Interventions to improve contact tracing for tuberculosis (TB) in specific groups and in wider populations: an evidence synthesis

Susan Baxter, School of Health Related Research, University of Sheffield
Elizabeth Goyder, School of Health Related Research, University of Sheffield
Duncan Chambers, School of Health Related Research, University of Sheffield
Maxine Johnson, School of Health Related Research, University of Sheffield
Louise Preston, School of Health Related Research, University of Sheffield
Andrew Booth, School of Health Related Research, University of Sheffield

Corresponding author: Dr Susan Baxter, School of Health and Related Research, University of Sheffield, Regent Court, Regent Street, Sheffield, South Yorkshire, UK. Telephone: 0114 2220852 Email: s.k.baxter@sheffield.ac.uk

Competing interests: None declared.

Key words: Tuberculosis control strategies; contact tracing; contact investigation; specific populations; hard to reach

Total report word count: 15,540

Important

This web report has been created once the normal NIHR Journals Library peer and editorial review processes are complete. The report has undergone full peer and editorial review as documented at NIHR Journals Library website and may undergo rewrite during the publication process. The order of authors was correct at editorial sign-off stage.

A final version (which has undergone a rigorous copy-edit and proofreading) will publish in a forthcoming issue of the Health Services and Delivery Research journal.

Any queries about this web report should be addressed to the NIHR Journals Library Editorial Office NIHRedit@soton.ac.uk.

The research reported in this web report was commissioned and funded by the HS&DR programme as part of a series of evidence syntheses under project number 13/05/12. For more information visit http://www.nets.nihr.ac.uk/projects/hsdr/130512

The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HS&DR editors have tried to ensure the accuracy of the authors' work and would like to thank the reviewers for their constructive comments however; they do not accept liability for damages or losses arising from material published in this web report.

This web report presents independent research funded by the National Institute for Health Research (NIHR). The views and opinions expressed by authors in this publication are those of the authors and do not necessarily reflect those of the NHS, the NIHR, NETSCC, the HS&DR programme or the Department of Health. If there are verbatim quotations included in this publication the views and opinions expressed by the interviewees are those of the interviewees and do not necessarily reflect those of the authors, those of the NHS, the NIHR, NETSCC, the HS&DR programme or the Department of Health.

ABSTRACT (500 words)

Background

The tracing and screening of people who have had contact with an active case of TB, is an important element of TB control strategies.

Objectives

This study aimed to carry out a review of evidence regarding TB contact tracing, with a particular emphasis on research that was applicable to TB contact tracing in specific population groups within the UK.

Design

An evidence synthesis of literature of any study design on TB contact tracing in developed countries was carried out.

Setting

Any setting

Population

Individuals found to have active TB disease, and people who have come into contact with them.

Interventions

Contact tracing investigations

Main outcome measures

Any outcome related to TB infection, contact investigations, and/or the views of staff, people with TB disease, or their contacts.

Data sources

Searches for research published 1995 onwards were undertaken in the following databases: Medline via OVID SP; Embase via OVID SP; EconLit via OVID SP; PsycINFO via OVID SP; Social Policy and Practice via OVID SP; CINAHL via EBSCO; Science and Social Science Citation Indices via Web of Science; and the Cochrane Library via Wiley Interscience.

Review methods

The study comprised a review of TB contact tracing in specific population groups, and a review in wider populations. A narrative synthesis was completed and a logic model was developed from the literature.

Results

We included 112 articles in the review; 23 related to specific populations, and 89 related to wider populations. The literature was of limited quality, with much general description of investigations. We identified only two (uncontrolled) studies which could be considered evaluative. While the limitations of the evidence should be recognised the review suggested the following: the value of a location-based approach; working with local communities and the media; partnership working; using molecular epidemiological testing; ensuring adequate systems; and addressing fear of stigma. The literature on investigations for specific populations has much concordance with that reporting findings from wider population groups. Recognised limitations of conventional investigation methods may however, be exacerbated in specific populations.

Limitations

The English language inclusion criteria may have limited the breadth of countries represented. Meta-analysis was not possible due to the nature of the literature. Relevant studies may have been missed by our searches, which used terminology relating to contact tracing, rather than active case finding or screening.

Conclusions

The review identified a sizeable volume of literature relating to contact investigations. However, it is currently predominantly descriptive, with little evaluative work underpinning investigations in either specific or wider populations. Our findings are therefore based on limited evidence. Further research is required if robust conclusions are to be made.

Future work

Research should further explore the development of measures that can be used to compare the effectiveness of different contact investigations, in studies using evaluative designs.

Study registration

The study was registered with the funder and protocol freely available via their website.

Funding details

This work was funded by the National Institute for Health Research, within the Evidence Synthesis Centre Production of Evidence Syntheses for the HS&DR Programme.

CONTENTS

List of Tables and Figures

LIST OF ABBREVIATIONS

AFB smear	Acid-fast bacilli smear
BCG	Bacillus Calmette-Guérin vaccine
DNA	Deoxyribonucleic acid
IGRA	Interferon Gamma Release Assay
LTBI	Latent tuberculosis infection
TB	Tuberculosis (either latent or active)
TST	Tuberculin skin test
UK	United Kingdom
USA	United States of America

GLOSSARY

Active case finding	Systematic screening for active tuberculosis.
Active TB disease	A person has signs of disease that is caused by Mycobacterium tuberculosis or other members of the Mycobacterium tuberculosis complex family in any part of the body, may be infectious, and spread TB bacteria to others.
Contact	An individual who is at risk for TB infection due to exposure to someone with active TB disease.
Contact investigation	A procedure for identifying and evaluating individuals who have been exposed to someone with active tuberculosis.
Index case	An individual with suspected or confirmed active TB disease who is reported to a TB infection control department, and is the case from which the contact investigation begins.
Latent TB infection	A person who is infected with Mycobacterium tuberculosis, but does not have active tuberculosis.
Positive skin reaction	Contacts who have a tuberculin skin test reaction at a cut off designated during an investigation.
Prophylaxis/ prophylactic treatment	Use of a drug for the prevention of active tuberculosis in someone thought to have latent infection.
Skin test conversion	A documented increase in reaction size on a TB skin test, indicative of recent TB infection.
Source case	A person with confirmed infectious TB who is responsible for transmitting TB infection to others. This individual may or may not be the index case.
Specific populations	Any sub-group of the wider population containing individuals or groups who may be at higher risk of TB infection. This includes people described as "hard to reach", those with drug or alcohol problems, homeless people, asylum seekers, immigrants and refugees, people from ethnic minorities, and prisoners.

PLAIN ENGLISH SUMMARY (250 words)

Tuberculosis (TB) is an infectious disease which affects more than two billion people worldwide. Because infection is passed in the air between people, it is important to test people who have been in close contact with a person who has the disease. The testing is to see if they either have signs of infection, or have active TB disease. Looking for people who might have been infected is termed TB contact tracing.

This study carried out a search for research on ways to carry out contact tracing. We aimed to bring together the findings of different studies. We wanted to find out the best ways to trace contacts. Because certain groups of people (such as the homeless or drug users) are more at risk of getting TB, we wanted to know what might work well for them.

We found 112 research papers or reports which were relevant to our study. The research mostly described contact investigations, and counted the number of people who were tested. This does not tell us how effective contact tracing is, as different people with TB will have different numbers of contacts. It was therefore difficult to get a clear understanding of what works best. The research highlighted that investigating places where infected people go is important. Also, the traditional method of asking people to give names of contacts has limitations (especially for people at greater risk). Research also emphasised the importance of local resources, staff skills, systems for managing data, and services working effectively together

SCIENTIFIC SUMMARY (2365 words)

Background

The tracing and screening of people who have come in to contact with an active case of TB, is believed to be a critical component in the control of transmission, and early detection of TB infection. The threat of TB, even in historically low-incidence countries such as the UK, requires the implementation of TB control strategies, including the use of contact tracing investigations. Individuals from specific populations (such as the homeless and substance misusers) are known to be at increased risk of infection. Contact investigations for specific groups may need to be specifically tailored, to maximise effectiveness.

Objectives

The review aimed to answer the following research questions:

- What is the effectiveness and cost effectiveness of specific interventions designed to improve TB contact tracing (such as use of community outreach workers/cultural facilitators, specific interviewing techniques, home/hostel/workplace visits, home/hostel/workplace screening and follow up of contacts) in specific population groups (such as migrants/the homeless)?
- What is the acceptability, feasibility, appropriateness and meaningfulness of specific interventions designed to improve TB contact tracing in these population groups?
- What are the barriers to, and facilitators of, delivery or uptake of contact tracing in these population groups?
- What are the elements of the contact investigation pathway from interventions to impact, for TB contact tracing in wider population groups?
- How might evidence from interventions for wider populations be applied to TB contact tracing in specific population groups including what are the similarities and differences, and what elements of the pathway may be important for feasible, applicable and effective interventions?

Methods

The review used a two stage process. We carried out initial mapping work to develop and refine the scope of the work. We aimed to identify the potential volume of literature that would be available to a full review of TB contact tracing in specific populations, and thereby examine the feasibility and usefulness of carrying out the work. The initial mapping work was then followed by two linked sub-reviews, comprising a review of contact tracing in specific populations and a review of contact tracing in wider populations. Targeted searches of key databases for research published 1995 onwards were undertaken using search terms from existing reviews, supplemented by the review protocol, and terms harvested from other relevant documents. The databases searched in October 2015 were: Medline via OVID SP; Embase via OVID SP; EconLit via OVID SP; PsycINFO via OVID SP; Social Policy and Practice via OVID SP; CINAHL via EBSCO; Science and Social Science Citation Indices via Web of Science; and the Cochrane Library via Wiley Interscience.

The initial focus of the review was TB contact tracing in specific population groups however, following the mapping phase of the work (which indicated only a small body of literature available) we broadened the scope to also include TB contact tracing in any population. The term "specific population groups" was used to mean any sub-groups of whole populations, including individuals or groups who may be at higher risk of TB infection. In order to examine research of most relevance to the UK we included research carried out in countries that are members of the OECD. Contact tracing was defined as any intervention or procedure for identifying and evaluating individuals who have been exposed to someone with active tuberculosis. We included any documents which included reference to contact tracing as part of a TB control strategy. Literature reporting studies of any design was eligible, including reviews and primary studies, and also grey literature in the form of reports and guidelines.

Search results were exported to a reference management database (EndNote version 7) and the software de-duplication process was applied. The database of citations was screened at title and abstract (where available) level initially by one reviewer, and blind second screening of the complete database was shared between two further reviewers. Potentially relevant studies were coded as either "specific populations" or "wider populations". Data in the included studies were systematically extracted to a data extraction form, encompassing: first

author and date; type of document; study design; country of origin; population; research methods; staff involved; measures used; results/data and main conclusions.

Quality appraisal

We had intended to use standard quality appraisal tools to appraise the evidence identified. However, we found that a large proportion of the studies did not use conventional designs such as experimental or longitudinal methods. Instead, studies typically provided narrative (descriptive) reports regarding what had happened during investigations, or re-examined documents recording previous investigations. Where data were provided, it related to numbers of people who had been investigated, and test results, and a large proportion of studies did not fit the criteria for available checklists. We identified only two studies that could be considered to be evaluative.

Synthesis methods

The content of the literature in each sub-review was categorised by characteristics such as country, and type of intervention. Narrative synthesis methods were used to provide an overview of the included studies within the two sub-reviews. The narrative included the exploration of similarities and differences between the sub-reviews, and highlighted data of importance for TB contact tracing in specific populations. In addition to the narrative, a logic model diagram was used to summarise the findings across the two sub-reviews. The purpose of the model was to integrate data from both reviews, in the form of a pathway for contact tracing investigations.

Results

Searching of the electronic databases, and screening of reference lists identified 112 articles of relevance to a review of contact tracing. We identified a total of 23 which related to specific populations and 89 papers relating to wider populations.

The quality of the available literature, as indicated by the proxy of study design, was generally extremely low. The literature was dominated by descriptive accounts of the management of TB outbreaks, where contact tracing investigations had been employed. These papers drew on data from examination of records/case notes, and focussed on reporting the number of index cases and contacts identified, or provided predominantly narrative

(description) regarding the process of the investigations, rather than precise data. The limited nature of the evidence in the area should be fully recognised when considering the findings of the review.

In order to integrate the elements described in the literature we developed a logic model which details factors which underpin contact investigations. These factors relate to: prioritisation and decision-making prior to and during investigations; investigation strategies; TB detection tools; moderating factors; intermediate outcomes; investigation outcomes; and impact. The review of evidence across wider populations tended to echo the findings of the specific populations review, with most elements of the contact investigation pathway outlined being common to both.

There was consensus across the two reviews that the initiation and scope of investigations should be determined by characteristics of the index case of active TB, features of locations of potential exposure, and characteristics of potential contacts. Studies in the two reviews considered approaches to contact investigation which had a population, individual, location, and/or increased quality (improved efficiency and/or effectiveness) focus. Both reviews described the value of social network analysis approaches to map connections between cases and contacts, and there was consensus regarding the importance of a location-based approach, not just tracing personal contacts. In terms of population based approaches, the value of using the media during investigations was emphasised, and also the need to work with local communities in order to provide information and reassurance. The review of specific populations highlighted the overlap between screening, active case finding and contact tracing within approaches to TB control. The use of screening amongst high risk communities was advocated, in particular the use of mobile digital X-ray among the homeless. We highlight that these findings are based on a limited set of studies.

We identified little evidence which permits robust assessment of effectiveness and cost-effectiveness of different interventions. Of the 112 included papers, only two were an (uncontrolled) evaluation of an intervention to improve the efficiency/effectiveness of investigations, and there was little data which permitted associations between strategies and outcomes. The two papers available indicated that interventions, such as providing community workers or providing additional training to staff may be of value. The type of outcomes reported by the majority of studies (number of contacts identified; number found to

have active or latent infection) are problematic for comparing effectiveness between investigations and between studies, as differing contexts will impact these outcomes.

Papers included in the review which used modelling methods to estimate effectiveness and cost effectiveness, indicated that contact tracing is an effective intervention. However, there are cautions that this may be only if it achieves relatively complete population coverage, and includes preventive therapy. Both of these areas were highlighted in the review of specific populations, as being challenging for investigations.

We found limited data regarding barriers and facilitators to investigations. The use of IGRA testing rather than TST was suggested to overcome barriers of loss to follow up, although cost implications were highlighted. The literature described the need for adequate resources and adequate systems for delivering investigations. The role of fear of stigma, and population beliefs/understanding in determining uptake of contact tracing, were common to investigations in both specific populations and wider groups.

The use of molecular epidemiology to augment investigations was described in both reviews, with the added value of the method recognised for both specific populations and wider groups. Partnership working was reported as important to increase the efficiency/effectiveness of investigations across all populations.

Conclusions

The review identified a substantive number of studies relating to contact investigations. The literature is predominantly descriptive however, with very little empirical work evaluating investigations in either specific or wider populations. Currently, studies which have used mathematical or economic modelling methods are the predominant means of examining the effectiveness of contact investigations, and the outcomes of different strategies. Studies using evaluative designs are required, if robust conclusions regarding associations between different contact investigation methods and outcomes are to be made. The results of the review highlight the complexity of the pathway from initial decision-making to achieving long term impact on the health of the population. The differing nature of the context of each investigation is problematic when endeavouring to make comparisons between the effectiveness of different contact investigations.

