Health Information and Quality Authority

An tÚdarás Um Fhaisnéis agus Cáilíocht Sláinte

Statement of Outcomes

Report on the outcome of the public consultation on the draft health technology assessment (HTA) of a selective BCG vaccination programme.

November 2015

About the Health Information and Quality Authority

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

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

Setting Standards for Health and Social Services – Developing person-centred standards, based on evidence and best international practice, for health and social care and support services in Ireland.

Regulation – Registering and inspecting designated centres.

Monitoring Children's Services – Monitoring and inspecting children's social services.

Monitoring Healthcare Quality and Safety – Monitoring the quality and safety of health services and investigating as necessary serious concerns about the health and welfare of people who use these services.

Health Technology Assessment – Providing advice that enables the best outcome for people who use our health service and the best use of resources by evaluating the clinical effectiveness and cost-effectiveness of drugs, equipment, diagnostic techniques and health promotion and protection activities.

Health Information – Advising on the efficient and secure collection and sharing of health information, setting standards, evaluating information resources and publishing information about the delivery and performance of Ireland's health and social care and support services.

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1. Introduction and overview

The Health Information and Quality Authority (HIQA) has a statutory remit to evaluate the clinical- and cost-effectiveness of health technologies, providing advice to the Minister for Health and to the Health Services Executive (HSE). It is also recognised that the findings of a health technology assessment (HTA) may have implications for other stakeholders in the Irish healthcare system, including patient groups, clinicians, other healthcare providers, academic groups and health technology industry.

Tuberculosis (TB) remains a major health challenge, with an estimated 9.6 million new cases globally in 2014. As with most other Western European states, the incidence of TB in Ireland is low. In line with global trends, TB incidence in Ireland has been in decline over the last 25 years, with over 95% of cases occurring in adults. In 2014, there were eight cases of TB in children aged less than 16 years.

The BCG vaccine provides protection against TB. Universal BCG vaccination of newborns was first introduced in Ireland in the 1950s. Due to declines in TB incidence, many European countries have ceased universal vaccination, mostly switching to selective vaccination of children at higher risk of contracting TB. At present in Western Europe, only Ireland and Portugal have universal vaccination programmes despite neither being considered a high TB incidence country. The purpose of this report was to determine the impact of changing from a universal to a selective national neonatal BCG vaccination programme.

The HTA examined proposed changes to the national neonatal BCG vaccination programme. It examined the clinical implications, cost-effectiveness, resource implications, budget impact, organisation and ethical aspects of selective BCG vaccination of high risk infants compared with the existing programme of universal vaccination, and a strategy of no vaccination.

2. The consultation process

The draft health technology assessment of a selective BCG vaccination programme was launched for consultation on 9 September 2015. The consultation process ran for a six week period (43 days) until 21 October 2015. Key stakeholders were also targeted via e-mail to alert them to the public consultation.

A consultation feedback form (see Appendix 1) was developed to assist people in making a written submission. The draft assessment and feedback form for the public consultation were made publically available in a downloadable format on the Authority's website: www.hiqa.ie.

3. Analysis of submissions

A total of 16 submissions were received through the public consultation on the HTA of a selective BCG vaccination programme – all via email. Of the 16 submissions, 10 were submitted on behalf of healthcare organisations and six were submitted in a personal capacity. Appendix 2 gives a full list of all the organisations that made a submission.

Each submission was read in its entirety, broken down into individual comments, and recorded to create a database of comments. We identified 146 comments in total.

Amendments to the report, where applicable, were made and responses to comments were documented. The comments and responses are listed in Table 1 below.

4. Comments received and responses

This section describes some specific points raised during the consultation process and provides a brief summary of HIQA's response. HIQA would be happy to discuss any issues raised in greater detail and can be contacted using the details provided in Appendix 1 of this report

Comment	Response
Given the recent resurgence of measles as a result of reduced uptake of MMR vaccinations, I believe that restricting BCG vaccination to only those deemed high risk is a poor decision and will potentially have serious consequences. It is already well documented that the vaccine is most effective when given during childhood and less effective when given to adults. Given the fact that we have a far more transient population, and that we receive migrants and refugees from areas where TB is more prevalent, and BCG vaccination is not so stringent, we are potentially putting some of the most vulnerable members of our population at risk of TB if this proposed plan is implemented.	We appreciate the concern about reducing the level of protection in the child population. For this reason, the report clearly states the need to enhance other aspects of TB control before a change is made to the BCG vaccination policy.
This makes no sense at a time when we are meant to be taking in refugees from Syria etc. These people will not be screened for contagious diseases & any outbreaks will surely cost more in the long run than the vaccination programmes. If need be, why not charge a SMALL fee for the vaccination?	BCG vaccination offers protection to children against TB infection. Other elements of TB control are more appropriate for identifying cases as they occur, and hence reduce exposure for the whole population rather than protecting only a portion of the population. The BCG vaccine is not 100% protective.
What system is in place to identify children to be targeted for BCG? Who is responsible for this work?	The process for identifying high-risk children will have to be developed if selective BCG vaccination is adopted as policy. The report highlights issues regarding high-risk identification. We have added text to emphasise the need to have clear lines of responsibility for identifying high-risk infants.
Where do we start in the current system when we may not be allowed access to the birth details and it is only a matter of time when someone calls a halt to the current system of the hospital sharing the birth list with us because of confidentiality?	A reliable and sustainable system will have to be in place to support the identification of high-risk children. This may require linkage between the maternity services and those responsible for delivering the BCG vaccination programme.
Birth details alone do not identify those children who may be at increased risk for developing TB disease.	Depending on the criteria adopted for defining which infants are considered high-risk, other details such as ethnicity may be required. Clearly the most efficient and appropriate approach to identifying high-risk infants will have to be determined.
Who is responsible if a child who should be offered the BCG vaccine - is missed and subsequently gets TB? Who should have identified this child for vaccination?	We have added text (section 6.1.10) to emphasise the need to have clear lines of responsibility for the BCG vaccination programme.

Person responsible for this work?	
The absence of PHN's in some areas makes targeted selection difficult by this group and will PHN's be happy about this extra work and responsibility of referring babies who meet criteria for selection (PHN's are in the community and see the families)? Will the hospital /consultants be responsible? Obstetric/Paediatric departments? If the hospital is responsible then who is responsible for home births?	Successful delivery of TB control, not just BCG vaccination, requires an integrated approach across different services and providers. Responsibilities will have to be determined and stated as part of the service delivery plan.
Will non nationals have enough knowledge of the English/Irish language to complete forms given to them if the plan is self selection? Who gives them these forms to complete? How is this done? What percentage of forms will be actually returned? Who is responsible for follow up of non responders? Is there a responsibility to follow up people who do not complete forms?	The method of high-risk identification has not been determined. Should a selective BCG vaccination policy be adopted, the most appropriate approach will have to be identified.
Post codes do not apply in Ireland as people at risk could be at any address (UK uses post code system)	Those at high-risk are likely to be a more transient population, which will pose challenges. The implementation of the system will have to be cognisant of these issues. It should be noted that the high-risk population currently receive BCG vaccination. One of the challenges will be to ensure continued uptake in that population when the general population are no longer part of the BCG vaccination programme.
Will there be a feeling of discrimination / racism - targeted / deemed not in target group and refused /excluded?	We have discussed these issues as part of the ethical analysis and have highlighted them as part of the advice to the Minister for Health.
Will there be an increase in the incidence of TB as seen across Western Europe where there was a change to targeted programmes (London)?	We have estimated that, in the absence of any other changes to TB control measures, it is likely that there will be a small increase in the number of cases of childhood TB. For this reason the report clearly states the need to enhance TB control measures before introducing a change to the BCG vaccination policy.
How much extra office work will there be in vetting children (inclusion /exclusion) for vaccination? Who does this extra work belong to - doctor / nurse / manager?	It is unclear how much additional work this will introduce, and is dependent on the system used to identify high-risk patients and the extent to which that capitalises on existing data collection.
Will this vaccination take a back seat to other programmes as it will not be included in KPI's and will staff be prioritised to other (vaccination) work	We state in the report that the BCG vaccination programme should be subject to evaluation to ensure that

when there is pressure on the system?	there is adequate uptake in the high-risk population.
Will there be a delay in offering the BCG vaccine due to the time factor needed to identify neonates requiring vaccine. Delays over three months will result in increased work on the service to deliver the programme – Mantoux clinics required if infant is over three months which means double the work and double the clinics. Long delays could potentially cause the BCG targeted programme to clash with other live vaccines such as the MMR vaccine scheduled at 12 months?	Other countries with selective vaccination programmes have introduced systems to identify high-risk infants in the antenatal period, thereby limiting any time delays in identification.
Will vaccinators be able to retain their skills (intradermal vaccination) if numbers fall and clinics are infrequent? Will poor vaccination skill result in an increase in the percentage of adverse reactions to BCG?	This issue is a concern and is discussed in the report, and may influence how a selective BCG vaccination programme is delivered.
1. "The TB-control programme should be optimised prior to any change in the vaccination programme." – Dr. Mairin Ryan There is no information in the draft indicating what actions and resources may be required to ensure our TB-control programme is optimal	We have added a new section (6.1.10) that goes into more detail on this issue.
2. The draft gives no sense of how a targeted programme would be rolled out, how will target cohort be identified, who will be responsible for indentifying children for targeting.	These are operational features. A detailed description was outside the scope of the report. However, we have added a further section to address this (6.1.10).
3. There is a definite risk of a feeling of discrimination arising in the targeted groups. There is a risk that the traveller community in particular will feel stigmatised and that BCG uptake by this group will be compromised.	We agree and have highlighted these issues in the ethical analysis.
4. There is no indication in the report that there will be a KPI for this work. When there is pressure on the system staffing/funding of KPI work is prioritised at the expense of other work.	We have added text regarding the need for ongoing evaluation of the BCG vaccination programme.
5. How will vaccination uptake be measured in this targeted group?	We have highlighted the difficulties of assessing uptake for a population which is not clearly defined.
This document lays out the rationale that can underpin a decision to stop universal BCG vaccination in Ireland, without recommending it. If this decision is made, it is an opportunity to re-direct vaccine resources to improve the Irish TB service. Specifically, targeted testing for Latent TB infection (LTBI), which is detailed in the Irish TB guidelines- but which has not been implemented – could be meaningfully effected.	The advice to the Minister for Health states that selective vaccination is the preferred option, but that it must be introduced after enhancing other elements of TB control, such as testing for latent TB infection.

