephone intervention to | Pharmacotherapy | | Abstinence at 24m | Low |

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|---|---|---|---|---|---|---|---|---|---|
| | | | | | | pharmacotherapy; smoker did not initiate contact | | (biochem, pp) | |
| Emmons 2005[272] | USA | 31 | NS | 47% | 794 | Telephone intervention; smoker did not initiate contact | Self-help or minimal intervention | Abstinence at 12m (SR, PP) | Unclear |
| Ferguson 2012[273] | UK: English QUITline | 38 | NS | 55% | 2591 | Additional proactive call(s) | Standard phonecall; Adjunct: NRT provided to both group | Abstinence at 6m (biochem, car) | Low |
| Fiore 2004 [274] | USA | 40 | NS | 58% | 961 | Adjunct telephone intervention to pharmacotherapy; smoker did NOT initiate contact | Pharmacotherapy | Abstinence at 12m (biochem, car) | Unclear |
| Flöter 2009[275] | Germany | 35.9 | NS | NS | 527 | Adjunct telephone intervention; smoker did NOT initiate contact | Brief intervention or counselling | Abstinence at 6m (SR, pp) | High |
| Gilbert 2006[276] | UK: English QUITline | 39 | NS | 66% | 1457 | Additional proactive call(s) | | Abstinence at 12m (SR, car) | High |
| Girgis 2011[277] | Australia | 29 | NS | 52% | 407 | GP-referral to telephone counselling | Usual care | Abstinence at 12m (SR, PP) | High |
| Graham 2011[278] | USA | 35.9 | NS | 51% | 2005 | Telephone intervention; smoker did not initiate contact | Self-help or minimal intervention | Abstinence at 18m (SR, PP) | High |
| Halpin 2006[279] | USA | 67% age 40+ | NS | 66% | 388 | Coverage by health insurance for telephone counselling and pharmacotherapy | Coverage by health insurance for pharmacotherapy alone | Abstinence at 6m (SR, pp) | High |
| Hennrikus 2002[280] | USA | 36 | NS | 50-64% | 2402 | Telephone counselling | Group therapy | Abstinence at 24m (biochem, | Unclear |

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| | | | | | | | | car) | |
| Hollis 2007[251] | USA Oregon QUITline | 41 | NS | 60% | 4500 | Additional proactive call(s) | Brief counselling | Abstinence at 12m (SR, car) | High |
| Joyce 2008[281] | USA | 65+ | NS | 60% | 7354 | Offer of quitline: Reactive or proactive counselling vs provider counselling | | Abstinence at 12m (SR, pp) | High |
| Katz 2004[282] | USA | 43/40 | NS | 56% | 1141 | Interactive TC | Information on guidelines, no specific advice | Abstinence at 6m (biochem, car) | High |
| Lando 1992[283] | USA | 47 | NS | 50% | 1827 | Telephone intervention; smoker did not initiate contact | Self-help or minimal intervention | Abstinence at 18m (biochem, car) | High |
| Lando 1997[284] | USA | 42 | NS | 56% | 509 | Adjunct telephone intervention to pharmacotherapy; smoker did not initiate contact | Pharmacotherapy | Abstinence at 12m (biochem, pp) | Unclear |
| Lichtenstein 2000[285] | USA | NS | NS | NS | 1006 | Telephone intervention; smoker did not initiate contact | Self-help or minimal intervention | Abstinence at 12m (SR, car) | High |
| Lichtenstein 2008[286] | USA | NS | NS | NS | 1821 | Telephone intervention; smoker did not initiate contact | Self-help or minimal intervention | Abstinence at 12m (SR, car) | High |
| Lipkus 1999[287] | USA | 49% aged > 50 | African American | 52% | 266 | Telephone intervention; smoker did not initiate contact | Self-help or minimal intervention | Abstinence at 16m (SR, pp) | High |
| MacLeod 2003[288] | Australia | 42 | NS | 51% | 854 | Adjunct telephone intervention to pharmacotherapy; smoker did not initiate contact | Pharmacotherapy | Abstinence at 6m (SR, CAR) | High |
| McBride | USA | 36 | NS | 100% | 580 | Telephone | Self-help or minimal | Abstinence | Unclear |

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| 1999[289] | | | | | | intervention; smoker did not initiate contact | intervention | at 15m (biochem, pp) | |
| McClure 2005[253] | USA | 33 | NS | 100% | 275 | Telephone intervention; smoker did not initiate contact | Self-help or minimal intervention | Abstinence at 12m (biochem, pp) | Unclear |
| McClure 2011[290] | USA | 44.5 | NS | 67% | 52 | Telephone intervention; smoker did not initiate contact | Self-help or minimal intervention | Abstinence at 6m (SR, pp) | High |
| McFall 1993[291] | USA | NS; 23% age 18 - 30, 40% age 31 - 45, 30% 45 - 64 | NS | 70% | 1745 | Offer of quitline: quitline + self help | Nothing | Abstinence at 24m (SR, pp) | High |
| Metz 2007[292] | Germany | 47 | NS | 41% | 290 | Adjunct telephone intervention; smoker did not initiate contact | Brief intervention or counselling | Abstinence at 12m (SR, pp) | High |
| Miguez 2002[293] | Spain | 35 | NS | 38% | 200 | Telephone intervention; smoker did not initiate contact | Self-help or minimal intervention | Abstinence at 12m (biochem, car) | Unclear |
| Miguez 2008[294] | Spain | 37 | NS | 46% | 228 | Telephone intervention; smoker did not initiate contact | Self-help or minimal intervention | Abstinence at 12m (sr, car) | Unclear |
| Miller 1997[295] | USA | 51 | NS | 49% | 1942 | Intensive intervention (TC and FTF) | Minimal intervention (TC + FTF) | Abstinence at 12m (biochem, car) | Low |
| Ockene 1991[49] | USA | 35 | NS | 57% | 1223 | Adjunct telephone intervention; smoker did not initiate contact | Brief intervention or counselling | Abstinence at 6m (SR, pp) | High |
| Orleans 1991[296] | USA | 44 | NS | 63% | 2021 | Telephone intervention; smoker | Self-help or minimal intervention | Abstinence at 16m | Unclear |

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|---|---|---|---|---|---|---|---|---|---|
| | | | | | | did not initiate contact | | (biochem, car) | |
| Orleans 1998[297] | USA | NS; 62% in 20 - 39 age group | African American | 64% | 1422 | Two different interventions during single call (tailored vs standard counselling) | | Abstinence at 6m (SR, pp) | High |
| Osinubi 2003[298] | USA | 52 | NS | 7% | 58 | Adjunct telephone intervention; smoker did not initiate contact | Brief intervention or counselling | Abstinence at 6m (SR, pp) | High |
| Ossip-Klein 1991[299] | USA | 43 | NS | NS | 1813 | Offer of quitline: quitline + self help | Self help | Abstinence at 18m (biochem, car) | Unclear |
| Ossip-Klein 1997[300] | USA | NS | NS | 61% | 177 | Telephone intervention; smoker did not initiate contact | Self-help or minimal intervention | Abstinence at 6m (SR, pp) | Unclear |
| Prochaska 1993[301] | USA | 43 | NS | 62% | 756 | Telephone intervention; smoker did not initiate contact | Self-help or minimal intervention | Abstinence at 18m (sr, pp) | Unclear |
| Prochaska 2001[302] | USA | 38 | NS | 56% | 1447 | Telephone intervention; smoker did not initiate contact | Self-help or minimal intervention | Abstinence at 18m (sr, car) | High |
| Rabius 2004[303] | USA | NS; (≤ 25/ > 25): 61%/67 % F, av.age 22/44, | NS | NS | 3522 | Additional proactive call(s) | | Abstinence at 6m (SR, car) | Unclear |
| Rabius 2007[303] | USA | 43 | NS | 70% | 6322 | Additional proactive call(s) | | Abstinence at 7m (SR, pp) | Unclear |
| Reid 1999[304] | Canada | 38 | NS | 48% | 396 | Adjunct telephone intervention to pharmacotherapy; | Pharmacotherapy | Abstinence at 12m (SR, pp) | Unclear |

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|---|---|---|---|---|---|---|---|---|---|
| | | | | | | smoker did not initiate contact | | | |
| Rimer 1994[305] | USA | 61 | NS | 63% | 1867 | Telephone intervention; smoker did not initiate contact | Self-help or minimal intervention | Abstinence at 12m (SR, pp) | High |
| Sims 2013[306] | USA | 21.3 | NS | 58% | 410 | Additional proactive call(s) | | Abstinence at 6m (SR, pp) | Unclear |
| Smith 2004[307] | USA | 42 | NS | 61% | 632 | Additional proactive call(s) | | Abstinence at 12m (sr, car) | High |
| Solomon 2000[308] | USA | 33 | NS | 100% | 214 | Adjunct telephone intervention to Pharmacotherapy; smoker did not initiate contact | Pharmacotherapy | Abstinence at 6m (biochem, pp) | High |
| Solomon 2005[309] | USA | 34 | NS | 100% | 330 | Adjunct telephone intervention to pharmacotherapy; smoker did not initiate contact | Pharmacotherapy | Abstinence at 6m (sr, pp) | High |
| Sood 2009[310] | USA | 43 | NS | 62% | 990 | Two different interventions during single call (reactive counselling vs self-help materials) | | Abstinence at 12m (SR, pp) | Low |
| Sorensen 2007a[311] | USA | 40 | NS | 6% | 231 | Telephone intervention; smoker did not initiate contact | Self-help or minimal intervention | Abstinence at 6m (SR, pp) | High |
| Swan 2003[153] | USA | 45 | NS | 57% | 1524 | Free and clear proactive TC (4 brief calls), access to quitline & self-help materials | Zyban Advantage Program (ZAP) tailored self-help materials, single telephone call, Zuban support line | Abstinence at 12m (SR, pp) | High |
| Swan 2010[312] | USA | 47.3 | NS | 67% | 1202 | Adjunct telephone intervention to pharmacotherapy; smoker did not initiate | Pharmacotherapy | Abstinence at 6m (SR, pp) | High |

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| | | | | | | contact | | | |
| Thompson 1993[313] | USA | 41 | NS | 59% | 382 | Two different interventions during single call (stage-based counselling vs general information) | | Abstinence at 6m (SR, pp) | Unclear |
| Tzelepis 2011[314] | Australia | 45 | NS | 50% | 1562 | Telephone intervention; smoker did not initiate contact | Self-help or minimal intervention | Abstinence at 13m (SR, car) | High |
| Velicer 2006[315] | USA | 51 | NS | 23% | 2054 | Adjunct telephone intervention to pharmacotherapy; smoker did not initiate contact | Pharmacotherapy | Abstinence at 30m (SR, car) | High |
| Young 2008[316] | Australia | 37 | NS | 53% | 318 | Telephone intervention; smoker did not initiate contact | Self-help or minimal intervention | Abstinence at 12m (SR, pp) | High |
| Zhu 1996[317] | USA (Quitline) | 36 | NS | 57% | 3030 | Telephone contact and self help | Self help | Abstinence at 13m (biochem, car) | High |
| Zhu 2002[318] | USA (Quitline) | 38 | NS | 56% | 3282 | Additional proactive call(s) | | Abstinence at 13m (SR, car) | High |
| Zhu 2012[319] | USA (Quitline) | approx. 45% 25 - 44 and 45% 45 - 64 | Chinese Vietnames eKorean | 10% | 2278 | Additional proactive call(s) | | Abstinence at 7m (SR, car) | Low |