The literature on investigations for specific populations has much concordance with that reporting research findings from wider population groups. The literature relating to both specific populations and wider groups highlights limitations of conventional contact tracing approaches, in particular asking index patients to name contacts. Recognised limitations of conventional investigation methods may however, be exacerbated in specific populations. Conventional methods of dividing contacts into groups of close versus casual contacts also requires further consideration and clarification. In particular for specific populations, casual contacts may be of most importance in transmission, and conventional prioritisation systems may need revising. The importance of considering contacts at locations of potential transmission was highlighted across both the sub-reviews, although here again this strategy may be of particular importance for investigations in specific populations.

Currently, there are indicative studies to suggest that the quality (efficiency and/or effectiveness) of investigations may be enhanced by the use of additional testing such as molecular epidemiology. Few studies describe how systems and processes during investigations may be optimised, to overcome the range of moderating factors which are described in the literature. The examination of outcomes more closely relating to these systems and processes may help to address the limitations of the current evidence base examining the relative effectiveness of different contact tracing strategies.

The limited nature of the evidence available should be fully recognised when considering the following implications for healthcare and research.

Implications for healthcare (in priority order)

1. Existing studies indicate the potential limitations of contact naming, with location-based methods recommended to establish a complete picture of contact networks. In particular a location-based strategy may be a more effective approach in specific populations. This finding was based on studies which described contact investigations, rather than evaluated interventions.

2. The available research suggests that contact investigations in specific populations may require greater prioritisation of investigation of casual contacts (non-household), than in other

groups. This finding was based on studies which described investigations, rather than which evaluated interventions.

3. The results of the review suggest that an emphasis on the evaluation of processes and intermediate outcomes (such as engaging with treatment), may provide valuable data regarding factors determining the effectiveness of investigations.

4. Available research indicates that adequate systems, process and resources including local expertise and skilled staff; sufficient workforce capacity; data management systems, and effective co-ordination between agencies are important. This finding is based on descriptions and recommendations in the included literature, rather than empirical work. One evaluative study provided limited evidence that additional staff training may be beneficial.

5. Research studies suggest that use of mass media and other avenues for provision of information and advice may be effective in improving communication with communities and individuals at risk during investigations. This finding is based on recommendations in the included literature, rather than empirical work.

Implications for research (in priority order)

1.. Future studies should aim to adopt an evaluative approach, to increase the evidence base regarding associations between different contact investigation strategies and outcomes. We identified only two studies which could be considered to be evaluative.

2. Research studies should further explore the development of measures that can be used to compare the effectiveness of different contact investigations. The reporting of numbers of contacts identified during an investigation as a measure of success, or number who tested positive has considerable limitations.

3. Interventions targeting local expertise and staff skills, workforce capacity, systems and processes (such as data management and co-ordination between agencies), and lay knowledge, beliefs and behaviour should be developed and evaluated, in order to address moderating factors reported in the literature. This is based on findings from qualitative studies, and recommendations from descriptive studies outlining contact investigations.

4. Researchers should include the measurement of intermediate indicators of effectiveness such as the timing of identification of cases/clusters, the promptness and efficiency of investigation, the accuracy and completeness of information, and awareness of symptoms/need for testing amongst contacts, when reporting investigations that have been undertaken. These factors were not reported in the literature, yet our logic model indicates that they may be important elements of the investigation pathway.

Study registration

This study forms part of ongoing work within the National Institute for Health Research Health Services and Delivery Evidence Synthesis Centre. As the work is developmental and ongoing the review was registered with the funder and protocol freely available on their website.

CHAPTER ONE; BACKGROUND

Tuberculosis (TB) is an infectious disease, with latent infection estimated at more than two billion people worldwide.[1] While approximately 95 per cent of cases of TB occur in developing countries, TB disease also exists in low-incidence countries, including the UK.[2] TB is known to disproportionately affect specific population groups including the socially disadvantaged, immigrants, and those with complex lifestyles (such as users of drugs or excessive alcohol).[3] While levels of TB may be low in countries such as the UK, TB control strategies, including the use of contact tracing investigations remain important to control levels of disease.

The priority of TB disease control programmes is the early identification and successful treatment of people with active infection to avoid further transmission. Strategies for TB control also include the efficient detection and treatment of latent infection to avoid further transmission. Approaches to identify individuals with either active or latent infection include the screening of high risk groups, active case finding, and also contact tracing.[4]

Transmission of TB occurs via inhalation of airborne particles from an infected person.[1] The tracing and screening of people who have had contact with an active case of TB, is therefore a critical component in the control of transmission, and early detection of infection.[5] Contact tracing/investigation has three main objectives.[6] Firstly, to identify additional cases of active TB amongst contacts (to initiate treatment and avoid further transmission); secondly, to identify contacts with latent TB infection in order to offer preventive treatment (to prevent progression to active TB infection); and thirdly, to identify and treat the source of an outbreak. Contacts who show evidence of latent TB infection and who complete a course of prophylactic treatment, may reduce the risk of progressing to active TB disease by 60-70 per cent.[7] Investigation to identify contacts of an individual with active TB disease is therefore considered a key tool in control of TB, to enable early detection of infection and disease, and for prevention of secondary cases.[8]

RESEARCH QUESTIONS

- What is the effectiveness and cost effectiveness of specific interventions designed to improve TB contact tracing (such as use of community outreach workers/cultural facilitators, specific interviewing techniques, home/hostel/workplace visits, home/hostel/workplace screening and follow up of contacts) in specific population groups (such as migrants/the homeless)?
- What is the acceptability, feasibility, appropriateness and meaningfulness of specific interventions designed to improve TB contact tracing in these population groups?
- What are the barriers to, and facilitators of, delivery or uptake of contact tracing in these population groups?
- What are the elements of the contact investigation pathway from interventions to impact, for TB contact tracing in wider population groups?
- How might evidence from interventions for wider populations be applied to TB contact tracing in specific population groups including what are the similarities and differences, and what elements of the pathway may be important for feasible, applicable and effective interventions?

CHAPTER TWO: REVIEW METHODS

The review used a two stage process. We carried out initial mapping work to develop and refine the scope of the work. This was then followed by two linked sub-reviews to identify and synthesise the most directly relevant evidence in this field.

Initial mapping work

An initial phase of mapping was used to broadly describe the published literature on contact tracing for TB in specific population groups, particularly that relevant to the UK NHS and similar healthcare systems. We aimed to examine the potential volume of literature on contact tracing in specific populations, to see if a full review of this evidence would be viable and provide potentially useful information. We used the term "specific population groups" to mean any sub-groups within whole populations (individuals or groups) who may be at higher risk of TB infection. This includes people described as "hard to reach", those with drug or alcohol problems, homeless people, asylum seekers, immigrants and refugees, people from ethnic minorities, and prisoners. The mapping exercise was intended to guide decisions regarding the focus of further review work in this area.

Mapping review search strategy

Targeted searches of key databases were undertaken using search terms in previous reviews, supplemented by the review protocol, and terms harvested from relevant evidence. We applied broad inclusion criteria and did not seek to distinguish between different potential purposes of contact tracing in tuberculosis prevention and management during the searching process or during the later stages of the review. The search focused on terms relating to people with tuberculosis, with terms relating to the intervention (contact tracing). While we were primarily interested in finding literature on specific populations that may be at greater risk of TB, we did not use any search terms for particular sub-groups. We felt that an *a priori* decision on terms relating to specific populations may lead to key groups being missed. The mapping review therefore used general population terms, with the aim of sifting out literature relating to sub-groups from the retrieved citations.

The terms relating to contact tracing were harvested from the NICE Evidence Review on Tuberculosis[9] and other relevant evidence. The search was limited to studies in English language, in human populations due to the restricted timescale for this work. Literature published between 2000 and 2015 was retrieved. It was expected that any significant earlier work would be included via review studies. The databases searched in October 2015 were: Medline via OVID SP; Embase via OVID SP; EconLit via OVID SP; PsycINFO via OVID SP; Social Policy and Practice via OVID SP; CINAHL via EBSCO; Science and Social Science Citation Indices via Web of Science; and the Cochrane Library via Wiley Interscience. We screened reference lists of included studies for relevant grey literature, and requested potentially relevant literature from topic advisors. The search terms used are provided in Appendix 1.

Mapping review sifting and identification of relevant literature

Search results were exported to a reference management database (EndNote version 7) and the software de-duplication process was applied. The database of citations was screened at title and abstract (where available) level initially by one reviewer, and blind second screening of the complete database was shared between two further reviewers. Potentially relevant studies on contact tracing were identified.

Full review methods

We incorporated the results of the mapping review into one of two sub-reviews. The full review encompassed: a sub-review of contact tracing in specific populations (including and extending the literature found in the mapping work); and a sub-review of TB contact tracing in wider populations.

Search strategy

We re-examined the citations retrieved in the mapping review searches, and also extended the date inclusion to 1995 onwards in a second search in March 2016, thus examining over 20 years of research. In addition to topic-based searching of electronic databases, we screened the reference lists of included studies.

Sifting and identification of relevant literature

Search results were exported to a reference management database (EndNote version 7) and the software de-duplication process was applied. The database of citations was screened at title and abstract (where available) level initially by one reviewer, and blind second screening of the complete database was shared between two further reviewers with approximately 95% agreement. Potentially relevant studies were coded as either "specific populations" or "wider populations".

Following this screening, all coded records were re-examined to identify literature relating to specific population groups (such as those described as hard to reach, minority ethnicity, substance abusers, homeless, migrants, drug users or prisoners) versus papers which related to wider populations or which included wider populations as well as particular sub-groups. We identified and excluded work carried out in countries of less relevance to the UK NHS (countries which are not members of the Organisation for Economic Collaboration and Development [OECD]).

Data extraction

We used a data extraction form developed using previous experience of the team, which was piloted on several studies before the final version was established. Data in the included studies were systematically extracted to the form, encompassing: first author and date; type of document; study design; country of origin; population; research methods; staff involved; measures used; results/data and main conclusions. See Appendix 2 and Appendix 3 for the completed data extraction tables.

Quality appraisal

We planned to select appropriate tools for quality appraisal based on the study designs that we found in the included literature. These included checklists such as that developed by the Cochrane Collaboration, and the Critical Skills Appraisal Programme.[10, 11] The literature that we found however was more limited than we had expected. Studies tended to be descriptive reports of contact investigations, either around the time that the investigation was carried out, or at a later point, where records completed at the time were retrospectively examined by the research team. This literature did not use evaluative experimental or observational designs that are typically included in systematic reviews, and was not suitable for appraisal using established checklists. Criteria that might be used to assess quality, such as sample size, were

not indicators of robustness, as a larger number investigated was not representative of a better quality investigation (indeed the reverse might be true). Other aspects that may be indicators of quality such as sampling strategy or robustness of outcome measures, were also not applicable for this literature which was dominated by descriptions of what happened during investigations with complex outcomes. Studies that we categorised as "qualitative" referred to interviews with cases and contacts however, qualitative data were not always provided. While grey literature is typically considered to be of lower quality than peer-reviewed published papers, many of the reports and guidelines we identified were based on reviews of the literature (some robust systematic reviews) and therefore was considered to not necessarily be weaker than the published studies. In the following synthesis however, we have separated the reports and guidelines from the other studies, by describing them last in each section.

Given these assessment challenges we considered whether and how to attempt to grade the identified literature on the basis of quality. We reached the conclusion that a quality criteria checklist approach was not feasible as there were no clear indicators of quality, and study methods were diverse. We therefore adopted an approach to quality appraisal whereby we highlighted those few studies of a stronger design, and any issues of particular concern during the narrative synthesis.

Approach to synthesis

The literature was divided into papers which focused on specific populations versus those which had a wider population focus, these groups of papers formed two sub-reviews. The content of the literature in each sub-review was categorised by characteristics such as country, and type of intervention. Narrative synthesis methods were used to provide an overview of the included studies within the two sub-reviews. The narrative included the exploration of similarities and differences between the sub-reviews, and highlighted data of importance for TB contact tracing in specific populations. In addition to the narrative, a logic model diagram was used to summarise the findings across the two sub-reviews. The purpose of the model was to integrate data from both reviews, in the form of a pathway for contact tracing investigations. The logic model diagram outlines key elements of the pathway, from initial decision-making regarding investigations, to outcomes and impacts.

Inclusion criteria

- The initial focus of the review was TB contact tracing in specific population groups however, following the mapping phase of the work, we broadened the scope to also include TB contact tracing in any population. We considered "specific population groups" as encompassing any sub-groups within whole populations, including individuals or groups who may be at higher risk of TB infection. This includes people described as "hard to reach", those with drug or alcohol problems, homeless people, asylum seekers, immigrants and refugees, people from ethnic minorities, and prisoners.
- We defined contact tracing as any intervention or procedure for identifying and evaluating individuals who have been exposed to someone with active tuberculosis. We adopted broad criteria for the types of studies of interest, including those which aimed to evaluate outcomes following contact tracing investigations, and also those describing or exploring the delivery of investigations. We aimed to focus on contact tracing activities rather than screening, active case finding, or other interventions to reduce infection and/or transmission. We recognised however, that these distinctions may not be clear cut, and there may be overlap between these purposes. We therefore included any papers which included reference to contact tracing as part of a TB control strategy.
- In relation to comparators, we included studies with any comparator, or studies with no comparator. As we intended to produce an inclusive review, studies of any design, including experimental, observational, cross-sectional, qualitative and reviews were eligible, together with grey literature in the form of reports and guidelines.
- We included studies which reported any outcome related to contact tracing activity.

Exclusion criteria

- We excluded research that was published prior to 1995.
- We excluded studies carried out in countries that are not members of the OECD. We intended to focus the review on low TB incidence countries which are most applicable to the UK.

- We excluded studies that comprised discussion or opinion, and did not relate to specific investigations.
- We excluded conference abstracts, theses, letters to the Editor and other commentaries.

CHAPTER THREE: RESULTS OF THE REVIEW

Results of the mapping work

Searching of the electronic databases identified 13 articles of relevance to a review of contact tracing in specific populations. Figure 1 provides an overview of the results of the mapping work.

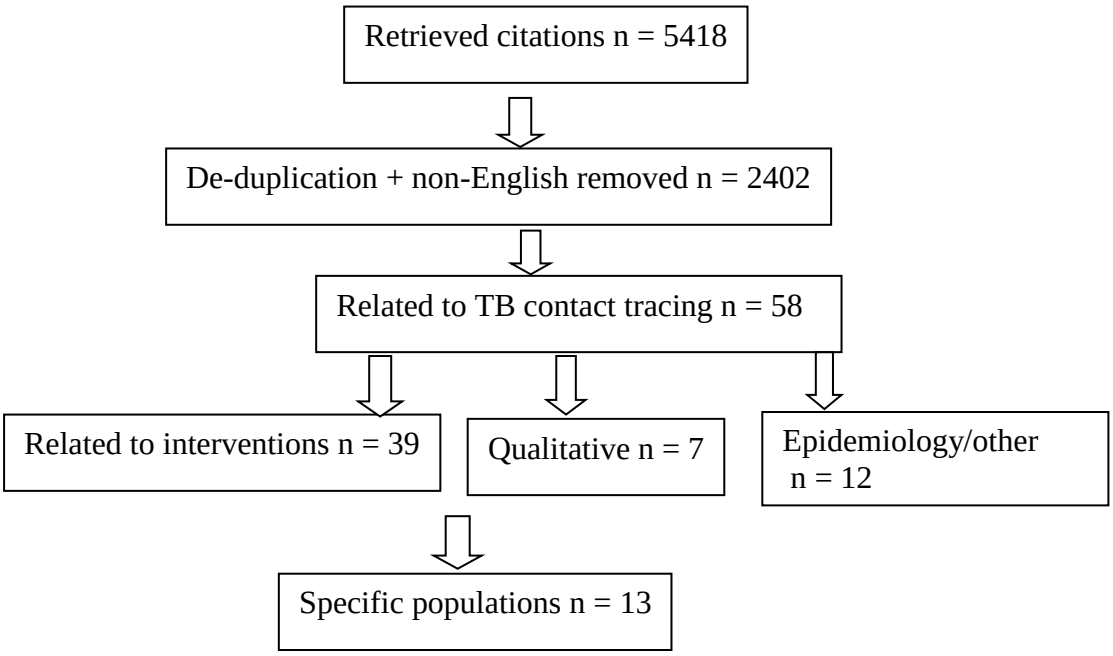

Figure 1. Results of the mapping work

The mapping exercise indicated that there was unlikely to be a large number of research studies on contact tracing in specific populations, and data identified were likely to derive from poor quality studies. It was anticipated that the conclusions which might be drawn from a full review of this literature would be restricted by the limited numbers and quality of available research studies. Following the mapping exercise we therefore proposed three potential options for further review work. The options below were presented for discussion

with local and national policy makers, topic experts, infectious disease and public health practitioners, specialists in the field and representatives of the review commissioners (the NIHR HS&DR programme).