It is my opinion that Ireland's TB programme would be immediately enhanced by 1. The appointment of a TB controller for the country: In an un-distractible manner, this person would be dedicated to TB elimination, and take ownership of our TB elimination efforts. 2. The universal application of directly observed therapy (DOT) to all cases of tuberculosis. With under 400 cases per year- this is not a huge undertaking. Using outreach workers to achieve this, we can expect near immediate benefit- by ensuring treatment completion and therefore no repeat disease in TB cases. 3. Latent TB infection (LTBI) testing and treating: The stepping up of LTBI diagnosis and treatment after targeted testing as outlined (but not implemented) in the national guidelines.	These comments have been taken on board and are reflected in changes to Chapter 6.
Page vii (PDF page 8 of 197) Change sentence "it is less effective in preventing respiratory disease" to it is not effective in preventing respiratory disease; which is the more common form in adults and the form which is responsible for the spread of the epidemic. BCG therefore does not interfere with the epidemic.	The text has been amended.
Comment on sentence page ix (PDF 9 of 197) Ireland is considered to have a well-functioning TB programme. See above*.	We have rephrased the text to reflect that the current TB control approach is well-functioning in the context of a universal BCG vaccination programme.
Page v (PDF 10 of 197) Add the following Treatment is also intended to prevent re-activation of infection in the future in the treated person. This is also a main outcome of treatment: to ensure that a disease -which responds quickly to antimicrobial therapy- remains inactive after therapy has finished. To achieve this, six months treatment at least is required, and no new regiment has shortened this treatment duration requirement - when measured against this important metric of disease return.	The text has been amended.
Page 8 of 195 Add comment In addition it should be noted that the United States has had more success in addressing the TB epidemic than Europe, and in that jurisdiction (the USA) BCG has never been used. Their success in areas such as New York are down to the interventions mentioned above* which we lack, and are unrelated to any effect (positive or negative) that BCG might have on the epidemic.	We have emphasised the need to enhance TB control measures in Ireland.

Page 11 of 197 It should be noted that a positive Mantoux is the only objective evidence of persisting immune memory after BCG vaccination. It is estimated that a neonate BCG vaccinated, would be reliably Mantoux positive for a period of one or two years only.	We have only given a very brief description of the Mantoux test as part of the general description of BCG vaccination.
Page 28 of 197 Add It should be noted that BCG has become resistant to isoniazid. As a consequence of this when patients become diseased with BCG, then they may be more difficult to treat than persons treated with isoniazid sensitive mycobacterial disease. (Please add reference, Watts M.R. et al., Clinical Infectious Diseases, 2010, 52).	We appreciate the information. As we do not describe the treatment for BCG-osis in the report, we have not added the reference.
Page 14 of 197 Where the 2010 school outbreaks in jurisdictions where the students had BCG? Should this comment be included, for balance, if you are going to comment that the 18 children in the cork outbreak lacked BCG vaccination?	There were insufficient data available on the BCG status of children affected by the school outbreaks in 2010 to enable a proper overview.
Page 43 of 197 section 3.3 An equally important outcome is to prevent TB reactivation/recurrence after treatment which will interfere with the epidemic spread (see above). We are currently preparing a report of a large number of these cases managed in Dublin – avoidable if DOT was used universally.	This information will clearly be useful as part of planning changes to TB control in Ireland.
Page 45 of 197 Drop the word primary in “associated with the primary TB infection” Primary TB is a term that should be reserved for new infection with Mtb that progresses directly to cause TB disease.	The text has been amended.
Table 4.4 on page 65 is unclear. Has this table been published? What are the numbers (denominator units) involved in generating the data? How is the data generated?	As described in the text, the table combined TB notification data with vaccine uptake data. The denominators use the best estimates for vaccine uptake, taking into account periods of no vaccination or selective vaccination in some part of the country.
Page 67 of 197 Is distance from the equator merely a surrogate marker for tuberculosis instances/ prevalence (and thus increased chances of exogenous re-infection) in the background population?	There are several hypotheses regarding the influence of distance from the equator. Irrespective of the exact cause of the relationship, it was reasonable to investigate the impact it may have on interpreting the effectiveness of BCG vaccination.

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Section 6.1.6 is entitled Screening. This section is unclear. I would recommend a different title to screening – which is poorly defined. Specifically a title called 'Targeted testing for latent TB infection and treatment' would serve us better. Screening is too non-specific a word and is open to misinterpretation. Although the discussion of LTBI testing and treating is good - it fails to bring notice to the fact that latent TB targeted testing and treatment is an integral part of the existing guidelines, but that these guidelines have had no universal implementation, in health care workers for instance. The advice of the guidelines is largely set aside by some institutions; as they are inconvenient and costly and no doctor wants to treat LTBI. Along with 1. Appointing a national TB controller, 2. The universal application of DOT; I consider that 3. The implementation of targeted testing of latent TB and its treatment is a fundamentally important aspect of the control of this disease in this country.	The section has been re-titled. In a new section we have added reference to the existing guidelines and the extent to which they have been implemented.
Special note is made of the advice in the TB guidelines - that all healthcare workers should be screened for latent tuberculosis infection and treated. In this regard the guidelines make special acknowledgement to high risk persons coming to work in this country, in the healthcare system, from countries with high tuberculosis prevalence. It is okay that hospitals continue to hire such persons without proper latent tuberculosis targeted testing and treatment? Such LTBI treatment structures are required to stop the healthcare worker reactivating TB on the job. This has two negative implications. 1. They become ill themselves 2. They potentially could spread the infection to a patient or an immune compromised person present in the hospital. For this reason special consideration might be given to improving the structures and implementing the advice of the national TB guidelines, whereby all hospitals have readily available access to latent TB testing and treatment in a manner that eliminates this risk of nosocomial TB infection from our health system.	While this is an important point, the scope of the report is focused on the neonatal BCG vaccination policy. Issues regarding the screening of healthcare workers are relevant irrespective of a change to the BCG vaccination policy.
Page 118 of the document or page 140 of 197 of the pdf Remove the comment about leprosy.	The reference has been removed.

Very comprehensive. Explains the pros and cons very well. We had reached this stage of considering stopping neonatal BCG about 15-20 years ago, but immigration levels rose. There will be some who will think that civil liberties may be infringed by being selective in targeted screening. What about Irish born individuals who go to work in an area where the level of TB is high? I am in full agreement with the overall thrust of the proposal.	The definition of high-risk may have to include infants born to parents who have lived for extended periods in high TB incidence countries.
Firstly, I think the document is very difficult to read and the layout does not make it easy to understand how conclusions were reached. It is not reader-friendly for a person working in the area not to mind a lay person.	Health technology assessments are technical documents. While we endeavour to make the document readable, we must strike a balance between lay and technical audiences. The document is primarily intended to serve the needs of the decision maker by including the relevant evidence.
There is an assumption that there is a good TB Control Programme in place – no evidence of this (IUATDL Criteria)	We have amended the text to reflect that the TB control programme is well-functioning in the context of a universal BCG vaccination programme.
The recommendations of 'Guidelines on the Prevention and Control of TB in Ireland 2010' document have not been implemented to date	We have included this in a new section (6.1.10).
There is no evidence that patients with latent TB are being identified and treated – this needs to be in place before any change to BCG policy. Difficulties managing those identified through contact tracing – do not have national figures on these	We have highlighted the need to both enhance existing TB control measures but also the need for a more integrated approach across services and providers.
Too much emphasis is being put on the risk of Disseminated BCG as side effect – very rare and no deaths from same in past 10 years. Evidence that BCG is a relatively safe vaccine with very high uptake	Although disseminated BCG is a rare event, based on international evidence it has a very high mortality rate associated with it. It is important to present both the risks and benefits of any intervention.
No evidence shown on how countries have fared that moved from universal programme to selective	The report includes data from the few countries that have published figures from before and after a change in national vaccination policy (in 6.1.7).
No costing of introducing a Selective BCG Programme – cost, uptake, staff, identification of high risk groups, follow up of these, budget impact	The costs associated with a change in BCG vaccination programme are outlined in detail in the economic evaluation section. Individual cost items are reported in the appendices.
There is evidence that BCG has been protective in a number of outbreaks – not considered	This information was considered as part of the evaluation of clinical effectiveness and safety in Chapter 4.

	It must be stressed that for the analysis we have adopted the best available evidence. Data from Ireland are observational in nature but have been taken into account in the sensitivity analyses.
Change would lead to increase in number of child cases of TB – this needs to be considered	This potential impact is stated clearly at various points in the report and in the advice to the Minister for Health. For this reason, we stress the need to enhance other aspects of TB control.
Finally, I think changing from current policy to selective one cannot happen without firstly putting in place a working TB Control programme which is properly resourced and audited to ensure it works. A proper explanation of how a selective programme would work in Irish setting – budget, resources, identification of cohorts, follow up, monitoring of uptake etc	We agree, and the document states this clearly.
This draft BCG HTA document addresses the options for BCG vaccination in Ireland. One of the criteria for discontinuing BCG vaccination is that we have a well-functioning TB control system. We would argue that we have a good TB contact tracing service but we do not have a good TB control programme. Earlier this year Dr. Tony Holohan Chief Medical Officer (CMO) in the DoH requested Dr. Stephanie O Keefe, HSE Director of Health and Wellbeing to undertake a full and comprehensive report on the TB prevention and control programme reflecting the HSE's performance and encompassing all aspects of the programme. A multidisciplinary committee comprising Respiratory Consultants, Infectious disease consultants, Consultants and Senior Medical Officers in Public health, Consultants in Microbiology, and Surveillance Scientist was convened to undertake this task. This committee was requested to assess whether Ireland's TB programme complied with the European Centre for Disease Prevention and Control's (ECDC) report entitled "Progressing towards TB elimination" and to identify any possible gaps in the TB control programme in Ireland. Many deficits were identified both with surveillance systems for TB (incomplete and missing data), laboratory facilities and TB control programmes (lack of contact tracing in high - risk situations such as migrant screening, prisons, healthcare workers etc.). We are of the opinion that there is not an effective TB control programme in Ireland and this requires to be urgently augmented to support the World Health Organisation goal of TB elimination by 2050. This would equate to a TB incidence rate of 1/1,000,000 population and a rate in Ireland of 4-5 cases per year.	We have amended the text to reflect that the TB control programme is well-functioning in the context of a universal BCG vaccination programme. A change in vaccination policy implies the need to enhance other elements of TB control to account for the reduced level of protection in children. Enhancing the current TB control programme will be facilitated by the TB control Guidelines developed by the Health Protection Surveillance Centre and by the assessment of the current TB prevention and control programme undertaken recently by the HSE.

