National Institute for Health and Clinical Excellence

Tuberculosis: clinical diagnosis and management of tuberculosis, and measures for its prevention and control

Scope Consultation Table
29.11.12 – 10.01.13

No	Type	Stakeholder	Section No	Comments	Developer's Response
1.	SH	ANHOPS	5.1.1b	University student population and those entering clinical professions	Thank you for your comment. The scope for this guidance will cover all adults, young people and children who have or are suspected to have active or latent TB, or are at an increased risk of infection with Mycobacterium tuberculosis complex (see sections 5.1.1a to c). We feel that this includes the university student population and those entering clinical professions**.**
2.	SH	ANHOPS	5.3.2a	Within Occupational Health (OH) setting i) HCW's diagnosed with latent TB (as not infective)--any work restrictions are not appropriate Investigation and treatment should be managed by their GP/public health. 'Inform and advise 'by Occupational Health could be sufficient ii) Many HCWs from high endemic countries would remain IGRA positive – what is the evidence that Igra results indicate infection and are not markers of past infection successfully cleared. iii) Numbers required to be screened with little evidence of anticipated outcome of prevention (see HPA BIOS 2005 report) iv) Is it effective use of resources – to be	Thank you for your comment. We agree that the identification, management and control of TB in occupational health settings are significant issues. However, it is felt that the issue of communicable diseases in the workplace goes beyond TB: activities relating to the identification, management and control of other diseases – such as influenza, HIV and hepatitis B and C – may also benefit from guidance. Since such occupational health risks may often affect the same groups of workers and are often managed by a single occupational health team using similar principles and practices, it was felt that a single piece of guidance that covers this area as a whole may be more appropriate than fragmenting guidance under individual diseases.

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				applied to ALL HCWs as opposed to those with high risk factors.	The Centre for Public Health Excellence is currently considering the management of communicable diseases in the workplace as a possible piece of guidance within their draft library of topics. More information on how topics are selected for public health guidance can be found in the Centre for Public Health Excellence's guidance and method guides: http://www.nice.org.uk/aboutnice/howwework/developingnicepublichealthguidance/publichealthguidanceprocessandmethodguides/public_health_guidance_process_and_method_guides.jsp
3.	SH	ANHOPS	5.3.2b Does contact tracing for latent TB need to be reviewed?	As latent TB is non infective – is contact tracing relevant? People with High Risk factors (those coming from high risk countries, Diabetes etc – should be tested and then managed by their GPs. OH assesses their risk at work to patients and colleagues	Thank you for your comment. The diagnosis of latent TB is an important part of TB prevention activities in that it identifies those who may go on to develop active TB. If latent TB is detected, a person may be treated or monitored for the emergence of active TB (and subsequently treated), therefore avoiding the morbidity and mortality associated with active TB in that individual, as well as limiting the potential infectivity of that individual that occurs if active TB were to arise.
4.	SH	ANHOPS	5.3.2c	a) Interpretation of IGRA tests rather than a binary view (of positive and negative) – positivity could just be a marker of past infection b) Is there a risk of resistance increasing if all positive IGRAs are treated (85%-90% - who may not develop disease are also treated) What are the risk factors for the 10% that go on to develop active disease?	Thank you for your comment. a) We feel that the CG117 evidence reviews for diagnosing latent TB in adults are still relevant and that the new evidence in this area would not change the current recommendations. The CG117 review areas relating to the diagnosis of latent TB that have been identified as requiring an update is paediatric diagnosis of latent TB, diagnosis of latent TB in people who are immunocompromised

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				c) HCW's travelling to high-incidence countries—should IGRA be used as screening tool on return and if so on what basis – e.g. duration of stay, risk assessment of what they did when abroad, both, etc d) Effectiveness of BCG – HPA studies show that more than 75% of HCWs who developed active disease had BCG. Is it therefore a more effective action than "educate and advise" within health care workers? Most agree that BCG vaccination is of little or no effectiveness against respiratory TB which is the main concern from an employment (OH) view – hence a review of promoting BCG vaccine (whose general effectiveness is dubious) to *ALL* HCWs should be considered – this leads to false assurance of immunity against TB and alertness for symptoms is reduced.	or at known risk of immunosuppression, and diagnosis of latent TB in new entrants from high incidence countries. Therefore, a new topic has been included under 5.3.1, 'key issues that will be covered': "h) Diagnosis of latent TB infection using Mantoux testing and interferon-gamma release assays in: • children • people who are immunocompromised, such as people with HIV or renal disease, or at known risk of immunosuppression, such as people about to start immunosuppressive regimens • new entrants from high incidence countries, in the context of opportunistic case-finding rather than proactive screening programmes." The threshold for interpreting an IGRA result as a diagnosis of latent TB will be considered as part of these reviews. The reviews for the diagnosis of latent TB in adults will not be updated. b) The risk factors for drug resistance will be reviewed in review question 5.5.1s. c) Although we agree that the issue of healthcare workers travelling to high-incidence countries is an important issue, it is not considered a priority for review in the new guidance. d) An evaluation of the effectiveness of the BCG

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					vaccination is beyond the remit of NICE. This area falls within the responsibilities of the JCVI and its current position is that the BCG vaccine offers some protection against TB. Where available, relevant evidence on BCG vaccination uptake and effective information and support for healthcare workers will be reviewed and considered by the GDG.
5.	SH	ANHOPS	Any other comments	We feel that HCWs must be looked at as a separate population to evaluate the current occupational risk of TB, the risk of communicating the disease and effectiveness of actions advised by guidelines in such a setting. TB is mainly a Public Health Issue and should be dealt with accordingly and only in select cases as ascertained by a risk assessment it becomes an occupational Health issue Function of OH re TB 1) to rule out active TB which is based on symptoms and hence questionnaire 2) risk assess need for further screening and BCG e.g in those with high risk factors 3) contact tracing in staff when criteria for this are met.	We agree that the identification, management and control of TB in occupational health settings are significant issues. However, it is felt that the issue of communicable diseases in the workplace goes beyond TB: activities relating to the identification, management and control of other diseases – such as influenza, HIV and hepatitis B and C – may also benefit from guidance. Since such occupational health risks may often affect the same groups of workers and are often managed by a single occupational health team using similar principles and practices, it was felt that a single piece of guidance that covers this area as a whole may be more appropriate than fragmenting guidance under individual diseases. The Centre for Public Health Excellence is currently considering the management of communicable diseases in the workplace as a possible piece of guidance within their draft library of topics. More information on how topics are selected for public health guidance can be found in the Centre for Public Health Excellence's guidance and method guides: http://www.nice.org.uk/aboutnice/howwework/developingnicepublichealthguidance/publichealthguidanceprocessandmethodguides/public_health_guidance_proces

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6.	SH	British HIV Association (BHIVA) and British Association for Sexual Health and HIV (BASHH)	5.1.1b	5.1.1 (d) bullet 3: BHIVA comment: can make reference to the BHIVA Guidelines on the Treatment of TB/HIV coinfection Published: *HIV Medicine* (2011), **12**, 517–524 Online: http://www.bhiva.org/TB-HIV2011.aspx	Thank you for your comment. Section 5.1.1 of the scope is intended to capture the population groups that will be covered in the new guidance. The scope would not refer directly to other related guidelines, except those produced by NICE (see section 6). However, the Guideline Development Group appointed to the guidance can consider existing guidance as part of their decision-making, where this is appropriate. Please see the NICE Guidelines manual (2012) for further details on our guidance development methodology.
7.	SH	British HIV Association (BHIVA) and British Association for Sexual Health and HIV (BASHH)	Any other comments	4.2 f) bullet 2: "people with HIV regardless of their age" BHIVA comment: We have a risk evaluation in the BHIVA TB guidelines	Thank you for your comment. Section 4.2 is meant to summarise current practice in the prevention, identification and management of TB. Bullets 4.2b to g reflect current best practice, as recommended by NICE clinical guideline 117 ('Tuberculosis: clinical diagnosis and management of tuberculosis, and measures for its prevention and control').
8.	SH	British HIV Association (BHIVA) and British Association for Sexual Health and HIV (BASHH)	Any other comments	5.3.1 b) Bullet 4 BHIVA comment: issue of drug / drug interactions e.g. use of rifabutin is covered elsewhere in scope but should be mentioned here	Thank you for your comment. We agree that drug-drug interactions are an important issue in the management of people coinfected with TB and HIV. It is already covered under section 5.3.1b: "Treatment of active TB. Specific consideration will be given to when treatment should deviate from the 'standard recommended regimen', taking into account factors such as the site and severity of the disease, and individual patient characteristics including age

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					and the presence of comorbidities such as HIV, renal or liver disease and drug dependency." Specifically, this will be considered under review question 5.5.1j: "In people co-infected with TB and HIV receiving drug treatment for both infections, what are the key pharmacological considerations that should be taken into account when selecting a treatment regimen for eradicating TB infection?"
9.	SH	British Society of Thoracic Imaging	5.1.1b	Yes	Thank you for your comment.
10.	SH	British Society of Thoracic Imaging	5.1.2	Yes	Thank you for your comment.
11.	SH	British Society of Thoracic Imaging	5.2	Yes	Thank you for your comment.
12.	SH	British Society of Thoracic Imaging	5.3.2	Yes	Thank you for your comment.
13.	SH	British Society of Thoracic Imaging	5.4	a) The scope is not specific in outlining the diagnostic tests to be evaluated. As such it is not incorrect but not focused i.e. different combinations of imaging, microbiology, interferon gamma and rapid molecular assays.	Thank you for your comment. a) The bullet points in section 5.1.1a are intended to provide a brief summary of the range of diagnostics that may be considered in the reviews for diagnosing

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				b) 'Diagnostic utility and accuracy of diagnostic strategies' will presumably be stratified according to risk groups eg. Symptomatic vs contact screening vs high risk populations eg prison c) While monitoring of patient response to treatment is specifically excluded when surgical management is being evaluated indications may include relapsed or failed treatment so I am sure patient selection for 'aggressive management' will be discussed (including imaging aspects)	active respiratory and non-respiratory TB. Those diagnostic tests listed are considered to be the most important for review, but the full range of tests that will be evaluated will be determined by the available evidence and by the Guideline Development Group. b) Where possible, subgroup analyses will be performed for key groups for whom the diagnosis and management of TB may vary. Section 5.1.1d gives examples of the types of groups that this may be the case for: "Where appropriate and when reported by study authors these may include, but are not limited to: • neonates, children and young people • adults older than 35 years • people with HIV and other comorbidities or conditions that impact on the diagnosis and management of TB." It should be noted that the subgroups to be included in each review will be subject to confirmation by the Guideline Development Group, who will consider the appropriateness of the proposed review protocols at their first meeting. c) We agree that relapse or treatment failure may be indications for surgical management. The reviewer will therefore include groups with these indications as subpopulations of interest in the protocol for review questions 5.5.1o and r. However, it should be noted that this is subject to confirmation by the Guideline Development Group, who will consider the

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					appropriateness of the proposed review protocols at their first meeting. Additionally, the role of relapse and treatment failure as risk factors for drug resistant TB will be examined in 5.5.1s, and the role of surgery in the management of drug resistant-TB will be reviewed in 5.5.1x.
14.	SH	British Thoracic Society	5.1.1b	a) LTBI in patients considered for biological therapies such as a/TNF (plus receptor) and a/IL1 antibody therapy b) LTBI in patients with CKD	Thank you for your comment. a) Since people about to start immunosuppressive biological therapies regimens who have latent TB are believed to be at particular risk of progressing to active disease, we agree they are an important subpopulation to include. Although we do not explicitly note them in section 5.1.1 ('Groups that will be covered'), we feel they are included under bullet c): "Adults, young people and children at increased risk of infection with Mycobacterium tuberculosis complex and/or at increased risk of progressing to the active disease." The diagnosis of latent TB in people on/about to start immunosuppressive regimens will be explicitly covered in review question 5.5.1ff: "Which diagnostic strategy is most effective in establishing an accurate diagnosis of latent TB in people who are immunocompromised or at risk from immunosuppression?" People on/about to start immunosuppressive regimens will also be included by the reviewer in the protocol for review questions 5.5.1hh (according to their risk factors, which people with latent TB should receive treatment?) and 5.51ii (which treatment

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					regimen is best for treating latent TB?) as populations of interest. It should be noted that this will be subject to confirmation by the Guideline Development Group, who will consider the appropriateness of the proposed review protocols at their first meeting. b) Again, although we do not explicitly note people with renal disease in section 5.1.1, we feel they are included under bullet c): "Adults, young people and children at increased risk of infection with Mycobacterium tuberculosis complex and/or at increased risk of progressing to the active disease." Additionally, we acknowledge that they may be a subgroup for whom the diagnosis and management of TB may vary. Therefore we feel that they are also reflected by the 3rd bullet point of 5.1.1d: "people with HIV and other comorbidities or conditions that impact on the diagnosis and management of TB" People with renal disease will be included as populations of interest in the protocol for review question 5.5.1k: "What comorbidities or conditions affect the choice of regimen for the treatment of active TB? How should the standard recommended regimen be adapted to accommodate these comorbidities or conditions?" Additionally, the diagnosis of latent TB in people with renal disease will also be explicitly considered in review question 5.5.1ff: "Which diagnostic strategy is most effective in

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					establishing an accurate diagnosis of latent TB in people who are immunocompromised or at risk from immunosuppression?" Again, it should be noted that the review questions and protocols will be subject to confirmation by the Guideline Development Group, who will consider their appropriateness at their first meeting.
15.	SH	British Thoracic Society	5.1.2	No	Thank you for your comment.
16.	SH	British Thoracic Society	5.2	? Hostels for the homeless	Thank you for your comment. As there many important settings in which activities relating to the prevention, identification and management of TB are received, provided or commissioned, section 5.2 has now been amended to state: "Any setting in which NHS or public health services for TB are received, provided or commissioned in the public, private and voluntary sectors." This includes hostels for the homeless, where appropriate.
17.	SH	British Thoracic Society	5.3.2	a) I agree with Onn Min Kon's suggestions of looking at evidence base and cost effectiveness of New entrant screening for LTBI b) I do not believe that consideration of configuration/ delivery of broader TB services (under public health/clinical banners) by NICE is important at this stage, whilst this is being	Thank you for your comment. a) The diagnosis of latent TB among new entrants from high incidence countries is now included under 5.3.1h: "Diagnosis of latent TB infection using Mantoux testing and interferon-gamma release assays in: • children • people who are immunocompromised, such as

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				debated and defined by TB stakeholders with PHE and DOH	people with HIV or renal disease, or at known risk of immunosuppression, such as people about to start immunosuppressive regimens • new entrants from high incidence countries, in the context of opportunistic case-finding rather than proactive screening programmes." Specifically, it will be undergo a clinical- and cost-effectiveness review under review question 5.5.1gg: "Which diagnostic strategy is most effective in establishing an accurate diagnosis of latent TB in people who are recent arrivals from countries with a high incidence of TB?" b) A review of effective and cost effective models for the delivery and configuration of TB services will be developed using the CCPs interim methods for developing service guidance. This will be presented to a subgroup of the GDG for consideration, with any recommendations ratified by the GDG. The review will cover service delivery across the care pathway, where evidence is available. The CCPs interim methods for service guidance will be available on the NICE website at http://publications.nice.org.uk/pmg8
18.	SH	British Thoracic Society	5.4 Are the outcomes in section 5.4.appropriate and correct?	I believe so.	Thank you for your comment.