1. Widen the population inclusion criteria to TB contact tracing in any population (not just specific populations) and explore in particular implementation processes and feasibility. The mapping work indicated that there would be a substantive number of studies available to synthesise.

2. Examine contact tracing in specific populations for other conditions drawing on data from existing systematic reviews. The other conditions included would need to be carefully considered, to ensure that findings from these research studies would be applicable to TB, with careful documentation regarding the criteria for judging applicability. The review would aim to examine what may be learned from tracing in specific population in other conditions, and applied to contact tracing in TB.

3. The mapping exercise indicated that social network approaches, and use of community workers may be promising approaches to TB contact tracing in specific populations. Further work could comprise a systematic review of these interventions in relevant conditions.

The three options presented seemed to offer different potential for adding to the knowledge base. The first option would have the advantage of keeping the focus on the condition and using instrumental lessons from the literature. However, coverage would be limited to approaches that have actually been implemented, and based on the mapping review of interventions in specific populations, there may be a limited number of and poor quality of research studies. The second option would focus on the conceptual/theoretical contribution of the wider literature. It might offer innovative solutions from other populations and settings however, might be limited by heterogeneity in the nature of "contacts" and issues of applicability. The third option might shed further light on the mechanisms and processes underpinning these promising interventions, and any issues of implementation reported in other conditions. However, differences in context and delivery may reduce the applicability to TB contact tracing.

Following consultation on the mapping review findings with topic experts in TB and Public Health, we received feedback that option two would have limited value due to the challenges inherent in applying findings from other conditions to contact tracing for TB. Topic experts expressed the opinion that, due to the relatively low transmissibility, the long and extremely variable incubation period, the limitations of existing diagnostic tests of infection and disease, and other issues, TB is sufficiently different to other infectious diseases for which contact tracing is conducted. These differences would severely limit the applicability of a review of contact tracing in other conditions, to research and practice in the area of TB. Following feedback and discussion with the HS&DR team, the decision was made that further systematic review work would include contact tracing in wider populations, with a particular focus on what could be learned and applied to interventions for specific population groups. We therefore progressed to implementation of option 1.

Results of the full review

Searching of the electronic databases, and screening of reference lists identified 112 articles of relevance to a review of contact tracing. We identified an additional 10 papers relating to specific populations (further to the 13 found in the mapping exercise) giving a total of 23. The remaining 89 papers related to wider populations. Figure 2 provides an overview of the inclusion process. Appendix 3 provides a list of papers excluded a full text and reasons for exclusion.

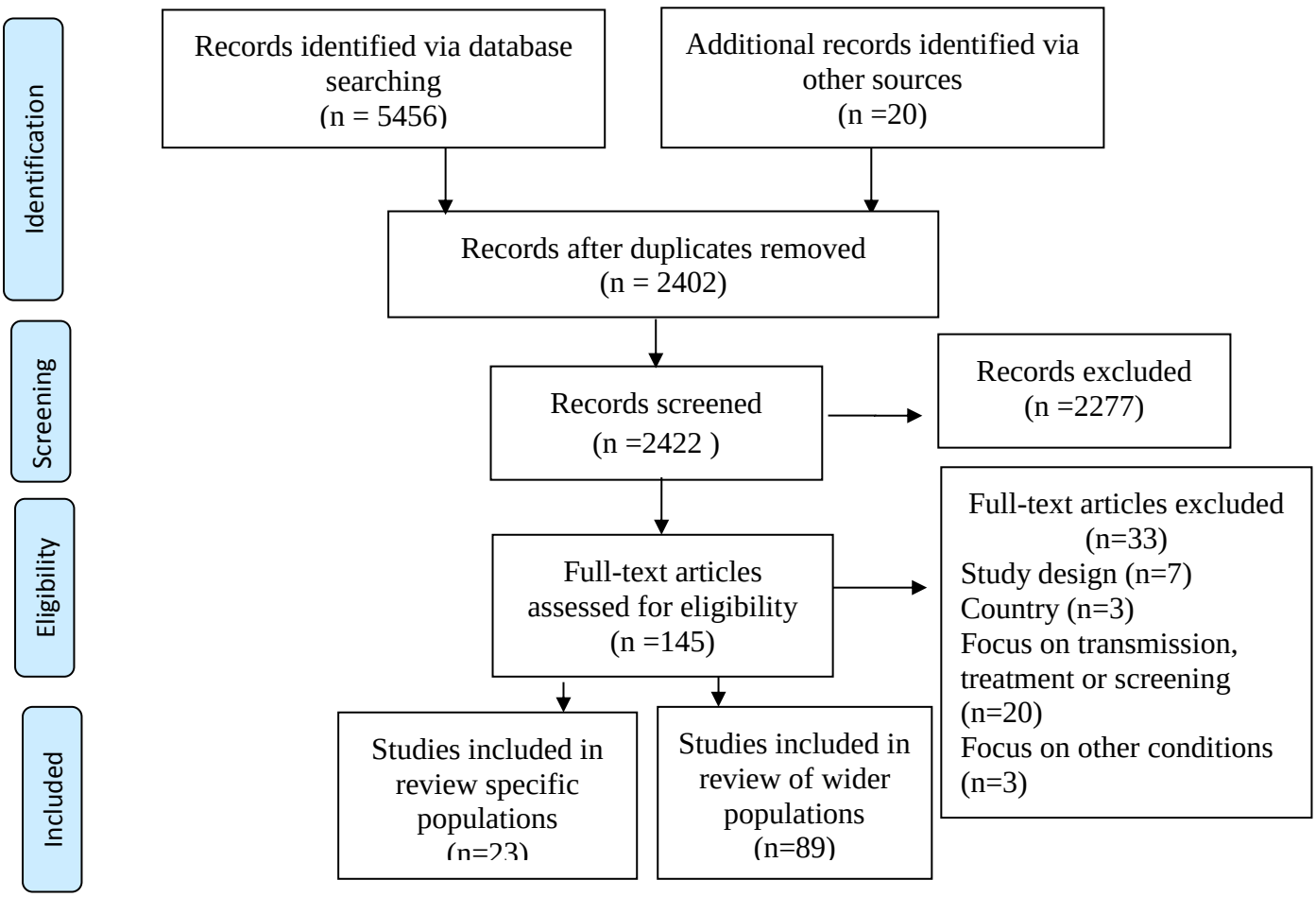

Figure 2. PRISMA diagram illustrating the inclusion process

RESULTS OF REVIEW OF TB CONTACT TRACING IN SPECIFIC POPULATIONS

Characteristics of the literature

We identified 23 papers with a focus on TB contact tracing in specific populations. Sixteen of the papers originated from North America [12-17 18 19 20 21 7 22 5 23 24 25] and five from Europe,[26-30] together with a systematic review from the UK[9] which formed the basis of national guidance.[31]

Five studies examined contact tracing in migrants,[18, 26-29] four in drug users (one included homeless persons)[7, 15, 19, 30] five in homeless people,[24 12-14, 21] one in an ethnic minority group,[25] one in prisoners,[5] one predominantly in individuals with human immunodeficiency

virus (HIV) who were described as "gay, transvestite or transsexual."[23] One study reported a contact investigation surrounding customers of a bar who mostly "used alcohol excessively",[16] and five further papers described individuals as being "hard to reach" or from a range of different population subgroups.[22 9, 17, 20, 31]

Quality of the literature

The quality of the available literature, as indicated by the proxy of study design, was generally low. We found one systematic review on rates of contact tracing in migrants versus local populations,[29] one review on the cost-effectiveness of control strategies among immigrants and refugees,[18] and an effectiveness and cost effectiveness review of interventions among hard to reach groups which was un-published report.[9] One study used an evaluative design to examine the period prior to introduction of a community worker intervention, compared to during the introduction period itself.[26] Two studies reported that they included elements of qualitative methods (interviews) although neither provided qualitative data.[19 20] The literature was dominated by studies which we term "descriptive accounts" of the management of TB outbreaks, where contact tracing investigations had been employed. These papers provided narrative about how an investigation was carried out, and often provided data reporting the number of index cases and contacts that were identified. These data do not provide an indication of effectiveness, as each investigation will inevitably differ in terms of number of contacts that should be approached, and identifying more contacts (rather than appropriately targeting) is not necessarily an optimal outcome. Table 1. provides an overview of the literature by study design.

Table 1. Literature classified by study design

Systematic review	Mulder et al. 2009[29]
Cost effectiveness review	Rizzo et al. 2011[9] (unpublished report) Dasgupta et al. 2005[18]
Uncontrolled comparator design	Ospina et al. 2012[26]
Reported qualitative elements	Ashgar et al. 2009[19] Wallace et al. 2003[20]
Descriptive accounts of investigations	Bur et al. 2003[5]

	McElroy et al. 2003[7] Li et al. 2003[12] Lofy et al. 2006[13] McElroy et al. 2003[14] Oeltmann et al. 2006[15] Kline et al. 1995[16] Malakmadze et al. 2005[17] Yun et al. 2003[21] Fitzpatrick et al. 2001[22] Sterling et al. 2000[23] Curtis et al. 2000[24] Cook et al. 2012[25] Van Loenhout-Rooyackers et al. 2002[27] Mulder et al. 2011[28] de Vries and van Hest, 2005[30]
Guidance	National Institute for Health and Care Excellence, 2012[31]

Decision to instigate contact tracing and prioritisation of contacts

The included papers highlighted factors in the decision-making process that occurs prior to, and during contact tracing investigations for specific populations. Factors that were described impacted on the degree and type of response following identification of a case of active TB infection, including the prioritisation of contacts to trace. These factors were: the infection level of the source case and perceived risk; the proportion of close contacts found to have active or latent infection; the estimated period of time for which the case had exhibited active TB; the potential locations of exposure; the potential intensity of exposure; and the susceptibility of contacts. One study emphasised that the diversity of elements that need initial and ongoing consideration, require that contact tracing investigation methods be tailored to particular circumstances.[20]

Types of contact tracing investigations

The included studies provide a range of descriptive data related to contact tracing investigations, with only one paper which could be considered to be evaluating an investigation.[26] Other papers reported strategies used during outbreaks, and/or discussed the use of different strategies during the investigation. The strategies described can be broadly categorised into: firstly, those which target all members of a specific population; secondly, those targeting individuals within a specific population; thirdly, those which target the locations frequented by infected individuals and members of a specific population; and finally, strategies which aimed to enhance the quality (efficiency/effectiveness) of contact investigations.

Population-based contact tracing strategies

Three studies described population-based strategies.[26 29 30] In relation to contact tracing strategies targeting all members of a specific population, authors described the use of local news/media to publicise an outbreak, and outlined how the media may be used to encourage those who may have been in contact with a case or those who may be exhibiting symptoms, to come forward for testing.[29] Community meetings were suggested as useful way of publicising an outbreak or providing health information.[26] One paper recommends the use of mobile digital X-ray units for screening among groups such as drug addicts and homeless persons, when there was expected to be poor compliance with skin testing.[30] The authors of this study provide data on numbers examined during the outbreak, but no data which evaluate use of the X-ray unit versus methods of contact investigation. The study emphasised the overlap between use of chest X ray during investigations, and activities which could be considered population screening. Indeed, following the outbreak, a programme of mobile X-ray screening for this population was reported to have been introduced. UK national guidance advocates the use of digital mobile radiography screening in settings where at risk people congregate.[31]

An un-published report of a systematic review of interventions which aimed to identify people with TB or raise awareness of TB among hard to reach populations[9] concluded that incentives to increase the take up of TST and enhance compliance in further investigation, are

effective and cost effective in drug users and homeless populations. The authors recommended that an active approach to case finding, rather than contact tracing, may be most effective in hard to reach or at risk populations. The report formed the basis of national guidelines.[31]

Contact tracing strategies targeting individuals

The literature frequently refers to "conventional contact tracing," a term used to refer to an investigation method based on interviewing an index case, and asking them to name individuals with whom they have been in contact. The conventional contact tracing approach uses principles termed "stone in the pond" or "concentric circles" to refer to widening an investigation from only named close contacts, to other contacts (usually described as casual or non-close). Several papers outlined the limitations of the conventional contact tracing method, in particular a reluctance to name contacts[19, 23] and the influence of perceived stigma underpinning this reluctance.[9, 29] It was highlighted that index cases may more freely reveal the names of household contacts and workplace contacts, than social contacts.[22]

Three papers highlighted the limitations of conventional contact naming approaches when investigating outbreaks centred on homeless shelters.[12-14] One paper[12] found that the number of contacts identified per homeless patient was significantly lower than for non-homeless patients (median 1 vs. 4, $p< 0.001$; mean 2.7 vs. 4.8, $p<0.001$). Homeless patients were four times more likely to have no contacts identified ($p<0.001$). The study suggested that investigation methods other than conventional contact tracing should be used, with strategies focused on identifying the location of exposure rather than eliciting names of contacts. The authors also suggested that conventional prioritisation systems for widening contacts may need to be revised, with being homeless at the time of diagnosis used as an indicator for prioritising prompt contact evaluation.

Another study reported similarly low numbers of contacts being named by homeless persons.[13] In this investigation the median number of named contacts was 3.5 (mean 4.8) per index patient, and 14% of patients named no contacts. Rather than relying on patient contact naming, the investigation had used attendance records where available, or staff recollections to prioritise TB screening. Prioritisation of locations for investigation was based on the number of infectious patients who visited each facility, and the prevalence of positive TST

results compared with other homeless sites. Contacts were prioritized for screening based on their cumulative number of exposed visits. It is important to note that while the methods outlined in this study were described as a contact investigation, they could also be considered to be population screening. The use of screening, rather than contact investigation in specific populations was highlighted in the study by Curtis et al.[24] The authors recommended that routine screening should be considered in homeless shelters, to overcome the limitations of the conventional contact tracing approach.

Contact tracing strategies focused on locations

Six papers emphasised that locations, rather than individuals are the key to TB transmission in specific populations.[7, 16, 17, 19, 22, 25] Authors of these papers argued that contact tracing investigations should therefore focus on identifying potential settings of transmission.

The use of a social network analysis approach (referred to as epidemiological investigation by some authors) which explores links between individuals (including the locations frequented), was described as valuable in populations of drug users, aboriginal communities and "hard to reach" populations. Network analysis methods create diagrams which illustrate links between key individuals and their contacts, together with the types of activities in which cases and contacts engage. Authors of one paper which outlined network methods[19] reported that the limitations of conventional contact naming methods could be overcome by investigation staff visiting and observing locations frequented by an index case. Of 187 contacts in their investigation, 49% were named and 10% were observed at a local "crack house". The contacts that were identified by observation were eight times more likely to have positive skin test results than those who were named (relative risk = 7.8, 95% confidence interval = 3.8-16.1).