Laboratory services Currently second line testing is not available in Ireland and isolates have to be referred to the Scottish National Reference Laboratory in Edinburgh, UK. The Irish Mycobacterium Reference Laboratory (IMRL) referred seven Mycobacterium Tuberculosis Complex (MTC) isolates to UK laboratories during 2013, four MDR-TB isolates, two M. tuberculosis strains and one M. bovis BCG. The cost per isolate referred to Scotland is approximately €800 inclusive of transport costs (€600 + VAT) The IMRL is the sole facility in Ireland performing MIRU- VNTR typing The IMRL have repeatedly requested funding to perform IGRA at St James's Hospital/HSE but to date have been unable to secure funding to set up a service. Currently the only public service laboratory providing (and charging for) IGRA testing is the Mater Hospital. One other private laboratory also performs IGRA testing in Ireland. The staffing complement of the IMRL is of 2 personnel only - a Chief Medical Scientist and a Specialist Medical Scientist. Additional staff are seconded from the Microbiology Department (SJH) to help provide the IMRL.	
The standard of care for patients with active TB is dedicated TB clinics, ideally multidisciplinary encompassing hospital based specialists and public health. These have been shown in the US to improve outcomes, both in relation to the direct treatment of TB, but also associated care such as universal HIV testing (TB guidelines recommendation 10.4).3These could also provide the framework for the screening for and treatment of LTBI. Dedicated TB clinics should be available in all HSE regions (TB guidelines recommendations 5.2-5.5). Currently there are dedicated TB outpatient clinics in St. Vincent's University Hospital, Dublin (SVUH), St. James Hospital, Dublin (SJH), Mater Misericordiae University Hospital, Dublin (MMUH), Galway University Hospital (GUH), Limerick University Hospital (LUH) and Mercy University Hospital (MUH) Cork leaving large gaps around the country. Even within their catchment areas not all patients are referred to the dedicated TB clinics. These clinics have developed on an ad-hoc basis without dedicated funding rather than as part of a co-ordinated TB service. Many of these clinics are combined respiratory and infectious disease clinics but do not have public health staff on site or a pharmacist for direct drug dispensing on site.	We have recommended that national clinical guidelines are developed with respect to TB control. This would help to address a number of the gaps identified in TB control.

Dedicated TB clinics should be appropriately resourced with medical, nursing, pharmacy, administrative staff and medically qualified interpreters. Currently SJH and MUH are the only clinics with consultants appointed with special interest in TB, and SJH is the only clinic with dedicated pharmacy support. For over 10 years there has been in place a plan to establish a Supra-Regional Tuberculosis Centre in a dedicated building at St. James's Hospital, Dublin. This plan is in response to the Comhairle Report 2000 and the ERHA Working Group Report on Tuberculosis Services 2004, which details its establishment in St. James's Hospital, and includes special reference to the necessary development of the Irish Mycobacterial Reference Laboratory on the St. James's campus, as a matter of urgency. Hospital services need to be reviewed to ensure that there are an appropriate number of isolation and negative pressure rooms for those patients who require hospitalisation including MDR-TB and XDR-TB cases. The provision of dedicated TB beds in all HSE regions should be proportionate to the number of TB cases reported per region per annum. The present system of admitting patients with possible highly resistant TB to general wards with single rooms is a major risk for our health service and needs to be urgently addressed. Dedicated TB clinics should have the required pharmacy support to allow direct dispensing of anti-tuberculous therapy on site. This would reduce errors in dispensing, allow for monitoring of adherence and remove the nominal GMS fee for TB drugs that this can act as a deterrent for some patients to obtaining medications. This is not current practise. In addition, some unlicensed high tech preparations can be difficult to access and are not free to the patient, for example the new treatment for MDR-TB. Funding should be made available to facilitate access to these new treatments. Whilst the St James TB treatment clinic has pharmacy support on site- this service is not provided to the TB contact tracing service in St James Hospital. This service is not provided at any TB contact tracing clinics nationally.	Changes to TB services should ideally occur as part of an overhaul to TB control to ensure a comprehensive and adequately resourced programme.
Dedicated TB clinics should have active case management as the model of care. Active case management is the key to successful treatment of TB, and this becomes more important as the patient groups with TB are increasingly marginalised. All clinics need to be resourced with case managers for the active management of TB cases (TB guidelines recommendations 5.2-5.5). Case managers can also facilitate improved communication and compliance by	We have recommended that national clinical guidelines are developed with respect to TB control. Such guidelines are an opportunity to set the standard of care for patients with TB.

integrating with interpreter services and directly observed therapy (DOT). DOT workers need to be exclusive to TB and not a component of a general public health role. Dr Terry O'Connor, Dr Joe Keane and Dr Anthony O'Regan (Irish Thoracic Society) have developed a proposal for three dedicated TB nurses who would actively case manage TB infected patients for Dublin (St. James's Hospital), Cork (Mercy University Hospital) and Galway (Galway University Hospital). These are the three main urban areas with the highest proportion of complex TB cases. However a formal needs assessment based on incidence and complexity is warranted. This model has proven highly effective to enhance DOT provision in US cities e.g. New York and San Francisco. However as DOT becomes the standard of care additional community based healthcare workers should be available to liaise with hospital based case managers. Resource requirement will be greatest in certain groups such as the homeless (TB guidelines recommendation: 9.11) and in those for whom English is not their first language. DOT should be the default setting for the treatment of all patients with active TB (TB guidelines recommendation 5.11). Currently it is not widely available or fully enacted when available, and is reliant on the good will of public health nurses. A structured national DOT programme resulting in a network of appropriately trained health care workers who would work with case managers needs to be established as per "HSE Guidelines for the delivery of Directly Observed Therapy in the community to persons with TB disease available at www.hpsc.ie. Guidelines in relation to DOT are not uniformly implemented in all areas. There is no provision of DOT for LTBI and thus no provision for the elimination of TB in the Irish context. Consideration to expanding the number of dedicated TB clinics or resourcing the existing clinics to provide a hub and spoke model of care with an understanding that all patients on TB therapy for active TB be seen in one of these clinics is recommended. All TB patients should be seen by or referred to a consultant with an interest in TB i.e. respiratory physician or infectious diseases consultant for treatment and supervision of care, in a similar manner to HIV or oncology referrals.	
The main elements of a public health TB Service include TB surveillance, public health follow-up of TB cases, TB outbreak management, TB contact tracing, chemoprophylaxis, Directly Observed Therapy (DOT) and in some instances BCG vaccination of unvaccinated TB contacts. This co-ordinated multifaceted approach to the public health	We refer to the guidelines in section 6.1.10, and also highlight the concern that the guidelines have been only partially implemented.

management of TB has been outlined in the Guidelines on the Prevention and Control of Tuberculosis in Ireland, 2010. There is much good practice, but quite a variation in the structure of TB contact tracing services across the country. Contact tracing is coordinated by a Specialist in Public Health Medicine in each Department of Public Health and is carried out by Senior Medical Officers (SMOs) with support from nursing and administrative staff where available. There have been difficulties in staffing these clinics. SMOs with training in TB contact tracing are being deployed to other duties at a time when the HSE has identified that we need a robust TB contact tracing service. This will have a significant detrimental impact on the service going forward. The Guidelines for the Control and Prevention of Tuberculosis in Ireland 2010 recommend as a model of best practice joint clinics staffed by respiratory physicians and public health doctors. This model is in operation in four hospitals nationally, Mater Misericordiae University Hospital Dublin, St James's Hospital Dublin, St. Vincent's University Hospital Dublin and University Hospital Limerick. In other areas contact tracing is carried out by public health doctors with limited nursing and administrative support in health centres or special clinics (Slainte Clinic in Cork). When a case is diagnosed in a workplace or an institution e.g. school, prison etc. then contact tracing may be carried out "on – site" by public health doctors with limited nursing and administrative support. Clinics would not have the capacity to deal with the sharp increase in demand and compliance rates are improved by bringing the service to the client. The elimination of TB will require chemoprophylaxis for all eligible patients diagnosed with Latent TB infection (LTBI). While chapter 3 of the TB Guidelines provides detailed advice on the management of LTBI, this may not be implemented on a national basis. The service provided is not uniform throughout the country. Three systems operate 1. Chemoprophylaxis provided to both adults and children 2. Chemoprophylaxis NOT provided to either adults or children. Contacts referred to acute respiratory services- 6-12 months waiting list 3. Chemoprophylaxis provided to adults only and children referred to paediatric services	

In situation 2 above we are aware of a TB case in one area where the index case was treated in hospital 1, the partner and oldest child referred to hospital 2 and the younger children referred to a paediatric unit in hospital 3 - needless to say this did not result in a positive outcome. In instances where contact tracing is undertaken by two Departments of Public Health e.g. index case living in one HSE region and working in another HSE region different approaches to chemoprophylaxis may be applied	We have highlighted the need for an integrated approach to the management of TB control in Ireland.
None of the TB contact tracing clinics has pharmacy support.	Issues such as this should be addressed as part of changes to TB control in Ireland.
The "Guidelines for the Control and Prevention of Tuberculosis in Ireland 2010" recommend screening of high risk populations. This would include migrants from areas of high TB incidence, prisoners, homeless people and those with medical conditions that place them at higher risk of disease. Although this is a public health issue it falls outside of the remit of the TB contact tracing services and would require significant resources to implement.	We have drawn attention to the fact that a number of elements of the TB control guidelines have not been or are only partially implemented.
There is currently no structured TB education programme for healthcare professionals. TB education should also be targeted to those statutory and voluntary agencies working with ethnic minority populations and those with chaotic lifestyles. However, training occurs in an ad-hoc basis through attendance at meetings, conferences and seminars.	We recommend the need for training of healthcare professionals in the context of delivering the BCG vaccination programme and identifying high-risk infants.
If selective vaccination is the preferred option we will still need to maintain competent vaccination teams and appropriate systems throughout the country. Children are born into high risk groups and in several maternity hospitals throughout the country. It is difficult to see that the staff provision outlined – middle paragraph page 106– 1.7 medical, 1.6 nursing and 1.5 administration could apply for an adequate national BCG programme.	The estimated staff requirements are based on the proportion of infants that will be eligible for selective vaccination coupled with the inefficiency associated with only vaccinating a subgroup of the population.
This is the first time a universal vaccine will be removed in Ireland. This may affect confidence in other vaccines. How will the concerns of people whose 'low risk children' who will be advised not to vaccinate/be refused vaccine.	For this reason, the report is emphatic about the need for a clear and comprehensive public awareness campaign. This would be necessary to minimise confusion, ensure high BCG coverage in the high-risk population, and to ensure continued high uptake of other vaccinations.
It is always challenging dealing with screening in congregate settings where children have been exposed to tuberculosis. It will be even more difficult doing contact tracing if we get case in a primary school teacher with a cohort of children who have not received the BCG. Not logistically, but dealing with	We appreciate the challenges associated with future TB cases. However, a vaccination programme should deliver more benefits than harms. The current low TB incidence in the childhood population is an