## Table 8.36 Updated review. Included studies: NRT versus placebo

| Study | Setting | Mean age | Female | Participants | Intervention dose | Control dose | Support | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|
| Tuisku 2016a[320] | Finland | 21 | 52% | 291 | NRT: Nicotine patch (10mg/16h) X 8/52 | Placebo Patch X8/52 | All received 20min counselling based on motivational interviewing x 22 | 6 month (PP, SR) | High |
| Ward 2013[321] | Aleppo, Syria | 40 | 22% | 269 | NRT: Nicotine patch (dose related to nicotine dependence) - 6 weeks | Placebo Patch | Individual behavioural counselling to both groups. 3x30 min individual counselling and 5x10min phone call | 12 month (prolonged, Biochem) | Low |

## Table 8.37 Updated review. Included studies: Bupropion plus Varenicline versus Varenicline

| Study | Setting | Mean age | Female | Participants | Intervention | Control | Adjunct | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|
| Ebbert 2014[322] | USA | 42.2 (Intervention) 41.9 (Control) | 45% (Intervention) 49% (Control) | 506 | Bupropion SR + Varenicline (12 weeks) | Placebo + Varenicline (12 weeks) | Brief advice to both groups | 12 month (prolonged, Biochem) | Low |

## Table 8.38 Updated review. Included studies: Varenicline plus NRT versus Varenicline

| Study | Setting | Mean age | Female | Participants | Intervention 1 | Intervention 2 | Adjunct | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|
| Ramon 2014[323] | Spain | 45.1 | 42% | 341 | NRT (Nicotine Patch 21mg for 11weeks) + Varenicline (12 | Placebo Nicotine Patch + Varenicline (12 weeks) | Both groups received behavioural support 10- | 6 month (CAR, Biochem) | Low |

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|---|---|---|---|---|---|---|---|---|---|
| | | | | | weeks) | | 15min x 5 | | |
| Koegelenberg 2014[324] | South Africa | 46.3 | 15% | 446 | NRT (Nicotine Patch 15mg for 14 weeks) + Varenicline | Placebo Nicotine Patch + Varenicline | | 6 month (CAR, Biochem) | Low |

## Table 8.39 Updated review. Included studies: Varenicline versus NRT versus Bupropion

| Study | Setting | Mean age | Ethnicity | Female | Participants | Intervention 1 | Intervention 2 | Intervention 3 | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|
| Zincir 2013[325] | Turkey | NS | NS | NS | 251 | NRT with patch or gum, or combination NRT (patch and gum) - 12 weeks | Varenicline (12 weeks) | Bupropion (12 weeks | 6 month (PP, Biochem) | High |

## Table 8.40 Updated review. Included studies: Varenicline versus NRT

| Study | Setting | Mean age | Ethnicity | Female | Participants | Intervention 1 | Intervention 2 | Intervention 3 | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|
| Tulloch 2016[326] | Canada | 48.61 | NS | 47% | 737 | NRT - 10 weeks (21mg daily) | NRT (35mg daily) + Nicotine gum or inhaler - 22 weeks | Varenicline (1mg BID) - 24 weeks | 12 month (CAR, Biochem) | High (open-label) |
| Study | Setting | Mean age | Ethicity | Female | Participants | Intervention 1 | Intervention 2 | | Outcome | Risk of bias |
| Tuisku 2016b[320] | Finland | 22 (NRT), 21 (Varenicline) | NS | 45% (NRT) 50% (Varenicline) | 291 | NRT: Nicotine patch (15mg/16h) | Varenicline | | 6 month (PP, SR) | High |

## Table 8.41 Updated review. Included studies: telephone interventions

| Study | Setting | Mean age | Ethnicity | Female | Participants | Intervention | Control | Adjunct | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|
| Killen 2008[327] | USA | Telephone support: M 46.56, F 44.59; CBT: M 45.9, F 46.23 | 82% White | 40% | 301 | CBT - on site - 30 mins x 4 sessions | Support telephone calls - 5 mins x 4 sessions | 9 weeks of Bupropion and 8 weeks of NRT to all participants in open-label 8 week period | 12 months, CAR, Biochem | Low |
| Zwar 2014[328] | Australia | 42.6 (Practice Nurse), 43.5 (QUITline), 42.1 (Control) | NS | 55% (PN), 55% (QUITline), 53% (Control) | 2390 | Practice nurse intervention (face-to-face or by telephone) | Usual care (GP care: brief advice) | Pharmacotherapy offered to all participants (NRT, bupropion or varenicline) | 12 months (CAR 10 Months, SR) | Low |
| *Zwar 2014* | Australia | 42.6 (Nurse), 43.5 (QUITline), 42.1 (Control) | NS | 55% (PN), 55% (QUITline), 53% (Control) | 2390 | QUITline referral by GP (proactive call) | Usual care (GP care: brief advice) | Pharmacotherapy offered to all participants (NRT, bupropion or varenicline) | 12 months (CAR 10 Months, SR) | Low |

## Table 8.42 Updated review. Included studies: Internet interventions

| Study | Setting | Mean age | Female | Participants | Intervention | Control | Adjunct | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|
| Borland 2013[258] | Australia | 42.1 | 60% | 3530 | Internet intervention: personalised tailored Internet-delivered (QuitCoach) | Minimal advice | No pharmacological adjunct | 7 months (6-month CAR), SR | Low |
| | Australia | 42.1 | 60% | 3530 | SMS intervention: interactive automated | Minimal advice | No pharmacological | 7 months (6-month CAR), | Low |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | SMS programme (onQ) | | adjunct | SR | |
| | Australia | 42.1 | 60% | 3530 | Combined Internet and SMS intervention | Minimal advice | No pharmacological adjunct | 7 months (6-month CAR), SR | Low |
| Stanczyk 2016[329] | Holland | 45.7 | 61% | 2099 | Enhanced Internet (video messages) | Brief generic text advice | No pharmacological adjunct | 12 months (CAR, Biochem) | Unclear |

## Table 8.43 Updated review. Included studies: Mobile phone interventions

| Study | Setting | Mean age | Female | Participants | Intervention | Control | Adjunct | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|
| Borland 2013[258] | Australia | 42.1 | 60% | 3530 | Internet intervention: personalised tailored Internet-delivered (QuitCoach) | Minimal advice | No pharmacological adjunct | 7 months (6-month CAR), SR | Low |
| Borland 2013 | Australia | 42.1 (Females) | 60% | 3530 | SMS intervention: interactive automated SMS programme (onQ) | Minimal advice | No pharmacological adjunct | 7 months (6-month CAR), SR | Low |
| Borland 2013 | Australia | 42.1 (Females) | 60% | 3530 | Combined Internet and SMS intervention | Minimal advice | No pharmacological adjunct | 7 months (6-month CAR), SR | Low |

## Table 8.44 Updated review. Included studies: motivational interviewing

| Study | Setting | Mean age | Ethnicity | Female | Participants | Intervention | Control | Adjunct | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|
| Bock 2014[246] | USA | 39.6 | 53% White | 69% | 846 | Motivational interviewing (45minstrained professional and follow-up telephone calls) + brief physician advice + NRT | Usual care: brief physician advice + NRT | All received 8 weeks NRT | 12 months (PP 7-day, Biochem) | Low |

## Table 8.45 Updated review. Included studies: individual behavioural counselling

| Study | Setting | Mean age | Ethnicity | Female | Participants | Intervention | Control | Adjunct | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|---|
| Killen 2008[327] | USA | Telephone support: M 46.56, F 44.59; CBT: M 45.9, F 46.23 | 82% White | 40% | 301 | CBT - on site - 30 mins x 4 sessions & telephone counselling | Support Telephone calls - 5 mins x 4 sessions | 9 weeks of Bupropion and 8 weeks of NRT to all participants in open-label 8 week period | 12 months (CAR, Biochem) | Low |

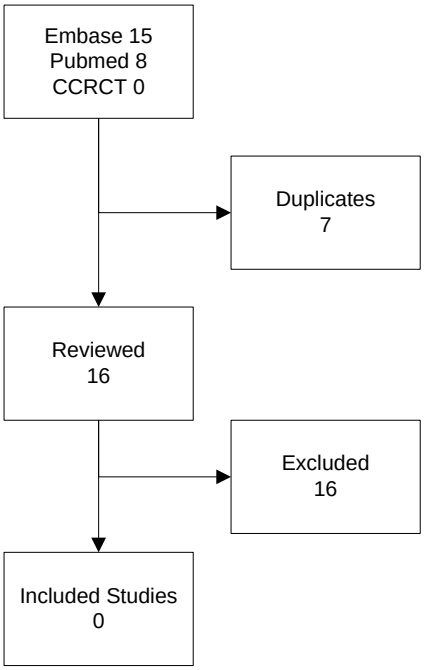
## Table 8.46 Updated review. Included studies: nursing interventions

| Study | Setting | Mean age | Female | Participants | Intervention | Control | Adjunct | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|
| Zwar 2014[328] | Australia | 42.6 (Practice Nurse), 43.5 (QUITline), 42.1 (Control) | 545% (PN), 57% (QUITline), 58% (Control) | 2390 | Practice Nurse Intervention (face-to-face or by telephone) | Usual care (GP care: brief advice) | Pharmacotherapy offered to all participants (NRT, bupropion or varenicline) | 12 months (CAR 10 Months, SR) | Low |
| Zwar 2014 | Australia | 42.6 (Practice Nurse), 43.5 (QUITline), 42.1 (Control) | 55% (PN), 57% (QUITline), 58% (Control) | 2390 | QUITline referral by GP (proactive call) | Usual care (GP care: brief advice) | Pharmacotherapy offered to all participants (NRT, bupropion or varenicline) | 12 months (CAR 10 Months, SR) | Low |