A study describing a contact investigation that was focused on a neighbourhood bar[16] reported that the index patient (a homeless person) named few contacts, but had spent most time in the bar. This index case proved to be highly infectious with 14 linked cases of active TB and 27 cases of latent infection detected. In most cases the bar was the only site where there was any contact with the index patient, for those who were found to be infected. Use of a network approach to investigation in another study[17] echoed the importance of investigating

potential locations for transmission. Construction of a social network diagram revealed several previously unrecognized locations of transmission, including a single-room occupancy hotel, homeless shelters, a bar, and crack houses. Another study using social networks methods[22] found that the majority of people identified with active TB disease were members of a single social network, and reported that the approach had been essential to identify this link.

Cook et al.[25] concluded from their discussion, that methods including social network analysis, geographic information systems and genomics could improve the assessment of transmission, together with the prioritising of contacts. These methods were needed to overcome a key limitation of conventional contact tracing approaches, which was described as not sufficiently taking account of the differing social structure of different populations.

UK guidance recommends that investigations should be co-ordinated at places where an index case spends significant amounts of time, and where people at risk congregate.[31]

Elements which enhance the quality (efficiency/effectiveness) of contact tracing investigations

A study outlining a contact investigation in both a prison and the community emphasised the importance of inter-agency working when carrying out an investigation.[5] Another paper reported that at least half of the outbreak patients who were living in homeless shelters, had spent time in prison or had visited the local Sexually Transmitted Diseases Clinic in the prior two year period.[14] The authors therefore suggested that TB control strategies would be enhanced by employing a joined up approach to TB control among the relevant agencies.

Other methods described to improve the efficiency/effectiveness of contact tracing investigations in specific populations, included the use of DNA fingerprinting/molecular epidemiology. These additions to an investigation were described as valuable to permit the further analysis of relationships between cases, and for the establishment of clusters. Use of these technologies was described by authors of several studies as being an essential part of TB control strategies, as contacts could be infected by cases other than the presumed

source.[16, 29] Also, DNA fingerprinting was recommended as useful for investigating cases once regular contact tracing procedures had been completed.[27]

The value of investigations having a location, rather than individual focus, was also echoed in a paper outlining the use of molecular epidemiology.[14] It was suggested that DNA fingerprinting may offer a useful impetus to further question a patient regarding routine, contacts, and places frequented, and thereby to uncover social networks in communities where contact naming is challenging.[14] A paper describing further investigation of a cluster of cases in a "hard to reach" population[17] found that by using genotyping methods in addition to conventional contact tracing, an additional 98 contacts which had been missed during routine contact investigation, were identified. The authors recommended that genotyping should be used alongside other methods of contact tracing, as it can aid detection of unapparent transmission before an increase in incidence, and thus will help identify clusters earlier. They highlighted however, that in order to be successful, a policy of genotyping isolates from all (not just some) patients with culture-positive TB is required in order to identify clusters.

Three papers referred to the value of using community workers during contact investigations.[15, 23, 26] One study evaluated a staff-based intervention which introduced trained community health workers in areas of high immigration.[26] The workers were described as benefitting the contact tracing process by acting as translators and cultural mediators, and also as facilitators during treatment. The study found a statistically significant increase in contact tracing coverage among immigrants during the intervention period, compared to the previous period of time (81.6% compared to 65% $p<0.001$). A second paper mentioned that community workers were used during contact tracing among "highly mobile" communities.[23] National guidance also recommended the use of peer educators where available and appropriate during investigations.[31] One paper describes the persistence and flexibility required by outreach workers investigating an outbreak among a group of illicit drug users.[15] Workers had to arrange meetings at times and locations convenient to the group, and spent many hours establishing trust in order to gain co-operation. The authors describe how screenings could take place in varying locations including street corners and in car parks. Often outreach workers were successful only after spending hours driving around the community, searching for patients and contacts.

UK guidance highlights the need for partnership working between organisations in high quality investigations.[31]

Factors which can influence contact tracing investigations

Sensitivity and specificity of tests

Three papers discussed the accuracy and feasibility of different testing tools used during investigations.[10, 26, 27] Authors describe potential issues of specificity with the Tuberculin Skin Test (TST), particularly from individuals in high-incidence TB countries.[29] A study describing an investigation in homeless shelters found that screening contacts with one sputum culture, was as sensitive as chest radiography in detecting active TB disease (77% versus 62%).[13] Authors of one paper examining contact investigations in drug addict and homeless populations, highlighted another factor influencing the success of investigations, namely the poor take up of testing.[30]

Systems and processes

Authors of two further papers mentioned other factors that could assist, or provide obstacles to effective contact investigations.[18,19] Factors that could assist included local expertise, local capability, communication and co-ordination, prompt action, effective data management and infrastructure systems.[22] Perceived social stigma., the identification of additional contacts after the investigation had closed, or failure to perform the initial evaluation due to error or lack of resources were obstacles described.[21]

Social factors

One study outlined the need to customise investigations to individuals, by taking into account language and cultural differences, and different settings.[20] This paper described challenges in conventional contact tracing in the foreign-born (due to different languages spoken), also in prison populations (due to different systems between prisons and states), and in the homeless (due to movement of individuals between shelters). In order to address these challenges the authors recommended: different agencies working together efficiently; accurate record keeping in shelters; and the use of photographs rather than relying on names when tracing contacts of homeless people. The work however, provides little or no data to support these recommendations. A second paper[24] highlighted that the refusal of an index patient to visit a hospital to investigate symptoms, could result in delay in instigating an investigation, and thereby increased the chance of disease transmission.

Outcomes and impacts following contact tracing investigations

Study authors[5, 16, 21] highlighted the issue of non-completion of treatment as hindering successful outcomes from contact tracing. In one study,[21] less than a third of infected prisoner contacts completed treatment, and in another study[5] only 44% of homeless people completed treatment. Kline et al.[16] reported that 19 of the 39 people with positive TSTs in their study attended follow up appointments. Of these, 13 contacts refused prophylaxis or did not complete their treatment, with three individuals progressing to active TB within two years. The authors highlighted that chronic alcoholism may be a high-risk factor for progression to active disease, and that major efforts to ensure completion of six months of isoniazid therapy are worthwhile in an alcohol-user population.

The outcomes most frequently reported by studies as indicating the effectiveness of contact tracing investigations were: firstly, the number of contacts identified (yield); and secondly, the number of positive skin test results. One study[18] examined the cost-effectiveness of TB control strategies including screening and contact tracing. The authors concluded that contact tracing (particularly in ethnic communities) may be more cost efficient and less intrusive than screening.

Main findings and implications from review of contact tracing in specific populations

The review found a small number of studies relating to contact investigation in specific populations. This is consistent with other related reviews such as Rizzo et al.[9] and Fox et al.[32] The findings of the review suggested that methods which focus on locations rather than individual naming of contacts, and approaches which draw on social network methods may be of value. The provision of community health workers may also enhance the efficiency/effectiveness of investigations. The use of screening rather than contact investigation may be useful in a homeless population. The evidence base however, is limited and underpinned by little empirical work. While we identified a total of 23 papers across specific populations, the data are predominantly descriptive rather than evaluative. The following review of contact tracing examining literature in wider populations, was carried out

with the aim of providing additional insight into what may be learned and applied to contact tracing in specific populations.

RESULTS OF REVIEW OF TB CONTACT TRACING IN WIDER POPULATIONS

Characteristics of the literature

We identified 89 papers which met our inclusion criteria for the review of wider populations.[1-3, 6, 8, 32-115] These studies originated from a variety of countries, with the greatest number from North America (see Figure 3). We excluded studies from countries which are not members of the OECD, therefore the included literature is from contexts most applicable to the UK. While these papers related to investigations in wider populations, some also included data relating to specific groups within their analysis, or mentioned elements of particular relevance for specific groups.

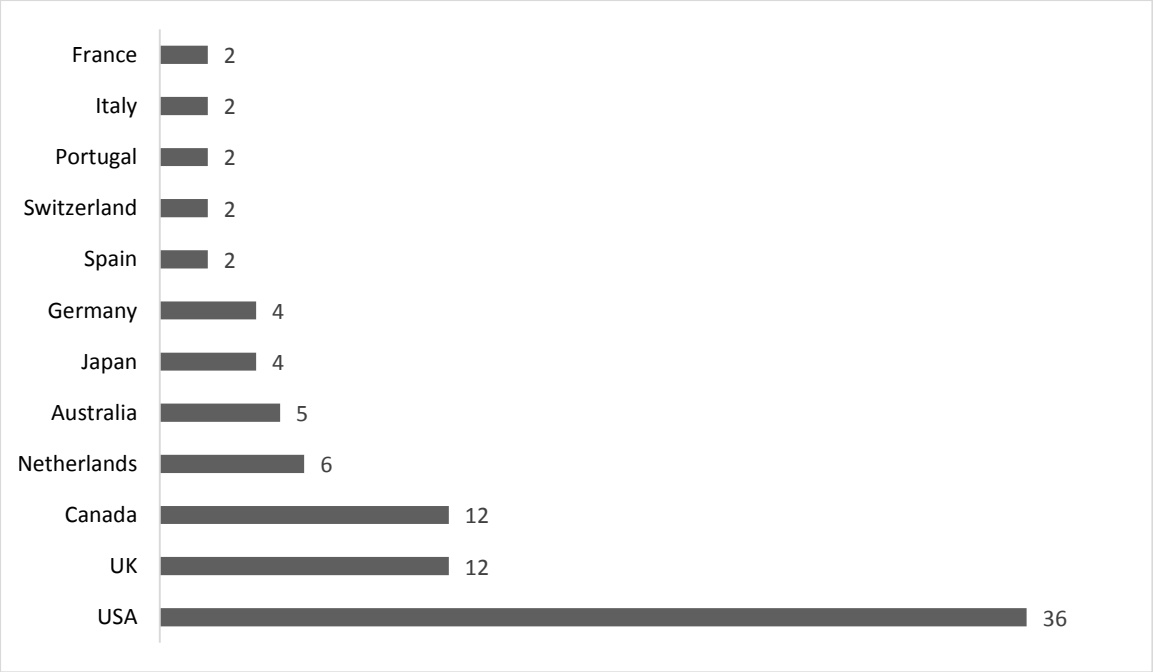

Figure 3. Number of studies by country of origin

Quality of the literature

As with the literature on contact tracing in specific populations, the quality of study design was generally low, with little empirical work evaluating contact tracing methods. The

majority of studies retrospectively examined either a group of investigations which had been completed in an area, or investigations carried out over a particular time period (see Figure 4). These papers scrutinised notes and patient records completed at the time to describe, and further examine the investigations. A second large group of studies "told the story" of a single investigation, describing the process and outcomes, with data relating to the number of cases and contacts, and often outlining where issues and obstacles had been encountered.

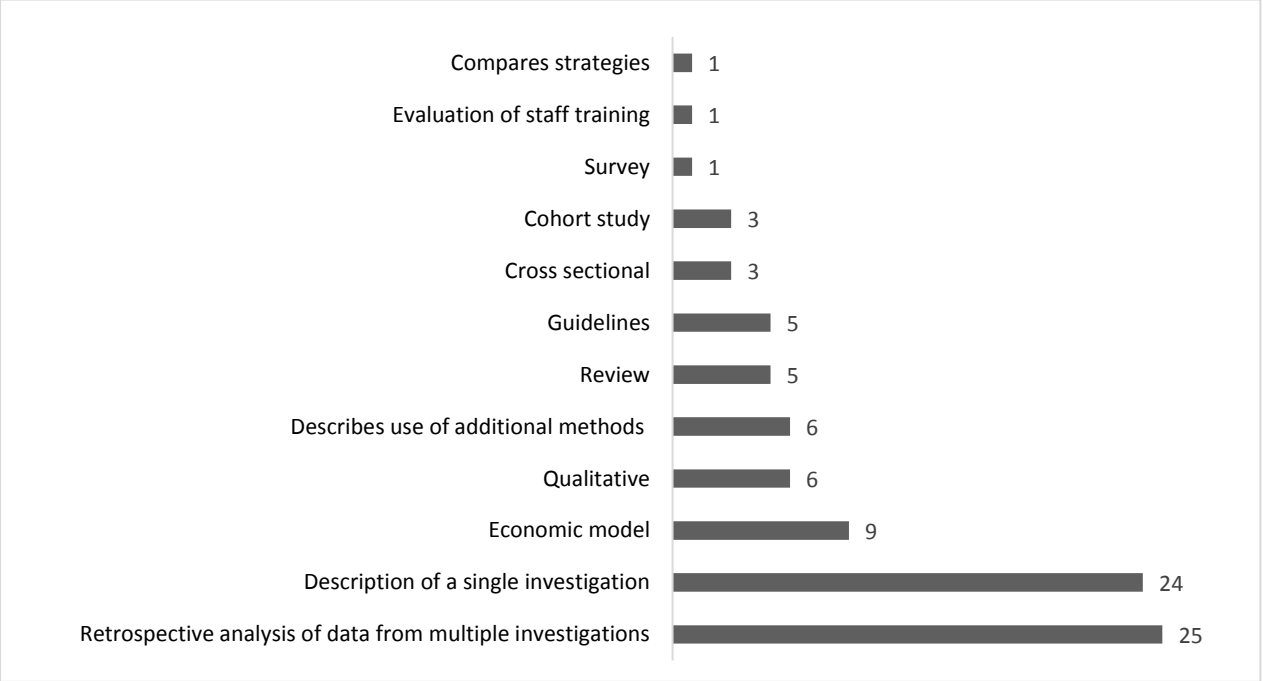

Figure 4. Number of studies by study design

As we have outlined in the Methods chapter, due the diversity of designs, predominantly descriptive data and unclear quality indicators in the included literature, established quality appraisal tools, such as the risk of bias tool developed by the Cochrane Collaboration, were not suitable for use in this review. Instead, we used study design as a proxy for quality, and characterised study types during the narrative synthesis, highlighting any particular concerns regarding quality of individual papers.

Integration and comparison of the specific population and wider population literature

We synthesised the elements of contact tracing described in the two sub-reviews, via use of a logic model, which sets out the elements of the contact investigation pathway (see Figure 5).

We used this model to describe and compare data in the review of wider populations with that in the review of specific populations, and highlight data of particular relevance to contact tracing in specific populations.

The elements of the model are drawn from the included literature. Elements in standard typeface were referred to in both reviews, the elements of the model that are in bold typeface were described only in regard to specific populations.

The model pathway progresses from left to right and details firstly, elements relating to prioritisation and decision-making required prior to commencing an investigation and during the investigation. The second column provides a categorisation of investigation activities, with the elements of these further itemised in the third column. Columns further to the right indicate the influence of TB detection and diagnosis tools used during investigations, followed by factors which may influence the process of an investigation and outcomes. The final columns detail outcomes which may be achieved during an investigation, and longer term impacts which may result from contact tracing investigations.