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19.	SH	British Thoracic Society	Any other comments	5.1.1- special consideration should be given to elderly persons with active TB, as side effects from medicines and drug interactions more likely	Thank you for your comment. Older people will be included in the protocol for relevant treatment reviews as a subpopulation of interest. However, it should be noted that this will be subject to confirmation by the Guideline Development Group, who will consider the appropriateness of the proposed review protocols at their first meeting. Additionally, the Summary of Product Characteristics for a particular drug formulation and the British National Formulary include issues that should be taken into consideration (such as adverse events and drug interactions) when treating different populations, including older people. This should be used to guide decisions regarding the monitoring of a patient's response to treatment.
20.	SH	British Thoracic Society & RCP	5.1.1b	Latent TB infection in pre-biological therapy immunosuppressed individuals (most pertinently pre-TNF) and chronic kidney disease are a notable omission here as this is a significant workload for most TB services and of value to those in related specialities.	Thank you for your comment. Since people about to start immunosuppressive biological therapies regimens who have latent TB are believed to be at particular risk of progressing to active disease, we agree they are an important subpopulation to include. Although we do not explicitly note them in section 5.1.1 ('Groups that will be covered'), we feel they are included under bullet c): "Adults, young people and children at increased risk of infection with Mycobacterium tuberculosis complex and/or at increased risk of progressing to the active disease." The diagnosis of latent TB in people on/about to start immunosuppressive regimens will be explicitly covered in review question 5.5.1ff: "Which diagnostic strategy is most effective in

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					establishing an accurate diagnosis of latent TB in people who are immunocompromised or at risk from immunosuppression?" People on/about to start immunosuppressive regimens will also be included by the reviewer in the protocol for review questions 5.5.1hh (according to their risk factors, which people with latent TB should receive treatment?) and 5.51jj (which treatment regimen is best for treating latent TB?) as populations of interest. Again, although we do not explicitly note people with renal disease in section 5.1.1, we feel they are also included under bullet c). Additionally, we acknowledge that they may be a subgroup for whom the diagnosis and management of TB may vary. Therefore we feel that they are also reflected by the 3rd bullet point of 5.1.1d: "people with HIV and other comorbidities or conditions that impact on the diagnosis and management of TB" People with renal disease will be included as populations of interest in the protocol for review question 5.5.1k: "What comorbidities or conditions affect the choice of regimen for the treatment of active TB? How should the standard recommended regimen be adapted to accommodate these comorbidities or conditions?" Additionally, the diagnosis of latent TB in people with renal disease will also be considered in review question 5.5.1ff: "Which diagnostic strategy is most effective in establishing an accurate diagnosis of latent TB in

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					people who are immunocompromised or at risk from immunosuppression?" It should be noted that the review questions and protocols will be subject to confirmation by the Guideline Development Group, who will consider their appropriateness at their first meeting.
21.	SH	British Thoracic Society & RCP	5.2	Community settings needs to be specific that this covers incidents involving schools/ colleges/ workplace assessments. Military establishments should be considered.	Thank you for your comment. As there many important settings in which activities relating to the prevention, identification and management of TB are received, provided or commissioned, section 5.2 has now been amended to state: "Any setting in which NHS or public health services for TB are received, provided or commissioned in the public, private and voluntary sectors." This includes schools, colleges, workplaces and military establishements, where appropriate.
22.	SH	British Thoracic Society & RCP	5.3.2a	a) There have been recent publications on the place of new entrant screening in a UK context examining the cost effectiveness of approaches and also the threshold of the screening – these have been published since CG117. The threshold suggested by CG117 hence needs revising and also the method by which screening can occur most effectively is now similarly clearer. Pareek M, Bond M, Shorey J, Seneviratne S, Guy M, White P, Lalvani A, Kon OM. Community-based evaluation of immigrant tuberculosis screening using interferon γ release assays and tuberculin skin testing:	Thank you for your comment. a) The diagnosis of latent TB among new entrants from high incidence countries is now included under 5.3.1h: "Diagnosis of latent TB infection using Mantoux testing and interferon-gamma release assays in: • children • people who are immunocompromised, such as people with HIV or renal disease, or at known risk of immunosuppression, such as people about to start immunosuppressive regimens

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				observational study and economic analysis. Thorax. 2012 Jun 12. Pareek M, Watson JP, Ormerod LP, Kon OM, Woltmann G, White PJ, Abubakar I, Lalvani A. Screening of immigrants in the UK for imported latent tuberculosis: a multicentre cohort study and cost-effectiveness analysis. Lancet Infect Dis. 2011 Jun;11(6):435-44. b) The evidence review should concentrate on latent TB detection and also in particular the issue of the two step versus one step cost effectiveness analysis. This field will have advanced given the more recent publications now evaluating IGRAs since 2008-9. In particular there have been more publications of IGRA's in immunocompromised individuals apart from HIV. The last UK renal guidance is from 2010 and for pre anti-TNF screening 2005. c) The algorithms for investigation of close contacts which were removed from the old guideline presumably for updating will hopefully be restored as an update. A review of the evidence for contact tracing would be helpful. For example ,the term "household contacts" is misleading. Many individuals working full time potentially spend more time in a work environment then in the home. The term "Close contacts" may be more helpful in identifying potential	• new entrants from high incidence countries, in the context of opportunistic case-finding rather than proactive screening programmes." Specifically, it will be undergo a clinical- and cost-effectiveness review under review question 5.5.1gg: "Which diagnostic strategy is most effective in establishing an accurate diagnosis of latent TB in people who are recent arrivals from countries with a high incidence of TB?" b) We feel that the CG117 evidence reviews for diagnosing latent TB in adults are still relevant and that the new evidence in this area would not change the current recommendations. The CG117 review areas relating to the diagnosis of latent TB that have been identified as requiring an update is paediatric diagnosis of latent TB, diagnosis of latent TB in people who are immunocompromised or at known risk of immunosuppression, and diagnosis of latent TB in new entrants from high incidence countries. Therefore, a new topic has been included under 5.3.1, 'key issues that will be covered': "h) Diagnosis of latent TB infection using Mantoux testing and interferon-gamma release assays in: • children • people who are immunocompromised, such as people with HIV or renal disease, or at known risk of immunosuppression, such as people about to start immunosuppressive regimens • new entrants from high incidence countries, in the context of opportunistic case-finding rather than

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				transmission. Individual assessment of each contact plays an important part of identifying those more at risk following exposure. d) Could the use of TB questionnaires be helpful in combination with mantoux/IGRA? Incorporating symptoms, medication, previous TB etc. Particular in groups where you would not necessarily look for latent TB just active disease. e) A review of the evidence with regard to paediatric TB active /latent screening would be useful.	proactive screening programmes." The reviews for the diagnosis of latent TB in adults will not be updated. c) Contact-tracing will be reviewed in terms of how latent TB should be diagnosed in defined groups. Please see the response above (b) for details. Additionally, a review of effective and cost effective models for the delivery and configuration of TB services will be developed using the CCPs interim methods for developing service guidance. Where evidence is available, the GDG subgroup will consider who should carry out contact tracing and when this should be done, but a full evaluation on the organisation of contact tracing activities is outside the scope of the guidance. Recommendations made by the GDG subgroup will be ratified by the GDG. d) Although we agree that TB questionnaires may be a useful tool for identifying those who may have latent TB, it is not considered a priority for review in the new guidance. e) The diagnosis of active TB in children and young people will be explicitly reviewed in the new guidance. For example, see review question 5.5.1b and d. Where not covered by a standalone review question, they will be included in the protocol for the relevant reviews as a subpopulation of interest. This means that, where possible, evidence on this population will be considered in isolation from the evidence for adults. However, it should be noted that this is subject

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					to confirmation by the Guideline Development Group, who will consider the appropriateness of the proposed review protocols at their first meeting. Children, along with people who are immunocompromised or at known risk of immunosuppression and new entrants from high incidence countries, have been highlighted as populations for whom the diagnosis of latent TB should be reconsidered. Therefore, a new topic has been included under 5.3.1, 'key issues that will be covered': "h) Diagnosis of latent TB infection using Mantoux testing and interferon-gamma release assays in: • people who are immunocompromised, such as people with HIV or renal disease, or at known risk of immunosuppression, such as people about to start immunosuppressive regimens new entrants from high incidence countries, in the context of opportunistic case-finding rather than proactive screening programmes."
23.	SH	British Thoracic Society & RCP	5.3.2b	a) We presume that the BCG efficacy issues will continue to be defined by the JVCI and hence will not need replicating here and in addition it appears to be covered in terms of improving uptake in section b) The configuration and delivery of TB services is an important topic but it is unclear how the process will help advise on a specific model apart from comparative systems descriptions in a variety of settings. It is	Thank you for your comment. a) The consultee is correct that the responsibility for recommendations on BCG efficacy lies with the JCVI. As outlined in section 5.5.2 of the scope, the evidence review for the area of BCG vaccination uptake will cover strategies and interventions to increase uptake and the barriers to uptake. The effectiveness of the vaccine will not be evaluated. To improve clarity, section 5.5.2pp will be removed from the scope.

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				difficult to see how a systematic review would be able to generate sufficient evidence to advocate a specific model. A national TB programme to ensure the broadest coverage of provision in a uniform and equitable manner is needed but given the current reconfiguration of commissioning is likely to lead to some significant changes and the cycle of review not allowing this publication till 2015 would seem to make this aspect redundant even if pursued.	b) A review of the evidence on effective and cost effective models for the delivery and configuration of TB services will be developed using the CCPs interim methods for developing service guidance, and will be presented to a subgroup of the GDG for consideration. Recommendations made by the subgroup will be ratified by the GDG. The review will aim to cover service delivery across the care pathway, where evidence is available. The CCPs interim methods for service guidance will be available on the NICE website at http://publications.nice.org.uk/pmg8
24.	SH	British Thoracic Society & RCP	5.5.1	a) 5.5.1b - needs to explicitly cover molecular tests now given the apparent improved sensitivity of these in sputum smear negative cases 5.5.1s – similarly the emergence of rapid and readily available PCR resistance platforms should explicitly be reviewed here b) However note is made of a 'paused' NICE diagnostics assessment – dependent on when this review is likely to proceed, it could be argued this is very relevant to the TB update.	Thank you for your comment. a) Molecular tests will be included as interventions of interest in the diagnostic reviews within the new guidance, both for drug susceptible and drug resistant TB. b) The reviewer is hoping to include the results of the ongoing review in the new guidance.
25.	SH	British Thoracic Society & RCP	Any other comments	a) 5.3.1b: Advice on management of hepatic reactions (which occur in approx 3% of cases). BTS guidance was published in 1996 and repeated in 1998 treatment guideline. b) 5.3.1b: Alternative regimens for use where	Thank you for your comment. a) We agree that liver toxicity may be an important adverse effect associated with the treatment of TB. Although it is not mentioned explicitly, we feel that

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				the 4th drug (Ethambutol) is relatively or absolutely contraindicated because of renal or visual impairment. c) 5.3.1j: Although currently unlicensed rifapentene is likely to become a mainstay agent for LTBI treatment in combination with isoniazid and as such may warrant a review. d) 5.5.1: In young children with active TB receiving drug treatment including ethambutol, is routine visual screening necessary and if so how should it be done? (NB Monitoring of patient response to treatment was specified as an issue which will not be covered)	hepatic reactions are covered under 'adverse events' – one of the outcomes to be considered in the treatment reviews (see 5.4b). However, it should be noted that this will be subject to confirmation by the Guideline Development Group, who will consider the appropriateness of the proposed review protocols at their first meeting. If included as an outcome of interest, recommendations on the treatment of TB will include a consideration of hepatic toxicity. It has also been noted that such adverse effects are a major source of non-adherence to treatment, and that detecting and swiftly managing these side effects may improve adherence to treatment. This issue will be included in the review of adherence to treatment for active and latent TB, where the available evidence on a range of interventions and approaches that support or prohibit treatment completion will be identified and assessed. Additionally, such adverse effects can lead to breaks in the continuity of treatment, which is believed to be a risk factor for relapse and treatment failure, as well as drug resistance. The best approach to management of these treatment interruptions will be addressed in review question 5.5.1z: "For people receiving drug treatment for active TB who experience treatment interruptions, what approach to re-establishing appropriate treatment is the most effective in reducing mortality and morbidity?" b) Although we do not explicitly note people with renal or visual impairment in section 5.1.1, we acknowledge

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					that they are subgroups for whom the diagnosis and management of TB may vary. We feel that this is reflected by the 3rd bullet point of 5.1.1d: "people with HIV and other comorbidities or conditions that impact on the diagnosis and management of TB" Additionally, the diagnosis of latent TB in people with renal disease will also be considered in review question 5.5.1ff: "Which diagnostic strategy is most effective in establishing an accurate diagnosis of latent TB in people who are immunocompromised or at risk from immunosuppression?" c) Whilst we note that rifapentine appears to be promising in the treatment of latent TB, it is not licensed in the UK. Therefore this guidance will not be able to make recommendations on its use. If studies comparing rifapentine regimens to regimens of drugs licensed in the UK are available, rifapentine may be included as a comparator in our evidence reviews. d) The Summary of Product Characteristics and British National Formulary for Children include details on the tests that should be conducted before a particular drug formulation is started. NICE urges prescribers to use this information to guide treatment decisions.
26.	SH	BSAC	5.1.1b	Include private health care providers eg dialysis for renal patients or indeed anywhere where NHS services are contracted out. The	Thank you for your comment. Private healthcare providers who provide NHS services are captured within section 5.2 of the scope,

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				appropriate level of infection control service is contracted for so that patients receive the same standard of care as within mainstream NHS provision.	which now states: "Any setting in which NHS or public health services for TB are received, provided or commissioned in the public, private and voluntary sectors."
27.	SH	BSAC	5.3.2	Pathology services are currently changing with networks of labs being formed and private providers on the scene. The guidance can ensure that access for direct molecular tests for TB is available within a short turnaround time irrespective of which lab the sample is sent to!	Thank you for your comment. A review of effective and cost effective models for the delivery and configuration of TB services will be developed using the CCPs interim methods for developing service guidance, and will be presented to a subgroup of the GDG for consideration, with any recommendations ratified by the GDG. This evidence review will consider the general configuration of TB services across the care pathway, however, the management and organisation of allied services that support the identification, management and treatment of TB services is a local decision. The CCPs interim methods for service guidance will be available on the NICE website at http://publications.nice.org.uk/pmg8
28.	SH	Children's HIV Association	5.2	yes	Thank you for your comment.
29.	SH	Children's HIV Association	5.3.2a	a) Drug dosages for children should be reviewed: Present statement is that BNF for children should be followed. However there is published evidence that higher doses are required for adequate treatment. This evidence should be reviewed. b) Review of fixed dose combination	Thank you for your comment. a) We agree that achieving appropriate dosages in a treatment regimen is an important part of managing TB. However, the guidance will not cover the specific dosages required by particular populations; instead, we ask that prescribers use the British National Formulary for Children and a formulation's Summary of Product Characteristics to inform their decisions for