concerns about the vaccine having been withdrawn.	important consideration.
Page ix "Ireland is considered to have a well-functioning TB programme with high quality of TB notifications" – We disagree with this comment – see all of the above issues "Criteria include selective vaccination of migrants, or children or grandchildren of migrants who have moved from high incidence countries (≥40/100,000 persons)". This could actually apply to Irish population as parents and grandparents of Irish children grew up in a time where there were much higher rates of TB. "In line with global trends, TB incidence in Ireland has been in decline over the past 25 years. The crude national incidence rate per 100,000 has fallen from 18.2 in 1991 to 7.0 in 2014". Figures for 2014 are provisional. Outbreak in Irish Prison in 2011 not mentioned- largest prison outbreak in Western Europe	We have rephrased the text to reflect that the current TB control approach is well-functioning in the context of a universal BCG vaccination programme. For parents and grandparents originating from a high TB incidence country, it would be on the basis of the current list of high TB incidence countries. Since 1990, Ireland has an incidence of less than 20 cases per 100,000. In terms of outbreaks, we have restricted our analysis to those that affected child populations.
Page xiii The terms screening and contact tracing need to be defined and consistently applied throughout this document "In the interest of public health, a change of vaccination strategy should be supported by a clear commitment to systematic and comprehensive TB control. Changes to TB control should be introduced before a change in vaccination policy to minimise the impact of reduced vaccine coverage." What is the governance structure behind these changes, who is responsible and how will it happen? Suggest National TB lead required to coordinate a uniform response.	We have included the suggestion of a national TB lead to support the implementation and oversight of TB control in Ireland.
Page 7 "A positive reaction likely indicates that an individual is infected or has active TB disease or has been previously vaccinated with BCG". Also could have been exposed to Non tuberculous mycobacteria. "Young children and those with strongly positive tests should have specialist paediatric or physician assessment" Please mention public health specifically as public health doctors are perfectly placed to look after these patients and indeed sometimes get referrals from paediatricians who are inexperienced in dealing with LTBI.	The text has been amended regarding non-tuberculous mycobacteria. Regarding referral, specialist paediatric or physician assessment is detailed as the relevant clinical pathway.

Page 9 "Ireland is considered to have a well-functioning TB programme with high quality of TB notifications" – We disagree with this comment as above.	We have rephrased the text to reflect that the current TB control approach is well-functioning in the context of a universal BCG vaccination programme.
Page 20 "DOT treatment is administered daily or on a reduced frequency regimen of three or five times a week using a modified dose regimen, as directed by the treating physician". This is an oversimplification. In the case of MDR –TB and XDR –TB regimes can be two or three times a day and also requires intravenous medication. It should also be stated that all doses on medication for MDR and XDR TB cases should be with DOT	The text has been amended accordingly.
Page 24 "In terms of parental nationality, the National Perinatal Reporting System maintained by the Healthcare Pricing Office records the nationality of mothers and, where available, fathers. High incidence countries were identified from the WHO TB incidence data as countries with an incidence of greater than or equal to 40 cases per 100,000 persons. All births where at least one parent came from a high incidence country were labelled as high TB risk births. Based on national births data from 2008 to 2013, 12.0% of births can be classified as high-risk based on parental nationality, although the percentage by county varies from 5.3% in Wexford to 20.1% in Dublin city. Data on the country of birth of grandparents is not captured by the National Perinatal Reporting System". How well is this information recorded? Has an audit been carried out regarding its reliability? We think that this will not be sufficient to identify high–risk. Also should we be looking at geography as well as ethnicity e.g. anybody coming from London where there is an incidence of TB >40/100,000 and should be considered at high risk irrespective of ethnicity.	The nationality of one or both parents was known for almost all births. As to whether the figures are reliable, they were very similar (but higher) than the proportion reported as part of the Growing Up In Ireland study, which was used by the National Centre for Pharmacoeconomics to estimate the proportion births that could be considered high-risk. We have included text regarding parents from high TB incidence areas within otherwise low TB incidence countries.
Page 43 "The vaccination status of TB cases is recorded in notification documents and can be used to determine the number of cases in the vaccinated and non-vaccinated cohorts". How well is this information recorded? Has an audit been carried out regarding its reliability?	Given the requirements for notification, we believe these are well-recorded. In interpreting the data, we took a conservative approach to classification. That is, if data on BCG status was unconfirmed then we assumed that the child had not been vaccinated.
Page 64 "No costs associated with identification of high-risk infants were included in the analysis. It was assumed that risk status could be determined from existing resources, such as maternity hospital records". See comments above- we would envisage that there will be significant cost associated with identification	The identification of high-risk infants is an operational feature. Within the report we assumed that identification could leverage on existing systems, such as maternity hospital data, and also on clerical staff involved in vaccination. We assumed that a

of high- risk clients. If ante-natal staff is envisaged as the group who will identify infants from the high risk community – are they willing to take on the responsibility of deciding which infants should/should not be offered vaccination? Need to develop logistics for this and for onward communication with vaccination teams.	selective programme would lead to inefficiencies which entailed double the staff compared to a pro rata allocation based on existing workloads.
Page 99 "As part of a policy to reduce vaccine coverage, additional TB control measures will be advisable to account for the reduced protection against TB in the child population". It is not clear what the additional control measures should be and the governance of the TB control programme. This needs to be spelt out more clearly.	The report has been strengthened in this regard, with an additional section on implementation. However, it was outside the scope of the report to address the wider TB control programme.
Page 104 "The BCG vaccination policy in Ireland at present is not consistent, with one county adopting a school-age vaccination policy. Given the relatively small population of Ireland, adoption of the same policy across all areas may be more efficient and, coupled with adequate training of clinicians and increased public awareness, may ensure greater coverage of the eligible population than the current approach". This also applies to the TB control programme as there is NOT a comprehensive uniform TB control programme. Also even within the current TB contact tracing programme there are inconsistencies as outlined in the discussion about the TB control programme above	Text has been added to section 6.1.10 to highlight issues of inconsistency in TB control in Ireland.
Page 105 "Healthcare professionals must be educated in how to identify high-risk infants" How and by whom? And at what cost? If ante-natal staff is envisaged as the group who will identify infants from the high risk community – are they willing to take on the responsibility of deciding which infants should/should not be offered vaccination. Need to develop logistics for this and for onward communication with vaccination teams.	These are operational features that were outside the scope of the assessment. We have reviewed the international literature to provide an overview of mechanisms used elsewhere to implement selective BCG vaccination policies.
Page 107 "A selective strategy would target high-risk groups which largely comprise ethnic minorities. There may be language and information barriers to obtaining informed consent. Staff administering the vaccine would require adequate training and access to translation services to ensure informed consent is obtained." These are already required by the current programme.	We agree. However, a change in policy could create confusion and therefore adversely affect uptake rates in the high-risk population.

Page 107 "It may not present a practical alternative in all areas, but may be more efficient in high volume maternity hospitals" This has not worked well in the Dublin maternity hospitals and had to be abandoned in most. If ante-natal staff is envisaged as the group who will identify infants from the high risk community – are they willing to take on the responsibility of deciding which infants should/should not be offered vaccination. Need to develop logistics for this and for onward communication with vaccination teams.	The details of a maternity hospital-based approach would have to be carefully considered, and it would be pertinent to review the previous system and why it was discontinued.
Page 109 "Screening provides a method of identifying those entering the country with active TB or with latent TB infection. Although screening is recommended for the high-risk population in Ireland there is no organised screening programme at present". This is a very important point and should be highlighted and costed.	It was outside the scope of this project to consider the costs of a latent TB infection screening programme.
Page 110 "A robust information system that facilitates the tracking of cases across health service regions within Ireland would also offer greater prospects for effective case management". This is also important for contacts and for information on high risk groups	The extent to which data are updated and managed will impact on the ability to use such a system for multiple purposes.
Page 121 "Classification of infants will therefore be based on information provided by the infant's parents or guardians in a clinic or hospital setting" As previously we would be concerned that this may not happen For those high-risk infants who are not vaccinated, it is anticipated that the protective effect of vaccination of the majority of people in the high-risk groups will be sufficient to confer a protective effect on all within the group' This is not logical as it seems to us that we are implying here that children will be the index case. The savings from either no vaccination or a selective vaccination strategy would not contribute much to an effective TB control programme with the ultimate goal of TB elimination. Selection of 'high risk children' for vaccination. The biggest effect of taking away BCG would be to remove the protection against tuberculosis that the BCG offers to young children and to some extent to adolescents. Where do children get exposed to TB –	In the absence of centralised population registers with data on ethnicity or parental country of origin, any system to identify high-risk infants must, to some extent, rely on information provided by an infant's parents or guardians. The reference to protective effect to unvaccinated children has been removed. We stress in the report that there should not be a change to the BCG vaccination programme without first enhancing other aspects of TB control. Those changes should focus on identifying TB and latent TB infection in adults.

• Home – family and carers • Creche/School • Extended family/ other. If go for the option of offering vaccination to children in the Irish Traveller and Immigrant communities we're essentially providing protection for the exposure these children might have within their family or ethnic group.	
Page 121 Will there be some criteria for offering vaccine to children not belonging to Traveller/Immigrant groups where there is a family history of TB? Children from low incidence groups may have substantial contact with adults from high risk groups – au-pairs, childminders, crèche workers, church groups, clubs etc. Grandparents are still reactivating in Ireland and they may have a lot of interaction with grandchildren including childcare roles. A few examples from the East – *<examples omitted>*	A comprehensive set of eligibility criteria will have to be determined as part of the planning process for a change in the vaccination policy.
If ante-natal staff is envisaged as the group who will identify infants from the high risk community – are they willing to take on the responsibility of deciding which infants should/should not be offered vaccination. Need to develop logistics for this and for onward communication with vaccination teams. Immigrant screening – what is the current practice? This is currently voluntary for asylum seekers. Does it focus solely on diagnosing active TB? Is there any screening for LTBI or provision of chemoprophylaxis? Is this necessary and if so does it need to be costed?	The operational features of a selective BCG vaccination programme and of enhancing the TB control programme would have to be developed if there is a decision to change the policy.
There is no service for other professional groups/ family members / language students etc. We in Dublin in the last year have been involved in contact tracing in several language schools	This is a general TB control issue that is not specific to neonatal BCG vaccination.
The HTA insufficiently emphasises the effectiveness of the BCG vaccine as seen in two outbreaks in the HSE South. While the BCG vaccine is most effective in reducing rates of TB meningitis and miliary TB, it also has a significant protective effect against pulmonary TB.	The data from the outbreaks in HSE South were considered. Sensitivity analyses were used to determine whether greater effectiveness would impact substantially on outcomes, and those results are included in Chapter 5.
The report outlines the high rate of disseminated BCG in the Irish population. Much of this is attributable to the much higher rate of disseminated BCG in the traveller population. In a selective BCG vaccination programme the traveller population are one of the groups targeted for BCG vaccination, so the rate of	As part of a sensitivity analysis we investigated the impact of a screening programme for infants from the Traveller community in terms of reducing the risk of disseminated BCG in that population. We found that it did