## Table 8.47 Search strategy for studies involving the Allen Carr method

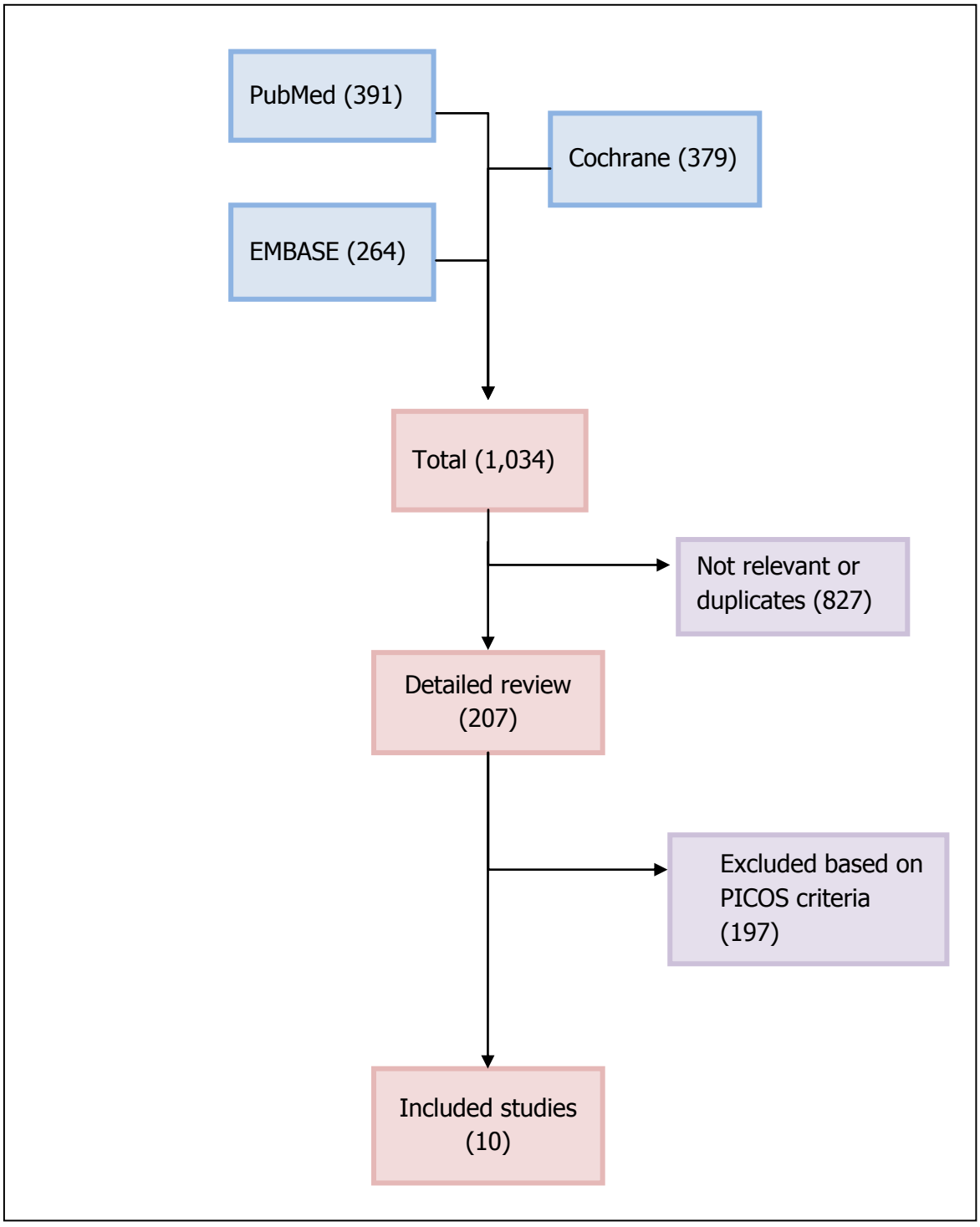
| Database (Date of search) | Search string | Results |
|---|---|---|
| Pubmed (20/5/2016) | Allen AND Carr AND smoking | 8 |
| Embase (20/5/2016) | Allen AND Carr AND smoking | 15 |
| Cochrane Registry of Controlled Trials (20/5/2016) | Allen AND Carr AND smoking | 0 |

## Figure 8.1 Flowchart of included studies for the Allen Carr smoking cessation intervention



# Appendix 9 Search details for review of smoking cessation interventions in pregnancy

## Figure 9.1 Flow diagram of included studies from the updated search: Psychosocial and pharmacological interventions for smoking cessation in pregnancy



## Table 9.1 Search string used in Medline (PubMed)

| Pubmed (Date 18/10/2016) | Search strings | Results |
|---|---|---|
| #1 | (("Smoking Cessation"[Mesh]) OR ("Tobacco Use Cessation"[Mesh]) OR (Stop* smoking) OR (Quit* smoking)) | 31604 |
| #2 | (("Pregnancy"[Mesh]) OR ("Pregnant Women"[Mesh]) OR ("Postpartum Period"[Mesh]) OR ("Postnatal Care"[Mesh]) OR (Pregnancy [tiab]) OR (Pregnant [tiab]) OR (Postpartum [tiab]) OR (Post-partum [tiab]) OR (Postnatal [tiab]) OR (Post-natal [tiab]) OR (Prenatal [tiab]) OR (Pre-natal [tiab])) | 984290 |
| #3 | #1 AND #2 | 2264 |
| #4 | #3 AND Filters (Years: 2013-2016, Type: RCT, Systematic Review, Meta-analysis, Humans) | 391 |

# Appendix 10 Included studies smoking cessation interventions in pregnancy

## Table 10.1 Included studies: NRT and BCS versus placebo and BCS, n=5

| Study | Country | Ethnicity | Participants (n) | Gestational cut-off (weeks) | Intervention | Control | BCS | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|
| Berlin 2014[330] | France | European (96%) | 402 | ≤ 20 | Nicotine patch 10mg/16hr or 15mg/16hr for eight weeks. Dose adjusted to max of 30mg/hr | Placebo patch | Behavioural support at each visit from a midwife or doctor who had been specifically trained. At least 10mins of counseling or visit | Continuous abstinence until birth and birth weight | Low |
| Coleman 2012[331] | England | White British (97%) | 1050 | ≤ 24 | Nicotine patch 15mg/16h | Placebo patch | Behavioural support provided by research midwives. First face-to-face and three by telephone. Face-to-face if collected a second month's supply | Continuous abstinence until birth | Low |
| Kapur 2001[332] | Canada | NS | 30 | ≤ 24 | Nicotine patch 15mg/18 hr for eight weeks followed by 10mg/18hr for two weeks followed by 5mg/18hr for two weeks | Placebo patch | Four counselling sessions. One of the investigators maintained weekly telephone contact | Point prevalence abstinence after eight weeks of treatment | Low |
| Oncken 2008[237] | US | Hispanic | 194 | ≤ 26 | Nicotine gum 2mgs for six weeks followed by a six week taper period | Placebo gum | Two 35min counselling sessions in English or Spanish delivered by a research assistant using a motivational interviewing approach | Seven day point prevalence abstinence after six weeks of gum use and at end of pregnancy | Low |
| Wisborg 2000 [333] | Denmark | NS | 250 | < 22 | Nicotine patch/16hr: 15mg/16hr for eight weeks followed by 10mg/16hr for three weeks | Placebo | Four sessions of smoking cessation counselling with midwife independent of routine antenatal care visits | Seven day point prevalence abstinence at 2nd, 3rd and 4th prenatal visits | Low |

BCS: behavioural cessation support

## Table 10.2 Included studies: NRT patches and BCS versus BCS, n=3

| Study | Country | Ethnicity | Participants (n) | Gestational cut-off (weeks) | Intervention | Control | BCS | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|
| El-Mohandes 2013[334] | US | African-American Hispanic | 52 | ≤ 30 | Nicotine patch 7mg or 14mg or 21mg/24 hr – two dosing schedules for 10 weeks based on baseline salivary cotinine levels | None | SCRIPT* programme – reinforcement and behavioural methods at four visits | Seven day point prevalence after six weeks and between 32 and 34 weeks' gestation | High |
| Hotham 2006[335] | Australia | NS | 40 | ≤ 28 | Nicotine patch 15mg/16h for 12 weeks | None | Counselled for approx 5mins at randomisation and for approx 2mins at subsequent visits by a researcher or midwives who has undergone training with QUIT | Self-reported abstinence at end of treatment and within 48 hours of birth | High |
| Pollak 2007[336] | US | White 69%, Black 24% | 181 | ≤ 25 | Nicotine patch or gum (2mg) or lozenge. Patch 7mgs/16hr if less than 10cigs/day, 14mg/16hr if 10-14 14 cigs/day and 21mg/day if ≥ 15 cigs/day | None | Six one-on-one counselling sessions. Five face-to-face at prenatal visits and one via telephone. Contacts designed to be relapse-sensitive and to coincide with prenatal visits | Seven day point prevalence after seven weeks of treatment and between 32-34 weeks' gestation | High |

BCS: behavioural cessation support *The SCRIPT (Smoking Cessation and Reduction in Pregnancy Treatment Program)

## Table 10.3 Included studies: Bupropion and BCS versus BCS, n=1

| Study | Country | Ethnicity | Participants (n) | Gestational cut-off (weeks) | Intervention | Control | BCS | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|
| Stotts 2015[337] | US | African-American Hispanic | 11 | ≤ 26 | Bupropion 150mg/day for three days followed by 150mg twice daily for eight weeks | Placebo | Four, weekly, 15-minute smoking cessation counselling sessions delivered by a research nurse | Seven day point prevalence abstinence at end of treatment | Unclear |

## Table 10.4 Included studies: counselling, n=44

| Study | Country | Ethnicity | Participants (n) | Gestational cut-off (weeks) | Intervention | Control | Comparison type | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|---|
| Baric 1976[338] | England | NS | 110 | < 20 | One-to-one counselling from a senior medical student. Half were given a diary and a gift of a free smoking diary | Usual care | Counselling (single intervention) versus usual care | Self-reported abstinence 11 weeks after baseline visit | High |
| Cinciripini 2000[339] | USA | NS | 82 | ≤ 30 | Control and posted a video with six 25-30 minute vignettes | Quit calendar and tip guide | Counselling (single intervention) versus less intensive intervention | Biochemically validated point prevalence abstinence within 2-3 days of quit, 4-5 weeks after quit and 1 month (0-5) postpartum | High |
| Cook 1995[340] | USA | NS | 150 | < 24 | Control and regular meetings with | Discussion of risks by a nutritionist | Counselling (multiple intervention) versus less | Biochemically validated at | High |

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| | | | | | smoking cessation counsellor + physician reinforcement at each visit. Feedback from urine cotinine | and resident physician at initial visit | intensive intervention | term or birth, > 50% reduction in mean cotinine and mean birth weight | |
| Cummins 2016[341] | USA | NS | 1173 | < 27 | Telephone counselling provided by veteran staff members of quitline and self-help materials | Self-help materials only | Counselling (multiple intervention) versus less intensive intervention | Self-reported abstinence; 30-day abstinence in third trimester (about 29 weeks), 90 day abstinence at two months postpartum and 190 abstinence at six months postpartum | High |
| Dornelas 2006[342] | USA | 66% Hispanic | 107 | < 30 | One 90 min psychotherapy session by mental health therapist. Bimonthly phone calls | Usual care and booklet, chart prompt and audited chart | Counselling (single intervention) versus less intensive intervention | Biochemically validated seven day point prevalence abstinence and six months (6-11) postpartum | High |
| Dunkley 1997[343] | UK | NS | 100 | < 18 | Brief contact (< 5mins) x eight visits with trained midwives | Usual care | Counselling (single intervention) versus usual care | Self-reported abstinence at 37 weeks and one month (0-5) postpartum | High |
| Eades 2012[344] | Australia | Aborginal or Torres Straight Islander | 263 | ≤ 20 | Advised to quit 'cold turkey' at first visit. Bring a support person to second visit. Offered NRT at | Usual care | Counselling (tailored intervention) versus usual care | Biochemically validated point prevalence abstinence at 36 weeks | High |