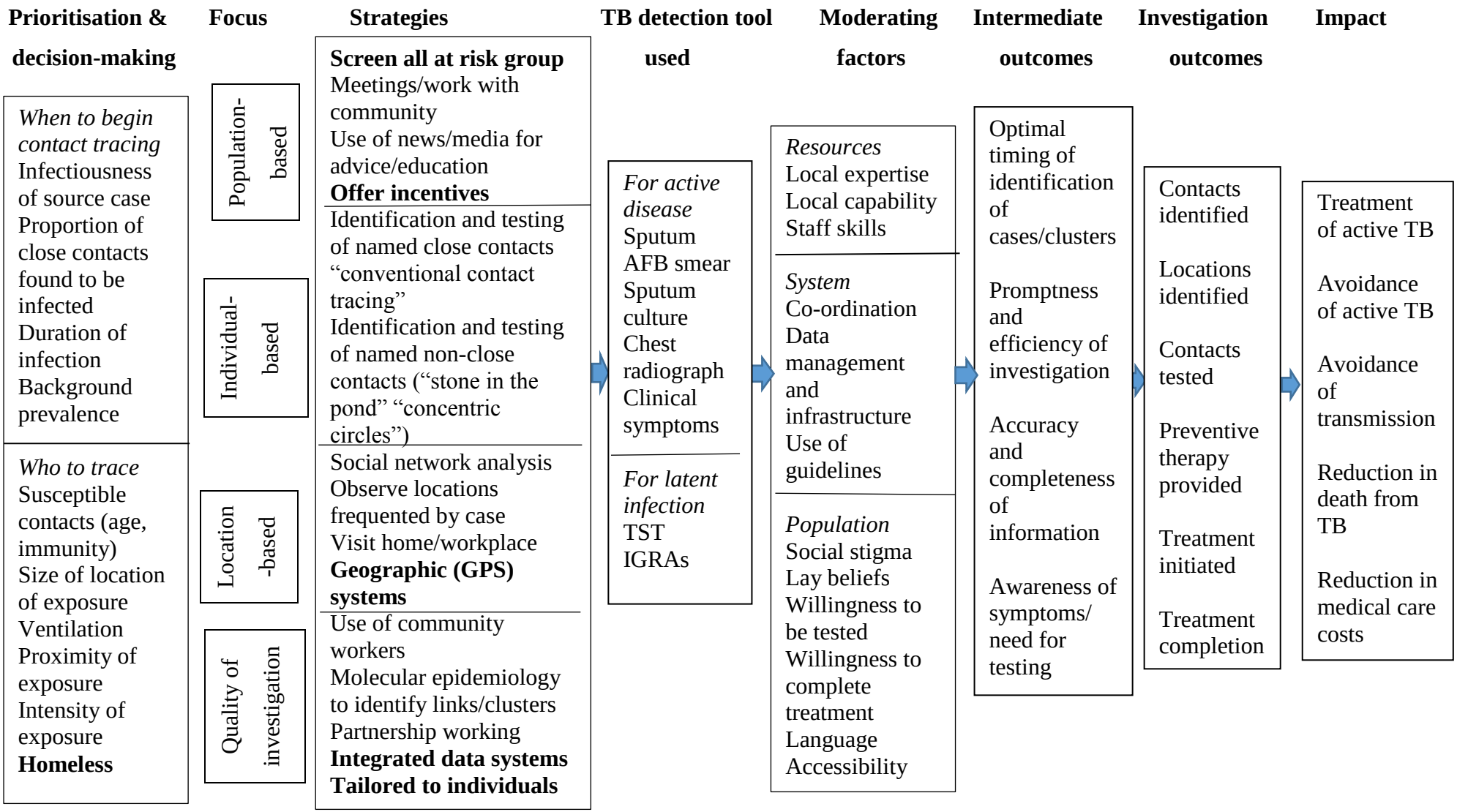

Figure 5. Logic model outlining elements of the contact tracing pathway (bold =reported in specific populations literature only)

Prioritisation and decision-making

There was a high level of consensus within the literature regarding elements to consider when making decisions about when to instigate contact tracing investigations, and then who should be prioritised for tracing and screening. The research studies included within the wider review echoed elements of prioritisation and decision-making that were described in the literature on contact tracing for specific populations. Authors described the need for a risk assessment approach[36, 60] based on the infection type, level and period of infection,[71, 87] characteristics of contacts such as younger age or reduced immunity[1, 8, 45, 82, 102] duration of exposure and proximity of exposure,[33, 47, 69, 115]. Elements relating to the specific environment also require consideration, such as the size of an area where people congregate, together with levels of ventilation in a location.[57, 59, 93]

Several studies highlighted the importance of considering the background prevalence of TB in population sub-groups, such as minority ethnicity communities or those born overseas in TB endemic countries. Having this information was described as a key element in decisions on when to commence or expand contact tracing, with some investigations reportedly expanded inappropriately when background prevalence had not been sufficiently taken into account.[32, 44, 62, 89, 94, 95] The authors of one study highlighted that the stone in the pond principle is only useful if accurate data regarding prevalence in specific communities (such as immigrants) is available.[95]

Three papers outlined decision trees or tools for use when considering priorities for investigations.[68, 83, 92] The first of these[68] evaluated use of a decision tree for a set of 3162 contacts. The authors reported that the decision tree had a 9% sensitivity, 22% specificity and a false-negative rate of 7-10%. It was estimated that use of the decision tree could lead to around a 20% reduction in the number of contacts investigated. The priorities for contact tracing detailed in the decision tree are: if the index case has cavitary disease; or the total exposure of a contact per month is more than 120 hours, or the contact is under age 15. If none of these criteria apply, then it is recommended that a case should only be investigated if: the contact was exposed to a smear positive case in their home, or the contact was exposed in a place where the ventilation was minimal. A second study[83] also described development of a checklist and decision tree. The tools were intended to be piloted, although it was reported

that no suitable investigations were started during the period of the study, therefore testing of the tools had not been carried out.

The Mohr study[92] consulted experts to develop a decision-making tool for contact tracing investigations following potential transmission to users of public transport. Nine elements were identified: symptoms of the index case; infectiousness of the index case; drug resistance pattern of index case; evidence of transmission to other contact person; the quality of contact between an index case and contact person (face to face/social interaction); the proximity of contact to case during exposure (more/less than 1 metre); the duration of exposure (more/less than 8 hours); the susceptibility of the contact (under 5 years of age/HIV/substance abuse/other disease); environmental factors (external ventilation present or not/with/without circulation).

Several sets of guidelines were identified during the review, which provide detailed recommendations regarding considerations of prioritisation.[1, 6, 33-35, 96] These guidelines confirm that priorities should be assigned to contacts (high/medium/low priority) based on firstly, the likelihood of infection, and secondly, the potential hazards to the individual contact if infected (including characteristics of the index patient, characteristics of the contact, and intensity, frequency and duration of exposure).

Population focused strategies

Four included studies describe the use of media and information provision to reach populations during an investigation[40, 41, 47, 65] A report of an investigation in a school[40] describes intense pressure from parents, addressed by holding information sessions, sending letters and factsheets to all parents, and providing a central point of communication. A second investigation in a school[41] found that it was important to counter public fears by providing simple, credible, accurate, consistent and timely information, and to let the public know what action they could take. An investigation focussed around a hospital[47] set up a Freephone telephone help-line, with press releases and media campaigns also used. A telephone helpline, and information about TB symptoms/mode of transmission/availability of effective treatment was made freely available to the population of an area where a public house was suspected to be a site of transmission.[65] Authors of another paper reporting an investigation around a

public house[97] described how several individuals had come forward as a result of awareness raising activities among the local population. The authors suggested that targeted health education programmes may improve contact detection.

Papers in the specific populations review[30, 31] highlighted the potential overlap between contact tracing for population sub-groups, and population screening activities. In the wider review we identified one study which compared the effectiveness of contact tracing versus population screening.[111] The paper supports the view that these interventions have areas of overlapping purposes. This UK study[111] compared contact tracing among residents in a deprived area of London, with screening all new entrants to the country. The authors concluded that tracing contacts of individuals who have been identified with smear-negative pulmonary TB was significantly more effective in identifying individuals requiring intervention, than routine screening of all new entrants (7.7% of contacts of people with smear negative pulmonary TB required full treatment or chemoprophylaxis, versus 3.1% of new entrants screened). This paper is particularly interesting in regard to specific populations, as it comments that in high incidence areas contact tracing could be seen as a way of screening communities at particularly high risk, thus emphasising the overlap between these strategies. Another paper included in the wider review[70] concluded from its examination of contact tracing in a workplace setting, that screening of all new employees from countries of high prevalence of TB should be considered.

Individual focused strategies

As found in the specific populations review, the literature in the wider populations review was dominated by reports of investigations which used "conventional contact tracing" methods to identify individuals with possible active or latent infection. These investigations consisted of an index case being asked to name their close contacts, and "stone in the pond/concentric circles" methods, to widen the pool of contacts tested from close/family contacts to less close/casual contacts.

Several papers echoed the review of specific populations, in describing limitations of contact tracing methods. Bock et al.[43] report a study where contacts were re-interviewed following the increase of an outbreak. Re-interviewing identified an additional 282 contacts from the

original 61 contacts (19% of these had positive TSTs). It was concluded that contacts were originally missed, because the normal daily connections between them were not recognized by investigators. In another study[74] it was reported that while 67% of cases identified all their contacts, 32% did not. The index case was less likely to identify contacts who were employed and those who were not a relative or co-habitant (OR=4.82 95% CI 1.71-13.54; and OR-0.22 95% CI 0.10-0.47 respectively).

An area of frequent debate within the literature related to the expansion of investigations from close/household contacts to casual contacts. Some investigations prioritised only household contacts.[105] Others concluded that screening of casual contacts was not cost-effective in low incidence areas,[38] or should only be carried out for smear-positive respiratory index cases,[102] or only for highly infectious cases,[33] or that there should be only limited screening of casual contacts.[87] Authors of one study found that screening of casual contacts was routinely omitted due to limited resources.[113] In contrast authors of another study argued that screening beyond close contacts must always be considered.[97]

While authors agreed that closeness was an important predictor of infection, and should guide prioritisation for investigation,[68, 108] the definition of close contact varied considerably,[32, 113] and different authors used different categories. For example one study defined close as having less than 4 hours exposure indoors or in a confined space, and a casual contact as exposure other than close.[39] Another study defined people who spent an estimated total of at least 40 to 100 hours with the index cases in the 3 months prior to diagnosis or during the infectious period as "close contacts," and those who shared the same front door with the index case were considered as "household contacts."[42] A study retrospectively examining a number of investigations, reported that in all of them "household contacts" were always defined as "close".[89] In other studies close contact was defined as exposure for more than 6 hours per week, and occasional contact as less than 6 hours per week,[48] or close contact as those spending more than 8 hours per week with the source case.[57] Another study reported that testing should be restricted to casual contacts having frequent (at least once a week) contact.[44]

A review of published data relating to the likelihood of tuberculin reactions in casual contacts,[69] defined casual contacts as "persons sharing the same air, but having no direct

contact with the index cases". It concluded that the decision to extend a contact investigation to a group of casual contacts in a work place or school should be based on: evidence of transmission from the index case to closer contacts; the number of hours of exposure; and the likelihood in the population to be screened of previous exposure.

National guidelines tended to provide descriptive information regarding categorisation of contacts. Guidelines from the USA defined close exposure as prolonged exposure in a small, poorly ventilated space or a congregate setting.[34] Guidelines from the UK[33] defined close contacts as being people from the same household sharing kitchen facilities, and very close associates such as boyfriend/girlfriend or frequent visitors to the home. They note however, that contacts at work or in a hospital ward may be as close as a household contact. Guidance from Canada divides contacts into high priority (household contacts plus non-household who are immunologically vulnerable), medium priority (close non-household contacts with daily or almost daily exposure including those at school or work), and low priority (casual contacts with lower amounts of exposure).[6]

Two included documents suggested that recommendations for expanding investigations in general population groups may require further consideration in specific populations.[6, 51] The first of these,[51] carried out a descriptive literature review of contact investigation methods. They concluded that, while conventional strategies have given priority to household contacts, the importance of casual contacts and locations in contact tracing for high risk or vulnerable groups is not always sufficiently recognised. It was recommended that closeness of contact should be based on the amount of time an individual is exposed, rather than environmental or social factors. The second document,[6] which comprised Canadian guidelines, included the statement that "the concentric circles approach does not take into account contacts who are vulnerable but may have had less exposure, and can be difficult to apply in congregate settings". The guidelines recommended was that level of priority should be the primary consideration, with most effort put into tracing contacts who are most at risk of being infected, and/or most at risk of developing active TB disease if infected.

Location focused strategies

Three studies examined outbreaks among work colleagues.[50,67,96] A paper reporting a retrospective review of data from outbreaks across five states in the USA[53] (which used a subset of data from another included study)[99] concluded that the potential for transmission of TB in the workplace needs further recognition. The study found inconsistent and limited recording of data collected during the investigations, and differences between the locations in regard to who was selected for screening and who was used as the primary source of information. Another study[70] also concluded that the workplace can be an important site for transmission.

In a further investigation,[96] co-workers had initially been classified as low priority however, a high rate of infection found in high priority cases (39%) led to expansion of the investigation to low priority contacts, and 15% of these subsequently had positive TSTs. Similarly, Duarte et al.[58] reported that expanding contact investigations to home and workplace visits increased the number of individuals screened and identified further patients with active and latent TB. Interviews had identified 950 contacts (estimate 0.75 cases of infection per index patient identified); expanding the investigation to home and workplace visits helped identify 2629 contacts (1.4 cases of infection per index patient). These results support the finding that locations such as the workplace can be important to consider in contact investigations.

A study from the UK examined the contact tracing investigation surrounding an outbreak of TB in the South West of England.[65] The paper highlighted that few conventional household contacts were identified, but a significant number of secondary cases were detected from tracing contacts at a single public house location. An investigation in a village in Spain[48] similarly found that few cases in the outbreak cluster appeared to have a close relationship, but many frequented some of the same bars. Authors of another study which highlighted the importance of bar locations,[55] concluded that contact investigation should examine the location itself, and not focus on personal contacts. While the bar in this study attracted a mixed clientele, it was located in a red light district, and next door to a hostel for homeless people, so the conclusions are particularly relevant for investigations in specific populations.

In contrast to these papers, a retrospective analysis[57] of 100 contact investigations carried out over a five year period in congregate settings (schools workplaces, drug treatment centres, single room hostels, and other locations) found that transmission at congregate sites was uncommon (22% of investigations examined in this analysis), concluding that these investigations are resource intensive. The study recommended that decisions to perform testing at a congregate setting (not just among household contacts) should be based on: infectiousness of the source case; size of location, level of crowding; number of windows at the setting; characteristics of contacts such as age and immune status; and the presence of case clusters.

Six papers outlined the benefits of a social network analysis approach to contact investigations.[2, 39, 52, 66, 76, 91] Findings from these studies builds on the positive findings from the papers in specific populations reported previously.[16, 17, 19, 22, 25] Bailey et al.[39] describe the development of network diagrams and calculation of reach, degree, and "betweenness" scores to examine relationships between an index case and contacts. The highest 20 scores and lowest 5 scores for each metric were used for prioritisation. The network diagram indicated that the index patient was directly linked to 56% and indirectly linked to 18% of secondary cases, and contacts prioritised using network analysis were more likely to have latent infection than non-prioritised contacts (odds ratio=7.8 95% CI=1.6- 36.6). A similar study,[91] explored an investigation including contacts from a local community, a prison, a hospital, and a school, concurred that the metrics calculated using social network methods enabled contacts with higher scores to be prioritised. Three contacts with high ranking "betweenness" scores were found to be links to the overall network. The authors concluded that network analysis provides a means to identify linkages among cases, quantify the magnitude of an outbreak, and assist prioritisation of contacts to screen. Gardy et al.[66] reported that social network analysis outperformed contact tracing in identifying a probable source case, as well as indicating several locations and persons who could be subsequently targeted for follow-up.

Another study supplemented routine investigation procedures with an interview to collect data on places of social aggregation for use in social network analysis.[52] TB patients not linked via conventional contact tracing were linked by mutual contacts or places of social gathering. An association was found between TST results and being in the denser area of a person-place network. ($p<0.01$) A UK study[2] re-interviewed patients using a social network

enquiry approach. They found that associations detected previously tended to be family-friend relationships, while over half of associations reported during the new interviews related to friends and socialising in public houses. Fourteen of the 43 epidemiological links were newly uncovered, although associations were not discernible for 45% of patients.