disseminated BCG may remain relatively high. However, the data included in the HTA were from 2005 to 2014; therefore the impact of the national SCID screening programme for traveller infants was not accounted for [page 101].	not substantively change the findings of our main analysis. As with a number of additional sensitivity analyses that were carried out to test parameter assumptions, the details of the analysis are not included in the report.
The HTA only considered high risk persons as being children with a parent from a high TB incidence country and Irish Traveller children. Therefore not all high risk persons were included in the cost analysis.	We have added text to draw attention to this fact, and that the figure for proportion high-risk infants may be an underestimate.
The process to identify high risk persons for selective BCG vaccination is both complex and challenging as demonstrated in UK. The challenge is not only in identifying high risk persons but also in ensuring that they participate in the programme. The HTA did not account for the resources that would be required to identify and implement an effective process to identify high risk persons. An assumption was made that risk status could be determined from existing resources, an assumption we would challenge. The uncertainty in the administration cost of a selective programme was acknowledged by the authors as a major contributor to uncertainty in the incremental budget impact. Without significant ongoing investment in an effective process the uptake rate will not be sufficient to protect these vulnerable children. Indeed the HTA acknowledges that administering vaccine in a selective programme is likely to be less efficient then in the current universal BCG vaccination programme.	The uncertainty surrounding the cost of administering the vaccine in a selective programme stems from a lack of evidence regarding how inefficient the programme would be. The inefficiency comes from the fact that the reduction in BCG clinics is unlikely to be in proportion to the reduction in eligible infants. Alternative modes of delivering the BCG vaccination programme may be more efficient.
Prior to the introduction of universal hepatitis B vaccination into the national childhood immunisation programme, selective vaccination was the recommended approach. This selective vaccination approach was sub-optimal.	The choice between selective and universal vaccination is highly context specific, and we cannot generalise from one programme to another.
In the absence of a culturally appropriate public awareness campaign, ample staff training and consistent risk classification, there may be a stigma associated with being targeted for BCG vaccination, which could make target groups harder to reach and therefore the selective BCG programme less effective and more resource intensive than anticipated.	The report stresses the importance of a public awareness campaign and the need to involve members of high-risk groups in the planning of a selective BCG vaccination programme.
There has to be an acknowledgement of the weaknesses of the current TB control programme in Ireland. The HTA analysis was on the existing approach to TB control in Ireland. There is insufficient management of TB cases. There is no national programme of screening of immigrants for LTBI. At present there are considerable difficulties actioning the recommendations of the National TB guidelines for the control of TB in Ireland, in particular initiating Directly Observed Therapy (DOT) for treatment of TB disease and LTBI. The rate of TB	Text has been added to Chapter 6 to highlight concerns regarding the existing TB control programme.

in children in Ireland has in the past been a concern and may be indicative of some of the challenges of the current TB control programme. As the authors state the operational features and likely budget impact of an adequate TB control programme need to be considered [page 99].	
During the recession there was a very significant reduction in the numbers of immigrants from highly endemic countries which would have contributed to the reduction in the number of cases of TB in Ireland. However, it could be anticipated that the numbers of immigrants from highly endemic countries will begin to rise again as our economy recovers and as the European migrant crisis continues. It is important to acknowledge the complex management issues that can occur, such as cultural and linguistic barriers. Indeed many TB cases and cases of LTBI occur in marginalised, socially excluded and disadvantaged communities and present many challenges in achieving successful treatment outcomes. The resources required to manage some of these issues can be enormous.	We have added text to the section on screening to point to the need to monitor migration patterns and the impact on demand for screening capacity.
The following should be in place and evaluated and stakeholders should be consulted, before a decision is made on whether or not to move to selective BCG vaccination: 1) An effective TB Control Programme in Ireland including: • Rapid access to high quality diagnostic and treatment services • Education programme for clinicians and other health care workers to ensure early recognition and treatment of TB • Consistent provision and resourcing of interpreting services at GP and hospital level, • Enhancement of compliance with treatment through access to DOT and other methods including appointment of TB outreach workers and TB case managers. • Additional resources for contact tracing • Additional resources for treatment of LTBI. • A national screening programme for immigrants from highly endemic countries and other high risk groups (e.g. homeless persons, asylum seekers, prisoners and Health Care Workers) • Strengthening of TB surveillance 2) A fully costed implementation plan for an effective TB control programme. 3) A fully costed implementation plan for the identification of high risk persons for selective BCG	We agree that changes to TB control should be carefully planned and costed prior to implementation. This has been addressed in a new section (6.1.10).

vaccination and the delivery of the targeted vaccination programme. Implementation plan would need to include IT system to record vaccination e.g. link with any proposed maternity e-health system/immunisation register. 4) The costs of implementing both the TB control programme and the system for identifying and vaccinating high risk persons should then be compared with the current cost of the universal programme. 5) There should be a recommendation on the need to develop a robust evaluation process to evaluate any change to the vaccination programme to ensure any potential negative impacts (e.g. low uptake rates amongst target population, increase in TB cases, stigma, dissatisfaction amongst population not targeted which could result in reputational damage or undermining of the national childhood immunisation programme) are identified in a timely manner.	
1. Section 7.6 does not clarify that in the absence of mainstream ethnic identifier, how the high-risk groups are going to be identified, especially, the Travellers. If that mechanism is absent, the high-risk groups may fall through the net and this could lead to a partial failure of the programme. Reliable and consistent use of ethnic identifiers across the health service is essential to avoid mistaken classification of infants as low or high TB risk. Ethnic identification is also vital to ensure accurate recording of BCG vaccine uptake rates in addition to TB incidence and prevalence in Irish Travellers. Measures of data completeness specifically with regard to Irish Travellers will be needed to be contained within the surveillance information collected.	Depending on how high-risk is defined, identification of high-risk infants will potentially require data on a number of characteristics. The need for an ethnic identifier will depend on how high-risk identification is implemented.
2. The consultation document acknowledges the role of improved socioeconomic conditions (through better housing and reduced overcrowding) and nutrition in the reduction of TB. According to section 2.1, “in Ireland, improvements in socioeconomic conditions (through better housing and reduced overcrowding) and nutrition as well as introduction of effective treatment in the 1940s led to a rapid decrease in the incidence and mortality rate from TB” (p.5). However, the document does not explain how this selective BCG vaccination alone will bring down the number of new cases of TB without concomitant improvements in the social determinants of health in the high risk group.	The decline in TB is due to a wide range of factors including improved socioeconomic conditions. Further declines in TB can be achieved through improved TB control in Ireland and in high TB incidence countries.
3. High risk groups are already being vaccinated through the Universal BCG Vaccination Programme. Therefore, it is not clear in any of the sections what	Improved outcomes in high-risk groups may come about by a reinvestment of resources in other elements of TB

additional health outcomes will be achieved for the high risk group following a switch to Selective BCG vaccination.	control which will benefit not just the child population but also adults.
4. There could be some reluctance from the high risk groups to participate in the selective programme as they may believe that the government is trying to blame them for TB in the country. Consequently, some people may not participate, fearing stigmatisation as outlined in section 7.8. Exactly how this fear will be overcome will need to be addressed.	As we have stated in Chapter 6, a public awareness campaign with particular cognisance of the high-risk population will be an important aspect for the successful transition from universal to selective BCG vaccination.
5. As section 7.8 notes, if vaccinated, high-risk groups may be subjected to possible side effects and scarring where those in the general population are not. This will need to be highlighted to the high risk group. Furthermore, visible scarring could potentially become an identifiable and associated mark with high-risk groups and may further stigmatise individuals belonging to those groups.	The needs of the high-risk population must be addressed in planning and providing information regarding changes to the BCG vaccination programme.
6. Following the switch from Universal to Selective BCG vaccination in Sweden, a drop in vaccine coverage to a level that was considered "too low to cover the risk group" was reported (Romanus, 2006). It is not clear from the consultation document how a potential drop in vaccine coverage in the high risk group with the introduction of selective vaccination in Ireland would be measured or rectified. Sections 6.1.3-6.1.5 outline practices in other jurisdictions in addition to respective advantages and disadvantages (p.105-108). However, the consultation document is tentative in terms of setting out which preferred strategies will be employed in the selective BCG vaccination of Irish Travellers. More detailed information should be provided such that it is apparent that the selective BCG vaccination programme will, in all probability, lead to enhanced delivery of the BCG vaccine to Irish Traveller children. http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=606	Childhood cases of TB are typically as a result of transmission from an infectious adult. As such, the notion of herd immunity is not applicable in the child population. A low uptake will mean a lower proportion of children will be protected against TB. A BCG vaccination programme aims to achieve 100% coverage. The benefits for the high-risk population in terms of continued protection should be clearly outlined as part of a public awareness campaign.
7. Section 7.4 states that "it is likely that there will be an increase in TB cases as a result of changing from universal to selective vaccination in Ireland" (p.120). This will need to be communicated very clearly to the general population.	The potential for increased cases is in the context of no other changes to TB control. The report strongly recommends that TB control be enhanced in Ireland prior to a change in BCG vaccination policy, which will reduce the likelihood of additional cases.

8. Section 7.7 states, "in the event that a child whose parents have refused vaccination later becomes infectious with TB, protection and detention measures may be necessary in order to prevent spread of the disease" (p.123). Detention measures are legislated for to manage situations where a "person is a probable source of infection with an infectious disease and that his isolation is necessary as a safeguard against the spread of infection" rather than vaccine refusals. The main grounds for detention, or the threat of detention, in Ireland are "non-compliance with anti-infective therapy"2 (Duffy, 2009). Detention measures, albeit rare, would be applicable to individuals from both low TB risk and high TB risk groups but it is not clear from the consultation document whether the detention provision would also be made known to individuals who, due to belonging to a low TB risk category, are not receiving the BCG vaccine. Hence, it appears inappropriate to make the connection between vaccine refusal and possible detention in relation to parental consent. This connection should not form part of the proposed selective BCG vaccination programme. 2 http://www.ncbi.nlm.nih.gov/pubmed/19091360	This section has been rephrased to clarify that detention measures are irrespective of vaccination or risk status. The use of detention is highly unusual and only in the context of an individual with TB refusing treatment.
The HTA on BCG models three scenarios, universal vaccination (current status quo), selective vaccination and no vaccination. The cost of control is modelled as the cost of current control measures, increased proportionate to the increased number of cases expected in the scenarios of selective or no vaccine. Current control measures are inadequate, and only work because we have universal vaccination, and therefore are unlikely to have outbreaks in young children and other young groups. In order to be able to provide adequate prevention and control of TB in a situation of selective or no vaccine, there would need to be a much enhanced control programme.	We have included text to state that there are concerns over the adequacy of existing control measures. It was not within the scope of the assessment to consider the costs associated with changes to TB control generally.
The models predict significant cost savings if BCG vaccination is given only to infants considered High-Risk (selective) or discontinued altogether. While this is acknowledged in the HTA we believe that it is a mistake not to include the cost of an enhanced TB control programme as part of the HTA and this should be factored in appropriately as a cost in the model for these two scenarios. Also as stated this would need to be put in place before any changes could be made to the BCG vaccination programme.	While we appreciate the importance of costing changes to TB control, it was not within the scope of the project to consider the costs associated with changes to TB control generally. We have stated clearly that savings generated by a switch to selective BCG vaccination are unlikely to be realised due to the need to reinvest in other elements of TB control.