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|---|---|---|---|---|---|---|---|---|---|
| | | | | | third visit. Follow-up visits with health workers and midwives | | | | |
| Ershoff 1989[345] | USA | 64% white | 242 | < 18 | Control and eight self-help booklets, taught behavioural strategies and asked to read first one, other mailed weekly | Two-page pamphlet, two minutes with a health educator and advised about free cessation programme | Counselling (single intervention) versus less intensive intervention | Biochemically validated abstinence at 34 weeks | High |
| Ershoff 1999[346] | USA | 60% white | 257 | ≤ 26 | Control and 4-6 x 10-15 min phone counselling sessions by nurse educators trained in motivational interviewing | Received a 32-page self-help booklet | Counselling (single intervention) versus less intensive intervention | Biochemically validated cessation at 34 weeks and mean cigs/day | High |
| Gielen 1997[347] | USA | African American: 81%, 89% | 391 | ≤ 28 | Written information, a 15 minute one-to-one counselling session, educational materials, reinforcement and two letters of encouragement | Usual clinic + inpatient smoking cessation | Counselling (multiple intervention) versus usual care | Biochemically validated seven day point prevalence abstinence in hospital after delivery, six months (6-11) postpartum, > 50% reduction in cotinine from baseline to late pregnancy | High |
| Hajek 2001[348] | NS | NS | 732 | 12 | Midwives received two hours of training on CO monitor and stage of change advice and CO assessments. | Midwives received one hour of training to discuss the study and were asked to provide usual care | Counselling (tailored intervention) versus usual care | Biochemically validated point prevalence abstinence at birth and self-reported | High |

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|---|---|---|---|---|---|---|---|---|---|
| | | | | | Participants received written advice, motivational materials and offer of buddying to another pregnant smoker for support | and any usual pamphlets | | continuous abstinence at six months (6-11) postpartum | |
| Hartmann 1996[349] | USA | White: 78%, 74% | 219 | ≤ 36 | Counselling by residents at each visit, Windsor's guide, contacted by smoking cessation counsellor and quitters sent encouraging postcard each week | Usual care | Counselling (multiple intervention) versus usual care | Biochemically validated abstinence at last prenatal visit, > 50% reduction in self-reported smoking and mean cigs/day | High |
| Haug 1994[350] | Norway | NS | 322 | ≤ 12 | GP advice < 15 minutes at first visit, written information, invited to consult GP after 1, 6, 12 and 18 months | Usual care | Counselling (multiple intervention) versus usual care | Self-reported smoking abstinence 6 months after study entry, biochemically validated 12 months after start (0-5 months postpartum), self-reported abstinence at 15 (6-11) and 18 (12-17) months postpartum | High |
| Hegaard 2003[351, 352] | Netherlands | NS | 647 | ≤ 22 | 30-40 minute consultation, written information, invitation to join smoking cessation programme based on CBT, all offered NRT | Usual care (included advice in a 30 minute consultation) | Counselling (tailored intervention) versus usual care | Biochemically validated cessation at 37 weeks, mean birth weight, low birth weight | High |

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| | | | | | (2mg gum or 15mg patch/16 hours) for 11 weeks + encouragement at subsequent clinic visits | | | and preterm births | |
| Kendrick 1995[352] | USA | NS | 1,885 | ≤ 32 | Based on stages of change but differed by state. 1-5 minutes counselling or brief clinic based counselling or six minutes with brochures and written materials | Usual care (not otherwise specified by usual clinic staff) | Counselling (multiple intervention) versus usual care | Biochemically validated point prevalence abstinence at eight months' gestation | High |
| Lawrence 2003[353] | UK | NS | 613 | ≤ 19 | Midwives trained on theory of transtheoretical model (TTM). Assessed by midwife and given TTM based self-help manual and interactive computer programme giving individualised advice | Usual care. Midwives asked to give a booklet to women | Counselling (multiple intervention) versus usual care | Biochemically validated point prevalence abstinence at 28-30 weeks, 10 days after birth and at 0-5 months postpartum | High |
| Lee 2015[354] | USA | 56% Black 12% Hispanic | 277 | ≤ 25 | Cognitive behavioural therapy provided by a health educator-two prenatal and two postnatal | Best practice - brief advice based on the 5A's | Counselling (multiple intervention) versus usual care | Biochemically verified seven day point prevalence abstinence in late pregnancy and at one and five months postpartum | High |
| Lillington 1995[355] | USA | 53% African American | 34 | NS | Assessment of motivation and intention. Bilingual health educators. 15 | Usual care. Printed information and group quit | Counselling (multiple intervention) versus usual care | Self-reported smoking cessation at nine months' | High |

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| | | | | | minute individual counselling, self-help guide, how to win prizes and booster postcard every month | message | | gestation and six weeks (0-5 months) postpartum | |
| Loeb 1983[356] | USA | NS | 963 | NS | Letter of invitation, reminder letter, group information meeting, individual session with trained smoking counsellor, six 1.5 hour group sessions, once a week and subsequent optional groups, individual sessions + phone calls | Usual care | Counselling (tailored intervention) versus usual care | Self-reported smoking cessation in late pregnancy. Biochemically validated with cord blood thiocyanate | High |
| Mayer 1990[357] | USA | 75% White | 149 | ≤ 28 | 20min 1:1 counselling and behavioural change manual focusing on contracting and self-monitoring (CBT) | Usual care which included printed information | Counselling (multiple intervention) versus usual care | Self-reported smoking cessation at 9 months' gestation and approx. 4.7 weeks (0-5months) postpartum | High |
| McBride 1999[358] | USA | 88% White | 501 | < 20 | Receive a personalised letter, a relapse prevention kit, a booklet, three antenatal counselling phone calls, three additional counselling calls in first four months after birth and three newsletters | Self-help booklet and suggestions for quitting | Counselling (multiple intervention) versus less intensive intervention | Self-reported and biochemically validated 7 day point prevalence abstinence at 28 weeks. Abstinence at two (0-5), six (6-11) and 12 (12-17) | High |

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| | | | | | | | | months postpartum (combined baseline smokers and spontaneous quitters) | |
| McLeod 2004[359] | New Zealand | NS | 272 | NS | Four armed approach. Intervention 1: midwife training-smoking cessation and support.<br>Intervention 2: midwife - breastfeeding support for smokers.<br>Intervention 3: Interventions 1 and 2 combined.<br>Intervention 4: Control and intervention 2 compared with interventions 1 and 3 | Usual care and midwife training and support to implement education and support for breastfeeding for women who smoked | Counselling (single intervention) versus usual care | Biochemically validated cessation at 28 and 36 weeks and at six weeks and four months (0-5) postpartum. Breastfeeding outcomes also reported | High |
| Messimer 1989[360] | USA | 98% White | 59 | < 28 | Control and use of American Lung Association materials, encouragement to send off for materials and slide tape presentation at first visit | Three counselling sessions with physicians, removal of ashtrays and staff asked not to smoke in front of patients | Counselling (multiple intervention) versus less intensive intervention | Self-reported smoking abstinence at 32-36 weeks and at first postpartum visit (0-5 months) | High |
| Moore 2002[361] | England | NS | 1090 | ≤ 32 | Midwives spent ≥ 5mins introducing a series of 5 self-help booklets based on | Usual care | Counselling (single intervention) versus usual care | Self-reported 7 day point prevalence abstinence at | High |

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| | | | | | stages of change theory. Given copy of first booklet and remainder posted | | | 26 weeks (94% biochemically validated). Self-reported mean cigs/day in late pregnancy | |
| Panjari 1999[362] | Australia | NS | 1013 | ≤ 20 | Control and four counselling sessions by a midwife specifically trained and employed to provide smoking cessation counselling using CBT. Video, interactive discussions and strong verbal messages. Followed by a 5-10min personalised counselling session | Usual care (advice and pamphlet distribution during a group info session) | Counselling (single intervention) versus less intensive intervention | Biochemically validated self-reported smoking cessation at 36 weeks, at six weeks (0-5 months) and at six months (6-11 months) postpartum. Mean birth weight, proportion < 2.5kg and preterm birth | High |
| Parker 2007[363] | USA | Majority White | 736 | ≤ 26 | Received quit kit, enrolled in quit and win monetary incentive lottery programme and up to three motivational interviewing (MI) phone calls | Received self-help materials (quit kit and video - SCRIPT) | Counselling (multiple intervention) versus less intensive intervention | Biochemically validated self-reported smoking cessation at 32 weeks, six weeks and six months postpartum (outcomes not reported) | High |
| Patten 2009[364] | USA | Alaskan natives | 33 | ≤ 24 | Self-help guide adapted from SCRIPT trials, 15-25 min face-to-face counselling based on | 5A's component treatment, five minute face to face at first visit and culturally | Counselling (multiple intervention) versus less intensive intervention | Biochemically validated tobacco use 60 days post-randomisation | High |

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| | | | | | 5A's, a video, 4 x 10-15 minute proactive interactive phone sessions | specific brochures | | (late pregnancy) | |
| Pbert 2004[365] | USA | NS | 434 | < 32 | Dissemination intervention consisted of provider training based on national CPGs, office management system and establishment of programme boards. Based on MI and 4 A's from the SCRIPT trial. | Usual care, in which no training or intervention occurred | Counselling (single intervention) versus usual care | Biochemically validated smoking cessation at one month postpartum (late pregnancy), at three (0-5) and at six (6-11) months postpartum. Mean cigs/day | High |
| Price 1991[366] | USA | 70% White | 141 | ≤ 28 | Tailored educational videotape for 6.5 minutes, pamphlet on quitting, a second four minute video one month later and questions answered by health educator | Usual care | Counselling (single intervention) versus usual care | Biochemically validated smoking cessation two or three weeks prior to delivery. Mean cigs/day | High |
| Rigotti 2006[367] | USA | NS | 421 | ≤ 26 | Control and a series of telephone calls accompanied by additional mailed written materials. Each participant had a trained counsellor who offered up to 90mins of counselling in pregnancy and up to 15mins postpartum | Usual care and mailed a validated smoking cessation booklet. Less than five minutes counselling at enrolment by a trained counsellor | Counselling (multiple intervention) versus less intensive intervention | Biochemically validated seven day point prevalence abstinence at 28 weeks to term, at three (0-5) months postpartum and > 50% reduction in cigs/day | High |
| Secker-Walker | USA | NS | 513 | < 25 | Counselling from a trained health | Usual advice about smoking | Counselling (multiple intervention) versus usual | Self-reported smoking | High |