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				treatments for children as available in high incidence countries and why these are not made available in UK. c) CG117: 1.6.1.5 and 1.6.1.6 Suggest should be reviewed. What is the evidence that a negative mantoux/ Interferon gamma test can adequately rule out latent/active TB in these very young children/ age groups. This does not mirror current practice within paediatric TB- often decided to complete latent treatment for neonates with maternal smear positive contact or for very young children with close smear positive contacts, despite negative testing. d) Also specific comment should be made with regard to contact tracing for index cases that are smear negative but culture positive. e) Evidence for repeat screening especially in young children and immunocompromised.	individual patients. Although the guidance will not address the option of higher doses for achieving adequate treatment levels, it will review the possibility of extending treatment regimens beyond the standard 6 months in certain circumstances (see review question 5.5.1l). b) Although we agree that access to appropriate formulations is central to the management of TB, it is not within NICE's remit to assess issues relating to the availability of formulations. c) The CG117 review areas relating to the diagnosis of latent TB that have been identified as requiring an update is paediatric diagnosis of latent TB, diagnosis of latent TB in people who are immunocompromised or at known risk of immunosuppression, and diagnosis of latent TB in new entrants from high incidence countries. Therefore, a new topic has been included under 5.3.1, 'key issues that will be covered': "h) Diagnosis of latent TB infection using Mantoux testing and interferon-gamma release assays in: • children • people who are immunocompromised, such as people with HIV or renal disease, or at known risk of immunosuppression, such as people about to start immunosuppressive regimens • new entrants from high incidence countries, in the context of opportunistic case-finding rather than proactive screening programmes." The reviews for the diagnosis of latent TB in adults will

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					not be updated. d) Contact-tracing will be reviewed in terms of how latent TB should be diagnosed. The groups that will be covered are discussed in the response above c). Additionally, a review of effective and cost effective models for the delivery and configuration of TB services will be developed using the CCPs interim methods for developing service guidance. Where evidence is available, a subgroup of the GDG will consider who should carry out contact tracing and when this should be done, but a full evaluation on the organisation of contact tracing activities is outside the scope of the guidance. Any recommendations made by the subgroup will be ratified by the GDG. e) Repeat screening will be included in the protocol for the updated paediatric reviews for diagnosing latent TB. However, it should be noted that this will be subject to confirmation by the Guideline Development Group, who will consider the appropriateness of the proposed review protocols at their first meeting.
30.	SH	Children's HIV Association	5.3.2b	Review of evidence for current recommendations: Contact tracing / screening for smear negative, culture positive index case within household. This is not specifically mentioned in guidance put young children are at greater risk of active/latent TB infection following this contact, as are children and adults who are immunocompromised. No specific recommendation for these circumstances.	Thank you for your comment. Contact-tracing will be reviewed in terms of how latent TB should be diagnosed. We feel that the CG117 evidence reviews for diagnosing latent TB in adults are still relevant and that the new evidence in this area would not change the current recommendations. The CG117 review areas relating to the diagnosis of latent TB that have been identified as requiring an update is paediatric diagnosis of latent TB, diagnosis

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				Review of evidence should be included for this.	of latent TB in people who are immunocompromised or at known risk of immunosuppression, and diagnosis of latent TB in new entrants from high incidence countries. Therefore, a new topic has been included under 5.3.1, 'key issues that will be covered': "h) Diagnosis of latent TB infection using Mantoux testing and interferon-gamma release assays in: • children • people who are immunocompromised, such as people with HIV or renal disease, or at known risk of immunosuppression, such as people about to start immunosuppressive regimens • new entrants from high incidence countries, in the context of opportunistic case-finding rather than proactive screening programmes." The reviews for the diagnosis of latent TB in adults will not be updated. Additionally, a review of effective and cost effective models for the delivery and configuration of TB services will be developed using the CCPs interim methods for developing service guidance. Where evidence is available, a subgroup of the GDG will consider who should carry out contact tracing and when this should be done, but a full evaluation on the organisation of contact tracing activities is outside the scope of the guidance. Any recommendations made by the subgroup will be ratified by the GDG.
31.	SH	Children's HIV Association	5.4	All areas that are covered in section 5.4 should specifically comment on the paediatric population and be based on evidence in	Thank you for your comment. Almost all review areas that will be covered by the Centre for Clinical Practice's methodology (see

No	Type	Stakeholder	Section No	Comments	Developer's Response
				children: eg diagnosis, treatment etc.	sections 5.3.1a to i) will include children and young people as a subpopulation of interest. This means that, where possible, paediatric evidence will be considered in isolation from the evidence base for adults. Review areas covered by the Centre for Public Health Excellence will also include children and young people, however the extent to which it will be possible for the GDG to make recommendations in this area will depend on the available evidence. Additionally, it should be noted that these inclusions will be subject to confirmation by the Guideline Development Group, who will consider the appropriateness of the proposed review protocols at their first meeting.
32.	SH	Children's HIV Association	Any other comments	General: The guideline seeks to act as both adult and paediatric guideline. Usefulness of diagnostic tests/ approaches to screening and treatment in children need to be based on paediatric evidence base. The paediatric focus of the guidance is split between various sections and could usefully be made more easily accessible to paediatricians and those dealing with children	Thank you for your comment. Almost all review areas that will be covered by the Centre for Clinical Practice's methodology (see sections 5.3.1a to i) will include children and young people as a subpopulation of interest. This means that, where possible, paediatric evidence will be considered in isolation from the evidence base for adults. Review areas covered by the Centre for Public Health Excellence will also include children and young people, however the extent to which it will be possible for the GDG to make recommendations in this area will depend on the available evidence. Additionally, it should be noted that these inclusions will be subject to confirmation by the Guideline Development Group, who will consider the appropriateness of the proposed review protocols at

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					their first meeting.
33.	SH	CPHVA	5.4 Are the outcomes in section 5.4 appropriate and correct?	Under 'g' 'education awareness and support', please add voluntary groups as well as 'relevant staff'	Thank you for your comment. We consider that 'relevant staff' covers voluntary groups and this level of additional detail will not be added to the scope.
34.	SH	Department of Health	5.2	Yes	Thank you for your comment.
35.	SH	Department of Health	5.3.2	There should be an update evidence review on the diagnosis of latent infection as the Department of Health are currently exploring the effectiveness of latent screening where there is a high incidence of tuberculosis. A review would help in assessing the effectiveness of latent tuberculosis screening.	Thank you for your comment. We feel that the CG117 evidence reviews for diagnosing latent TB in adults are still relevant and that the new evidence in this area would not change the current recommendations. The CG117 review areas relating to the diagnosis of latent TB that have been identified as requiring an update is paediatric diagnosis of latent TB, and diagnosis of latent TB in new entrants from high incidence countries. In addition to this, two new populations of interest have been highlighted: people with renal disease and people about to start immunosuppressive regimens. A new topic has been included under 5.3.1, 'key issues that will be covered': "h) Diagnosis of latent TB infection using Mantoux testing and interferon-gamma release assays in: • children • people who are immunocompromised, such as people with HIV or renal disease, or at known risk of immunosuppression, such as people

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					about to start immunosuppressive regimens • new entrants from high incidence countries, in the context of opportunistic case-finding rather than proactive screening programmes." The reviews for the diagnosis of latent TB in adults will not be updated.
36.	SH	Department of Health	5.3.2	Service models should be looked at in order to develop a better understanding of commissioning of tuberculosis services, hence providing advice to clinicians and Public Health staff in a wide range of settings.	Thank you for your comment. A review of effective and cost effective models for the delivery and configuration of TB services will be developed using the CCPs interim methods for developing service guidance, and will be presented to a subgroup of the GDG for consideration and ratified by the GDG. The review will cover service delivery across the care pathway, where evidence is available. The CCPs interim methods for service guidance will be available on the NICE website at http://publications.nice.org.uk/pmg8
37.	SH	Department of Health	5.3.2 Does contact tracing for latent TB need to be reviewed?	Yes	Thank you for your comment. Contact-tracing will be reviewed in terms of how latent TB should be diagnosed. We feel that the CG117 evidence reviews for diagnosing latent TB in adults are still relevant and that the new evidence in this area would not change the current recommendations. The CG117 review areas relating to the diagnosis of latent TB that have been identified as requiring an update is paediatric diagnosis of latent TB, diagnosis of latent TB in people who are immunocompromised or at known risk of immunosuppression, and diagnosis

No	Type	Stakeholder	Section No	Comments	Developer's Response
					of latent TB in new entrants from high incidence countries. Therefore, a new topic has been included under 5.3.1, 'key issues that will be covered': "h) Diagnosis of latent TB infection using Mantoux testing and interferon-gamma release assays in: • children • people who are immunocompromised, such as people with HIV or renal disease, or at known risk of immunosuppression, such as people about to start immunosuppressive regimens • new entrants from high incidence countries, in the context of opportunistic case-finding rather than proactive screening programmes." The reviews for the diagnosis of latent TB in adults will not be updated. Additionally, a review of effective and cost effective models for the delivery and configuration of TB services will be developed using the CCPs interim methods for developing service guidance. Where evidence is available, the GDG subgroup will consider who should carry out contact tracing and when this should be done, but a full evaluation on the organisation of contact tracing activities is outside the scope of the guidance.
38.	SH	Department of Health	5.3.2 Should NICE consider the configuration and	yes	Thank you for your comment. A review of effective and cost effective models for the delivery and configuration of TB services will be developed using the CCPs interim methods for developing service guidance, and will be presented to a subgroup of the GDG for consideration. The CCPs

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			delivery of broader public health, clinical or all TB services as part of this update?		interim methods for service guidance will be available on the NICE website at http://publications.nice.org.uk/pmg8
39.	SH	Department of Health	5.4 Are the outcomes in section 5.4 appropriate and correct?	yes	Thank you for your comment.
40.	SH	Department of Health	5.3.2 Does contact tracing for active TB need to be reviewed?	Yes	Thank you for your comment.
41.	SH	Homerton University Hospital	5.1.1b	Groups with high risk of MDRTB (but included later as 5.5.1.r) and s)	Thank you for your comment. 5.1.1a to c states that this guidance will cover all adults, young people and children who have or are suspected to have active or latent TB, or are at an increased risk of infection with Mycobacterium tuberculosis complex. 5.1.1e has been added to reflect that these will be considered in terms of both drug susceptible and drug resistant strains of Mycobacterium tuberculosis complex.

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					Which groups are at an increased risk of drug resistant-TB will be investigated under review question 5.5.1s: "In people with suspected or confirmed active TB, which relative risk factors are associated with a higher level of: (i) multidrug resistance, or (ii) any drug resistance?"
42.	SH	Homerton University Hospital	5.1.2	No	Thank you for your comment.
43.	SH	Homerton University Hospital	5.2	Community settings should include both hostels for the homeless and local hotspots for TB defined by geographical mapping	Thank you for your comment. As there many important settings in which activities relating to the prevention, identification and management of TB are received, provided or commissioned, section 5.2 has now been amended to state: "Any setting in which NHS or public health services for TB are received, provided or commissioned in the public, private and voluntary sectors." This includes hostels for the homeless, where appropriate.
44.	SH	Homerton University Hospital	5.3.2	a) Monitoring of treatment: this should include action to take when no improvement observed at 2 months and the need to confirm cure of culture-positive pulmonary TB at the end of treatment. The recent knowledge about the variability of drug levels should incorporate guidance for HPAs in terms of giving the MICs and how/when to measure drug levels. Our aim must be to prevent MDRTB arising.	Thank you for your comment. a) The reviewer will insert 'no improvement observed at 2 months of treatment' and 'persistence of a positive culture result at the end of treatment' as possible risk factors for drug resistance into the protocol for review question 5.5.1s. However, it should be noted that this will be subject to confirmation by the Guideline Development Group, who will consider the appropriateness of the proposed review protocols at

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				b) We should also include evidence regarding the restarting of TB treatment after drug-induced hepatitis in a) alcoholics, where LFTs may have been abnormal because of a binge and b) true drug-induced hepatitis. Again the aim is to prevent monotherapy for any significant duration which could facilitate drug resistance developing (see 5.5.1.bb). [These could be included under section 5.4.b]	their first meeting. b) The restarting of treatment after a treatment interruption will be considered in review question 5.5.1z: "For people receiving drug treatment for active TB who experience treatment interruptions, what approach to re-establishing appropriate treatment is the most effective in reducing mortality and morbidity?" The examples of drug-induced hepatitis in alcoholics and true drug-induced hepatitis will be included by the reviewer in the protocol for this question. Again, it should be noted that this will be subject to confirmation by the Guideline Development Group, who will consider the appropriateness of the proposed review protocols at their first meeting.
45.	SH	Homerton University Hospital	5.4 Are the outcomes in section 5.4 appropriate and correct?	a) Infection control should include comments on coughing behaviour (so-called cough hygiene). b) The distinction between transmissibility of TB from HIV negative to HIV-coinfected should be recorded. c) The value of recording doses taken to assess adherence could be usefully included as an adjunct to self-administered treatment.	Thank you for your comment. a) The reviewer will include cough hygiene as a measure of interest in the protocol for review questions 5.5.1aa to cc. However, it should be noted that this is subject to confirmation by the Guideline Development Group, who will consider the appropriateness of the proposed review protocols at their first meeting. b) We agree that the risk of infection with TB may be different for people with HIV compared to people without HIV. They will be included as a subpopulation of interest in the protocols for review questions

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					5.5.1aa to dd. Again, it should be noted that the review questions will be subject to confirmation by the Guideline Development Group, who will consider the appropriateness of the proposed review protocols at their first meeting. c) As outlined in section 5.5.2 a review of evidence for interventions and strategies to promote the uptake and adherence to treatment for active and latent TB will be carried out to inform the guidance. Section 5.4 of the scope lists only the key outcomes and is not intended to be an exhaustive list. The detail suggested by the consultee will therefore not be added to section 5.4 of the scope, but where relevant evidence is identified, the value of recording doses taken to assess adherence will be considered by the GDG.
46.	SH	London TB workforce group	5.1.1b	a) On section 5.1.1c: to clarify that increased risk of infection and disease progression could be due to both medical conditions and social risk factors, including diabetes. b) Anti TB Treatment dosage (rifampicin) of drug users on methadone would be different and review of evidence on optimal treatment would be useful.	Thank you for your comment. a) 5.1.1c has not specified that an 'increased risk' can stem only from medical conditions or from social risk factors. Instead, the population in 5.1.1c has been left broad to permit the Guideline Development Group to consider people at an increased risk of infection and/or at increased risk of progressing to the active disease from a range of perspectives. These will be defined by the reviewers and the Guideline Development Group during the development of the evidence reviews. b) We acknowledge that drug users receiving methadone may be a subgroup for whom the management of TB may vary. We feel that this is

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					reflected by the 3rd bullet point of 5.1.1d: "people with HIV and other comorbidities or conditions that impact on the diagnosis and management of TB" This group will be included as a population of interest in the protocol for review question 5.5.1k: "What comorbidities or conditions affect the choice of regimen for the treatment of active TB? How should the standard recommended regimen be adapted to accommodate these comorbidities or conditions?" However, it should be noted that this is subject to confirmation by the Guideline Development Group, who will consider the appropriateness of the proposed review protocols at their first meeting.
47.	SH	London TB workforce group	5.2	This section is rather ambiguous. For example, community setting would include the specific settings would include educational and community-based centres. It is not clear what national and regional public health centres are referring to, and need clarification to what is meant by this.	Thank you for your comment. We recognise that this section is very broad. However, as there many important settings in which activities relating to the prevention, identification and management of TB are received, provided or commissioned, section 5.2 has now states: "Any setting in which NHS or public health services for TB are received, provided or commissioned in the public, private and voluntary sectors."
48.	SH	London TB workforce group	5.3.2	a) 5.3.2d: a review of reliability of an IGRA test after Mantoux should be reviewed as it may result in false positive result. With new evidence on IGRA tests, there should be better evidence-based guidelines that can be used by the commissioning bodies. It would be useful to review the evidence on the most appropriate test for various age groups, e.g. <5 or >35. The cut off point for	Thank you for your comment. a) We feel that the CG117 evidence reviews for diagnosing latent TB in adults are still relevant and that the new evidence in this area would not change the current recommendations. The CG117 review areas relating to the diagnosis of latent TB that have been identified as requiring an update is paediatric

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				diagnosing and treating latent infection is currently 35, but it there are differing practices in different countries (and different clinics in the UK). It would be useful to review the evidence. b) International guidance for long-haul air travel exists, but not for other forms of long-distance travels such as coaches (e.g. international routes). c) In light of data available from TB Cohort Reviews it would be useful to review cost-effectiveness of household contacts of non-pulmonary cases and comparing them too to other contact groups, e.g. new entrants screening or incident contacts. d) There is a need for further guidance on universal HIV screening at TB clinics for all suspected or diagnosed cases, irrespective of age. e) New Entrant screening and the threshold for high incidence countries, i.e. 40/100,000 should be reviewed in light of new evidence. f) Clearer infection control guidelines in community and healthcare setting, in particular in relation to MDR and XDR TB would be appreciated. Isolation of patients,	diagnosis of latent TB, and diagnosis of latent TB in new entrants from high incidence countries. In addition to this, two new populations of interest have been highlighted: people with renal disease and people about to start immunosuppressive regimens. Therefore, a new topic has been included under 5.3.1, 'key issues that will be covered': "h) Diagnosis of latent TB infection using Mantoux testing and interferon-gamma release assays in: • children • people who are immunocompromised, such as people with HIV or renal disease, or at known risk of immunosuppression, such as people about to start immunosuppressive regimens • new entrants from high incidence countries, in the context of opportunistic case-finding rather than proactive screening programmes." The reviews for the diagnosis of latent TB in adults will not be updated. b) We feel that this represents a small proportion of the overall amount of transmission. This, in conjunction with the scarcity of evidence in this area, means that a review of this issue would not add as much value to efforts to control the spread of TB as other review areas, such as the infection control measures or the optimum regimen for treating latent TB infection. Therefore, although we agree that long-distance travel, such as by coach, may play a role in the transmission of TB, it is not considered a priority for review in the new guidance.