One included paper cautions against uncritical acceptance of studies advocating the use of social network analysis.[76] It found that while betweenness scores (but not centrality scores) were useful to identify contacts at greater risk of latent TB infection (significant association for contacts with higher betweenness score and latent TB infection OR 2.12 p=0.020 95% CI 1.14-3.96). However, the complexity and time-consuming nature of the method reduces the potential for its incorporation within routine contact investigations. The study by Bailey et al. mentioned above,[39] also outlines potential issues of implementation. The authors reported that, while data required to perform network analyses is already routinely collected, it needs to be organised into the proper format for analysis. While the costs to carry out network analysis may be beyond some programmes, the authors recommended that principles such as pursuing repeatedly named contacts should be widely adopted.

Strategies to improve the quality (efficiency/effectiveness) of investigations

We identified only one paper which reported an intervention to improve the delivery of a conventional contact tracing investigation.[67] Gerald et al.[67] examined existing contact tracing protocols. They found considerable variance among field workers regarding their understanding of terms used in the protocols. There was also variance in understanding of methods for eliciting information from index cases, and in the use of concentric circle analysis. The authors developed standardised definitions and procedures as part of a new Contact Exposure and Assessment Worksheet. They also introduced training sessions to increase TB field worker adherence to the protocols. The quality of the training sessions was evaluated by self-reported questionnaires. Sessions were rated at mean 4.61, and the overall value of the training received was rated 4.71 (scale 1-5 with 5=excellent). It was mentioned that "some further training was required when data entry errors and misunderstandings were identified".

The review of specific populations had indicated the potential value of community health workers during investigations. In the wider review, one paper[86] described the perception of nurses that outreach workers would be of value.

One included study reported the linking of data from two different healthcare data systems during a contact investigation based around a maternity ward (hospital-based electronic medical records to identify patients exposed to the index case, and an electronic immunization registry to obtain contact information for exposed infants). There are limited data evaluating the impact of using the integrated system. However, the authors reported that the integrated system aided the identification, notification and evaluation of contacts, thereby reducing the resource burden required for the investigation.[103]

A sizable group of papers focused on improving the quality of investigations via the use of epidemiological testing, predominantly with the aim of identifying clusters of cases. This echoes the specific population literature. These approaches were described as complimentary strategies to contact tracing[80] so have been included in this review. The use of molecular epidemiology, referred to in the papers as DNA fingerprinting, or genotyping, or whole genome sequencing, or spoligotyping, using IS6110-based restriction fragment length polymorphism analysis (RFLP) or Mycobacterial interspersed repetitive unit 12 typing (MIRU-12) or 24 loci mycobacterial interspersed repetitive units variable number of tandem repeats (MIRO-NNTR) was described in nine papers in the review of wider populations.[42, 46, 55, 61, 66, 78, 80, 114]

Lambregts et al.[80] reported that DNA fingerprinting can be useful to confirm suspected epidemiological links, and to identify new links where transmission is not suspected, and where links between cases of TB are vague or with long periods in between. In their retrospective analysis of clusters over a five year period in The Netherlands, DNA fingerprinting established an epidemiological link in 31% of clustered cases where no link had been assumed or documented. Cluster feedback significantly improved the confirmation of documented epidemiological links ($p<0.001$). In another study[42] it was reported that DNA fingerprinting demonstrated that 30% of contacts with tuberculosis developed the disease at nearly the same time as, but not as a result of transmission from the index case. Authors of a further study which used molecular epidemiology to examine an investigation at a workplace

in Italy[61] also reported that genotyping was important to establish linkages. Yeo et al.[114] examined public health data over a four year period, and carried out additional genotyping. Genotyping by the research team identified up to 14 possible additional index cases. The authors described the contact investigations as extensive. The investigations had mostly been able to identify latent tuberculosis infection, but had been less successful in identifying the source cases.

Authors of one paper[78] analysed data from an initiative to DNA fingerprint all new cases of TB during a five year period. Fingerprints were obtained and stored in a database and pattern matching software was used, with a network diagram approach also used and centrality scores calculated. DNA fingerprinting was reported to be valuable in identifying the size of outbreaks, and in leading to recognition of the importance of location (bars) in understanding of an outbreak. Contact investigation had identified only 12 links among 27 cases. The index case could not be linked to any other case, and half (51%) of cases could not be linked to another case via contact investigation. Analysis using the additional strategy found that around 80% of the patients could be linked by other people or places, and individuals were often linked by multiple places providing several opportunities for infection.

One study compared DNA fingerprinting with whole sequence molecular epidemiology, to conventional contact tracing and social network analysis methods.[66] The authors reported that DNA fingerprinting had suggested that the outbreak had a single TB lineage, whereas more in-depth whole sequence molecular epidemiology revealed two lineages. Genotyping and contact tracing alone did not capture the true dynamics of the outbreak. Genome sequencing allowed the social network to be divided into sub-networks associated with specific genetic lineages of the disease. Genotyping was also reported to be valuable in excluding social relationships that could not have led to transmission according to the genomic data. This was described as greatly reducing the complexity of the network, and aiding identification of index patients.

A study of particular relevance to specific populations,[46] highlighted that molecular epidemiological methods tended to identify non-household links. These methods also identified more individuals from precarious economic circumstances and social difficulties (p-=0.002) than conventional contact tracing. A second study of note for specific populations

[55] reported that conventional contact tracing is insufficient for the detection of chains of transmission in some harder to reach communities. The study found that 12 of 20 cases with confirmed recent transmission could only be determined by DNA fingerprinting. The authors highlighted that DNA fingerprinting can not only provide important information regarding recent infection of one patient by another; it also allows structural weaknesses in an investigation to be identified.

TB detection and diagnosis tools

Thirteen papers[54, 56, 63, 72, 79, 90, 110 37, 38, 44, 57, 60, 104] highlighted how the specific test used for screening for latent or active TB infection, proved to be important during contact tracing investigations. Four papers considered how the process of contact tracing could be influenced by the particular test.[37, 38, 57, 104] In the first of these,[37] the authors reported that uptake and completion of chemoprophylaxis may be higher when latent TB infection is diagnosed with IGRAs (Interferon-c release assays) rather than TSTs. This finding was echoed in a second paper,[104] which similarly found that contacts tested using IGRAs were more likely to complete screening.

One study of particular relevance to specific populations, outlined the need for difference in the testing process for individuals in congregate settings versus other contacts. This investigation[57] reported that testing should be carried out for high risk groups as soon as possible, and again 10-12 weeks later. For other individuals, the authors recommended that testing was performed only once; 10-12 weeks after exposure.

A further study[38]described the effects of a change in policy regarding follow up of contacts. Previously, close contacts had been invited for follow up annual radiological surveillance. Under the changed policy close contacts were either discharged or referred to the chest clinic following their initial screening, with no annual follow up. The study found that compared with the results of the previous protocol, fewer contacts were unnecessarily screened. However, as a result of the new policy, referrals to the chest clinic increased, and the number of contacts given chemoprophylaxis also increased.

Nine further papers provide evaluations regarding the usefulness, effectiveness or cost effectiveness of IGRAs (either the QuantiFERON-TB-Gold In Tube assay or the T-Spot) instead of, or in addition to TSTs.[44, 54, 56, 60, 63, 72, 79, 90, 110] Borgen et al.[44] concluded that use of IGRAs could improve the positive predictive value of testing, and also enables TST for those with BCG vaccination. Another study similarly concluded[60] that IGRA tests are more sensitive in detecting latent TB infection than TST. The authors of this literature review recommended that a positive TST should be followed by IGRAs, as IGRAs may be superior to TST in predicting latent infection becoming disease (although they recognised that this finding was not consistent across all the literature). They also recommended that where only a TST is used, a cut-off point for positivity must be decided with decisions regarding sensitivity versus specificity. The likelihood of infection and BCG status should be considered.

Other papers echo the superiority of IGRAs over TST for detecting latent TB infection[54 56 72] Diel et al.[54] estimated that the use of IGRAs (either QuantiFERON TB Gold [QFT-GIT] or T-Spot) as a replacement for the TST, would decrease the number of contacts to be investigated by approximately 70%. IGRAs were described as particularly useful for people who show tuberculin reactivity due to past BCG vaccination.[63] An economic modelling study from Canada cautions against widespread use of QFT-GIT,[90] This study found that the most cost effective strategy, was to administer QFT-GIT in BCG-vaccinated contacts, and to reserve TST for all others (at an incremental net monetary benefit cost of $3.70 per contact). The least cost-effective strategy was QFT-GIT for all contacts (an incremental net monetary benefit cost of $11.50 per contact). Trieu et al.[110] similarly concluded that QFT-GIT was particularly useful for contacts from countries with BCG coverage, however also raised the issue of cost. The authors estimated that QFT-GIT was 16 times more expensive than TST. They also highlighted the need for field workers to be trained in taking blood samples, and that specimens needed to be transported to a laboratory for analysis within 16 hours of collection. In addition to people who are BCG vaccinated, the authors recommended use of the test with people who are hard to follow up, such as the homeless, as the test requires only a single encounter.

An economic model was constructed by authors of another study,[79] to compare high resolution computed tomography to chest X-ray tuberculosis (in combination with QFT or

TST) for the detection of active TB during contact investigations. The study found that a strategy which comprised QFT followed by high resolution computed tomography, yielded the greatest benefits at the lowest cost. High resolution computed tomography, rather than chest X-ray, was therefore recommended to evaluate and manage contacts with active TB infection.

Moderating factors

We grouped factors which could reportedly influence (or moderate) an investigation, into those relating to available resources, those relating to systems, and those relating to the population.

Resources

Studies described how contact investigations are complex, challenging and labour-intensive, and require immediate availability of a large workforce.[41, 64] Screening was described as costly, and diverted staff from other duties.[100] National standards in Canada[6] outline the need for good organisation, and adequate staffing and resources.

One study[43] described how the quality of an investigation was hampered by an inexperienced workforce. The authors reported that as TB rates were historically low in the area, no specialised/experienced team was available to conduct contact tracing. Wilce et al.[113] found variability in levels of training received by staff involved in investigations. A qualitative study exploring the perceptions of patients with active TB and staff involved in contact investigations, concluded that programmes may be enhanced by staff receiving training in listening, and culturally appropriate interviewing techniques.[106] This need for training for staff in interviewing techniques, was echoed in a second study,[61] and further supported by Bock et al.[43] who described how patients who were re-interviewed by "experienced interviewers" named an additional 282 contacts that had not been identified in the first interview. Wilce et al.[113] described how, in one investigation, the content of the interview was typically left to the discretion of the interviewer.

An interesting finding regarding resources was described by Duarte et al.[58] This study compared investigations during two study periods (during the first period the investigation

interview targeted close contacts; during the second period visits to home and workplace were also included) and found that while there was an increase in workload, investigations including assessment of locations could be carried out within the same resource.

Systems

System-based elements which could impact on an investigation, included the degree of communication and co-ordination between staff and between agencies.[77, 106] One study[50] described how the requirement for contact across different agencies had provided additional complication to an investigation. The authors described how good communication among services was required to overcome this. This finding regarding working practices was echoed in another study, which reported that multidisciplinary team working is essential for effective management of an investigation.[65] A narrative overview of the literature[51] concluded that there needs to be a focus on local capability and expertise, co-ordinated approaches, and strategies including the development of questionnaires, and electronic data management. The importance of effective data management systems was also highlighted by Reichler et al.[99]

As detailed in the section outlining characteristics of the literature, we identified several sets of guidelines during the review.[1, 6, 33-35] The provision of written policies and procedures for investigations was described as improving the efficiency and uniformity of investigations.[34] However, the included literature contained many references to inconsistency in use of guidelines, and a requirement for training and support to improve adherence, and thereby increase the standard of contact tracing investigations.[53, 84, 95, 100, 113]

One study found inconsistent and limited recording of data collected, and differences in regard to who was selected for screening and who was used as the primary source of information.[53] Researchers who retrospectively analysed a TB data registry for children, found limited documentation regarding the labelling of level of closeness of contact among those screened.[112] They suspected that the labelling of close/not close was made after the investigation has been completed. Another study, which examined the decision-making of public health nurses during investigations, found evidence of scaling up of an investigation from close to casual contacts which was not required. Staff perceived the criteria for classification as being unhelpful/ambiguous, and there was reported difficulty in interpreting background population prevalence data.[95] The nurses tended to identify more contacts than

just those at substantial risk of infection, with a perception that screening as many contacts as possible gave a more comprehensive view of the level of infectiousness of the index case. Staff expressed concerns regarding missing contacts, and this omission then leading to further transmission.

Population

Moderating factors associated with the population, related predominantly to the reported influence of perceived stigma amongst people with active TB, and also among contacts. A UK study explored the views of contacts who had attended for screening versus those who had not.[86] The findings highlighted the importance of working with a community to allay fears, educate, and reduce the stigma. Fears regarding stigma, loss of employment or loss of housing, and alienation or abandonment were described.[106] Another study similarly described reports of a fear of social discrimination.[55] In one investigation, perceived stigma had led the index case to claim that they were unemployed, which delayed investigation of contacts at their workplace.[61]

Three papers further described how the influence of lay beliefs could delay the initiation or course of an investigation. In one study,[55] people with active disease reported irritation over the contact tracing procedure, which was perceived to be intrusive. It was reported that more than a quarter of patients identified with active TB had failed to seek medical attention. Those patients who did go to see a doctor delayed doing so for an average of seven weeks after the onset of symptoms. Some cases reported trying to shield drinking partners from "bullying methods" of the "health police" by naming only contacts in more distant bars, or by naming more transient contacts, such as neighbours.

Another study[3] found that, while patients understood the concept of airborne transmission, and contact, prolonged contact was not thought to be required for infection. Modes of TB transmission were not always fully understood, with patients describing potential infection via airborne transmission, sharing utensils, consumption of infected foods/drink, and exchange of bodily fluids. Authors of another study[106] echoed the importance of understanding lay beliefs in TB control strategies. They highlighted differences in understanding of the terms "contact" and "at risk contact"; these were terms that could be vague or understood incorrectly. Some patients in this research were unclear about the

purpose of naming contacts, it was not clear to them that the focus wasn't getting the names, it was finding the people who may have been infected. Patients reported preferring to inform contacts themselves, prior to people receiving contact from the health department.

A failure to attend for screening could delay or limit the effectiveness of investigations, and one study described how non-attenders at screening appointments could be unaware of their missed appointment.[86] Contact details could be inaccurate, shared houses with muddled incoming post were described, a limited understanding of the need for screening, being unable to take time off work, and childcare issues were all given as reasons for non-attendance at testing. The paper outlines a range of recommendations to aid the progress of contact investigations including: building good working relationships between TB services and GPs: sending letters to the patient to distribute to contacts: using outreach workers to trace contacts via home visits/telephone calls: walk in appointments for screening; having testing sessions in GP surgeries rather than hospitals; and using telephone text reminders.

Outcomes

The logic model depicts two columns relating to outcomes associated with contact investigations. These outcomes differ according to their place in the pathway, with the intermediate outcomes underpinning the investigation outcomes. While the intermediate outcomes are of significance, as they help to explain investigation outcomes, it was the investigation outcomes (number of contacts identified, and number tested and treated), that were typically the focus of the literature.

Guidelines[6, 33] refer to the importance of indicators of effectiveness, the timing of investigations, efficiency of processes and systems, and accurate data recording. Few studies however, provided data regarding these indicators. Wilce et al.[113] highlighted the variability in accuracy of information recorded, and the need for improvement in this area. Only one paper[97]referred to awareness raising as an outcome from an investigation.