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|---|---|---|---|---|---|---|---|---|---|
| 1994[368] | | | | | educator. Follow up at second visit, 36 weeks and six weeks postpartum | provided by obstetrician or midwife | care | cessation at 36 weeks (75% biochemically validated). Self-reported cessation at 8-15 months (6-11), 16-24 months (18) and 25-54 months postpartum. Mean + low birth weight, PPROM, placenta praevia + placental abruption | |
| Secker-Walker 1997[369] | USA | 98% White | 49 | NS | Control and a 29 minute video of four women going through process of quitting during pregnancy. Based on social learning theory | Advice from obstetrician or nurse-midwife and a booklet on quitting | Counselling (single intervention) versus less intensive intervention | Biochemically validated cessation at 36 weeks | High |
| Secker-Walker 1998[370] | USA | NS | 291 | NS | Structured smoking cessation protocol provided by physicians trained in its use. First, second, third and fifth visits | Received a baseline questionnaire, a booklet, physician advice, CO measured and a brief standardised health risk message from a research nurse | Counselling (multiple intervention) versus less intensive intervention | Biochemically validated seven day point prevalence abstinence at 36 weeks and one year postpartum. Mean birth weight, low birth weight, mean cigs/day | High |

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|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | at 36 weeks and one year postpartum. Preterm births | |
| Stotts 2002[371] | USA | NS | 269 | 28 | Control and 20-30 mins of motivational interviewing (MI) telephone counselling, a personalised stages-of-change based feedback letter and a final MI call 4-5 days after the feedback letter was sent | Provided with MI counselling (3-5 minutes) and a series of eight motivational self-help books | Counselling (multiple intervention) versus less intensive intervention | Biochemically validated cessation at 34 weeks. Self-reported smoking cessation at six weeks and three and six months postpartum | High |
| Stotts 2004[372] | USA | NS | 54 | < 28 | MI intervention over eight weeks consisting of one face-to-face MI session, three MI based telephone counselling calls and a personalised feedback letter providing assessment results | Usual care which included physicians or nurses acknowledging smoking and advising quitting | Counselling (multiple intervention) versus usual care | Biochemically validated cessation at post treatment assessment (late pregnancy) | High |
| Tappin 2000[373] | Scotland | NS | 97 | NS | Received 2 to 5 MI sessions (mean 2.6hrs) at home by a midwife with 3 weeks training in smoking cessation counselling | Usual care (received usual advice which should include information about smoking) | Counselling (single intervention) versus usual care | Biochemically validated cessation at greater than or equal to 27 weeks. Mean birth weight, preterm birth and stillbirths | High |
| Tappin 2005[374, 375] | Scotland | NS | 756 | ≤ 24 | Control and offered 2-5 additional home visits of about 30mins from same study midwife | Midwives provided standard health promotion including information from a | Counselling (single intervention) versus usual care | Biochemically validated and self-reported quitting after the 36 week | High |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | book given to all pregnant women in Scotland | | visit , mean birth weight, low and very low birth weight, perinatal deaths, admission to NICU, preterm delivery, stillbirths and neonatal deaths | |
| Thornton 1997[376] | Ireland | NS | 367 | NS | Control and structured one-to-one counselling by a trained facilitator. Partners invited to be involved in the programme. Received an information pack which included a self-help booklet and invited to join a support group. A CO monitor was available for the intervention group. | Routine prenatal advice on a range of health issues from midwives and obstetricians | Counselling (tailored intervention) versus usual care | Biochemically validated abstinence and relapse prevention at delivery and at three months postpartum, mean birth weight, low birth weight, preterm birth, perinatal deaths and admission to NICU | High |
| Tsoh 2010[375] | USA | NS | 42 | < 26 | Tailored advice from 'Video Doctor' designed to simulate an ideal discussion with a prenatal healthcare professional who provided non-judgemental counselling following | Usual care | Counselling (multiple intervention) versus usual care | Self-reported 30 day abstinence after one month and two months. Mean reduction in cigs smoked per day and | High |

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| | | | | | principles of MI. At the end of each session two documents printed automatically (a cueing sheet for providers and education worksheet for participants) | | | days smoked | |
| Valbo 1996[377] | Norway | NS | 130 | 18 | Anaesthetist provided two 45min sessions at 2 week intervals of a protocol-based script (Handbook of the American Society of Clinical Hypnosis). Two different tapes played after hypnosis established | Usual care | Counselling (single intervention) versus usual care | Self-reported abstinence at birth, mean cigs per day at birth and self-reported reduction in smoking | High |
| Walsh 1997[378] | Australia | NS | 252 | < 26 | CBT. 2-3 minute standardised information from doctor, 14 minute video, 10 minute standardised information, counselling from midwife after video, self-help manual, 4 packets of confectionary gum, lottery chance for biochemically validated abstinence at next visit, social support, letters, 34 weeks, 5 minute counselling from doctor and 1-2 | Women advised to stop smoking by doctors and midwives. Midwife provided a package which included (sticker, pamphlet and a two page cessation guide, not specifically tailored to pregnancy) | Counselling (tailored intervention) versus less intensive intervention | Biochemically validated abstinence at 34 weeks and at 6-12 weeks postpartum and preterm births | High |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | minute risk advice from doctor | | | | |
| Windsor 1985[379] | USA | 57% Black | 206 | < 32 | Received a 10min standardised counselling session from a health educator, a self-help guide to quit smoking and a pamphlet | Smoking cessation advice routinely given at prenatal visits: 2-3 minutes within a group prenatal education session at the first visit | Counselling (multiple intervention) versus usual care | Biochemically validated point prevalence abstinence mid-pregnancy, during last month of pregnancy, or within 48hrs of birth. Self-reported reduction in late pregnancy | High |
| Windsor 1993[380] | USA | 52% Black | 814 | < 32 | 15 minute standardised cessation skills and risk counselling session based on CBT from trained female health education counsellor, a 7 day self-directed cessation guide, clinic reinforcement, social support and monthly newsletter | Two minute talk in a 30 minute group session. Given two pamphlets, including details and contact of local quit programme | Counselling (multiple intervention) versus less intensive intervention | Biochemically validated point prevalence abstinence at four to eight weeks after first visit and at 32 weeks | High |
| Windsor 2011[381] | USA | NS | 993 | < 32 | Received Assist procedures 4 through 8: 14 min video, written guide with 10 day self-help guide, a ≤ 10 min MI counselling session | Received four elements of the '5A's' best practice guidelines | Counselling (multiple intervention) versus less intensive intervention | Biochemically validated point prevalence abstinence in late pregnancy (> 60 days after first visit and < 90 days postpartum) | High |

## Table 10.5 Included studies: health education studies, n=6

| Study | Country | Ethnicity | Participants (n) | Gestational cut-off (weeks) | Intervention | Control | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|
| Burling 1991[382] | USA | 52% White | 139 | any | Personal letter + pamphlet, CO test mentioned and simple guidelines for self-directed smoking cessation | Usual care | Biochemically validated point prevalence abstinence at 34 weeks | High |
| Herbec 2014[383] | UK | 94% White | 200 | NS | Fully automated smoking cessation website targeted to pregnancy (tailored, personalised and structured) 'MumsQuit' | Information only website | Self-reported continuous abstinence (4 week abstinence) 8 weeks post-baseline | High |
| Hjalmarson 1991[384] | Sweden | | 653 | < 12 | Self-help manual on stopping smoking, based on Windsor 1985 | Given information sheet by their doctor as included in the last pages of the self-help manual | Biochemically validated abstinence at 30-34 weeks and at eight weeks (0-5 months) postpartum. Mean birth weight, births < 36 weeks, low birth weight*, mean cigs/day at 30-34 weeks among baseline smokers | High |
| Lilley 1986[385] | England | | 145 | < 28 | Control + 10 min advice from junior doctor based on booklet, a leaflet and copies of booklet for family, letter to GP, letter to woman and pre-planned home visit | Usual care with possible exposure to a concurrent television series on stopping smoking in pregnancy | Self-reported abstinence 9-16 weeks after booking visit. Mean cigs per day | High |
| Naughton 2012[386] | England | 100% White | 198 | < 21 | Tailored self-help leaflet by post. Automated tailored text messages. 80 texts sent over eleven weeks. Participants could request instant response supportive text 24 hours a day | Non-tailored self-help leaflet and the same assessment texts as intervention | Biochemically validated 7 day point prevalence abstinence at three month follow-up. Self-reported four week point prevalence abstinence initiation | High |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | arm but no intervention texts | and frequency of quit attempts and seven day point prevalence abstinence at three and seven weeks after enrolment | |
| Petersen 1992[387] | USA | Majority White | 90 | ≤ 24 | Brief counselling by a healthcare professional. Pregnancy specific self-help manual and an audiotape on safe exercise and relaxation posted to participants. Behavioural strategies for quitting and maintenance section for postpartum period | Brief repeated counselling by a healthcare professional and information about community resources posted to participants | Self-reported abstinence at six months gestation and at eight weeks (0-5) postpartum | High |

## Table 10.6 Included studies: financial incentives studies, n=3

| Study | Country | Ethnicity | Participants (n) | Gestation (weeks) | Intervention | Control | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|
| Harris 2015[388] | USA | 88% White | 17 | ≤ 12 | A web-based contingency management programme and financial incentives ($100 cash) | A phone-delivered cessation counselling programme (Smoking Cessation for Healthy Births) | Biochemically validated continuous abstinence in late pregnancy. Abstinence was determined by self-reported smoking using a timeline follow-back calendar and urinary cotinine values | High |
| Ondersma 2012[389] | USA | 90% Black | 114 | ≤ 27 | Incentives. Maximum of five episodes of reinforcement (in the form of retail gift cards | Usual care | Biochemically validated seven day point prevalence | High |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | worth $50) | | abstinence at 10 week follow-up | |
| Tappin 2015[390] | UK | NS | 612 | < 24 | Routine care and the offer of up to £400 of shopping vouchers. £50 for attending a face to face appointment and setting a quit date, another £50 if at four weeks' post-quit date exhaled carbon monoxide confirmed quitting; a further £100 was provided for continued validated abstinence of exhaled carbon monoxide after 12 weeks; a final £200 voucher was provided for validated abstinence of exhaled carbon monoxide at 34-38 weeks' gestation | Usual care (offer of a face to appointment), offer of free NRT x 10 weeks if set a quit date, 4 weekly support phone calls | Biochemically validated point prevalence abstinence at 34-38 weeks | High |