Factors which need to be included as part of the HTA with respect to additional TB control measures include: Combined Physician/Public Health TB clinics. Despite recommendations combined clinics are not in place throughout the country. Follow-up of identified cases of TB. Most HSE areas do not have dedicated TB nurses/case workers. In an enhanced TB control programme dedicated case workers would be an essential component. Compliance with TB treatment. Ensuring cure would become even more important if universal vaccination were discontinued. This would require enhanced provision of Directly Observed Therapy (DOTS) among TB cases, with obvious resource implications.	These issues would need to be considered as part of a review of TB control in Ireland and an implementation plan for proposed changes.
Screening of migrants. Over 40% of TB cases in Ireland now occur in migrants. It is currently recommended that migrants from countries with high rates of TB be screened. However this is not implemented. If children are not routinely vaccinated with BCG, in order to protect children from exposure to TB, at a minimum a programme of screening is required for migrants who would be working with children, e.g. in childcare, schools and healthcare. This would be likely to identify more cases of latent TB infection of which the treatment and follow-up would have further resource implications.	We have acknowledged the TB control guidelines in the report and the fact that some elements of the guidelines have not been fully or partially implemented.
Screening of all those working with children and in healthcare. In addition a pre-placement screening would have to be provided for all those taking up work in crèches and preschools, junior primary cycle teachers and those working in healthcare. Current HSE pre-employment screening provides checks for those entering HSE employment. There is no screening for those in private healthcare provision e.g. private nursing homes.	A coherent and cross-sectoral approach to TB control would be welcome, and may eliminate some of the highlighted inconsistencies.
Uptake of vaccine in a selective programme. Where a programme is selective as opposed to universal then the uptake may be lower. Is there any data from countries where this programme change has already happened?	These data are described in the report (6.1.5) and used as part of the analysis.

Latent Tuberculosis Infection (LTBI). Is there any data on the protective effect of BCG against LTBI? If reduced in an unvaccinated population the number of cases of LTBI would be higher per case than the estimate used for our current vaccinated population. The cost of treating same has implications.	We have added a section to the report (4.4.2) that reviews the evidence regarding the protective effect of BCG vaccination against latent TB infection.
Staffing cost savings may be less than expected. BCG clinics afford opportunities for staff to interact with parents and monitor child development. An extra Child Health visit may need to be provided for children who do not get BCG in a selective programme.	Changes to the BCG vaccination programme may have consequences for the delivery of other services, and planning should be cognisant of this.
Cost of identification/Follow-up of High Risk Infants. Some costings should be included.	We assumed that high-risk identification could leverage off existing data and staff, taking into account the reduced efficiency likely in a selective BCG vaccination programme. We have highlighted this as a limitation of the evaluation. The cost of identification would be dependent on the mode of delivery of the programme and what groups are defined as high-risk.
The HTA models 3 scenarios: universal BCG vaccination, Selective BCG vaccination and no BCG vaccination. The current universal programme is costed and costs compare unfavourably with other BCG programmes. It is unclear if like is being compared with like in the costings, i.e. are vaccine purchase costs comparable, are same grades of healthcare staff involved in the programmes, are salaries of those staff comparable?	Programmes in other countries may use different grades of staff. We have stated that it is unclear if the comparisons are fair, and whether the international studies are accurate or if they represent underestimates of the cost.
There is no cost applied to the ancillary benefits of the neonatal BCG clinics which are often used as an occasion for health promotion and dealing with concerns new mothers may have about infant welfare, feeding and growth.	Changes to the BCG vaccination programme may have consequences for the delivery of other services, and planning should be cognisant of this.
The report does not explore how infants are to be selected for a selective programme or who might do this work. It may be that effective selection of babies for a targeted vaccination programme will also have costs associated, which may be considerable.	The report includes a high-level review of the methods used in other countries. However, a detailed description of how it might be implemented in Ireland is an operational feature and outside the scope of the assessment.
It is unlikely that, in a selective vaccination programme, the number of BCG clinics will decrease in proportion to the number of babies to be vaccinated.	If there was no reduction in the number of clinics then the continued use of community-based clinics would be highly inefficient. For this reason, it will be important that an implementation plan for a selective programme would determine the optimal approach to delivering the

	programme.
The HTA states that TB control measures will need to be enhanced if a selective programme of vaccination is introduced. However, the enhancements required have not been detailed in the HTA. Nor have the increased costs associated been included in the costs of a selective vaccination programme. Such costs might include: • Dedicated TB nurses/case workers in Depts of Public Health • Provision of Directly Observed Therapy among TB cases • Routine screening of migrants from countries with high rates of TB, particularly for migrants working with children.	We have included additional detail in Chapter 6. However, the assessment was focused on the neonatal BCG vaccination programme rather than the wider TB control programme. As such, only a high-level review was feasible.
If there is a possibility that numbers of cases of Latent Tuberculosis Infection could rise, then increased costs associated with treatment of this should also be included in costings for selective programme.	The costs associated with treatment for latent TB infection are included in the analysis.
If we are to change from current universal BCG vaccination programme to a targeted programme, it is essential that a detailed implementation plan be developed which will set out and cost how selection of babies/persons to be vaccinated is to be done and who is to do this work, and how TB control measures are to be enhanced.	The need for an implementation plan is highlighted in section 6.1.10.
The current universal programme is costed and costs compare unfavourably with other BCG programmes. It is unclear if like is being compared with like in the costings, i.e. are vaccine purchase costs comparable, are same grades of healthcare staff involved in the programmes, are salaries of those staff comparable?	The published international studies do not give a breakdown of staff grades. We have stated that it is unclear if the comparisons are fair, and whether the international studies are accurate or if they represent underestimates of the cost.
The Mid West area is mixed urban and rural and we run community BCG clinics in a variety of locations to provide a service relatively close to home for mothers and babies. In a selective programme, there will still be a requirement for clinics in remote areas, even though the actual numbers attending may be greatly reduced.	For this reason we expect a reduction in efficiency in moving from universal to selective BCG vaccination, and that has been factored into the analysis. The optimal approach to delivering the BCG vaccination programme needs to be determined.
The current neonatal BCG programme achieves very high uptake (>95%) and it is not clear that programmes with which our current programme is being compared achieve similar uptake.	There is a description of uptakes rates in section 6.1.5 of the report.
Neonatal BCG clinics in the community provide other services at the same time as neonatal BCG vaccination they are opportunities for new mothers to link with Public Health Nurses and Community Health Doctors about any concerns they may have regarding infant welfare, feeding and growth. There may be a	Changes to the BCG vaccination programme may have consequences for the delivery of other services, and planning should be cognisant of this.

necessity to have additional child welfare clinics in some areas to make up for opportunities lost by non-attendance at BCG clinics.	
The HTA states that TB control measures will need to be enhanced if a selective programme of vaccination is introduced. However, the enhancements required have not been detailed in the HTA.	We have added a section (6.1.10) to address this. However, it was outside the scope of the HTA to carry out a detailed review of TB control measures other than neonatal BCG vaccination.
BCG is a very acceptable vaccination to most parents in our area. It may be that many parents will request BCG vaccination for their children even if those children are not part of the target cohort. Will there be sufficient quantities of BCG vaccine available to be able to facilitate this?	The extent to which BCG vaccine will be available on request to non-high-risk infants in a selective programme will be a matter for the HSE and the Department of Health.
BCG vaccination has been proven to be effective in preventing invasive tuberculosis in young children, therefore any change in BCG vaccination strategy can be expected to impact the epidemiology of paediatric M. Tuberculosis cases. As tuberculosis is a notifiable disease for which BCG is a preventative measure, the decision regarding changing to a "Selective Vaccination Programme" should be made by the Medical Officers of Health, whose statutory function is to "prevent spread and remove conditions favourable to such infection." A Public Health Risk Assessment should also be carried out prior to a final decision on any change to the BCG vaccination programme.	HIQA's statutory functions include the assessment of health technologies and the provision of advice on request to the Minister for Health to inform national health policy decisions. It would not be appropriate for HIQA to make statements about who should be involved in the decision-making process.

The Efficacy of Current TB Control Measures The International Union Against TB and Lung Disease Criteria for Considering Universal BCG Vaccination Discontinuation clearly states that having a well functioning existing TB Control Programme in place is essential prior to vaccine discontinuation. Current TB Control Measures TB control services in Ireland are generally considered to be inadequate by Medical Officers of Health as: delayed diagnosis is common increasing prolonged avoidable exposure; there is very limited access to DOTs; there is limited co-ordination of expert services and limited in-patient treatment sites especially for MDR-TB and XDR-TB etc. This is supported by the findings of the multidisciplinary committee established by the Health and Wellbeing Directorate at the request of the CMO at the Department of Health to assess if Ireland's TB control service met the standards described in the ECDC report "Progressing towards TB elimination". The committee identified a number of deficits in the current TB control programme including: • Deficits in the surveillance system, • Gaps in laboratory facilities, • Inconsistent active case management, • Lack of dedicated specialized in-patient TB treatment facilities and in • Deficits in public health TB control.	We have amended the text to reflect the fact that the TB control programme can be considered well-functioning in the context of the current universal BCG vaccination programme.
Concerns Specific to the HSE Midlands Area There are also some specific concerns related to the area served by the Department of Public Health, HSE Midlands including; • Two counties (Laois and Offaly) are without access to a Respiratory Physician. • Cases of active pulmonary TB are frequently managed by general physicians. • The role of diagnosing and treating Latent TB infection is undertaken by the Senior Medical Officer, with minimal support from secondary or tertiary referral centres. • Children diagnosed with latent TB have difficulty accessing paediatric services which are extremely busy in the area. • There have also had several cases of TB in the area with a delayed diagnosis which is associated with a need for extensive contact tracing. There are similar anecdotal accounts of other jurisdictions in Ireland whereby cases with confirmed LTBI can wait 6-9 months for treatment and there are issues relating to access to DOTS.	We have stated that there are concerns over the implementation of TB control measures and that there is regional variation.