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				de-isolation and discharging criteria from hospital need clearer guidance. g) Some aspects of service model will benefit from a review by the NICE, including ratio of patient to nurse/physician/admin/outreach worker and the role of MDT meetings in case management. h) Boundaries for calculating TB rates, in relation to BCG vaccination, e.g. local authority level or the whole town/city/metropolis.	c) Although we agree that this may be useful in the organisation of TB screening services, it is not considered a priority for review in the new guidance. d) Although NICE acknowledges that the identification of HIV in patients with TB is important, its explicit inclusion in the scope falls outside the remit provided by the Department of Health. This guidance is concerned with the prevention, identification and management of tuberculosis, not with the identification of HIV. e) The diagnosis of latent TB among new entrants from high incidence countries is now included under 5.3.1h: "Diagnosis of latent TB infection using Mantoux testing and interferon-gamma release assays in: • children • people who are immunocompromised, such as people with HIV or renal disease, or at known risk of immunosuppression, such as people about to start immunosuppressive regimens • new entrants from high incidence countries, in the context of opportunistic case-finding rather than proactive screening programmes." Specifically, it will be undergo a clinical- and cost-effectiveness review under review question 5.5.1gg: "Which diagnostic strategy is most effective in

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					establishing an accurate diagnosis of latent TB in people who are recent arrivals from countries with a high incidence of TB?" f) Infection control, including for instances in which MDR-TB is suspected, will be covered by review questions 5.5.1aa to dd. The isolation of patients, including the necessary period of isolation, will also be addressed in review questions 5.5.1aa to dd. g) A review of effective and cost effective models for the delivery and configuration of TB services will be developed using the CCPs interim methods for developing service guidance, and will be presented to the GDG for consideration. The review will cover service delivery across the care pathway, where evidence is available. The CCPs interim methods for service guidance are available on the NICE website at http://publications.nice.org.uk/pmg8 h) Calculating boundaries for TB rates, as requested by the consultee, will not be addressed by a specific research question on BCG vaccination in the scope. However, if there is evidence available when we review the area of BCG vaccination uptake, the GDG will consider it.
49.	SH	London TB workforce group	5.4	Treatment for latent infection.	Thank you for your comment.

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50.	SH	National Treatment Agency for Substance Misuse (NTA)	5.4 Are the outcomes in section 5.4 appropriate and correct?	these outcomes appear appropriate	Thank you for your comment.
51.	SH	National Treatment Agency for Substance Misuse (NTA)	Addition to 5.1.1 d	We suggest adding 'people with substance misuse problems' and 'homeless people' to the list of subgroups. The Health Protection Agency has identified these groups as being at increased risk of contracting TB. Some people who are receiving TB treatment will also be receiving treatment or assistance for their substance misuse problems	Thank you for your comment. Section 5.1.1d gives examples of key subgroups for whom the diagnosis and management of TB may vary, but it should be noted that special consideration in the evidence reviews and discussions of the Guideline Development Group will not necessarily be limited to the groups listed in this section of the scope. The Guideline Development Group may choose to highlight a certain subgroup for special consideration if that group is known to be managed differently from other groups, and therefore may require recommendations unique to their situation or characteristics.
52.	SH	National Treatment Agency for Substance Misuse (NTA)	Any other comments	*5.3.1 n)* The NTA agrees that ensuring support for those receiving TB treatment is delivered from treatment start to treatment completion is important. In the case of those also receiving treatment or help for substance misuse, liaison with the local substance misuse treatment sector will likely be important in ensuring that TB treatment is completed. We suggest this point could be made more specifically in the draft scope.	Thank you for your comment. The scope is not intended to be exhaustive in detail and the detail requested by the consultee will not be added to the scope. Where relevant evidence on multi-intervention approaches is identified it will be considered by the GDG.
53.	Ices	NHS	5.1.1b	Transient workers within communities that	Thank you for your comment.

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	SH	Wiltshire		potentially from high risk countries (Indian restaurants) (Not sure this sits here)	The scope for this guidance will cover all adults, young people and children who have or are suspected to have active or latent TB, or are at an increased risk of infection with Mycobacterium tuberculosis complex (see sections 5.1.1a to c). We feel that this includes transient workers who may be from countries with a high rate of TB incidence and prevalence.
54.	SH	NHS Wiltshire	5.2	Should we consider shelters for homeless people? (Again, I am not sure this sits here)	Thank you for your comment. As there many important settings in which activities relating to the prevention, identification and management of TB are received, provided or commissioned, section 5.2 has now been amended to state: "Any setting in which NHS or public health services for TB are received, provided or commissioned in the public, private and voluntary sectors." This includes shelters for homeless people, where appropriate.
55.	SH	NHS Wiltshire	5.3.2	Yes Public Health is significant in controlling and ensuring the services are in place	Thank you for your comment.
56.	SH	North Central London TB Network	3	Background - Activities….need to include raising awareness in non public health settings	Thank you for your comment. Section 3, 'Background', within the scope is intended to provide a summary of the context for the guidance. We feel that 'raising awareness in non-public health settings' is covered within the setting described within section 5.2: "Any setting in which NHS or public health services for TB are received, provided or commissioned in the public, private and voluntary sectors."
57.	SH	North	4.1 a	Need for guidance - The last phrase is for the	Thank you for your comment.

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		Central London TB Network		UK but in London the percentage is less and it would be useful to put in a phrase that more properly reflects the differences across the Boroughs and BME communities as increased levels of non pulmonary TB can lead to delays in diagnosis etc	We agree that it is important for us to consider the variations in the epidemiology of TB across geographical regions and amongst people from different ethnic and socioeconomic backgrounds. However, we feel that this has been captured in 4.1e and f of the scope. Because the guidance will cover the whole of England and Wales, and because this section is intended only as a summary, it was felt that noting the significance of urban areas more generally (see 4.1f) was more appropriate than highlighting a particular city.
58.	SH	North Central London TB Network	4.1 c	Almost all cases of TB…. Add in percentages of active TB and latent TB progression?	Thank you for your comment. Section 4.1 is only intended to provide a brief summary of the need for the guidance. However, in section 4.1d we have included the following relevant information: "People infected with TB bacteria subsequently have a lifetime risk of progressing to active respiratory TB of about 10%, with the highest risk falling in the first few years after infection. The risk of progressing to the active disease can be much higher in groups such as children, older people, people who are immunocompromised, and people with chronic poor health. For example, people who are co-infected with HIV and TB that are not treated are 21 to 34 times more likely to develop active TB; this risk is lower in those receiving antiretroviral therapy."
59.	SH	North Central London TB Network	4.1 e	In England, rates of TB…. Using a comparison of 2011 with 2010 is misleading and it might be more useful to use a rolling 3 year average as HPA do for some of their work or how the TB rates/notification numbers have changed	Thank you for your comment. The comparison is now made against the incidence rate in 2001.

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				over the last 5 or 10 years.	
60.	SH	North Central London TB Network	4.1 h	According to the HPA strains of TB …. A (large) proportion of MDRTB is likely to be imported – can this be reflected in the wording?	Thank you for your comment. Section 4.1 is only intended to provide a brief summary of the need for the guidance. However, a new bullet point (4.1j) has been added to indicate the groups in which MDR-TB is most commonly found, including people born outside of the UK: "Drug resistant TB is most commonly found in people born outside of the UK and in those with social risk factors for TB, including a history of substance misuse, homelessness and a history of imprisonment." Currently, it cannot be definitively concluded whether the TB found in people born abroad was 'imported' or whether transmission occurred whilst in the UK; this is reflected in terminology used.
61.	SH	North Central London TB Network	4.1 i	In 2011, there were increases… See 4.1 e. It is the overall trend that is important as a single year can be an outlier for many reasons or reflective of the overall trend.	Thank you for your comment. The comparison is now made against the incidence rate in 2001.
62.	SH	North Central London TB Network	4.2 f -	a) "people with evidence of scarring caused by TB, as shown on a chest x-ray, but who were not adequately treated" The scope suggests that this group should be offered treatment for latent TB infection. Is there an age limit associated with this? It is hard to determine whether this only applies to those 35 years or younger or all ages. b) ? include 'immunosuppressive treatment regimens' as this is an increasing	Thank you for your comment. Section 4.2 represents a short summary of current practice in the prevention, identification and management of TB. Bullets 4.2b to g reflect current best practice, as recommended by NICE clinical guideline 117 ('Tuberculosis: clinical diagnosis and management of tuberculosis, and measures for its prevention and control'). a) According to recommendation 1.6.1.1, there is no

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				workload/patient issue. relates to section 5	age limit restricting which people within this group ("people with evidence of scarring caused by TB, as shown on a chest x-ray, but who were not adequately treated") should receive treatment for latent TB. It should be noted, however, that the new guidance will update this part of CG117 b) Since this population was not explicitly considered in CG117, it has not been included section 4.2. However, since people about to start immunosuppressive regimens who have latent TB are believed to be at particular risk of progressing to active disease, we agree they are an important subpopulation to include. Although we do not explicitly note them in section 5.1.1 ('Groups that will be covered'), we feel they are included under bullet c): "Adults, young people and children at increased risk of infection with Mycobacterium tuberculosis complex and/or at increased risk of progressing to the active disease." The diagnosis of latent TB in people on/about to start immunosuppressive regimens will be explicitly covered in review question 5.5.1ff: "Which diagnostic strategy is most effective in establishing an accurate diagnosis of latent TB in people who are immunocompromised or at risk from immunosuppression?" People on/about to start immunosuppressive regimens will also be included by the reviewer in the protocol for review questions 5.5.1hh (according to their risk factors, which people with latent TB should

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					receive treatment?) and 5.51ii (which treatment regimen is best for treating latent TB?) as populations of interest. It should be noted that this will be subject to confirmation by the Guideline Development Group, who will consider the appropriateness of the proposed review protocols at their first meeting.
63.	SH	North Central London TB Network	5.1 d	Consideration will be given…. Add a 4th bullet point to include 'people on immunosuppressive treatment regimens'	Thank you for your comment. Since people on or about to start immunosuppressive regimens who have latent TB are believed to be at particular risk of progressing to active disease, we agree they are an important subpopulation to include. Although we do not explicitly note them in section 5.1.1 ('Groups that will be covered'), we feel they are included under bullet c): "Adults, young people and children at increased risk of infection with Mycobacterium tuberculosis complex and/or at increased risk of progressing to the active disease." The diagnosis of latent TB in people on/about to start immunosuppressive regimens will be explicitly covered in review question 5.5.1ff: "Which diagnostic strategy is most effective in establishing an accurate diagnosis of latent TB in people who are immunocompromised or at risk from immunosuppression?" People on/about to start immunosuppressive regimens will also be included by the reviewer in the protocol for review questions 5.5.1hh (according to their risk factors, which people with latent TB should receive treatment?) and 5.51ii (which treatment

No	Type	Stakeholder	Section No	Comments	Developer's Response
					regimen is best for treating latent TB?) as populations of interest. It should be noted that this will be subject to confirmation by the Guideline Development Group, who will consider the appropriateness of the proposed review protocols at their first meeting.
64.	SH	North Central London TB Network	5.1.1b	See 5.1.d	Thank you for your comment.
65.	SH	North Central London TB Network	5.2	Add in hostels or support for the homeless as *community settings* does not always cover those specifically.	Thank you for your comment. As there many important settings in which activities relating to the prevention, identification and management of TB are received, provided or commissioned, section 5.2 has now been amended to state: "Any setting in which NHS or public health services for TB are received, provided or commissioned in the public, private and voluntary sectors." This includes hostels for the homeless, where appropriate.
66.	SH	North Central London TB Network	5.3.1 m	Areas not in the original guideline… Not sure if this was in the original guideline. ? add in 'key staff groups i.e. A&E, GPs who TB patients often have initial health care professional contact.	Thank you for your comment. During the development of CG117 the GDG made some suggestions on communication and patient information and these are included at section 4.2 of CG117. For this update, the evidence that will be reviewed to inform recommendations on educating and raising awareness of TB will cover the general population with a focus on specific subgroups. It is NICE's intention that key staff groups, as suggested by the consultee, will be discussed by the GDG and

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					provided relevant evidence is available, recommendations will be made in this area. However, the text suggested by the consultee is too detailed for inclusion at section 5.3.1m of the scope so it will not be changed.
67.	SH	North Central London TB Network	5.3.2	a) Recognition of the move to use IGRA in situations where CG117 currently recommends Mantoux first and then IGRA. b) Contact tracing – has improved since cohort review implemented and need to look at the reports from cohort review specifically on contact tracing. c) Service models where there has been significant improvement in TB notifications i.e. continuation of universal BCG when TB rates have gone below 40/100,000 or implementation of universal BCG, where TB rates are below 40/100,000, is pragmatic in areas which border high incidence areas or service provision is different to the usual TB service provision. This would need to be underpinned by knowledge of how local demographic changes may have also influenced TB rates.	Thank you for your comment. a) We feel that the CG117 evidence reviews for diagnosing latent TB in adults are still relevant and that the new evidence in this area would not change the current recommendations. The CG117 review areas relating to the diagnosis of latent TB that have been identified as requiring an update is paediatric diagnosis of latent TB, and diagnosis of latent TB in new entrants from high incidence countries. In addition to this, two new populations of interest have been highlighted: people with renal disease and people about to start immunosuppressive regimens. Therefore, a new topic has been included under 5.3.1, 'key issues that will be covered': "h)Diagnosis of latent TB infection using Mantoux testing and interferon-gamma release assays in: • children • people who are immunocompromised, such as people with HIV or renal disease, or at known risk of immunosuppression, such as people about to start immunosuppressive regimens • new entrants from high incidence countries, in the context of opportunistic case-finding rather than proactive screening programmes."