## Table 10.7 Included studies: social support studies, n=7

| Study | Country | Ethnicity | Participants (n) | Gestation (weeks) | Intervention | Control | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|
| Albrecht 1998[391] | USA | 63% African-American | 84 | ≤ 28 | Teen Fresh Start (TFS) plus peer support compared with TFS and control | 30 minute education session with project nurse and provision of brochures | Biochemically validated point prevalence abstinence 4-6 wks after baseline | High |
| Albrecht 2006[392] | USA | NS | 95 | ≤ 28 | TFS plus a peer buddy | Usual care. Given educational materials and explanation at a 45-60 minute meeting, attendance incentive (lipstick or nail polish) | Biochemically validated point prevalence abstinence after eight weeks and at one year after the intervention (6-11 months) | High |
| Bullock 2009[393] | USA | 95% White | 66 | < 24 | Received eight booklets and nurse delivered social support | Pamphlet from AHA, research team member to call each month to | Biochemically validated point prevalence abstinence | High |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | arrange salivary sample, measure exposure, ask some questions for two more interviews | at 28-32 weeks and at six weeks (0-5 months) postpartum | |
| Hennrikus 2010[394] | USA | 67% racial minority | 82 | ≤ 28 | Control and one in-person visit and monthly phone sessions with peer supporters. Given a pregnancy scrapbook with pages that related to smoking cessation tasks | One in-person counselling session to increase motivation to quit and to provide information about community cessation resources | Biochemically validated smoking status just prior to EDD and at three (0-5) months postpartum | High |
| Malchodi 2003[395] | USA | Majority Black | 142 | < 20 | Control and peer counselling (trained) from lay community outreach workers (phone or home visits) | Usual care which included a programme of AAA, provision of self-help materials, smoking cessation counselling as per protocol at each visit | Biochemically validated abstinence at 36 weeks, mean birth weight and proportion low birth weight | High |
| McBride 2004[396] | USA | 77% White | 180 | ≤ 20 | Control and booklet, gift items, six counselling calls based on motivational interviewing (three in antenatal period and three in postnatal period) and partner assistance | Usual care, provider advice, mailed American Cancer Society self-help guide designed for pregnant women | Self-reported ppa at 28 weeks (baseline smokers and baseline quitters reported separately) combined continued abstinence at two (0-5), 6 (6-11) and 12 (12-17) months postpartum | High |
| Solomon 2000[397] | USA | Majority White | 151 | NS | Control + if intended to quit offered phone peer support by a healthcare professional. Phone peer support from a trained female ex-smoker - weekly, average duration 10 minutes | Brief smoking cessation advice from trained healthcare professionals at each of three prenatal visits and provided with printed materials | Biochemically validated seven day point prevalence abstinence at 28-34 weeks | High |

## Included studies: Feedback studies, n=4

| Study | Country | Ethnicity | Participants (n) | Gestation (weeks) | Intervention | Control | Outcome | Risk of bias |
|---|---|---|---|---|---|---|---|---|
| Bauman 1983[398] | USA | 56% Black | 79 | ≤ 32 | Control and exhaled CO with feedback on result | A 135 word script which described the relationship between cigarette smoking and CO, and the harmful consequences of smoking during pregnancy was read | Biochemically validated abstinence six weeks after intervention | High |
| Cope 2003[399] | England | NS | 270 | NS | Urinary CO with feedback on result. Quit date set and given a leaflet. Information, feedback and encouragement protocol followed at every visit until 36 weeks | Urinary CO measured but without feedback | Biochemically validated point prevalence abstinence at 36 weeks, mean birth weight and preterm birth | High |
| Stotts 2009[400] | USA | NS | 240 | ≤ 26 | Three armed RCT. Best practice counselling, feedback on results of ultrasound and information about effect of cigarette smoke on the fetus and one 45-50min fac-to-face session of motivational interviewing-based counselling | 5A's, 5R's, 10-15 minute counselling (best practice counselling) | Biochemically validated abstinence at eight months gestation | High |
| Valbo 1994[401] | Norway | NS | 111 | 18 | Offered Windsor self-help manual, extra ultrasound at 32 weeks and two reminders | Information about harm at time of 18 week ultrasound. Given a pamphlet and encouraged to quit | Self-reported abstinence, self-reported reduction, mean cigs per day at delivery and stillbirths | High |

# Appendix 11 Studies smoking cessation interventions in pregnancy that were excluded from this review

| | Exclude | Reason for Exclusion | Explanation |
|---|---|---|---|
| 1 | Belizan 1995 | Intervention | Intervention included advice on nutrition, alcohol and drugs. |
| 2 | Bullock 1995 | Intervention | Intervention included advice on nutrition, alcohol and drugs. |
| 3 | Byrd 1993 | Outcome | Smoking status not reported by intervention group. |
| 4 | Campbell 2006 | Comparison | Assessed the differential effectiveness of two methods of disseminating a smoking cessation programme. |
| 5 | Cinciripini 2010 | Comparison | Counselling compared to an Alternative (traditional health education or MI). |
| 6 | Donatelle 2000 | Comparison | Comparison - incentives was part of a multiple intervention, compared to a less intensive intervention. |
| 7 | Donovan 1977 | Outcome | No data on smoking cessation (just mean cigs/day). |
| 8 | El-Mohandes 2011 | Intervention | Smoking cessation part of multi-component intervention. |
| 9 | Graham 1992 | Outcome | Unclear how many smokers were in each arm. |
| 10 | Haddow 1991 | Outcome | No data on smoking cessation. |
| 11 | Haug 2004 | Population | Opioid dependent only. In addition, actual figures not reported. |
| 12 | Heil 2008 | Comparison | Intervention group (contingent voucher) verus control (non-contingent voucher) - equally intensive alternative. |
| 13 | Hiett 2000 | Outcome | Outcomes not reported. |
| 14 | Hughes 2000 | Outcome | Outcomes not reported. |
| 15 | LeFevre 1995 | Outcome | No specific smoking intervention provided. No data on cessation outcomes. |
| 16 | Lowe 1997 | Population | Spontaneous quitters within 3 months of first prenatal visit. |
| 17 | Lowe 2002 | Intervention | Dissemination trial. Smoking cessation rates not included as an aim of this study. |
| 18 | Manfredi 1999 | Population | Unable to separate pregnant women from women attending family planning and paediatric clinics. |
| 19 | Moore 1998 | Outcome | Not clear what proportion of outcomes related to smokers. Low birthweight and preterm births were study outcomes. |
| 20 | Moore 2002 | Outcome | Outcomes for smokers and recent quitters are combined in analysis. |
| 21 | Olds 1986 | Intervention | Multicomponent intervention (nutrition, alcohol, drugs, enhancement of informal support systems; high intensity) . |

| | | | |
|---|---|---|---|
| 22 | Olds 2002 | Outcome | Only mean reduction in cotinine reported. |
| 23 | Polanska 2004 | Outcome | Outcomes in late pregnancy not reported - 'shortly after delivery at home' (0 to 5 months postpartum). |
| 24 | Reading 1982 | Comparison | Three arms based upon visualisation of ultrasound; no specific smoking cessation component. Also, control outcomes not reported. |
| 25 | Strecher 2000 | Population | Included women who had quit since becoming pregnant. In addition, no late pregnancy outcomes (only postpartum). |
| 26 | Tuten 2012 | Population | Methadone users only. |
| 27 | Vilches 2009 | Outcome | Abstinence not reported: mean cigs/day reported in late pregnancy. |

# Appendix 12 Estimating the opportunity cost of a GP visit for a patient with a GMS or GP Visit Card

For the purposes of the economic model it was necessary to estimate the opportunity cost of a GP attendance for those with a Medical or GP Visit Card. Primary healthcare services are free at the point of care through the General Medical Services (GMS) scheme. Eligibility is means-tested based on the total income in a household. There are two types of eligibility:

- full GMS or Medical Card, which entitles the holder to free access to:
    - GP services
    - Prescribed medicines or aids listed for reimbursement by the Primary Care Reimbursement Service (PCRS) subject to a prescription charge[1];
- a GP Visit Card which entitles the holder to free GP services only.

Medical Card coverage is near universal for those aged over 70 years although means testing is applied. Medical Card coverage is universal for those aged less than six years. In 2015, almost 2.2 million people or 47% of the population were covered by a Medical Card or a GP Visit Card. In the subsequent text we will refer to patients with a Medical Card or GP Visit Card as 'public patients', and all those who must pay at the point of care as 'private patients'. The purpose of this analysis was to determine the opportunity cost of a GP visit for public patients; prescription costs were considered separately in the economic evaluation and are not considered here.

## Methods

The opportunity cost of a GP visit is a function of the number of GP visits, total income of GP services, and other services that must be funded through that income.

### *GP visits*

We reviewed datasets available through the Irish Social Science Data Archive, the Central Statistics Office (CSO), and other published sources that included evidence of GP visit rates. Rates were extracted at the highest level of detail with regard to age, sex and Medical Card status. Where there was no clear distinction between Medical Card and GP Visit Card, we assumed the same visit rate for Medical Cards applied to both groups. Where a visit rate was computed for an age range, we assumed that the same rate applied to each single year of age within that age band. Use of single year of age enabled calculation of total number of visits for different age ranges for comparison across datasets.

[1] For those aged less than 70 years, a €2.50 prescription charge applies per item dispensed (subject to a monthly ceiling of €25 per family ). The prescription charge for persons aged 70 years & over, and their dependents, is €2.00 per item and the monthly cap for prescription charges is €20.00 for this cohort.

### *Population data*

The relevant population is the total population of Ireland classified by age, sex and Medical Card status. The Medical Card population was estimated for males and females using PCRS data for 2015.[1] Total population by single year of age for 2015 was extracted from the CSO website.[2]

### *Income for GP services*

GPs are paid through a mix of capitation fee per Medical Card patient, fee-per-item, allowances and investment in general practice development. The capitation fee per patient is a function of the age and sex of the patient. In 2015, total fees and allowances of €489.69m were paid to GPs for provision of services through the PCRS, which covers services provided to public patients.[1] PCRS funding is used to pay towards practice premises, equipment, disposables, running costs, and staff.

Income is also generated by patients who pay out of pocket at the point of care. This is a combination of consultation fees to attend the GP and a practice nurse. Data on typical consultation fees were extracted from the www.WhatClinic.com website which includes data on 1,651 clinics (or 95% of practices).[3] A subset of 644 (39%) of the listed clinics include data on the cost of a GP consultation. The locations of the subset of practices were mapped to counties and the estimated mean cost was weighted by the expected number of private patient visits.

A 2010 survey of 123 (7%) GP practices by the National Consumer Agency found an average cost of €51 for a GP consultation.[4] Inflation in doctors' fees as measured in the consumer price index was unchanged from 2010 to 2015.[5]

### *Practice nurse data*

Included in PCRS payments to GPs is funding for practice nurses who provide clinical consultations. Practice nurses provide a wide range of services within primary care such as carrying out immunisations, phlebotomy, weight management, wound management, and travel vaccinations. To account for this in estimates of opportunity cost, data on practice nurses was included.