Potential Future Challenges to TB Control Measures due to changing demography in Ireland Civil unrest and poverty are precipitants for large scale population movements in Europe in 2015. With climate change, it is expected that major hydrological changes throughout the world will lead to even larger scale population movements later in this century. This could alter the incidence rates of TB in Europe and in Ireland. "Imported" cases of TB from countries of high endemicity are associated with increased incidences of MDR-TB and XDR-DB. Large scale population migration also increases the populations of vulnerable people, including homeless people, who are known to be high risk for contracting TB.	The recommendations in the report are based on the available evidence regarding TB incidence over the last decade. In the event of changing patterns of TB and MDR-TB then it would be appropriate to review TB control measures to determine whether changes are necessary.
The result of increasing immigration would be a change in the demography in Ireland. In Ireland immigrants are integrating into the general population in crèches, schools etc and are not segregated as may be the case in other countries with large cities where whole areas of cities may be a particular ethnic group. Immigrants are as mentioned often vulnerable groups, and may be more likely to work in relatively low paid jobs such as in childcare settings. Indeed, many come to work in healthcare and social care settings (nursing homes etc). Between the census of 2002 and 2011, the non-Irish national population increased by 143% and now accounts for 12% of the population resident in Ireland 4. The majority (74.4%) of the non-Irish national population comprises people from just 12 countries (UK, USA, Germany, Poland, Latvia, Lithuania, Romania, Slovakia, Philippines, India, China and Nigeria)4. This list of countries includes the two countries (India and China) that have the highest burden of MDR and XDR TB and countries of Eastern Europe which have the highest rates of MDR TB according to the WHO5. Immigration is likely to increase further over the coming years and so assumptions about the anticipated rates of TB are unlikely to hold.	It is important to recognise that during a period of high inward migration in the 2000s there was an increase in adult cases of TB but not in childhood cases, which were subject to an ongoing decline. While BCG vaccination offers protection to infants, it is does not entirely eliminate transmission to those exposed to infectious individuals. For this reason, it is important to focus on other elements of TB control that reduce exposure.
In addition, the prevalence of diabetes is increasing globally but the increase is most rapid in low and middle income countries which already carry a greater burden of TB. Evidence indicates that diabetes increases the risk of TB three fold and is also associated with higher rates of treatment failure and of relapse6.	The HTA focussed on neonatal BCG vaccination and the impact on a child population within which the prevalence of diabetes is low. If, in the future, the prevalence increases to the extent that this could have implications for TB control, then it would be appropriate to review TB control measures at that point.

The UK moved to a selective BCG vaccination programme and their rates of both TB and drug resistant forms of TB have increased over the last two decades7. To avoid the potential for a similar increase in rates here, it would be useful if a more comprehensive analysis of the potential demographic changes and the global changes in TB epidemiology outlined above could be undertaken. This would allow the potential effect of these changes on TB incidence and prevalence in Ireland to be accounted for before a change to the current BCG vaccination system is undertaken.	The neonatal BCG vaccination programme provides protection to children, and the analysis in the report assumes that protection extends to the age of 15. When comparing rates across counties in relation to BCG vaccination policies it is important to focus on childhood cases rather than all cases.
Studies of BCG efficacy have shown considerable variation. A meta-analysis of the efficacy of BCG vaccination carried out by Colditz et al8 showed considerable variation in BCG efficacy between different studies. They found that geographic latitude of the study location and study validity score explained 66% of the heterogeneity among the trials in a random effects regression model. This finding of improved efficacy of BCG at greater latitudes has been found in other studies in particular a further meta-analysis by Mantangi et al9 which found that the variation of efficacy between studies could be explained by three factors; latitude of study location, BCG given in infancy or school age with stringent tuberculin testing and studies with a lower likelihood of diagnostic detection bias. The authors note that many studies date from a time before standard methods for the conduction and reporting of trials were in place.	In the analysis of clinical-effectiveness we investigated the association between geographic latitude and vaccine efficacy. We included a sensitivity analysis that used a predicted vaccine efficacy for Ireland based on the latitude.
The evidence from the crèche outbreak in Cork, where there were no cases in vaccinated children and 18 cases in unvaccinated children, would indicate high efficacy of BCG in young children in Ireland and has not received sufficient weight when reaching conclusions on the possible efficacy of BCG in the Irish setting.	We have used the best available evidence to estimate clinical effectiveness – that is, from randomised controlled trials. Irish data were included in the report and the results of the economic evaluation are discussed in relation to the possible vaccine efficacy based on Irish data.
BCG vaccination has also been shown to reduce disease due to mycobacteria other than the M. tuberculosis complex10.	We have added a section on the non-specific effects of BCG vaccination (section 4.4.3).
There has not been a universal BCG programme in all areas of Ireland, with recent introduction in Cork (2008), Mayo (2009) and Roscommon (2012). Recent declines in TB figures in those under 15 years could be related to this.	The changes in Cork, Mayo and Roscommon are recent and as a result there are still large cohorts in those counties that are unprotected. It is also important to consider the longer-term secular trend observed for declining childhood TB cases in Ireland that predates changes in Cork, Mayo and Roscommon.

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Although the efficacy of the BCG Vaccination has been the cause of some controversy, it is still the only vaccine in use for the prevention of TB in humans and results from well conducted trials have shown considerable protection when given to neonates or stringently tuberculin tested populations.	We agree, and this is reflected in the findings of the chapter on clinical effectiveness and safety.
A more detailed review of the nature of the BCG reactions reported is required. The IMB in its Drug Safety newsletter in 2007, reports 54 case reports related to BCG as being received in 2006. The report states that" the majority of reports received during 2006 continued to involve local reactions, some of which were considered serious". It is important to carefully define what constitutes an adverse reaction to BCG as opposed to a normal response. Venkataran et al (2015) in their paper describe induration at the injection site with subsequent ulceration, crusting and scarring within six weeks and axillary lymphadenopathy <1cm as a normal response to BCG vaccination11. In determining a population rate for adverse events for BCG it would be important to distinguish between normal reactions and adverse effects. In the paper by Venkataran et al (2015) which looked at BCG complications over a six year period (2008-2013) in East London, only one case of systemic complications was identified. This was a case of osteomyelitis in a child who was subsequently found to have a potential defect in macrophage/T cell signaling and was treated with interferon gamma therapy. Most children presented with isolated axillary lymphadenitis (65%) or isolated injection site reactions (30%). As this was a hospital based study it was not possible to provide a population estimate of adverse events.	We refer to the data from the Health Products Regulatory Authority as adverse reaction reports. As such, we cannot state what the severity of those cases was. For the study, we have focused on reported adverse events as they are assumed to require clinical assessment. As such, papules, mild ulcers and scars are not considered unusual reactions in the assessment.

The paper referred to by Bolger et al 2006 was triggered by an initial case report and covers a time period when a recent change in the strain of vaccine in use was necessary due to the withdrawal from the market of a major vaccine supplier12. The new strain was known to have greater reactogenicity and therefore an increase in reactions both normal and adverse would be expected. A report into the factors affecting the efficacy and safety of BCG (Milstein and Gibson 1990) found that all identified "outbreaks" of BCG Lymphadenitis occurred after a change in the vaccine strain in use13. This led to a recommendation that changing the preparation of BCG in use in a country should be avoided if possible. Bolger et al have attempted to estimate an adverse event rate but as hospitals in Ireland do not have a defined catchment area, it is not possible to estimate a population rate from presentations at a single hospital. Previous mapping exercises for service planning purposes have indicated a footprint for Our Lady's Hospital in Crumlin that would be greater than the combined area of the former Eastern Regional Health Authority and South-eastern Health Board areas referred to in this paper.	The Bolger study is based on the same strain of BCG vaccine as is currently in use. We appreciate the difficulties in accurately defining hospital catchments in Ireland. The data from the Bolger study was in agreement with the data obtained from the Health Products Regulatory Authority (HPRA). As part of the assessment we used the HPRA data to estimate the rate of adverse events requiring some degree of hospital treatment.
Disseminated BCG as a severe possible side effect of BCG is described and children with severe combined immunodeficiency SCIDs (which occurs at a higher rate among travellers) are considered at high risk. The rate of disseminated BCG reported in Ireland is acknowledged in the report as being out of synch with that reported elsewhere. As only one of the cases of disseminated BCG was in a child from a traveller family, the higher incidence of SCID in travellers is unlikely to be the explanation for the higher rate. But if this reason is part of the decision to move to a selective vaccination programme which selects travellers to be given BCG then the risk of giving BCG to a child with SCIDs remains.	We agree, and the report recommends that consideration should be given to evaluating a formal neonatal screening programme (for all newborns) to identify infants with severe combined immunodeficiencies.
The department feels there is certainly a need for a more inclusive "High Risk" category, that would include not only children from countries of high endemicity, or from the travelling community, but would also include the children of prisoners, homeless persons etc.. In Ireland we have had an ongoing outbreak in prison populations over the past few years with some cases of severe destructive disease. Irish figures for TB in children 15 and under show that 40% occur in those in the risk groups identified for selective vaccination, indicating that 60% occur in those outside of these risk groups. Failing to offer BCG to these other vulnerable groups would put these groups at risk of TB infection.	For the purposes of the study, it was pragmatic to determine the size of the high-risk population based on the criteria of country of origin of parents and member of the Traveller community in Ireland. These two groups are estimated to comprise the vast majority of high-risk cases. We have added text to the report acknowledging that there may be other high-risk groups such as children who are homeless or children of prisoners.

The cost of identifying at-risk children and demonstrating an adequate uptake rate has not been included. To do these two essential tasks will entail significant resources both human and financial. A selective BCG vaccination programme is in operation in the UK, however it is not possible to determine the uptake rates at either a national or sub-national level as the denominator population (i.e. at risk population) is not known7. The uptake rate of a selective vaccination programme for high-risk children would need to be of the order of 95% to ensure the programme is effective. However, page 59 of the document states that some studies have found that, after a switch from universal to selective vaccinations "lower uptake figures in the region of 50% have been reported….." If rates were as low as 50% the programme would not be effective and this would impact on the theoretical cost-effectiveness of selective vaccination.	Lower vaccine uptake in the high-risk population will lead to increased cases of TB. However, due to the small proportion in high-risk and the low probability of TB infection, a reduced uptake will not lead to a much higher number of childhood TB cases. In the sensitivity analyses we tested the impact of an uptake rate of 59%, and the results are reported in Section 5.5. As no capital expenditure was identified in the analysis, a change in uptake rate has a negligible impact on the estimate of cost-effectiveness.
Correct identification of infants at risk and the proportion that receive BCG would be of paramount importance. This would require the implementation of a national register/database with its associated costs. A clear pathway is needed to establish which healthcare professionals identify the at risk population. A need for role clarity and clear responsibilities would be essential.	It is not clear that a national register is required, and this has not been used in other countries with selective vaccination programmes. The potential ethical issues associated with such a register would also have to be considered.
Once the population at risk is identified, ensuring that the vaccine is delivered is crucial. The options are whether to vaccinate on postnatal wards or in the community. Vaccination on post natal wards in other countries is associated with high vaccination coverage. However, with shorter hospital stays now the norm postnatally this relies on the availability of staff to visit the wards on a daily basis to vaccinate a relatively small number of eligible newborns. The limited number of trained staff to administer the vaccine could impose restrictions on this practice. It is also dependent on midwives to identify those infants who are considered high risk and therefore eligible for the vaccine. Vaccination in the communities could lead to a lower uptake rate as parents may not bring their children to appointments. BCG vaccine is currently provided through a different delivery mechanism than the other routine primary immunisations due to the skills required for intra-dermal injection. With a declining cohort for vaccination the throughput necessary to maintain the high level of skill among vaccinators may not be there, raising the possibility of a potential increase in side effects.	We have highlighted the need for any implementation plan to carefully consider the settings within which the BCG vaccination programme could be delivered. Such a plan would need to outline who is responsible for the vaccination programme, and how it is to be delivered.