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					The reviews for the diagnosis of latent TB in adults will not be updated. b) Cohort review was considered in PH37, 'Identifying and managing tuberculosis among hard-to-reach groups' (see recommendation 3). It is our aim that PH37 be incorporated into the updated guidance, if appropriate. Given that PH37's recommendation on cohort review advises that "those participating in a cohort review should review the results and evaluate local services", we feel that the role of cohort review in organising contact-tracing activities has been covered. Additionally, since PH37 was only published in March 2012, updating its reviews and recommendation is not considered a priority in the new guidance. c) A review of effective and cost effective models for the delivery and configuration of TB services will be developed using the CCPs interim methods for developing service guidance. This will be presented to a subgroup of the GDG for consideration, with any recommendations ratified by the GDG. The review will cover service delivery across the care pathway, where evidence is available. However, guidance on the provision of population level BCG vaccination falls within the remit of the Joint Committee of Vaccination and Immunisation (JCVI). The CCPs interim methods for service guidance will be available on the NICE website at http://publications.nice.org.uk/pmg8

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68.	SH	North Central London TB Network	5.3.2 d	Diagnosis of latent infection using Mantoux testing and interferon-gamma testing…. Comment 1 The current guidance is not clear or specific regarding assessment prior to the use of anti-TNF therapy. Will the updated guidance deal with this in particular? Comment 2 Apply comment 1 to immunosuppressive treatment regimens	Thank you for your comment. Since people about to start immunosuppressive regimens who have latent TB are believed to be at particular risk of progressing to active disease, we agree they are an important subpopulation to include. Although we do not explicitly note them in section 5.1.1 ('Groups that will be covered'), we feel they are included under bullet c): "Adults, young people and children at increased risk of infection with Mycobacterium tuberculosis complex and/or at increased risk of progressing to the active disease." The diagnosis of latent TB in people on/about to start immunosuppressive regimens will be explicitly covered in review question 5.5.1ff: "Which diagnostic strategy is most effective in establishing an accurate diagnosis of latent TB in people who are immunocompromised or at risk from immunosuppression?" People on/about to start immunosuppressive regimens will also be included by the reviewer in the protocol for review questions 5.5.1hh (according to their risk factors, which people with latent TB should receive treatment?) and 5.51ii (which treatment regimen is best for treating latent TB?) as populations of interest. It should be noted that this will be subject to confirmation by the Guideline Development Group, who will consider the appropriateness of the proposed review protocols at their first meeting.
69.	SH	North	5.4 Are the	Relate to the 2004 National TB Action Plan	Thank you for your comment.

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		Central London TB Network	outcomes in section 5.4 appropriate and correct?	actions	
70.	SH	North Central London TB Network	5.4 c	Infection control - another group to be considered here are people with latent TB infection and those who may get re-infected after LTBI treatment	Thank you for your comment. Latent TB is not thought to be infectious. Therefore, the implementation of infection control measures – such as the wearing of masks or isolation in negative pressure rooms – following a diagnosis of latent TB is not considered a priority for review in the new guidance.
71.	SH	North Central London TB Network	5.4 d	bullet point *"other measures of adherence"* Comment 1 Suggest NICE include within their examples not only pill counting and blood tests but also urine assessment? The request is made as this is an area that is very poorly assessed and where there is wide practice pattern variation at present. Comment 2 Add in 'dosette' boxes and there are now smart tablet bottle available which send a signal when they have been opened Comment 3 DOT including Virtual Observed Therapy (VOT) as being used by the London TB Find and Treat team	Thank you for your comment. Section 5.4 of the scope is intended to list the key outcomes only; it is not an exhaustive list. Where data on relevant outcomes are identified, these will be presented to the GDG. The scope will not be changed.
72.	SH	North	5.5.1 m, n	Draft review questions - Can NICE please	Thank you for your comment.

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		Central London TB Network		clarify if areas within the "draft review questions" need to be included for both respiratory and non-respiratory disease. This is in particular with regard to bullet point number n, as it would be surprising if most clinicians currently consider surgery for drug sensitive pulmonary tuberculosis, given the excellent results associated with appropriate anti-microbial therapy.	The population of interest is covered within the review questions. Review questions 5.5.1m and n (now 5.5.1 n and o) refer to active, drug susceptible respiratory TB.
73.	SH	North Central London TB Network	5.5.1 v	Treatment of drug resistant TB - In addition to what is currently stated, suggest that NICE should also look at monitoring for, and prevention of, adverse events associated with medication used to treat drug resistant tuberculosis e.g. renal and ototoxicity associated with long term aminoglycoside usage.	Thank you for your comment. The Summary of Product Characteristics and British National Formulary include details on the monitoring of adverse effects that should be conducted for a particular drug formulation. NICE urges prescribers to use this information to guide decisions regarding the monitoring of a patient's response to treatment. However, it is also noted that the adverse effects of tuberculosis treatment regimens are a major source of non-adherence to treatment, and that detecting and swiftly managing these side effects may improve adherence to treatment. This issue will be included in the review of adherence to treatment for active and latent TB, where the available evidence on a range of interventions and approaches that support or prohibit treatment completion will be identified and assessed.
74.	SH	North Central London TB Network	5.5.1 x	Management of and referral for drug resistant TB - The section on routes of referral for drug resistant tuberculosis is sensible and to be welcomed, though sounds like service organisation and delivery. The previous rubric had suggested that this was beyond the scope of the NICE guidelines. Can this be clarified	Thank you for your comment. Section 5.5.1 of the scope has been updated to remove specific reference to referrals for drug resistant TB, separate to service delivery. Where evidence is available, referral for drug resistant TB will be considered by the GDG subgroup.

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				please?	
75.	SH	North Central London TB Network	Whole scope	Commissioning - Given the changes in NHS commissioning and potentially service delivery, will NICE also focus on some aspects of TB commissioning or seek to avoid discussion of this area as commissioners are in key to ensuring delivery of guidelines?	Thank you for your comment. A review of effective and cost effective models for the delivery and configuration of TB services will be developed using the CCPs interim methods for developing service guidance, and will be presented to a subgroup of the GDG for consideration. Any recommendations made by the subgroup will be ratified by the GDG. This aspect of the guidance will be of particular interest to those involved in commissioning TB services – for more information about the interim approach to this aspect of the guidance and what it will cover see http://publications.nice.org.uk/pmg8
76.	SH	North Central London TB Network	Whole scope	Other guidelines - Will NICE be using this opportunity to bring in the NICE Public Health guidelines for the hard to reach, PH37 and the RCN case management and cohort review guidance to ensure a joined up approach along integrated care path?	Thank you for your comment. We anticipate that the recommendations from PH37 will be incorporated with the new guidance.
77.	SH	Oxford Immunotec	5.1	5.1.1.b Adults, young people and children who have an increased risk of latent infection with *Mycobacterium tuberculosis* complex, but not clinical disease.	Thank you for your comment. 5.1.1b refers explicitly to those who have been identified as having latent TB infection. Those who are at an increased risk of infection, but who may not actually be infected, are included under 5.1.1c: "Adults, young people and children at increased risk of infection with Mycobacterium tuberculosis complex and/or at increased risk of progressing to the active disease." This group are of particular importance in

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					protection/prevention activities.
78.	SH	Oxford Immunotec	5.2	The section describing the treatment of LTBI should not be limited to isoniazid and rifampicin. The use of short course therapy including rifapentine should be discussed.	Thank you for your comment. Whilst we note that short course therapy with rifapentine appears to be promising, rifapentine is not licensed in the UK. Therefore this guidance will not be able to make recommendations on its use. If studies comparing rifapentine regimens to regimens of drugs licensed in the UK are available, rifapentine may be included as a comparator in our evidence reviews.
79.	SH	Oxford Immunotec	Any other comments	5.5.1.hh. When determining who should receive treatment for LTBI the current suggested cut-off age (35) for provision of therapy should be reconsidered in light of more accurate tests for LTBI (reducing the likelihood of testing non-infected subjects) and with the advent of new, shorter drug regimens.	Thank you for your comment. The cut-off age for latent TB treatment of 35 years was based upon the belief that there is an increased risk of serious adverse treatment effects in those over 35. This recommendation will undergo review in the new guidance under review question 5.5.1hh: "According to their risk factors, which people with either latent TB infection or in close contact with people who have active TB should receive drug treatment to prevent the development of active TB?" People over the age of 35 will be included as a population of interest in the protocol for review question 5.5.1ii. However, it should be noted that this is subject to confirmation by the Guideline Development Group, who will consider the appropriateness of the proposed review protocols at their first meeting.
80.	SH	Primary care respiratory society	Any other comments	We are very comfortable that the scope is comprehensive and addresses aspects of TB diagnosis and management that are relevant	Thank you for your comment.

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		(PCRS-UK)		to primary care.	
81.	SH	RCGP	5.1.1b	No	Thank you for your comment.
82.		RCGP	5.1.2	No	Thank you for your comment.
83.		RCGP	5.2	Can you specifically include street homeless people with no fixed address and students in university placements who may need care in 2 settings	Thank you for your comment. As there many important settings in which activities relating to the prevention, identification and management of TB are received, provided or commissioned, section 5.2 has now been amended to state: "Any setting in which NHS or public health services for TB are received, provided or commissioned in the public, private and voluntary sectors." This includes street homeless people with no fixed address and students in university placements, where appropriate.
84.	SH	RCGP	5.3.2	The organisation of TB clinics is important. Bothamley (2011) highlights a ratio of 40 notifications or less per TB nurse should be implemented nationally (the current TB control documents do not specify this target). Bothamley et al. Tuberculosis in UK cities: workload and effectiveness of tuberculosis control programmes BMC Public Health 2011, 11:896 http://www.biomedcentral.com/1471-2458/11/896	Thank you for your comment. A review of effective and cost effective models for the delivery and configuration of TB services will be developed using the CCPs interim methods for developing service guidance. This will be presented to a subgroup of the GDG for consideration, with any recommendations ratified by the GDG. The review will cover service delivery across the care pathway, where evidence is available. The CCPs interim methods for service guidance will be available on the NICE website at http://publications.nice.org.uk/pmg8

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				With the reorganisation of the health service from PCTs to CCGs and the incorporation of public health into local authorities some assessment of models of service delivery should be considered to reflect the different needs of different populations	
85.	SH	RCGP	5.4 Are the outcomes in section 5.4 appropriate and correct?	Yes. Can consideration be given to reduce the disruption to people and their families lives of ways of multiple hospital attendances	Thank you for your comment. Section 5.4 of the scope is intended to be a summary of key outcomes, not a definitive list. This additional level of detail will not be added to the scope. Where evidence is available and acceptability of treatment interventions is being discussed by the GDG, the point raised by the consultee will be considered.
86.	SH	TB Alert	5.1	TB Alert is pleased that "adults, young people and children at increased risk of infection" (i.e. communities disproportionately affected by TB) are among the groups that are included in the draft scope and will be covered by the new guidance. Regarding the specific subgroups "for whom the diagnosis and management of TB may vary", TB Alert suggests that *"hard-to-reach" groups, including vulnerable migrants*, be added to this list for consideration when developing the guidance. This is especially relevant as the new guidance will bring together both the clinical and public health elements of the illness. Including "hard-to-reach" groups, including vulnerable migrants, to the subgroups considered will substantiate the recommendations made in PH37 "Identifying and managing tuberculosis among	Thank you for your comment. Hard-to-reach groups, including vulnerable migrants, have not been stated as a subpopulation of interest within 5.1.1d as we do not plan to update the evidence reviews underpinning PH37, 'Identifying and managing tuberculosis among hard-to-reach groups'. We intend for the recommendations from PH37 to be incorporated with the new guidance, if appropriate. Section 5.1.1d gives examples of key subgroups for whom the diagnosis and management of TB may vary, but it should be noted that special consideration in the evidence reviews and discussions of the Guideline Development Group will not necessarily be limited to the groups listed in this section of the scope. The Guideline Development Group may choose to highlight a certain subgroup for special consideration if that group is known to be managed differently from other groups, and therefore may require recommendations unique to their situation or

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				hard-to-reach groups". PH37 recognises that "hard-to-reach" groups are those whose social circumstances, language, culture or lifestyle (or those of their parents or carers) make it difficult to: recognise the clinical onset of TB; access diagnostic and treatment services; self-administer treatment and attend regular appointments for clinical follow-up. This definition includes certain migrant communities as well as newly arrived people and it is therefore imperative that the scope and following guidance recognises the specific needs of these populations. TB Alert would like to stress that within the "hard-to-reach" definition it is vital to consider the distinction between communities and people who are "hard-to-reach" (i.e. find and diagnose) and those who are "hard-to-treat" and therefore for whom management may vary.	characteristics.
87.	SH	TB Alert	5.2	TB Alert is encouraged to see that the scope will consider the delivery of NHS or public health services in community settings. We strongly suggest that the role of Third Sector Organisations (TSOs) working with affected communities in these settings is explored and utilised regarding the support and delivery of services.	Thank you for your comment. As there many important settings in which activities relating to the prevention, identification and management of TB are received, provided or commissioned, section 5.2 has now been amended to state: "Any setting in which NHS or public health services for TB are received, provided or commissioned in the public, private and voluntary sectors."
88.	SH	TB Alert	5.3.2	a) TB Alert is keen that point c) *Monitoring of*	Thank you for your comment.