The cost of a practice nurse consultation was provided by only three practices in the www.WhatClinic.com data, ranging from €20 to €45.[3] We assumed that the recouped cost of a private practice nurse visit was an average of €25 with relatively wide confidence bounds to reflect uncertainty in the true mean (95% CI: €20.55 to €30.41). That is, it was assumed that a private consultation with a practice nurse would generate an average €25 for the practice. Salaries for practice nurses are not set according to a specified scale. The Irish Nurses & Midwives Organisation recommends that the minimum salary of the Practice Nurse should be the salary at the maximum point of the staff nurse scale, which is €42,469 based on the January

2016 Revised HSE Consolidated Payscales,[6] plus any other allowance that is applicable (such as dual qualification).[7] Approximately 13% of practice nurses are Clinical Nurse Specialist Grade[8] and the remainder are a mix of Staff Nurse Grade, Senior Staff Nurse Grade, Dual Qualified Practice Nurse and Senior Dual Qualified Practice Nurse. Based on this distribution of grades, we assumed an average salary of €50,000, which approximately represents the mid-point of the scale for a clinical nurse manager, clinical nurse specialist or public health nurse. In accordance with national guidelines, salaries were adjusted to take into account pay-related costs.[9] After taking into account employers' PRSI, pension contributions and overheads, the average practice nurse salary was estimated to be €69,875 per annum. The total number of full time equivalent practice nurses was derived from a national study.[10]

Data on the number of practice nurse consultations for people aged 15 years and over were extracted by age, sex and medical card status from the 2015 Healthy Ireland survey.[11]

### *Statistical methods*

Given the uncertainty in a number of the parameters required for estimating the opportunity cost of a GP visit, a simple simulation model was used. Uncertainty in the number of GP visits, practice nurse visits, and cost of a private GP consultation was captured using bootstrapping of the survey data. Uncertainty in practice nurse numbers, salary and consultation fee was set by statistical distributions informed by the available data.

We used sensitivity analysis to explore some of the assumptions that were supported by limited evidence.

## Findings

### *Data sources on GP visits*

We identified eight sources of GP visit data (Table 13.1). Seven are nationally representative population surveys that include a question on GP utilisation. The question is predominantly phrased as utilisation in the 12 months prior to the survey. The Healthy Ireland survey is based on four-week recall. We identified one nationally representative survey of GPs, which provided supply-side data based on reported productivity per session, and number of sessions provided per week.

### Table 13.1 Details of sources of GP visit data

| Source | Sample size | Sample type | Recall period | Year | Age range |
|---|---|---|---|---|---|
| *Broad age range* | | | | | |
| Living in Ireland[12] | 14,510 | National | 12 months | 2004 | 16+ |
| CSO QNHS 2010[13] | 15,673 | National | 12 months | 2010 | 18+ |
| Irish Health Survey[14] | 10,323 | National | 4 weeks | 2015 | 15+ |
| Healthy Ireland[11] | 7,539 | National | 4 weeks | 2015 | 15+ |
| *Narrow age range* | | | | | |
| Growing Up in Ireland[15, 16] | 19,600 | National | 12 months | 2013 | <10 |
| TILDA[17] | 8,175 | National | 12 months | 2013 | 50+ |
| *GMS only* | | | | | |
| EU-SILC[18] | 13,793 | National | 4 weeks | 2015 | 15+ |
| *Supply-side* | | | | | |
| GP Survey[19] | 464 practices | National | 1 week | 2015 | All |

An 2013 audit of six general practices by Behan *et al.* was also identified.[20] The study collected data on GP and practice nurse visits over the course of 12 months. As GP and practice nurse consultations could not be disaggregated in the reported study data, the study was not included in this analysis.

#### *Volume of visits*

The Living in Ireland, CSO Quarterly Household Survey, and Healthy Ireland survey all generate similar estimates for the number of visits by the total population aged 18 years and over (Table 13.2). The Irish Health Survey generates a much higher estimate of utilisation (55% higher than the next highest estimate).

In terms of only the Medical Card population, the Living in Ireland, CSO Quarterly Household Survey, and Healthy Ireland again all generate similar estimates. The study by Behan et al. generates a higher estimate (16% higher than Living in Ireland) while the EU-SILC data generates a much higher estimate (54% higher than Healthy Ireland survey), as does the Irish Health Survey (59% higher than Healthy Ireland).

The Irish Longitudinal Study on Ageing (TILDA) asks about GP utilisation in a cohort of people aged 50 years and older. It generates a lower estimate of utilisation than any of the other datasets including the equivalent age range. Growing Up In Ireland was the only dataset identified estimating visit rates for those aged less than 15 years.

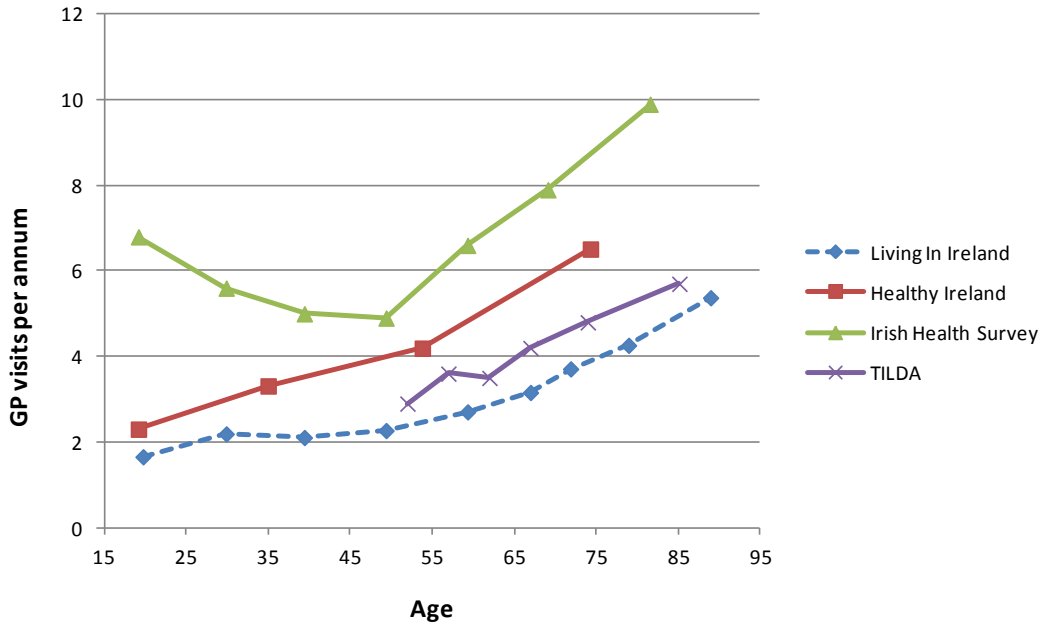
The GP Survey did not provide figures by age, but enabled calculation of a total number of visits for all patients. Based on the GP Survey an estimated 17.1 million patients are seen each year.

With one exception, the data sources on visits are based on surveys of the general population and potentially subject to recall bias. The Healthy Ireland survey is the only source that used four-week recall, with all other identified general population surveys using 12-month recall. There is the potential for substantial recall bias over a longer time span, although it is not clear whether this would result in systematic under- or over-reporting. A shorter time span should limit the risk of recall bias, but may introduce other bias if the survey is carried out at a time of year when visit rates are higher (e.g., Winter) or lower (e.g. Summer). The Healthy Ireland surveys were carried out between Autumn 2014 and Summer 2015, capturing data over almost a 12-month period. This provides reassurance that the data are likely to limit seasonal bias. The Quarterly National Household survey results for 2010 have an unusual pattern for public patients in that the visit rate peaks for those aged 55-64 years.

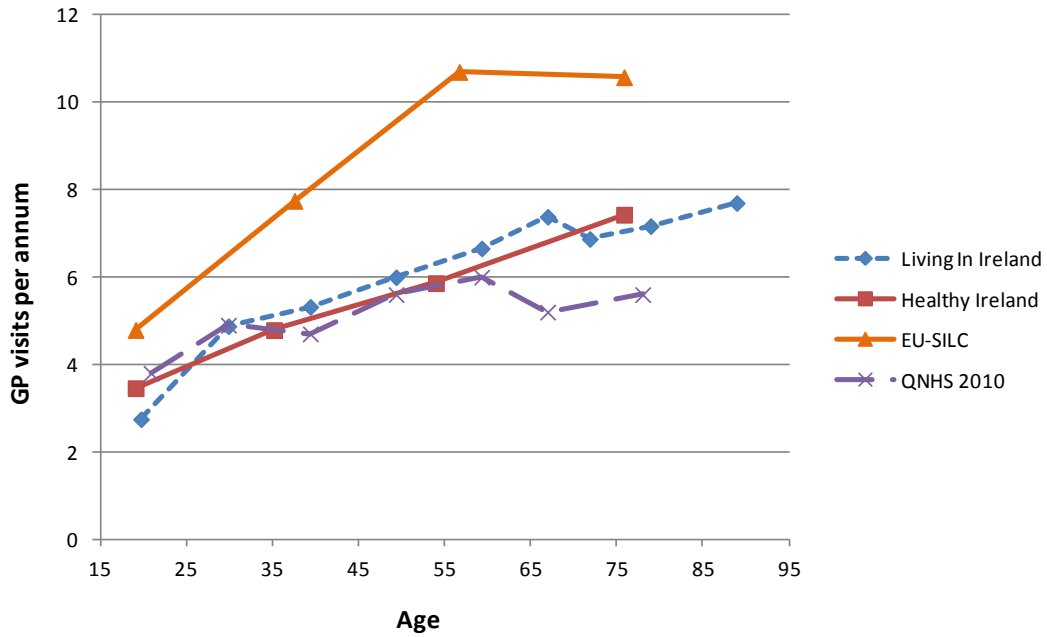
Two of the surveys generated substantially higher estimates of total visits: the Irish Health Survey and the EU-SILC survey, both conducted by the CSO. The former survey was carried out for the first time in 2015, and there are limited details available on the survey results. The Irish Health Survey estimates that 74% of respondents consulted a GP in the previous month, which is very similar to the 72.3% estimated in the Healthy Ireland survey. As it is based on a cross-European survey, it does not ask questions such as Medical Card status, so it is not possible to interrogate whether the higher visit rates apply to both private and public patients, or just to a subset. The Irish Health Survey is unique in the datasets in the visit rate does not follow a curve of increasing attendance with age – visit rates decrease from age 16-24 years to a minimum at age 45-54 years before increasing thereafter. This raises questions about the methodology used and the applicability of the data.

The EU-SILC survey only gathers data with respect to "free GP visits" and therefore excludes private patients. The results obtained by the EU-SILC survey would appear to be an outlier, generating estimated visit rates well in excess of any of the other data sources for an equivalent population.

## Figure 13.1 Number of visits per annum by age (for public and private patients)




## Figure 13.2 Number of visits per annum by age (public patients only)



## Table 13.2 Estimated numbers of GP visits per annum

| | Estimated visits | | | | | All ages | | |
|---|---|---|---|---|---|---|---|---|
| Source | 18+ (all)[a] | 18+ (public only)[a] | 50+ (all)[a] | <15 (all)[a] | <15 (public only)[a] | Public[b] | Private[b] | Total[b] |
| *Broad age range* | | | | | | | | |
| Living in Ireland | 13,408,472 | 8,464,929 | 7,308,414 | | | 10,482,782 | 5,673,650 | 16,156,432 |
| CSO QNHS 2010 | 12,284,036 | 7,784,524 | 6,210,329 | | | 9,296,519 | 5,274,371 | 14,570,890 |
| Irish Health Survey | 21,318,315 | | 10,238,417 | | | | | 25,534,391 |
| Healthy Ireland | 13,796,808 | 7,976,554 | 7,410,240 | | | 9,481,691 | 6,594,875 | 16,076,566 |
| *Narrow age range* | | | | | | | | |
| Growing Up in Ireland[c] | | | | 1,877,700 | 1,275,581 | | | |
| TILDA | | | 5,660,838 | | | | | |
| *GP side* | | | | | | | | |
| GP Survey | | | | | | | | 17,092,628 |
| *GMS only* | | | | | | | | |
| EU-SILC (GMS only) | | 12,272,314 | | | | 14,580,205 | | |

Notes:

[a] To facilitate comparison, data are presented for age ranges available across a number of datasets.