In the future there will also be a need to consider vaccinating previously unvaccinated children who are at high risk of TB, due to for example coming into contact with a case of active pulmonary TB. An effective system would need to be in place to identify children outside of infancy who fall into the risk groups.	As the assessment was concerned with the neonatal vaccination programme, the issue of revaccination or later vaccination was outside the scope of the project. However, vaccination of high-risk children would fall within the overall TB control programme.
The literature review included in this report regarding economic evaluations of neonatal BCG vaccines failed to always include treatment costs, or the costs incurred by contact tracing. Included in the limitations and key messages section is "The selective vaccination strategy modelled here did not include a specific cost for identifying high-risk infants, which may increase the budget impact of such a programme and reduce the estimated cost-effectiveness". This limitation casts doubt over the comparison of costs, as we have absolutely no idea of the costs of implementing selective vaccination in Ireland. In fact, we have no successful model of implementing selective vaccination to significant numbers of people in Ireland, so we cannot be sure if this is even feasible.	The manner in which high-risk infants are identified is partly dependent on the setting in which the BCG vaccination programme is delivered. It is also important that the programme capitalises on existing resources such as data and IT systems.
With an increasingly non-TB-immune population, TB outbreaks can be expected to increase in number, as seen by the outbreak of TB in 2 crèches in Co. Cork where there was no universal neonatal BCG vaccination programme. It may be economically difficult to measure, but the cost of dealing with an outbreak is greater than simply the cost of administering drugs to those who become infected.	The data on TB incidence used in the model incorporates the data on outbreaks. We used sensitivity analyses to test the impact of alternative approaches to including that data but it had limited impact on the results, and did not change the interpretation of the main findings.
Before consideration can be given to changing BCG immunization from a universal to a selective programme, Ireland must be able to demonstrate that it has a well functioning TB control programme. This is not currently the case. The deficits identified by the review conducted by the multidisciplinary team convened by the HSE Health and Wellbeing Directorate must be implemented before any change is considered. In other countries where there was a change from a universal to a selective BCG programme, transient increases in severe forms of tuberculosis particularly TB meningitis were seen14. If Ireland moves to implement a selective BCG programme, it is essential that a well functioning TB control programme is in place prior to the change in order to detect and response to any increase in cases particularly in children.	In the report, we acknowledge the concerns about the current TB control programme in Ireland. Our advice clearly states that enhancements should be made to TB control before any change is made to the BCG vaccination programme.

Further analysis of the efficacy of BCG vaccination as it applies to the Irish population is required. Previous studies span a considerable period of time and in many instances predate current accepted research methodologies. Studies conducted with varying levels of research rigor and at different latitudes cannot be generalized to the Irish population.	We incorporated the best available evidence for determining clinical efficacy. We appreciate that methodology and reporting have improved. However, randomised controlled trial evidence is superior to observational data. We reviewed the observational data from Ireland and we have discussed the results in the context of the Irish data, and the extent to which the findings may or may not be applicable to Ireland.
The demography of Ireland has changed rapidly in the last decade and with large areas of conflict and poverty in the world driving migration, it will continue to change. In addition the rapid rise of diabetes especially in low and middle income countries like India and China which already have a high burden of both TB and drug resistant TB is likely to impact on current TB control measures at a global level. The impact of these changes on TB epidemiology in Ireland should be analysed in order to fully inform the effects of changing to a selective BCG programme.	The analysis was based on childhood TB incidence in Ireland over the last ten years. Any analysis to predict future migration flows would be subject to substantial uncertainty and would have to be cognisant of changing TB incidence globally.
Identifying and monitoring BCG coverage in target groups is important and will necessitate new measures to ensure and record high uptake in at-risk groups. There is also a requirement to improve the quality of information on BCG status and incorporate a measure of BCG eligibility in the TB surveillance system. All of these changes will have a financial cost and this should be factored into the analysis to give a more accurate comparison between the costs and benefits of a selective versus a universal programme.	The report gives an overview of some of the issues relating to measuring uptake, and the challenges in determining uptake for a changing population. Regarding the costs, we have outlined the limitation of the study in terms of the types of data available and included in the analysis.
The Medical Officers of Health have a statutory function in relation to all notifiable disease including TB to “prevent spread and remove conditions favourable to such infection”. In the area of TB, BCG vaccination is a key tool for both of these actions. Any decision to weaken the resources available in the control of TB should consider the Precautionary Principle, taking into account that there is inadequate evidence and much uncertainty in relation to the benefits and costs of all options. We know that BCG is effective against all forms of TB including MDR and XDR TB when given as part of a well designed vaccination programme. Without alternative community protection methods, reducing the community protection from BCG appears to go against this Precautionary Principle.	The report clearly states that TB control needs to be enhanced before any change to the BCG vaccination programme is implemented. That is, BCG vaccination is part of TB control and a reduction in protection must be balanced by investment in other elements of TB control.

This document lays out the rationale that can underpin a decision to stop universal BCG vaccination in Ireland, without recommending it. If this decision is made, it is an opportunity to re-direct vaccine resources to improve the Irish TB service. Specifically, targeted testing for Latent TB infection (LTBI), which is detailed in the Irish TB guidelines- but which has not been implemented – could be meaningfully effected.	The report clearly states that any budgetary savings from a switch to selective BCG vaccination are unlikely to be realised due to the need to reinvest in other elements of TB control.
Ireland's TB programme would be immediately enhanced by 1. The appointment of a TB controller for the country: In an un-distractible manner, this person would be dedicated to TB elimination, and take ownership of our TB elimination efforts. 2. The universal application of directly observed therapy (DOT) to all cases of tuberculosis. With under 400 cases per year- this is not a huge undertaking. Using outreach workers to achieve this, we can expect near immediate benefit- by ensuring treatment completion and therefore no repeat disease in TB cases. 3. Latent TB infection (LTBI) testing and treating: The stepping up of LTBI diagnosis and treatment after targeted testing as outlined (but not implemented) in the national guidelines.	Some of these issues are addressed in Chapter 6, along with the recommendation to develop national clinical guideline for TB control. A Ministerially-mandated clinical guideline would help to ensure a coherent and comprehensive approach is adopted to TB control in Ireland.

5. Changes to the report

In response to the feedback received, we added additional sections to the report and added text to some existing sections. The main changes are listed below:

Sections added:

- Protection against latent TB infection (section 4.4.2)
- Non-specific effects of BCG vaccination (section 4.4.3)
- Preparing for a vaccination policy change (section 6.1.10)

Text was added to the following sections:

- Section 2.2 – reworded text on the adequacy of existing TB control measures.
- Section 3.4 – listed some additional population groups that may be considered high-risk.
- Section 5.4.2 – included results on the risk of TB in different population subgroups.
- Section 5.7.3 – included text on the effect of vaccine against latent TB infection.
- Section 5.7.3 – included text on high-risk groups not included in the analysis.
- Section 6.1.2 – included text to acknowledge BCG supply issues.
- Section 6.1.3 – additional text on identification of high-risk infants.
- Section 6.1.5 – additional text on uptake, in particular in relation to monitoring uptake.
- Section 6.1.6 – additional text on demand for screening in relation to migration patterns.

6. Conclusions

We received extensive feedback from a diverse range of people and organisations. As a result of this we have updated various sections of the report to include additional information or to clarify certain aspects of the evaluation. This document will also serve as a useful companion report to the HTA on a selective BCG vaccination programme, as it clarifies issues that were identified in the public consultation.

We also received many suggestions and queries regarding the operational issues that will need to be addressed during the planning and implementation phase of introducing a selective BCG vaccination programme. While these are outside the scope of this assessment, they are provided here for the benefit of those involved in any future work in this area.

We would like to thank all those who made submissions as part of the consultation process and express our gratitude for their contribution to ensuring that this assessment benefited from the views of people from all backgrounds and experiences.

Appendix 1: Public consultation feedback form

Health Information and Quality Authority
An tÚdarás Um Fhaisnéis agus Cáilíocht Sláinte

Health technology assessment of a selective BCG vaccination programme

For public consultation

Consultation Feedback Form

September 2015

Your feedback is very important to us. We welcome responses to all questions as well as any additional comments you would like to make.

When commenting on a specific section of a document, it would help if you can identify which element you are commenting on and the relevant page number.

The closing date for consultation is 5pm on Wednesday 21 October 2015

You may email or post a completed form to us.

About you

Name	
Address	
Contact details	
Date	

General Information and Questions

You may provide us with feedback on the specific questions (see questions that follow), or alternatively you may provide us with general comments.

Part 1

Are you replying in a personal capacity or on behalf of an institution or organisation?

☐ Personal capacity

☐ On behalf of an institution

☐ On behalf of an organisation

Part 2

Please outline any general or specific feedback on the documents. In your response, where applicable, please specify the section to which you are referring.

Please comment

Thank you for taking the time to give us your views.

After the closing date, we will assess all feedback and use it to finalise our documents. The final documents and the Statement of Outcomes (a summary of the responses) will be published on http://www.hiqa.ie.

If you wish to do so, you can request that your name and/or organisation be kept confidential and excluded from the published summary of responses. Please note that we may use your details to contact you about your responses. We do not intend to send responses to each individual respondent.

Please return your form to us either by email or post:

consultation@hiqa.ie

BCG Public Consultation
Health Information and Quality Authority
George's Court
George's Lane
Dublin 7

Please return your form to us either by email or post before 5pm on Wednesday 21 October 2015

Please note that the Authority is subject to the Freedom of Information Acts and the statutory Code of Practice regarding FOI.

For that reason, it would be helpful if you could explain to us if you regard the information you have provided as confidential. If we receive a request for disclosure of the information we will take full account of your explanation, but we cannot give an assurance that confidentiality can be maintained in all circumstances.

Appendix 2: List of organisations that made submissions

Community Medical Department, Community Health Office 3
Community Medical Service, Sligo/Leitrim/West Cavan
Department of Public Health, Health Service Executive (HSE) Midlands
Department of Public Health, HSE Mid-West
Department of Public Health, HSE South East
Irish Medical Organisation
Irish Thoracic Society
National Principal Medical Officer Group of the HSE
Pavee Point Traveller and Roma Centre
TB Contact Tracing service, HSE East / Department of Public Health, HSE East