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				patient response to treatment, and follow-up after treatment completion be removed from the list of issues that will not be considered by the new guidance. In light of the growing issue of drug resistance in the UK, TB Alert believes it is vital to address issues affecting adherence to medication. The significance of adherence is reflected in 5.3.1 of the draft scope that states that *promoting adherence to treatment of active TB, including the effectiveness of DOT, reminder systems and counselling* will be considered. However, we believe that the monitoring of patient response to treatment, especially with regard to their experience of side-effects, is a vital component of promoting adherence that is not included in 5.3.1. TB Alert is aware, through our role in facilitating the TB Action Group (TBAG) - the only TB patient advocacy group in the UK - that side-effects to the medication affect how patients proceed with their treatment regime, regardless of social risk factors identified in PH37. We believe it is important to explore whether closer monitoring of patient response to treatment, and side-effects they experience, could reduce the likelihood of long-term ill health or disability as a result of the medication (including, but not limited to: sight loss, mobility issues, hearing loss/tinnitus, liver or kidney damage). b) Similarly, TB Alert believes that the	a) Most of the points raised by the consultee will be included in the review of evidence on adherence to treatment in active and latent TB, where we will be considering evidence on a range of interventions and approaches that impact on treatment completion and other outcomes. However, it is also important to note that the Summary of Product Characteristics and British National Formulary include details on the monitoring of adverse effects that should be conducted for a particular drug formulation. This should be used to guide decisions regarding the monitoring of a patient's response to treatment. b) Although we agree that the follow-up of patients after treatment completion is important, it is not considered a priority for review in the new guidance. Recommendations from CG117 relating to the follow-up of patients after treatment completion will be incorporated into the new guidance. c) A review of effective and cost effective models for the delivery and configuration of TB services will be developed using the CCPs interim methods for developing service guidance, and will be presented to a subgroup of the GDG for consideration. Where evidence is available, the subgroup will consider who should carry out contact tracing and when this should be done, but a full evaluation of contact tracing is outside the scope of the guidance. d) National screening programmes for TB are not the remit of NICE, and fall under the work of the National

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				development of new guidance, incorporating both the clinical and public health aspects of the illness, provides a unique opportunity to consider the long-term effects of TB, which have previously been over-looked. Therefore the follow-up of patients post-cure is vital not only for the psychological and physical well-being of the individual, but to further understand the familial, social and economic impact of tuberculosis in the UK. c) TB Alert believes it would be beneficial to include an evidence review for contact tracing in the new guidance. In order to improve TB services in the UK, and reduce incidence of the illness, TB Alert believes that it is necessary to review how beneficial and cost effective the contact tracing procedure is as it is currently implemented, with regards to reach, up-take and number of people identified and treated (if appropriate). To this end, it would be useful to explore and make recommendations for how contact tracing for both active and latent TB infection could be improved. For example, TB Alert has received anecdotal feedback from TB Nurses regarding the difficultly in accessing "hard-to-reach" groups to carry out contact tracing. d) Similarly, TB Alert strongly encourages the review of contact tracing for latent TB infection in light of the growing debate around the	Screening Committee, who are currently working with the Health Protection Agency / Public Health England to consider a national screening programme for migrant communities for active and latent TB. Although NICE may make recommendations on certain aspects of case-finding activities, such has how to diagnose latent TB, it is felt that duplicating the efforts of the NSC is not an appropriate use of resources. e) A review of effective and cost effective models for the delivery and configuration of TB services will be developed using the CCPs interim methods for developing service guidance, and will be presented to a subgroup of the GDG for consideration. This review will present evidence across clinical and public health TB services with the intention of reducing fragmentation wherever possible. The CCPs interim methods for service guidance will be available on the NICE website at http://publications.nice.org.uk/pmg8

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				implementation of a national screening programme for latent TB infection amongst migrant communities. Pilots are taking place at a local level in a variety of locations, which would provide the basis for an evidence review. Screening for latent TB infection also raises pertinent ethical issues regarding its treatment. The development of NICE guidance would provide the appropriate forum for these issues to be discussed and recommendations made for practitioners. e) TB Alert believes that NICE should consider the configuration and delivery of all TB services as part of this update. With responsibility for public health aspects of TB moving into local authorities under the current reforms it is especially important to consider the configuration of all TB services to avoid fragmentation between public health and clinical services. There is a need for clear recommendations regarding a combined approach to TB to ensure that all local TB services are based upon comprehensive and integrated plans. NICE guidance that incorporates both the clinical and public health elements of the illness is an ideal authority to establish such recommendations.	
89.	SH	TB Alert	5.4 Are the outcomes in section 5.4	TB Alert is pleased to see that "acceptability of approach" is included in all the main outcomes to be achieved by the new updated TB guidance. This is in line with current health	Thank you for your comment. a) A review of effective and cost effective models for the delivery and configuration of TB services will be

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			appropriate and correct?	policy that promotes greater choice for patients. a) TB Alert encourages exploration of varied options regarding how services are delivered, providing more accessible options to many individuals and communities that are disproportionately affected by the illness. Especially with regard to education, awareness and support, case finding and treatment adherence, TB Alert strongly suggests that the role of Third Sector Organisations working with affected communities is explored as a potentially beneficial and cost effective option for service provision. TB Alert also promotes the coordination between trained Third Sector Organisations and local TB services for more effective referrals, which could have a positive impact on the speed of diagnosis. b) TB Alert is encouraged to see that point g) *Education, awareness and support* states "improved health, social and economic outcomes for people affected by TB" as a main outcome of the guidance. It is imperative that the guidance addresses the psychological impact of diagnosis, treatment and the after effects that TB illness has on patients and their families. Support for TB patients and their families must be consistently available throughout the patient	developed using the CCPs interim methods for developing service guidance, and will be presented to a subgroup of the GDG for consideration. Where evidence on the role of third sector organisations is presented to the subgroup this will be considered, and appropriate recommendations made and ratified by the GDG. The CCPs interim methods for service guidance will be available on the NICE website at http://publications.nice.org.uk/pmg8 b) Thank you. As outlined in section 5.5.2, the review of evidence on education, information and support intends to address the points raised by the consultee. In addition, where relevant evidence is identified on the psychological impact of diagnosis, treatment and the impact of TB on individuals this will be presented to the GDG for consideration.

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				pathway: before and after diagnosis, during treatment and post-cure (due to the long-term effects of the illness and medication experienced by some who undergo treatment). Again, the guidance should explore how this support can be best provided, in a way that is acceptable and accessible for diverse individuals and communities.	
90.	SH	Terrence Higgins Trust	5.2	We suggest the inclusion of settings where HIV testing occurs and HIV health care and treatment is given including community testing and support services provided by the charity/voluntary sector.	Thank you for your comment. As there many important settings in which activities relating to the prevention, identification and management of TB are received, provided or commissioned, section 5.2 has now been amended to state: "Any setting in which NHS or public health services for TB are received, provided or commissioned in the public, private and voluntary sectors." This may include settings where HIV testing occurs and HIV health care and treatment is given.
91.	SH	Terrence Higgins Trust	5.3.2	5.3.2 e) Effectiveness of BCG vaccination *Much research shows that the effectiveness of the BCG vaccine can be limited, especially in extra-pulmonary TB in people with HIV, effectiveness is also limited in adults and benefits after 10 years of vaccination are minimal. Therefore it is not clear to what extent BCG vaccination is effective. Awareness of this issue without clear clinical guidance is a potential barrier to ensuring that*	Thank you for your comment. An evaluation of the effectiveness of the BCG vaccination is beyond the remit of NICE. Responsibility for this area lies with the Joint Committee on Vaccination and Immunisation (JCVI) who have the remit to evaluate the effectiveness of the vaccine and issue recommendations to the NHS. An ongoing HTA research project on the duration of protection offered by BCG vaccination against TB intends to inform future BCG vaccination policy. This research is due for publication in March 2013 (see

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				those eligible and at risk are vaccinated. It would be helpful to have a statement in particular on the efficacy of BCG in adults diagnosed with HIV. *It may also be useful to know of developments in TB vaccination.* *References:* *International Journal of Epidemiology: BCG vaccine effectiveness in preventing tuberculosis and its interaction with human immunodeficiency virus infection- http://ije.oxfordjournals.org/content/29/6/1085.long* *Immunisation against infectious disease - 'The Green Book'; Immunisation against infectious disease - 'The Green Book', Dept of Health (various dates)* *Colditz GA, Brewer TF, Berkey CS, et al; Efficacy of BCG vaccine in the prevention of tuberculosis. Meta-analysis of the published literature. JAMA. 1994 Mar 2;271(9):698-702. [abstract]* *Rodrigues LC, Diwan VK, Wheeler JG; Protective effect of BCG against tuberculous meningitis and miliary tuberculosis: a meta-analysis. Int J Epidemiol. 1993 Dec;22(6):1154-8. [abstract]* *Sterne JA, Rodrigues LC, Guedes IN; Does the efficacy of BCG decline with time since vaccination? Int J Tuberc Lung Dis. 1998 Mar;2(3):200-7. [abstract]*	HTA website for more details http://www.hta.ac.uk/project/1750.asp). With regards to developments in TB vaccination, where the evidence is relevant to new strategies and interventions to promote the uptake of vaccination and/or barriers to uptake, these will be included for discussion by the GDG. The references provided by the consultee will be passed to the review team and included in the evidence base where relevant.

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				Science Daily http://www.sciencedaily.com/releases/2012/08/120828134936.htm **Better Vaccines for Tuberculosis Could Save Millions of Lives** Aug. 28, 2012 — Cases of one of the world's deadliest diseases—tuberculosis—are rising at an alarming rate, despite widespread vaccination. Reasons for the ineffectiveness of the vaccine, especially in regions where this infectious disease is endemic, as well as arguments for replacing the existing vaccine with novel synthetic vaccines, are presented in a review published online August 28th in *Trends in Molecular Medicine*. "Tuberculosis is a global health threat, and it is a highly communicable disease that may influence practically anyone and everyone," says senior author Javed Agrewala of the CSIR-Institute of Microbial Technology in Chandigarh, India. "There is a serious need and challenge for the scientific community to develop alternative vaccination approaches for the control of the disease." Tuberculosis is a bacterial infection caused by Mycobacterium tuberculosis (Mtb). About one third of the world's population is infected with Mtb, which causes about two million deaths each year. Vaccines may be the best strategy for controlling tuberculosis, but the only available vaccine—Bacillus Calmette-Guerin (BCG)—does not reliably prevent the disease	

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				in adults, especially in regions where tuberculosis is endemic. In the review, Agrewala explains that BCG does not work well in these regions because exposure to prevalent mycobacterial strains triggers the production of antibodies that counteract the vaccine. In addition, infections with parasitic worms called helminths interfere with protective immune responses induced by BCG. To overcome these limitations, Agrewala proposes the use of novel vaccines called lipidated-promiscuous-peptide vaccines. These synthetic vaccines are safer than BCG because they do not contain infectious material. Moreover, they generate long-lasting, protective immune responses and are not influenced by pre-existing antibodies. This type of vaccine strategy has already proven to be successful in an animal model of tuberculosis and is being tested in human clinical trials for other infectious diseases and cancer. "We believe that lipidated-promiscuous-peptide vaccines have all the essential qualities that can make them successful in tuberculosis-endemic countries," Agrewala says. "Such vaccines can impart better protection than BCG and will have a long-reaching positive impact on millions of people." Gowthama et al. "Lipidated promiscuous	

No	Type	Stakeholder	Section No	Comments	Developer's Response
				peptides vaccine for tuberculosis-endemic regions" Story Source: The above story is reprinted from materials provided by Cell Press, via EurekAlert!, a service of AAAS. *Note: Materials may be edited for content and length. For further information, please contact the source cited above.* Journal Reference: 1. Gowthaman, Pradeep K Rai, Nargis Khan, David C Jackson, Javed N Agrewala. Lipidated promiscuous peptides vaccine for tuberculosis-endemic regions. *Trends in Molecular Medicine*, 2012 (in press)	
92.	SH	Terrence Higgins Trust	5.4 Are the outcomes in section 5.4 appropriate and correct?	Yes	
93.	SH	Terrence Higgins Trust	Any other comments	a) Promoting adherence to the treatment of active TB *z) In people receiving drug treatment for active TB, which adherence-promoting strategies are effective in ensuring cure and/or treatment completion?*	Thank you for your comment and the information provided, which is extremely helpful. The commentary and references provided will be passed to the relevant review teams. NICE will be issuing a call for evidence on this topic in the near future and we would encourage you to submit this and any other information or evidence that you have in response. All

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				For people on self-administered treatment, help with remembering drug regimens can assist with ensuring treatment adherence and completion. Medication logs or diaries can be useful either in printed or electronic form. For those with ready access to the internet, membership websites that allow patients to 'log-on' and record their health status including appointments and treatment regime including drug timings can be very useful. Terrence Higgins Trust has experience of this from providing such a service on our 'myHIV' website. Text and email alerts to remind patients to take their medication at the right time can also be helpful in ensuring adherence. Community based support can help patients to adhere to medication regimens and be retained in care. Evidence for this was presented in the case of HIV medication at the Washington AIDS conference in 2012: *Community-based adherence support improves retention* *Adults receiving community-based adherence support were significantly less likely to be lost to follow-up and had lower mortality and improved virological suppression after starting ARVs, according to a prospective cohort study that compared patients receiving community-based adherence support to those not receiving community-based adherence support from ARV initiation.*	stakeholders will be notified of this call.

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				Clinic-based, community-outreach adherence-support healthcare workers called 'patient advocates' were introduced in 2004 by Kheth'Impilo, a South African NGO that supports district scale-up of ARV treatment in 142 public-sector health sites. The patient advocates ensure ongoing adherence, counselling and psycho-social support at the community level and support community services to ensure the continuum of care. *Six per cent (1185 of 19,668) of the patients who received community-based adherence support were lost to follow up, compared to 9.5% (4498 of 47,285) in those who did not receive support (p< 0.0001): Virological suppression at six months was also higher in the group receiving support at 76.6% (95% CI: 75.8%-77.5%), compared to 72% (95% CI: 71.3%-72.5%) in those who did not receive support (p< 0.0001). Only 4.9% of the supported patients died, compared to 6.3% of those who were not supported (p< 0.0001).* References Fox M An introduction to the cascade of care. 19th International Conference on AIDS, abstract WEAE0201, Washington, DC, July 2012. Ardura Garcia C et al. Risk factors and true outcomes of children lost to follow-up from antiretroviral therapy in Lilongwe, Malawi. 19th International Conference on AIDS, abstract WEAE0203, Washington, DC, July 2012.	

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				Fatti G et al. Community-based adherence support associated with improved virological suppression in adults receiving antiretroviral treatment: five-year outcomes from a multicentre cohort study in South Africa. 19th International Conference on AIDS, abstract WEAE0204, Washington, DC, July 2012. Scheibe F et al. High rates of loss to follow-up during first year of pre-antiretroviral therapy for HIV at primary health care level in rural Uganda. 19th International Conference on AIDS, abstract WEAE0206, Washington, DC, July 2012. Baggaley R et al. Improving retention at all points in the HIV care cascade: the WHO perspective. 19th International Conference on AIDS, abstract WEAE0207, Washington, DC, July 2012. View information on the session, including links to the abstracts and slides from the presentations, on the conference website. *aa) For which people receiving drug treatment for active TB is DOT effective in ensuring cure and/or treatment completion, compared with self-administered treatment? Who is the most effective observer and in what setting?* DOT is particularly effective for people who have issues taking their medication at home which may be due to a variety of reasons such as disclosure issues (e.g. living with family, friends or flatmates who are not aware of the	

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				health condition or possible associated health conditions such as HIV), dementia and other cognitive difficulties, depression, chaotic lifestyles (e.g. IV drug users, other people with alcohol or drug misuse/dependency issues). Effective observers can be doctors, nurses, health advisors or pharmacists in a clinical setting either in the public health sector or in the charity/voluntary sector. b) BCG vaccination uptake *oo) Which strategies and interventions are effective and cost effective at increasing the uptake of BCG vaccination in key groups?* For people living with HIV who are at risk of TB infection, an effective and cost effective strategy would be to target these people in clinics, in community settings, in peer-support groups and when accessing non-clinical services such as those provided by HIV charities, drug agencies and African community organisations as well as any other organisations that deal with key groups. Knowledge about which key risk groups are eligible for BCG vaccination or that vaccination can be offered to adults at all seems to be limited in third sector organisations that do not specialise in TB from our experience and more could be done to raise awareness in charity/voluntary organisations that deal with people in high risk groups.	