Papers predominantly reported the number of contacts who were screened, as a measure of success of a contact investigation. The size of investigations varied substantially between studies, including those who had screened less than a hundred to two hundred contacts;[41, 61, 65]

to those that screened many thousands.[44, 81] The number of contacts screened per index case also varied substantially, for example in the Aissa et al. study[36] the mean number of contacts screened per case was 6 (with a range of 1-122). In another study the median number of contacts per case was 3, and the highest number 150.[45]. Sprinson et al.[107] reported the mean number of contacts per case was 10.5 (range 0-170). A further study estimated 102 contacts needed to be evaluated per prevalent case diagnosed (95% CI 90–115).[37]

It is interesting to note that identifying high numbers of contacts appeared to be mostly reported as a positive outcome within the studies, despite the resource implications of increasing the size of investigations. There was little reference to appropriateness of the contacts being identified (apart from one study which described inappropriate widening of investigations,[95] and another describing local pressure to expand an investigation).[40] A study which reports the advantages of using IGRA testing, describes one benefit as being a reduction in the number of contacts requiring screening.[54] Another study examining testing protocols, similarly reports a reduction in inappropriate screening as a positive outcome.[38]

Several studies reported that a proportion of index cases named no contacts. For example Jereb et al.[73] found that 10% of index cases had no contacts listed. Sprinson et al.[107] reported 11% of cases had no reported contacts. Data of particular importance to the consideration of specific populations are reported in two studies. Marks et al.[89] noted that fewer close contacts were identified by homeless, males and Asian/Pacific islanders. No contacts were identified for 8% of index cases. Homelessness was significantly correlated with having no identified contacts (RR 1.3 95% CI 1-1.5). Similarly, Reichler et al.[99] found that 13% of index cases had no contacts identified, and an additional 11% had no close contacts identified. Patients with no contacts listed were more likely to live in a homeless shelter (13% versus 2% $p<0.001$).

Several studies highlighted the sizable numbers of contacts who might withdraw at different points during the process of screening and treatment. In one, 14.7% of contacts declined screening,[87] in another[57] 83% of contacts were tested, 20% had latent infection, and 52% of these completed treatment. An even lower rate of 44% of contacts with latent infection completing treatment, was reported in another paper.[73] An evaluation of a programme across one USA state[107] reported that 66% of contacts started treatment, and 64.2% completed.

Around half chose to stop, 17% moved, and for 17%, the reason for non-completion was unknown. The study found that only 31% of areas investigated met the target of 85% treatment completion. Another study reported similar latent TB infection treatment completion rates of 67%, with 40% of contacts identified with latent TB infection either refusing or stopped treatment.[81] One paper[104] provides data of particular interest to consideration of specific populations, in reporting that contacts were less likely to complete screening if they were of working age, male, black, or from the Indian subcontinent.

The Anger et al.[37] study concluded that contact screening is effective, even when completion rates for latent TB infection treatment are below ideal levels. The authors calculated the absolute risk reduction afforded by chemoprophylaxis initiation to be 1.1% (95% CI, 6%–1.9%), which equates to approximately 88 contacts needing to be treated, in order to prevent one case of active TB (95% CI, 53–164). Another study[109] emphasised however, how increasing treatment completion among contacts could substantially improve effectiveness. This study estimated that reducing loss to follow up to a 10% level, could lead to significant benefits in infection rates (5.4% prevented p=0.02).

Impacts

Two included papers used modelling methods to estimate the longer term impact of contact tracing investigation. The first of these[71] developed a computational model using notification data during a 10 year period. The model indicated that conventional contact tracing using the stone in the pond/concentric circles approach significantly reduced TB incidence (by 18.6%) and deaths (23.7%) compared to passive diagnosis only. The model indicated that around one fifth of recently transmitted cases may be identified by contact tracing. The results of the model also relate to considerations regarding when to instigate contact tracing, as the model indicated that investigation of only smear-positive cases has a negative impact on effectiveness, rather than also including smear-negative cases (including both smear negative and smear positive reduces incidence avoidance to 10.4% and deaths to 13.2%).

A second study[75] developed an agent-based simulation model of a TB epidemic. The model was used to compare household contact tracing to active case finding in the community. The

model indicated that the maximum 5-year reduction in TB incidence achievable by household contact tracing was 10 to 15% (2–3% per year), although any impact would be lower with imperfect coverage or reduced sensitivity. The authors concluded that contact tracing can have substantial epidemiologic impact (up to 7% reduction in incidence per year), but only if it achieves relatively complete population coverage, is sustained over time, and includes preventive therapy. They noted that contact tracing evaluation should encompass longer-term evaluation of latently infected contacts.

Six papers (five studies) provided cost-effectiveness data for contact tracing investigations.[49, 85, 88, 98, 107, 109] The first of these[107] estimated the cost of contact investigations during a single year in one US state to be $4.8 million. Two linked papers examined the cost-effectiveness of investigations following potential in-flight transmission.[49, 88] The first paper[49] used an average cost-per-contact estimate of $16.76, and calculated cost-effectiveness for a range of expenditures per contact ($28, $47, $134 and $164). The model indicated that every $1 spent on investigations and treatment (contact tracing and also testing/treating TB disease and latent TB infection) resulted in more than $1 of saving at moderate/high rates of infection and disease. However, low rates of infection and disease resulted in negative returns.

The second paper from the same team[88] compared contact investigations instigated within 3 months (versus within 6 months of the flight) and also investigation instigated only for those with sputum positive TB by culture or nucleic acid amplification test, and sputum smear positive for acid-fast bacilli and cavitation on chest X-ray. The model indicated that introduction of the new protocol could result in an estimated 409 fewer contacts investigated (half the investigations), of whom 115 might test positive (3 with active disease). The estimated risk for new protocol was 1.4-19%, and for the old protocol was 1.1-24%. The estimated cost under the old protocol was $222,000 to $1,300,000, and under the new protocol was $99,449 to $584,824. The authors concluded therefore, that the new protocol (reducing the time period between exposure and investigation, and increasing the stringency of test results) would be more cost efficient, while retaining an acceptable level of public health risk.

A study from Australia[85] compared cost per case prevented in three scenarios. Firstly, contact tracing as it had been carried out in 1991, secondly, a scenario where the investigation was

carried out adhering to guidelines in place at the time (1991), and finally a scenario where up to date evidence-based guidelines were adhered to. The cost for contact investigations in 1991 was estimated at $309,065 per case prevented. During this period the study found that prevention was not considered a priority, and few infected contacts identified had received preventive therapy. The authors estimated that if guidelines in 1991 had been correctly followed, that the cost would have been reduced to $58,742 per case prevented. If current guidelines had been followed, the cost per additional case prevented was estimated at $3,881. It was noted that lower referral rates, lower rates of preventive therapy, and lower efficacy of preventive therapy than the rates used during the calculations would impact on these estimated costs.

Pisu et al.[98] in the USA carried out a cost-effectiveness analysis using a decision-analytic model to compare conventional concentric circle contact tracing, with a contact priority model (using exposure hours, home, poorly ventilated environment). The aim was to explicitly categorise contacts as high risk and requiring testing, or low risk and not requiring testing. Conventional concentric circles contact tracing was found to be more effective, but more costly than a contact priority model. Savings would be made on cost of TSTs however, there would be higher costs from active disease. The concentric circles approach was estimated to prevent one additional case of active disease for a cost of $92,934 and one additional life year at a cost of $185,920. Estimated cost per 1000 contacts was $339,896 for concentric circles and $294,596 for contact priority. There would be an estimated one or two additional cases of active disease per 3000 contacts if a contact priority, rather than conventional tracing model was used.

Another study examined prioritisation models used mathematical modelling.[109] Using the model it was estimated that targeting investigations by prioritising by age (children under 9 years old are traced first) and ethnicity (first nation individuals traced first) could improve the effectiveness of contact tracing compared to non-prioritisation (preventing 11% of cases over 20 years $p<0.0001$).

Authors of a study from Canada carried out a comparison of scenarios with contact tracing and without.[109] The scenario involving no contact tracing, indicated a higher average prevalence of TB infection than a scenario with contact tracing. The study found that the

benefit of tracing the first 45% of contacts was greater than tracing the second 45%, indicating a diminishing return. Also, in contrast to work described in regard to network analysis, this study found that prioritising contacts on the basis of number of times that they have been named had adverse outcomes. Also, the work concluded that increasing the speed of the investigation (90% of contacts are tested within 30 days of diagnosis) did not lead to projected significant improvement in active cases or prevalence of infection.

CHAPTER FOUR: DISCUSSION

What is the effectiveness and cost effectiveness of specific interventions designed to improve TB contact tracing?

We identified a limited number of studies that permit robust assessment of effectiveness and cost-effectiveness of different interventions. Of the 112 included papers, only one from the specific population review could be considered to be an evaluation of an intervention to improve the quality of investigations.[26] This study indicated that the addition of trained community workers improved the coverage of investigations. One study in the review of wider populations[68] similarly described an intervention with staff to improve the conduct of investigations. Both these papers provide very limited evaluation data but do suggest benefits from these interventions.

While we identified several studies that reported the value of various strategies during investigations, there was little robust data to permit identification of associations between strategies and outcomes. The main area of strength and consistency of findings was that location-based strategies might lead to identification of an increased number of contacts. Included research studies tended to report the influence of factors such as workforce and lay views and perceptions during investigations, rather than identifying interventions that might address these moderating factors. We also found few studies reporting intermediate outcomes in the pathway from investigations to impact. Studies predominantly reported data regarding the yield of investigations, rather than attempting to measure elements relating to the conduct of the investigation, or any effect on the target population knowledge, beliefs or behaviour.

The review of specific populations highlighted the overlap between screening, active case finding and contact tracing within approaches to TB control.[31] The use of screening amongst high risk communities was advocated, in particular the use of mobile digital X-ray among the homeless.[30, 31 24] One study however, concluded that contact tracing (particularly in ethnic communities) may be more cost efficient and less intrusive than screening.[18] A second study (comparing contact tracing with the screening of immigrants)[111] also concluded that contact tracing was more effective than large scale screening. The authors commented that contact tracing could be considered a form of screening, as contacts may be located in at risk groups.

The type of outcomes reported by the majority of studies (number of contacts identified; number found to have active or latent infection) are problematic for comparing effectiveness between investigations and between studies, as differing contexts will impact these outcomes. For example (as reported in the studies) different index cases have very different numbers of contacts, and environmental factors influence rates of infection. Comparing these outcome data between investigations is therefore of limited value. An indication of effectiveness of the investigation processes may be determined, if numbers of contacts tested and numbers who completed treatment as a proportion of the total number identified is provided however, this calculation was rarely included.

Papers included in the review which used modelling methods to estimate effectiveness and cost effectiveness, indicated that contact tracing is an effective intervention. However, there are cautions that this may be only if contact tracing achieves relatively complete coverage of contacts, and includes provision of preventive therapy to contacts. Both of these areas were highlighted in the review of specific populations as being challenging for investigations.

What is the acceptability, feasibility, appropriateness and meaningfulness of specific interventions designed to improve TB contact tracing in these population groups?

We identified no studies which provide data to answer this research question.

What are the barriers to, and facilitators of, delivery or uptake of contact tracing in these population groups?

We found a limited number of research studies examining barriers and facilitators. The use of IGRA testing rather than TST was suggested to overcome barriers of loss to follow up, although cost implications were highlighted. The use of financial incentives to increase number of contacts tested was described by one study in hard to reach populations.[8] The literature described the need for adequate resources and adequate systems for delivering investigations. The role of fears of stigma, and population beliefs/understanding in determining uptake of contact tracing, were common to investigations in both specific populations and wider groups.

What are the elements of the contact investigation pathway from interventions to impact, for TB contact tracing in wider population groups?

We developed a logic model which details elements of the pathway relating to prioritisation and decision-making prior to and during investigations, investigation strategies, TB detection tools, moderating factors, intermediate outcomes, investigation outcomes, and impact. The review of studies examining wider populations tended to echo the findings of the specific populations review, with most elements of the contact investigation pathway outlined being common to both.

How might evidence from interventions for wider populations be applied to TB contact tracing in specific population groups including what are the similarities and differences, and what elements of the pathway may be important for feasible, applicable and effective interventions?

The literature on investigations for wider populations described a similar pathway to that in specific population groups. Recognised limitations of conventional investigation methods in wider populations however, were amplified in specific populations. We constructed a logic model from the elements described in the included studies, to explore the processes and systems that may influence the feasibility, applicability and effectiveness of contact investigations. This model sheds light on intermediary elements in the pathway from investigations to outcomes and impact that require consideration.

There was consensus across the two reviews that the initiation and scope of investigations should be determined by characteristics of the index case of active TB, features of locations of potential exposure, and characteristics of potential contacts. One study in the review of specific populations, highlighted that homelessness of a person found to have active TB should be a particular trigger for prioritising the commencement of contact investigations.[12] The wider populations literature emphasised the need to explore the likelihood, in the population to be screened, of previous exposure to TB infection.[69]

Studies in the two reviews considered approaches to contact investigation which had a population, individual, location, and/or increased quality focus. Reported intervention strategies did not differ between the reviews, although issues of cases identifying zero contacts, non-attendance at screening, and failure to complete treatment or follow up are particularly pertinent in specific populations.

In terms of population based approaches, the value of using the media during investigations was described in both reviews, and also the need to work with local communities in order to provide information and reassurance.

The review of strategies used for specific populations was dominated by critique of the conventional contact naming method. Papers in the wider review echoed these criticisms, highlighting that more generally the naming of contacts by people with active TB infection was problematic.[73] Papers in the wider review mirrored the specific population studies, in reporting that issues regarding contact naming are particularly apparent in specific groups, especially the homeless.[89]

While the specific populations review focused on the limitations of contact naming as part of conventional contact investigations, the wider review highlighted that conventional methods used to widen an investigation from close to less close contacts could also be problematic. The challenge when making decisions about expanding investigations, related to unclear definitions of different categories of contact, with reports of investigation staff disregarding guidelines when widening investigations, or being unsure of different classifications.[6, 51] Of particular importance to consideration of specific populations, one study noted that while casual contacts may be less important in wider populations and therefore not included in

investigations, they may be of particular importance for detecting transmission amongst harder to reach populations.[51]

The review of contact tracing in specific populations emphasised the importance of investigating locations of transmission. This was echoed in the wider review, with bars/public houses featuring as key locations in studies.[65, 97] The wider review also described the value of investigations at workplace locations.[53, 58] Both reviews indicated the value of social network analysis approaches, to map connections between cases and contacts. There was consensus regarding the importance of a location-based approach, not just tracing personal contacts.[55] Across the literature in both reviews there was an emphasis that the context will have a significant impact on the outcomes of an investigation, and particular features of each investigation.

The use of molecular epidemiology to augment investigations was described in both reviews, with the added value of the method recognised for both specific populations and wider groups. Partnership working was reported as important to increase the efficiency/effectiveness of all investigations. The introduction of integrated data systems across organisations (such as prisons and local health services was advocated in one specific populations study,[103] and the importance of addressing individual needs (such as culture/language) was described in another.[20]

Limitations

The nature of the included studies precluded evaluation of the data via meta-analysis. The limited quality of the literature, in particular the lack of experimental study designs and single study which could be described as evaluative, meant that the use of established quality appraisal tools was not indicated. As the evidence as a whole was from studies with weak designs, it was not appropriate to compare the strength and volume of evidence for different aspects of contact tracing investigations. The purpose of the review was to provide a synthesis of the literature in order to inform future commissioning of research in the area. The inclusion of a diverse range of study designs permitted examination of a substantial number of research studies that lie beyond the scope of many conventional systematic reviews.