[b] The estimated number of cases for all ages was calculated by including data from the Growing Up in Ireland and Healthy Ireland surveys for age ranges not included. For the Irish Health Survey and EU-SILC the data for the additional age ranges were adjusted to account for the higher estimate in the observed data. For example, the EU-SILC data produced a 54% higher estimate in the 18 years and over group, so data on under 18 year olds were multiplied by 1.54 before being included.

[C] The Growing Up in Ireland data only provided data for infants, three year olds and nine year-olds. It was assumed that visit rates for 10-14 year olds would be the same as for 5-9 year olds.

The remaining data source investigated utilisation from the supply-side. The GP Survey was based on a 23% national sample and achieved a 72% response rate. GPs were asked to report the number of clinical sessions worked per week and the average number of patients seen in a session. Using the GP survey data generated a total estimate only 2% larger than that calculated using data from the Healthy Ireland survey combined with Growing Up in Ireland data for children aged less than 15 years.

### *Practice nurse visits*

The Healthy Ireland survey data included a question on the number of practice nurse visits in the previous four weeks. From this, it was possible to estimate the rate of visits by age, sex and public/private status. Data were only available for respondents aged 15 years and over. For the population aged less than 15 years, the ratio of practice nurse visits to GP visits for the corresponding sex-GMS status group aged 15 to 24 years was applied to the available GP visit data for those aged less than 15 years.

The total estimated number of practice nurse visits was 5,883,598 per annum (3,724,532 for public patients; 2,159,066 for private patients).

### *Total visits to General Practice*

The combined number of visits (including GP and practice nurse) was 21,960,164 visits per annum across public and private patients.

### *Opportunity cost of visits*

Based on data from the 2015 GP Survey, only 6.9% of GPs work in purely private practice, and 9.0% work in purely GMS practice.[19] In other words, 84.1% of GPs have a mix of public and private patients. Income from both public and private practice is therefore combined to provide total income that is used to fund resources in terms of staff, equipment, and premises. We sought to estimate total income for general practice by combining income from public and private practice.

The opportunity cost of a GP visit was calculated as:

$$cost_{GP} = \frac{\left[\begin{array}{c} income_{pcrs} + \left(cost_{privateGP} * visits_{privateGP}\right) \\ +\left(cost_{privatenurse} * visits_{privatenurse}\right) \\ -(N_{nurse} * salary_{nurse}) \end{array}\right]}{\left(visits_{publicGP} + visits_{privateGP}\right)}$$

Where: $income_{pcrs}$ = total income from PCRS (€489.7m in 2015)

$cost_{privateGP}$ = mean GP consultation fee for private patient, €49.97

$visits_{privateGP}$ = total number of GP visits by private patients

$cost_{privatenurse}$ = mean practice nurse consultation fee for private patient, €25

$visits_{privatenurse}$ = total number of practice nurse visits by private patients

$N_{nurse}$ = total number of practice nurses

$salary_{nurse}$ = average salary for a practice nurse

$visits_{publicGP}$ = total number of GP visits by public patients

The above figure represents the opportunity cost across both public and private patients. The opportunity cost of a public patient GP visit was calculated as:

$$cost_{publicGP} = \frac{cost_{GP} - cost_{privateGP} * p_{private}}{p_{public}}$$

Where: $p_{private}$ = proportion all GP visits by private patients

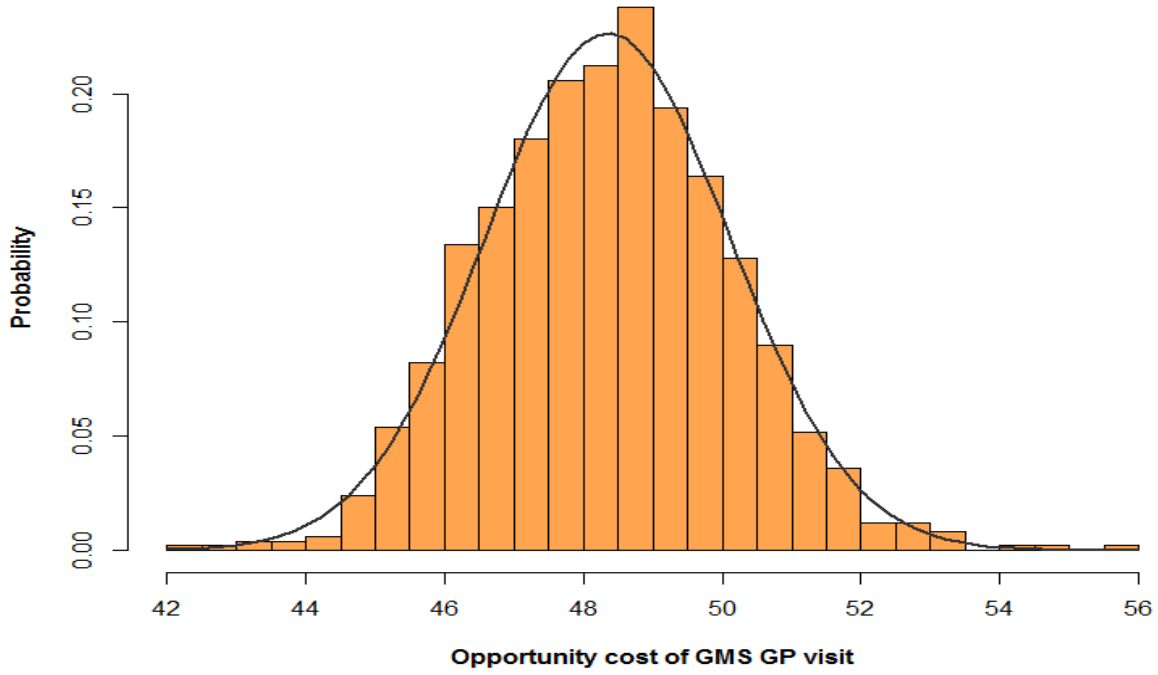
$p_{public}$ = proportion all GP visits by public patients

The opportunity cost of seeing a GP across both public and private patients based on the WhatClinic data, $cost_{GP}$, was estimated to be €49.01 (95% CI: 47.07 to 51.04) in 2015.

The opportunity cost of seeing a GP for public patients only, $cost_{publicGP}$, was estimated to be €48.35 (95% CI: 45.18 to 51.83) in 2015. The modelled distribution of costs was approximately normal with a mean of €48.35 and standard deviation of 1.76 (Figure 13.3).

Using the higher National Consumer Agency estimate of private GP visit costs, the average opportunity cost of seeing a GP for public patients only, $cost_{publicGP}$, was estimated to be €48.42 (95% CI: 45.22 to 52.08).

## Figure 13.3 Distribution of estimated opportunity cost of a public patient GP visit




### *Sensitivity analysis*

The cost of a private practice nurse visit was supported by very limited data. If the cost recouped was €20, the opportunity cost of a public GP visit would be €47.21 (95% CI: €43.95 to €50.78). If the cost recouped was reduced to €15, then the opportunity cost of a public GP visit would be €46.07 (95% CI: €42.98 to €49.42).

## Discussion

We identified a range of data sources reporting GP utilisation data. There is substantial variability in the estimated total number of GP visits per annum for both the total population and for the population of public patients. The Healthy Ireland survey was considered the most applicable dataset due to the short recall period (four weeks), nationally representative sample, limited potential for seasonal bias, and the fact that it was carried out relatively recently. In addition, the Healthy Ireland survey also gathered relevant data on practice nurse consultations. The cost associated with a public patient GP visit was estimated to be €48.35 (95% CI: 45.18 to 51.83). This is very similar to the average cost of a private GP visit (€49.97).

It should be remembered that the figures estimated here reflect an opportunity cost. That is, it is intended to reflect what a GP could have done in the time taken for a consultation. In the context of the smoking cessation HTA, a patient presenting to obtain a prescription or advice on smoking cessation displaces another patient. By including the total PCRS expenditure on general practice, we recognise that what is displaced is the average consultation. Clearly some patients generate more income

per visit than others, but we are interested in the average consultation. An alternative approach would be to micro-cost a consultation in terms of duration of a consultation, income of a typical GP, the cost of the practice premises, equipment and auxiliary staff, training, etc. However, in the absence of data on all of these individual contributors to cost, a pragmatic approach is to use the total annual spend on general practice by the PCRS divided by the activity that is covered by that spend. It is understood that investment in equipment and premises must be funded through the PCRS income or through revenue generated by private patients. Given the similarity in the estimated average value of a consultation, it is unlikely that private practice subsidises GMS practice other than potentially through economy of scale. Indeed, PCRS funding can provide grants for auxiliary staff and equipment that may in effect subsidise private practice when a practice is being developed.

The figures presented here represent an average across the system. Within individual practices the mix of patient demographics, ratio of PCRS to private income, and practice set-up will mean that opportunity costs will vary. For the purposes of the HTA, the average opportunity cost is the relevant figure.

The methodology used here is subject to some limitations. A large portion of GMS income is generated on the basis of fee-per-item. Private practice, on the other hand, has been represented solely through consultation fees. Many practice charge for certain services, for example 24-hour blood pressure monitoring, which may generate profits over and above what is required to cover the cost of the equipment or associated testing. There is little basis for determining how much income is generated in this manner, and hence we have not included it. We have also not taken into account that some practices charge a lower fee for repeat visits and repeat prescriptions. It is not possible to determine what proportion of practices charge a lower fee for repeat visits or what proportion of visits would classify as repeat visits. It must also be assumed that the reason why a repeat visit may incur a lower fee is because it is shorter than a standard consultation, and hence may incur a similar cost per minute as a full consultation. Failure to include additional income will have biased the average cost downwards, while not accounting for reduced repeat visit fees may have biased the estimated cost upwards. The data on private GP consultation costs come from a commercial website. Approximately 95% of practices are listed, of which 39% have provided data on GP consultation fees. As the advertising of consultation fees is optional, there may be a bias in the figures. Practices with higher fees, for example, may be less inclined to advertise fees if they perceive that it will discourage prospective patients on the basis of cost. However, the average cost is similar to that determined from a smaller survey by the National Consumer Agency and a sensitivity analysis showed that using the latter dataset had a minimal impact on the estimated mean opportunity cost of a public GP visit.

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