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				qq) What are the barriers to uptake of BCG vaccination? Resistance to the idea of vaccination in general within the general population (i.e. public health concerns about possible side effects), concern that the vaccine is not effective enough, confusion about who is in a key group for vaccination. People who have recently arrived in the UK from countries with high TB prevalence may not be aware that they are eligible for vaccination. c) Information and support *ss) Which strategies and interventions are effective and cost effective at providing and delivering information and support to people affected by TB, for example, the person, their families and/or carers, and staff?* From Terrence Higgins Trust's experience of developing and providing information and support to people living with HIV, it is important to have a variety of strategies and interventions to deliver information and support. Web and other electronic based media can be very effective and are certainly most cost effective compared to printed resources; however there are issues with accessibility for many people especially those living in poverty. Disclosure issues also need to be taken into account when devising strategies as patients may be uncomfortable	

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				with their health status being known to others including family and friends especially in shared accommodation. There may also be related anxiety about TB being connected to other conditions such as HIV or Hepatitis B/C. So for some people, one-to-one interventions will be most effective but for others, some more remote access such as web, text or email based interventions may be more useful. Printed materials are often requested by client groups who do not have easy or confidential access to electronic media. References: Sigma Research Framework for better living with HIV in England http://sigmaresearch.org.uk/go.php?/projects/policy/project35/ What do you need? 2007-2008: findings from a national survey of people with diagnosed HIV http://sigmaresearch.org.uk/go.php?/reports/report2009b/ *tt) What information and support (including access to support networks) should be given to people affected by TB?* For people living with HIV coinfected with TB: Helplines, peer support, facilitated group work, health support training and other services such as community volunteer support are	

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				available from community/voluntary organisations such as Terrence Higgins Trust. Our online resources at www.tht.org.uk/myHIV provide information on TB and our community forum provides online support for people living with HIV including an area to discuss co-infections such as TB. People affected by TB should also have information about local authority social care support.	
94.	SH	The Leeds NHS Teaching Hospitals trust	5.1.2	please see additional comments section at end of document	Thank you for your comment.
95.	SH	The Leeds NHS Teaching Hospitals trust	5.2	y	Thank you for your comment.
96.	SH	The Leeds NHS Teaching Hospitals trust	5.3.2	please see additional comments section at end of document	Thank you for your comment.
97.		The Leeds NHS Teaching Hospitals trust	Any other comments	Recommendations for 1.BCG and 2. diagnosis and treatment of latent TB differ for new healthcare workers compared	Thank you for your comment. We agree that the identification, management and control of TB in occupational health settings are significant issues. However, it is felt that the issue of communicable diseases in the workplace goes

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				with the general population in the current CG117 and are both resource intensive for occupational health screening, and place specific obligations on health care workers (which some h.c.ws are very uncomfortable about). I note that the scope now includes draft review questions for both these issues (5.5.1 hh), ii) and 5.5 pp) for general populations. If there is to be specific guidance for new healthcare workers which differs from the general population, as there is in CG117, should there be a review of available evidence for the healthcare workers as a specified population group?	beyond TB: activities relating to the identification, management and control of other diseases – such as influenza, HIV and hepatitis B and C – may also benefit from guidance. Since such occupational health risks may often affect the same groups of workers and are often managed by a single occupational health team using similar principles and practices, it was felt that a single piece of guidance that covers this area as a whole may be more appropriate than fragmenting guidance under individual diseases. The Centre for Public Health Excellence is currently considering the management of communicable diseases in the workplace as a possible piece of guidance within their draft library of topics. More information on how topics are selected for public health guidance can be found in the Centre for Public Health Excellence's guidance and method guides: http://www.nice.org.uk/aboutnice/howwework/developingnicepublichealthguidance/publichealthguidanceprocessandmethodguides/public_health_guidance_process_and_method_guides.jsp
98.	SH	The Royal College of Paediatrics and Child Health (RCPCH)	5.1.1b	Adults, young people and children who have latent infection with Mycobacterium tuberculosis complex and are due to start Biologic therapies and in particular anti-tumour necrosis factor-alpha treatment.	Thank you for your comment. Since people about to start immunosuppressive biological therapies who have latent TB are believed to be at particular risk of progressing to active disease, we agree they are an important subpopulation to include. Although we do not explicitly note them in section 5.1.1 ('Groups that will be covered'), we feel they are included under bullet c): "Adults, young people and children at increased risk of infection with Mycobacterium tuberculosis complex

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					and/or at increased risk of progressing to the active disease." The diagnosis of latent TB in people on/about to start immunosuppressive regimens will be explicitly covered in review question 5.5.1ff: "Which diagnostic strategy is most effective in establishing an accurate diagnosis of latent TB in people who are immunocompromised or at risk from immunosuppression?" People on/about to start immunosuppressive regimens will also be included by the reviewer in the protocol for review questions 5.5.1hh (according to their risk factors, which people with latent TB should receive treatment?) and 5.5.1ii (which treatment regimen is best for treating latent TB?) as populations of interest. It should be noted that this will be subject to confirmation by the Guideline Development Group, who will consider the appropriateness of the proposed review protocols at their first meeting.
99.	SH	The Royal College of Paediatrics and Child Health (RCPCH)	5.2	Yes	Thank you for your comment.
100.	SH	The Royal College of Paediatrics and Child	5.3.2	We disagree with not updating the section 1.1.1. a) *Diagnosing latent TB: page 11 section*	Thank you for your comment. a) It is felt that, in general, the evidence reviews for diagnosing latent TB in CG117 are still relevant and

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		Health (RCPCH)		*1.1.1.8.* The evidence provided by the GDG does not support doing both an interferon gamma release assay IGRA and Mantoux test at 6 weeks after a negative Mantoux test in contacts. There is no evidence that doing both increases sensitivity or reduces false negative results. There is now good evidence of an equivalent sensitivity and specificity in contacts without previous BCG immunisation and the GDG needs to focus the literature search update on this issue. Our recommendation is to do an IGRA at 6 weeks if there was a previous BCG immunisation to avoid false positives due to enhancement, and a repeat Mantoux if there was no previous BCG. An additional painful procedure, which dual testing implies, is not justifiable, particularly in young children. *Page 29 and 30 section 1.6.1.1.* The authors need to make clear the difference between "screening" and "opportunistic screening". In children aged 1-15 years the authors regard as latent tuberculosis infection for which treatment should be considered children without previous BCG who have a Mantoux test result >15mm. This is an error as without previous BCG, >6mm should be the cut off. In children, particularly those under 2 years of age, it increases the potential risk to choose a cut-off of 15 mm for latent infection, even with	that the new evidence in this area would not change the current recommendations. However, we agree that the CG117 review of diagnosis of latent TB in children might benefit from update. The reviews for the diagnosis of latent TB in adults and in people with HIV will not be updated. A new topic has been included under 5.3.1, 'key issues that will be covered', which lists the discreet populations for whom the diagnosis of latent TB will be reviewed: "h) Diagnosis of latent TB infection using Mantoux testing and interferon-gamma release assays in: • children • people who are immunocompromised, such as people with HIV or renal disease, or at known risk of immunosuppression, such as people about to start immunosuppressive regimens • new entrants from high incidence countries, in the context of opportunistic case-finding rather than proactive screening programmes." b) Since people on or about to start immunosuppressive regimens who have latent TB are believed to be at particular risk of progressing to active disease, we agree they are an important subpopulation to include. Although we do not explicitly note them in section 5.1.1 ('Groups that will be covered'), we feel they are included under bullet c): "Adults, young people and children at increased risk of infection with Mycobacterium tuberculosis complex and/or at increased risk of progressing to the active

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				previous BCG, as such a cut-off lacks evidence. There is however evidence showing that the diameter of duration of the positive Mantoux test is smaller in young children (Critselis E et al. The effect of age on whole blood interferon-gamma release assay response among children investigated for latent tuberculosis infection. J Pediatr 2012; 161:632-8). The guideline development group needs to review the evidence for validity of Mantoux test induration thresholds for labelling as infected in young children. *Page 31, section 1.6.1.5* There is no evidence or justification for treating neonates differently from other young infants less than 3 months old. There is no justification to do 3 tests: 2 Mantoux tests and one IGRA at 3 months in an infant with an initially negative Mantoux test in the neonatal period. To do one repeat Mantoux test and an IGRA test should be sufficient. Two Mantoux tests ("double checking") is not justified by any evidence and would only be appropriate if there was doubt about performance of the test. The authors need to use the same approach for excluding infection in the infant who started screening as a neonate as in the infants who starting screening after 4 weeks of age as used in section 1.6.1.6. (at least for consistency). *Page 32 section 1.6.1.7.* Even with previous BCG a threshold in the	disease." The diagnosis of latent TB in people on/about to start immunosuppressive regimens will be explicitly covered in review question 5.5.1ff: "Which diagnostic strategy is most effective in establishing an accurate diagnosis of latent TB in people who are immunocompromised or at risk from immunosuppression?" People on/about to start immunosuppressive regimens will also be included by the reviewer in the protocol for review questions 5.5.1hh (according to their risk factors, which people with latent TB should receive treatment?) and 5.5.1ii (which treatment regimen is best for treating latent TB?) as populations of interest. It should be noted that this will be subject to confirmation by the Guideline Development Group, who will consider the appropriateness of the proposed review protocols at their first meeting. c) Although we agree that the collection of sputum samples from adults who are unable to expectorate spontaneously is important, it was not considered a priority for review in the updated guidance. It was felt that updating the evidence review would not change the recommendations made in CG117. However, we agree that collecting sputum samples in children is a significant issue, and this will therefore be reviewed in the new guidance (see 5.5.1b: "What is the optimum method of collecting sputum samples from children unable to expectorate spontaneously?").

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				Mantoux test of 15 mm for labelling as infected in young infants is not evidence-based and may increase risk, as the immature immune system within the first 3 months of age may not mount a large enough induration on Mantoux testing (see above). The guideline should use the threshold of >6mm in children less than 2 years regardless of previous BCG immunisation because missing a child with early active tuberculosis could pose a risk by delaying appropriate treatment. The authors use the IGRA as a safeguard at six weeks in children with a Mantoux <15 mm but if they don't want to lower the cut-off for the Mantoux positivity should at least add "window period prophylaxis" in infants using isoniazid pending the result as in section 1.6.1.6. *Page 33, section 1.6.1.9.* The authors should add children less than 2 years of age to this list. b) *CG117 section 1.1.* Diagnosis latent TB does not give specific recommendations on how to screen for latent TB subjects who are due to start Biologic therapies and in particular anti-tumour necrosis factor-alpha treatment. This could be incorporated as a separate sentence following section 1.1.1.13. Increased risk to develop active TB in subjects receiving anti-tumour necrosis factor-alpha treatment is mentioned in section 1.6.1.9 but	d) Although we agree that the follow-up of patients after treatment completion is important, it is not considered a priority for review in the new guidance. Recommendations from CG117 relating to the follow-up of patients after treatment completion will be incorporated into the new guidance e) We feel that the CG117 evidence reviews for diagnosing latent TB in adults are still relevant and that the new evidence in this area would not change the current recommendations. The CG117 review areas relating to the diagnosis of latent TB that have been identified as requiring an update is paediatric diagnosis of latent TB, diagnosis of latent TB in people who are immunocompromised or at known risk of immunosuppression, and diagnosis of latent TB in new entrants from high incidence countries. Therefore, a new topic has been included under 5.3.1, 'key issues that will be covered': "h) Diagnosis of latent TB infection using Mantoux testing and interferon-gamma release assays in: • children • people who are immunocompromised, such as people with HIV or renal disease, or at known risk of immunosuppression, such as people about to start immunosuppressive regimens • new entrants from high incidence countries, in the context of opportunistic case-finding rather than proactive screening programmes."

No	Type	Stakeholder	Section No	Comments	Developer's Response
				no specific recommendations are made regarding treating latent TB in these subjects. In my opinion, diagnosis and treatment of latent TB in subject identified by screening before starting Biologic Therapies should be specifically covered as this is an expanding population managed by different medical specialities. c) Why are NICE not looking at specimen collection in patients who do not produce spontaneous sputum? In children, many clinicians do not try and collect samples at all. Others think sample collection is an essential part of investigation. There is little available guidance about this although there is some literature available for review. d) There is marked heterogeneity in follow-up arrangements for children with active Tb disease across the UK. Is there any guidance about what should be provided? e) 5.3.2d Diagnosis of latent infection should be reviewed including reviewing research findings on the use of interferon-gamma testing compared Mantoux in different sub-groups.	The reviews for the diagnosis of latent TB in adults will not be updated.
101.	SH	The Royal College of Paediatrics	5.4 Are the outcomes in section	Outcomes could include "appropriate screening for latent TB in subjects starting Biologic therapies".	Thank you for your comment. Since people about to start immunosuppressive regimens who have latent TB are believed to be at

No	Type	Stakeholder	Section No	Comments	Developer's Response
		and Child Health (RCPCH)	5.4 appropriate and correct?		particular risk of progressing to active disease, we agree they are an important subpopulation to include. Although we do not explicitly note them in section 5.1.1 ('Groups that will be covered'), we feel they are included under bullet c): "Adults, young people and children at increased risk of infection with Mycobacterium tuberculosis complex and/or at increased risk of progressing to the active disease." The diagnosis of latent TB in people on/about to start immunosuppressive regimens will be explicitly covered in review question 5.5.1ff: "Which diagnostic strategy is most effective in establishing an accurate diagnosis of latent TB in people who are immunocompromised or at risk from immunosuppression?" People on/about to start immunosuppressive regimens will also be included by the reviewer in the protocol for review questions 5.5.1hh (according to their risk factors, which people with latent TB should receive treatment?) and 5.51ii (which treatment regimen is best for treating latent TB?) as populations of interest. It should be noted that this will be subject to confirmation by the Guideline Development Group, who will consider the appropriateness of the proposed review protocols at their first meeting.
102.	SH	The Royal College of Paediatrics and Child Health	Any other comments	Page 3, d): line 4: Put "active respiratory tuberculosis"; line 6: Put " Adults with a normal immune system" Page 7, 5.1.2.a); put "non-tuberculous"	Thank you for your comment. Your suggestions have been noted.

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		(RCPCH)		instead of "opportunist" Page 35, section 1.7.4.1 The authors should correct to >500 per 100 000. Section 1.8.7.3: To avoid discrimination, immigrant children should have the same screening rules as for opportunist screening of the indigenous population.	
103.	SH	The Royal College of Pathologists	5.1.2	a) Pregnant women and management of TB should be included. b) Patients with renal and liver failure	Thank you for your comment. a) Section 5.1.1d has now been updated to include the following 3 subgroups: • "neonates, children and young people • adults older than 35 years • people with HIV and other comorbidities or conditions that impact on the diagnosis and management of TB" We feel that the 3rd bullet point covers pregnant women, as pregnancy may be a condition that impacts on the management of TB. However, the reviewer will insert pregnant women into the protocol for review questions 5.5.1k as a possible subgroup of interest. It should be noted that this inclusion will be subject to confirmation by the Guideline Development Group, who will consider the appropriateness of the proposed review protocols at their first meeting, as well as the availability of appropriate evidence. b) We feel that people with renal or liver failure are included under bullet c): "Adults, young people and children at increased risk of infection with Mycobacterium tuberculosis complex

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					and/or at increased risk of progressing to the active disease." Additionally, we acknowledge that they may be a subgroup for whom the diagnosis and management of TB may vary. Therefore we feel that they are also reflected by the 3rd bullet point of 5.1.1d: "people with HIV and other comorbidities or conditions that impact on the diagnosis and management of TB" People with renal or liver failure are also covered by 5.3.1d, and will be included as populations of interest in the protocol for review question 5.5.1k: "What comorbidities or conditions affect the choice of regimen for the treatment of active TB? How should the standard recommended regimen be adapted to accommodate these comorbidities or conditions?" Additionally, as populations who are often immunocompromised or at risk of immunosuppression, the diagnosis of latent TB in people with renal or liver failure will be considered in review 5.5.1ff: "Which diagnostic strategy is most effective in establishing an accurate diagnosis of latent TB in people who are immunocompromised or at risk from immunosuppression?" It should be noted that the review questions and protocols will be subject to confirmation by the Guideline Development Group, who will consider their appropriateness at their first meeting.
104.	SH	The Royal College of Pathologists	5.3.2	**For update**: a) Number of sputum samples as WHO has	Thank you for your comment. a) Although we agree that the collection of sputum

No	Type	Stakeholder	Section No	Comments	Developer's Response
				changed their recommendations b) Monitoring of patient response to treatment as there have been advances in this area c) Management of abdominal TB d) Pregnant women with TB	samples from adults who are unable to expectorate spontaneously is important, it was not considered a priority for review in the updated guidance. It was felt that updating the evidence review would not change the recommendations made in CG117. However, we agree that collecting sputum samples in children is a significant issue, and this will therefore be reviewed in the new guidance (see 5.5.1b: "What is the optimum method of collecting sputum samples from children unable to expectorate spontaneously?"). b) We agree that monitoring of patient response to treatment is an important part of managing TB. It is felt that there are two key features of monitoring that may need to be considered in this guidance. Firstly, the use of monitoring to detect people in which treatment is failing or has failed, including instances in which this results from drug resistance. The review of possible risk factors for drug resistance will include indicators detected through monitoring of treatment response (that is, indicators that treatment is failing or has failed) into the protocol for review question 5.5.1s: "In people with suspected or confirmed active TB, which relative risk factors are associated with a higher level of: (i) multidrug resistance, or (ii) any drug resistance?" Secondly, we feel that the adverse effects of tuberculosis treatment regimens are a major source of non-adherence to treatment, and that detecting and swiftly managing these side effects may improve adherence to treatment. This issue will be included in the review of adherence to treatment for active and

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					latent TB, where the available evidence on a range of interventions and approaches that support or prohibit treatment completion will be identified and assessed. However, the Summary of Product Characteristics and British National Formulary include details on the monitoring of adverse effects that should be conducted for a particular drug formulation, and this should be used to guide decisions regarding the monitoring of a patient's response to treatment. It should be noted that these inclusions will be subject to confirmation by the Guideline Development Group, who will consider the appropriateness of the proposed review protocols at their first meeting, as well as the availability of appropriate evidence. c) This has been included as a site of interest in the reviews of diagnosis and treatment of non-respiratory TB. d) Section 5.1.1d has now been updated to include the following 3 subgroups: • "neonates, children and young people • adults older than 35 years • people with HIV and other comorbidities or conditions that impact on the diagnosis and management of TB" We feel that the 3rd bullet point covers pregnant women, as pregnancy may be a condition that impacts on the management of TB. However, the reviewer will insert pregnant women into the protocol for review questions 5.5.1k as a possible subgroup of interest. It

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					should be noted that this inclusion will be subject to confirmation by the Guideline Development Group, who will consider the appropriateness of the proposed review protocols at their first meeting, as well as the availability of appropriate evidence.
105.	SH	The Royal College of Pathologists	5.4	5.4 Rapid diagnosis and early institution of correct therapy together with promotion of adherence to active TB are the key to cure and interruption of disease transmission and resources should be focused on these areas. Promotion of adherence should be considered in the broadest sense as there are several diseases (Eg Diabetes, hypertension) where long term therapy is essential and lessons could be learnt. Studies of what incentives are really effective would be very useful.	Thank you for your comment. As outlined in section 5.5.2 of the scope, the evidence on strategies and interventions to promote uptake and adherence to treatment for active and latent TB will be reviewed. As raised by the consultee, it is our intention to review the literature in communicable disease areas other than TB to ascertain whether any lessons on uptake and adherence to treatment can be learnt and effective interventions applied to TB.
106.	SH	The Royal College of Pathologists	Any Other comments	Broad and clear scope. Comments from earlier scoping meeting incorporated. Further comments below	Thank you for your comment.
107.	SH	The Society and College of Radiographers	5.1.1b	New immigrants to the UK	Thank you for your comment. The scope for this guidance will cover all adults, young people and children who have or are suspected to have active or latent TB, or are at an increased risk of infection with Mycobacterium tuberculosis complex (see sections 5.1.1a to c). We feel that this includes new immigrants to the UK.
108.	SH	The Society and College of Radiographers	Any other comments	a) Should there be guidance on the use of the chest radiograph in young children and the radiological diagnosis of TB.	Thank you for your comment. a) Chest radiography for the diagnosis of active respiratory TB will be considered under review

No	Type	Stakeholder	Section No	Comments	Developer's Response
				b) There is no mention of use of imaging to monitor effectiveness of treatment which probably should be included. c) Also, chest x-ray for the non-symptomatic – not quite a screening programme but perhaps targeted to vulnerable groups identified ("The majority of TB cases recorded in 2011 were in urban areas, and occurred in young adults, people from countries with a high incidence of TB and people with social risk factors for TB, including a history of substance misuse, homelessness and a history of imprisonment") d) Overall the protection of health workers is clearly identified – the chest x-ray remains as part of the primary diagnosis. Increase in numbers being assessed maybe an issue but most plain film departments have the equipment. Maybe something about access to suitable radiographic diagnostic facilities/systems that limit exposure to those most at risk might be a sensible comment in this world of high volume productive radiography.	questions 5.5.1b (explicitly considers children) and 5.5.1c (children will be considered in a subgroup analysis, if possible). b) We agree that monitoring of patient response to treatment is an important part of managing TB. One reason is that monitoring enables the detection of people in whom treatment is failing or has failed, including instances in which this results from drug resistance. However, the use of imaging as a monitoring tool was not considered a priority for review in the new guidance. c) It is felt that this was adequately covered by PH37, 'Identifying and managing tuberculosis among hard-to-reach groups'. We aim to incorporate the recommendations from PH37 with the new guidance, if appropriate. d) We agree that the identification, management and control of TB in occupational health settings are significant issues. However, it is felt that the issue of communicable diseases in the workplace goes beyond TB: activities relating to the identification, management and control of other diseases – such as influenza, HIV and hepatitis B and C – may also benefit from guidance. Since such occupational health risks may often affect the same groups of workers and are often managed by a single occupational health team using similar principles and practices, it was felt that a single piece of guidance that covers this area as a whole may be

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					more appropriate than fragmenting guidance under individual diseases. The Centre for Public Health Excellence is currently considering the management of communicable diseases in the workplace as a possible piece of guidance within their draft library of topics. More information on how topics are selected for public health guidance can be found in the Centre for Public Health Excellence's guidance and method guides: http://www.nice.org.uk/aboutnice/howwework/developingnicepublichealthguidance/publichealthguidanceprocessandmethodguides/public_health_guidance_process_and_method_guides.jsp
109.	SH	UK National Screening Committee	5.1	5.1.1 d. Just aware that examination of this group could stray into screening whole population territory. The UKNSC is working with NICE and the HPA to examine this prospect (screening for latent TB) so please can you steer the scope away from the possibility of overlap	Thank you for your comment.

These organisations were approached but did not respond:

Abbott Laboratories
Action for Children
Action on Smoking & Health (ASH)
African Health Forum
African HIV Policy Network

Aintree University Hospital NHS Foundation Trust
Air Products PLC
Alcohol Concern
Alder Hey Children's NHS Foundation Trust
Alliance Boots
Allocate Software PLC
ASPECT
Association for Perioperative Practice
Association of Anaesthetists of Great Britain and Ireland
Association of Directors of Childrens Services (ADCS)
Association of Directors of Public Health
Association of Medical Microbiologists/British Infection Society
Axis Shield
Balance, North East Alcohol Office
Barnsley Hospital NHS Foundation Trust
Barnsley Primary Care Trust
Bayer HealthCare
Black Health Agency (BHA)
Black Mental Health UK
Bradford District Care Trust
Brighton and Sussex University Hospital NHS Trust
British Association for Adoption and Fostering
British Association of Prosthetists & Orthotists
British Association of Spinal Surgeons

British Dietetic Association
British Global and Travel Health Associaton
British Heart Foundation
British Infection Association
British Lung Foundation
British Medical Association
British Medical Journal
British National Formulary
British Orthopaedic Association
British Paediatric Allergy, Immunology & Infection Group
British Paediatric Neurology Association
British Paediatric Respiratory Society
British Psychological Society
British Retail Consortium (BRC)
British Society for Rheumatology
British Society of Paediatric Gastroenterology Hepatology and Nutrition
Calderdale and Huddersfield NHS Trust
Cambridge University Hospitals NHS Foundation Trust
Cancer Research UK
Capsulation PPS
Cardiff School of Social Sciences (SOCSI)
Cardio Wellness
Care Quality Commission (CQC)
Cellestis Limited

Central London Community Healthcare NHS Trust
Central Manchester and Manchester Children's Hospital NHS Trust
Centre for Reviews and Dissemination (CRD)
Chartered Institute of Environmental Health
City and Hackney Teaching Primary Care Trust
College of Occupational Therapists
Commission for Social Care Inspection
Community Health Action Trust (CHAT)
Community Infection Control Nurses Network
Constructing Better Health
Co-operative Pharmacy Association
Criminal Justice Womens Strategy Unit
Crisis
Croydon Primary Care Trust
Cwm Taf Health Board
David Lewis Centre, The
Department for Communities and Local Government
Department for Education
Department of Health, Social Services and Public Safety - Northern Ireland
Derbyshire DAAT
Diabetes UK
Directorate of High Security, H M Prison Service
Doctors of the World UK
East and North Hertfordshire NHS Trust

Economic and Social Research Council
Education for Health
Faculty of Occupational Medicine
Faculty of Occupational Medicine
Faculty of Public Health
Family Action
Find and Treat
Gloucestershire Hospitals NHS Foundation Trust
Gloucestershire LINk
Great Western Hospitals NHS Foundation Trust
Greater Manchester and Beyond Coalition of PLW & HIV
Guy's and St Thomas' NHS Foundation Trust
Hammersmith and Fulham Primary Care Trust
Health & Safety Executive
Health Protection Agency
Healthcare Improvement Scotland
Health Quality Improvement Partnership
Health, Social Services and Public Safety of Northern Ireland
Healthcare Improvement Scotland
Healthcare Infection Society
Hertfordshire Partnership NHS Trust
Hindu Council UK (HCUK)
Hindu Forum of Britain
HIV i-Base

HMP Pentonville
Hull and East Yorkshire Hospitals NHS Trust
Humber NHS Foundation Trust
Imperial College London
Inclusive Health
Infection Control Nurses Association
Institute of Biomedical Science
Isle of Wight NHS Primary Care Trust
Janssen
JCVI (Joint Committee on Vaccination and Immunisation)
Jenny Craig
John Radcliffe hospital/Oxford health
Kings College London (School of Medicine)
Lambeth Community Health
Lancashire Care NHS Foundation Trust
Leeds City Council
Leeds Community Healthcare NHS Trust
Leeds Metropolitan University
Leeds Metropolitan University - Centre for Health Promotion Research
Leeds Primary Care Trust (aka NHS Leeds)
Lilly UK
Lincolnshire County Council
Liverpool Community Health
Liverpool PCT

Liverpool PCT Provider Services
Liverpool Primary Care Trust
Local Government Association
London Chest Hospital (Barts and the London NHS Trust)
London Development Centre for Mental Health
London School of Hygiene and Tropical Medicine
London TB Clinical Reference Group
Luton and Dunstable Hospital NHS Trust
Luton Borough Council
Maidstone and Tunbridge Wells NHS Trust
Mast Diagnostics
Mayday healthcare trust
MDDA - Muslims Doctors and Dentist Association
Medical Foundation for AIDS and Sexual Health
Medical Research Council
Medicines and Healthcare products Regulatory Agency
Met Office
Metro Centre
Ministry of Defence
NAM Publications
National AIDS Trust (NAT)
National College for School Leadership
National Commissioning Board
National Electronic Library for Infection

National Heart Forum
National Institute for Health Research Health Technology Assessment Programme
National Obesity Forum
National Patient Safety Agency
National Public Health Service for Wales
National Screening Committee
NHS Alliance
NHS Bedfordshire
NHS Blackpool
NHS Bournemouth and Poole
NHS Bradford and Airedale
NHS Brent
NHS Clinical Knowledge Summaries
NHS Connecting for Health
NHS County Durham and Darlington
NHS Darlington
NHS Direct
NHS East London and the City
NHS East Riding of Yorkshire
NHS East Sussex
NHS Evidence
NHS Gloucestershire
NHS Great Yarmouth and Waveney PCT
NHS Harrow
NHS Health Scotland

NHS Hertfordshire
NHS Information Centre for health and social care
NHS Leeds
NHS Lothian
NHS Newcastle
NHS Norfolk
NHS North of Tyne
NHS North West
NHS Northamptonshire - Provider Services
NHS Nottingham City
NHS Nottinghamshire County
NHS Oxfordshire
NHS Plus
NHS Quality Improvement Scotland
NHS Redcar and Cleveland
NHS Sheffield
NHS Tameside and Glossop
NHS Walsall
NHS Western Cheshire
NHS Worcestershire
NIA
North East London TB Network
North Essex Partnership Foundation Trust
North Tees and Hartlepool NHS Foundation Trust
North West London Perinatal Network
North West School of Public Health
North Yorkshire & York Primary Care Trust
Northwick Park and St Mark's Hospitals
Nottinghamshire County LINk
Offender Health - Department of Health
Pennine Acute Hospitals NHS Trust
PERIGON Healthcare Ltd
Pfizer

Pharmaceutical Services Negotiating Committee
Positively UK
Public Health Laboratory Service Board
Public Health Medicine Environmental Group
Public Health Wales NHS Trust
Race Equality Foundation
Refugee Action
Respiratory Etc
Royal Brompton Hospital & Harefield NHS Trust
Royal College of Anaesthetists
Royal College of General Practitioners in Wales
Royal College of Midwives
Royal College of Nursing
Royal College of Obstetricians and Gynaecologists
Royal College of Paediatrics and Child Health , Gastroenetrology, Hepatology and Nutrition
Royal College of Pathologists
Royal College of Psychiatrists
Royal College of Radiologists
Royal College of Surgeons of England
Royal Pharmaceutical Society
Royal Society of Medicine
Sacyl
Safer North Tyneside – North East Council on Addictions
Sandwell and West Birmingham Hospitals NHS Trust
Sandwell Primary Care Trust
Scarborough and North Yorkshire Healthcare NHS Trust
Scientific Advisory Committee on Nutrition (SACN)
Scottish Executive
Scottish Intercollegiate Guidelines Network
Sheffield Childrens Hospital
Sheffield Hallam University
Sheffield Primary Care Trust
Sheffield Teaching Hospitals Foundation Trust

Social Care Institute for Excellence
Society and College of Radiographers
Society for Acute Medicine
Society for Cardiothoracic Surgery of Great Britain and Ireland
Society for General Microbiology
Society of British Neurological Surgeons
Society of Local Authority Chief Executives (SOLACE)
Solutions 4 Health
South Asian Health Foundation
South Asian health Foundation+B2015
South Tees Hospitals NHS Trust
South West Yorkshire Partnership NHS Foundation Trust
St Ann's Hopsital
St Mary's Hospital
St Mungos
Stockport Managed Care
Stockport Primary Care Trust
Stonewall
Swansea University
Target Tuberculosis
Thames Reach
The British Psychological Society
The Children's HIV Association
The NIHR Evaluation, Trials and Studies Coordinating Centre (NETSCC)
The Rotherham NHS Foundation Trust
The Royal Free Hampstead NHS Trust
TUC (Trades Union Congress)
UK Clinical Pharmacy Association
UK Society for Behavioural Medicine
UK Specialised Services Public Health Network
Unite the union/ CPHVA
United Kingdom National External Quality Assessment Service
Univ. of East Anglia

Universal Hospital Supplies Ltd
University College London
University College London - Children's Immunisation
University College London Hospital NHS Foundation Trust
University of Southampton
University of Stirling
Walsall Local Involvement Network
Walsall Teaching Primary Care Trust
Well UK
Welsh Government
Welsh Scientific Advisory Committee
West Midlands East Health Protection Unit
West Sussex Public Health
Western Health and Social Care Trust
Westminster Local Involvement Network
Worcestershire PCT
Working Well Solutions Ltd
York Hospitals NHS Foundation Trust