We recognise that the English language inclusion criteria will potentially have limited the number of studies included and breadth of countries represented, The review however, includes study from 12 countries which offers a valuable overview of the international literature. We acknowledge that there was no public and patient involvement in this work, which was intended to assist with developing future research strategy. We also acknowledge the degree of overlap between contact investigation and other forms of TB control strategies. There is the potential for relevant data to have been missed by our searches, which used terminology relating to contact tracing, rather than other active case finding and screening. We believe that this potential limitation was mitigated to some extent via additional searching processes such as reference list screening.

CHAPTER FIVE: CONCLUSIONS

The review identified a substantive number of studies relating to contact investigations. The literature is predominantly descriptive however, with little robust empirical work evaluating investigations in either specific or wider populations. Currently, studies which have used mathematical or economic modelling methods are the predominant means of examining the effectiveness of contact investigations, and the outcomes of different strategies. Further studies are required, if robust conclusions regarding associations between different contact investigation methods and outcomes are to be made. The results of the review highlight the complexity of the pathway from initial decision-making to achieving long term impact on the health of the population. The differing nature of the context of each investigation was emphasised throughout the literature, and is problematic when endeavouring to make comparisons between the effectiveness of different contact investigations.

The literature on investigations for specific populations has much concordance with that reporting research findings from wider population groups. The literature relating to both specific populations and wider groups highlights limitations of conventional contact tracing approaches, in particular asking index patients to name contacts. Recognised limitations of conventional investigation methods may however, be exacerbated in specific populations. Conventional methods of dividing contacts into groups of close versus casual contacts also require further consideration and clarification. In particular for specific populations, casual

contacts may be of most importance in transmission, and conventional prioritisation systems may need revising. The importance of considering contacts at locations of potential transmission was highlighted across both the sub-reviews, although here again this strategy may be of particular importance for investigations in specific populations.

Currently, there are indicative studies to suggest that the quality of investigations may be enhanced by the use of additional testing such as molecular epidemiology. Few studies describe how systems and processes during investigations may be optimised, to overcome the range of moderating factors which are described in the literature. The examination of outcomes more closely relating to these systems and processes may help to address the limitations of the current evidence base examining the relative effectiveness of different contact tracing strategies.

The limited nature of the evidence available should be fully recognised when considering the following implications for healthcare and research.

Implications for healthcare (in priority order)

1. Existing studies indicate the potential limitations of contact naming, with location-based methods recommended to establish a complete picture of contact networks. In particular a location-based strategy may be a more effective approach for investigations in specific populations. This finding was based on studies which described contact investigations, rather than evaluated interventions.

2. The available research studies suggest that contact investigations in specific populations may require greater prioritisation of investigation of casual contacts (non-household), than in other groups. This finding was based on studies which described investigations, rather than which evaluated interventions. One evaluative study suggested that employing community workers may assist in gaining participation from individuals in high risk populations.

3. The results of the review suggest that an emphasis on the evaluation of processes undertaken during investigations, and also intermediate outcomes such as engaging with treatment, may provide valuable data regarding factors determining the effectiveness of investigations. Our logic model constructed from the data suggests the potential importance

of these intermediary outcomes and elements of process however, there were little data regarding these processes in the literature identified.

4. Available research indicates that adequate systems, process and resources including local expertise and skilled staff; sufficient workforce capacity; data management systems, and effective co-ordination between agencies are important to consider. This finding is based on descriptions and recommendations in the included literature, rather than empirical work. One evaluative study provided limited evidence that additional staff training may be beneficial.

5. Research studies suggest that use of mass media and other avenues for provision of information and advice may be effective in improving communication with communities and individuals at risk during investigations. This finding is based on recommendations in the included literature, rather than empirical work.

Implications for research (in priority order)

1. A large proportion of included literature describes investigations. Future studies should aim to adopt an evaluative approach, to increase the evidence base regarding associations between different contact investigation strategies and outcomes. We identified only two studies which could be considered to be evaluative.

2. Research studies should further explore the development of measures that can be used to compare the effectiveness of different contact investigations. The reporting of numbers of contacts identified during an investigation as a measure of success, or number who tested positive has considerable limitations. Measures such as the number of contacts who are tested/complete treatment as a proportion of those who were identified, can be more useful to gauge the effectiveness of investigation processes.

3. Interventions targeting local expertise and staff skills, workforce capacity, systems and processes (such as data management and co-ordination between agencies), and lay knowledge, beliefs and behaviour should be developed and evaluated, in order to address moderating factors reported in the literature. This is based on findings from qualitative studies, and recommendations from descriptive studies outlining contact investigations.

4. Researchers should include the measurement of intermediate indicators of effectiveness such as the timing of identification of cases/clusters, the promptness and efficiency of investigation, the accuracy and completeness of information, and awareness of symptoms/need for testing amongst contacts, when reporting investigations that have been undertaken. These factors were not reported in the literature, yet our logic model indicates that they may be important elements of the investigation pathway.

ACKNOWLEDGEMENTS

Contributions of authors

Susan Baxter (Research Fellow) led the study and took the lead in analysis and report writing.

Elizabeth Goyder, (Professor of Public Health) led development of the protocol and provided expertise and advice during the study.

Duncan Chambers (Research Fellow) contributed to the review processes.

Maxine Johnson (Research Fellow) contributed to the review processes.

Louise Preston (Information Specialist) developed the search strategy and carried out electronic database searching.

Andrew Booth (Reader) provided methodological input to the review processes.

DATA SHARING

All available data can be obtained from contacting the corresponding author.

CHAPTER SIX: REFERENCES

1. Canadian Agency for Drugs and Technologies in Health. *Contact Investigations following Patient and Staff Exposure to Active Tuberculosis Infections: A Review of the Clinical Evidence and Guidelines*. Ottowa: Canadian Agency for Drugs and Technologies in Health; 2014.

2. Jackson AD, Seagar AL, Reid ME, Doig C, Forbes KJ, Laurenson IF, *et al.* Characterising transmission of a tuberculosis genotype in Scotland: a qualitative approach to social network enquiry. *Int J Tuberc Lung Dis* 2009;**13**:486-93.

3. Jackson AD, McMenamin J, Brewster N, Ahmed S, Reid ME. Knowledge of tuberculosis transmission among recently infected patients in Glasgow. *Pub Health* 2008;**122**:1004-12.

4. Begun M, Marks GB, Wood JG, Newall AT. Contact Tracing of Tuberculosis: A Systematic Review of Transmission Modelling Studies. *PLOS One* 2013;**8**: e72470 doi: 10.1371/journal.pone.00724470.

5. Bur S, Golub JE, Armstrong JA, Myers K, Johnson BH, Mazo D, *et al.* Evaluation of an extensive tuberculosis contact investigation in an urban community and jail. *Int J Tuberc Lung Dis*.2003;**7**:S417-S23.

6. Rea E, Rivest, P. *Canadian Tuberculosis Standards: 7th Edition*: Ottowa: Public Health Agency of Canada; 2014.

7. McElroy PD, Rothenberg RB, Varghese R, Woodruff R, Minns GO, Muth SQ, *et al.* A network-informed approach to investigating a tuberculosis outbreak: implications for enhancing contact investigations. *Int J Tuberc Lung Dis* 2003;**7**:S486-93.

8. Verdier JE, de Vlas SJ, Kidgell-Koppelaar ID, Richardus JH. Risk factors for tuberculosis in contact investigations in Rotterdam, the Netherlands. *Infect Dis Reports* 2012;**4**:101-5.

9. Rizzo M, Martin A, Cliff-Matthews V, Jamal F, Lehmann A, Llewellyn A, *et al. Evidence review on the effectiveness and cost-effectiveness of interventions aimed at identifying people with tuberculosis and/or raising awareness of tuberculosis among hard-to-reach groups*. London: Matrix Evidence; 2011.

10. The Cochrane Collaboration: Cochrane handbook for systematic reviews of interventions, version 5.1.0, 2011. Available from: Handbook.cochrane.org. Accessed 14/4/2016.

11. Critical Skills Appraisal Programme (CASP) qualitative research checklist. Available from http://www.casp uk.net/wpcontent/uploads/2011/11/CASP_Qualitative_Appraisal_Checklist_14oct10.pdf. Accessed 14/4/16.

12. Li J, Driver CR, Munsiff SS, Fujiwara PI. Finding contacts of homeless tuberculosis patients in New York City. *Int J Tuberc Lung Dis* 2003;**7**:S397-S404.

13. Lofy KH, McElroy PD, Lake L, Cowan LS, Diem LA, Goldberg SV, *et al.* Outbreak of tuberculosis in a homeless population involving multiple sites of transmission. *Int J Tuberc Lung Dis* 2006;**10**:683-9.

14. McElroy PD, Southwick KL, Fortenberry ER, Levine EC, Diem LA, Woodley CL, *et al.* Outbreak of tuberculosis among homeless persons coinfected with human immunodeficiency virus. *Clin Infect Dis* 2003;**36**:1305-12.

15. Oeltmann JE, Oren E, Haddad MB, Lake LK, Harrington TA, Ijaz K, *et al.* Tuberculosis Outbreak in Marijuana Users, Seattle, Washington, 2004. *Emerg Infect Dis* 2006;**12**:1156-9.

16. Kline SE, Hedemark LL, Davies SF. Outbreak of Tuberculosis among Regular Patrons of a Neighborhood Bar. *New England J Med* 1995;**333**:222-7.

17. Malakmadze N, Gonzalez IM, Oemig T, Isiadinso I, Rembert D, McCauley MM, *et al.* Unsuspected recent transmission of tuberculosis among high-risk groups: implications of universal tuberculosis genotyping in its detection. *Clin Infect Dis* 2005;**40**:366-73.

18. Dasgupta K, Menzies D. Cost-effectiveness of tuberculosis control strategies among immigrants and refugees. *Eur Respir J* 2005;**25**:1107-16.

19. Asghar RJ, Patlan DE, Miner MC, Rhodes HD, Solages A, Katz DJ, *et al.* Limited utility of name-based tuberculosis contact investigations among persons using illicit drugs: results of an outbreak investigation. *J Urban Health* 2009;**86**:776-80.

20. Wallace CE, Cruise P, Tyree AB, Shevick G. Approaches to contact investigations in Texas. *Int J Tuberc Lung Dis* 2003;**7**:S358-62.

21. Yun LW, Reves RR, Reichler MR, Bur S, Thompson V, Mangura B, *et al.* Outcomes of contact investigation among homeless persons with infectious tuberculosis. *Int J Tuberc Lung Dis* 2003;**7**:S405-11.

22. Fitzpatrick LK, Hardacker JA, Heirendt W, Agerton T, Streicher A, Melnyk H, *et al.* A preventable outbreak of tuberculosis investigated through an intricate social network. *Clin Infect Dis* 2001;**33**:1801-6.

23. Sterling TR, Thompson D, Stanley RL, McElroy PD, Madison A, Moore K, *et al.* A multi-state outbreak of tuberculosis among members of a highly mobile social network: implications for tuberculosis elimination. *Int J Tuberc Lung Dis* 2000;**4**:1066-73.

24. Curtis AB, Ridzon R, Novick LF, Driscoll J, Blair D, Oxtoby M, *et al.* Analysis of Mycobacterium tuberculosis transmission patterns in a homeless shelter outbreak. *Int J Tuberc Lung Dis* 2000;**4**:308-13.

25. Cook VJ, Shah L, Gardy J. Modern contact investigation methods for enhancing tuberculosis control in aboriginal communities. *Int J Circumpolar Health* 2012;**71**:18643.

26. Ospina E, Orcau A, Millet J-P, Sanchez F, Casals M, Cayla JA. Community health workers improve contact tracing among immigrants with tuberculosis in Barcelona. *BMC Public Health* 2012;**12**: 158.

27. van Loenhout-Rooyacke JH, Sebek MM, Verbeek AL. Contact tracing using DNA fingerprinting in an asylum seeker with pulmonary tuberculosis. *Netherlands J Med* 2002;**60**:281-4.

28. Mulder C, Van Deutekom H, Huisman EM, Meijer-Veldman W, Erkens CGM, Van Rest J, *et al.* Coverage and yield of tuberculosis contact investigations in the Netherlands *Int J Tuberc Lung Dis*. 2011;**15**:1630-6.

29. Mulder C, Klinkenberg E, Manissero D. Effectiveness of tuberculosis contact tracing among migrants and the foreign-born population. *Euro Surveill* 2009;**14**:56-62.

30. De Vries G, Van Hest RA. From contact investigation to tuberculosis screening of drug addicts and homeless persons in Rotterdam. *Eur J Pub Health* 2006;**16**:133-6.

31. NICE. *Identifying and managing tuberculosis among hard-to-reach groups*. London: NICE; 2012.

32. Fox GJ, Barry SE, Britton WJ, Marks GB. Contact investigation for tuberculosis: a systematic review and meta-analysis. *Eur Respir J* 2013;**41**:140-56.

33. Joint Tuberculosis Committee of the British Thoracic Society. *Control and prevention of tuberculosis in the United Kingdom: Code of Practice. London: Joint Tuberculosis Committee of the British Thoracic Society*, 2000.

34. National Tuberculosis Controllers A. Guidelines for the investigation of contacts of persons with infectious tuberculosis: recommendations from the National Tuberculosis Controllers Association and CDC. *MMWR: Morbid Mortal Weekly Rep* 2005;**54**:1-47.

35. New York City Department of Health and Mental Hygiene. *Tuberculosis Clinical Policies and Protocols 4th Edition* New York: New York City Department of Health and Mental Hygiene, 2008.

36. Aissa K, Madhi F, Ronsin N, Delarocque F, Lecuyer A, Decludt B, *et al.* Evaluation of a model for efficient screening of tuberculosis contact subjects. *Am J Respir Crit Care Med* 2008;**177**:1041-7.

37. Anger HA, Proops D, Harris TG. Active case finding and prevention of tuberculosis among a cohort of contacts exposed to infectious tuberculosis cases in New York City. *Clin Infect Dis*2012;**54:** 1287-1295.

38. Ansari S, Thomas S, Campbell IA, Furness L, Evans MR. Refined tuberculosis contact tracing in a low incidence area. *Respir Med* 1998;**92**:1127-31.

39. Bailey WC, Gerald LB, Kimerling ME, Redden D, Brook N, Bruce F, *et al.* Predictive model to identify positive tuberculosis skin test results during contact investigations. *JAMA* 2002;**287**:996-1002.

40. Banner P. Tuberculosis contact tracing within a school environment: lessons for the future. *New South Wales Pub Health Bulletin* 2013;**24**:27-8.

41. Bargman C, Reeves. R., Parker, M., Belknap, R., Bettridge, J., Bedell, D. et al. *Transmission of Mycobacterium tuberculosis in a High School and School-Based Supervision of an Isoniazid-Rifapentine Regimen for Preventing Tuberculosis - Colorado, 2011-2012*. Atlanta: Centers for Disease Control & Prevention, 2013.

42. Behr MA, Hopewell PC, Paz EA, Kawamura LM, Schecter GF, Small PM. Predictive value of contact investigation for identifying recent transmission of Mycobacterium tuberculosis. *Am J Respir Crit Care Med* 1998;**158**:465-9.

43. Bock NN, Mallory JP, Mobley N, DeVoe B, Taylor BB. Outbreak of tuberculosis associated with a floating card game in the rural south: lessons for tuberculosis contact investigations. *Clin Infect Dis* 1998;**27**:1221-6.

44. Borgen K, Koster B, Meijer H, Kuyvenhoven V, van der Sande M, Cobelens F. Evaluation of a large-scale tuberculosis contact investigation in the Netherlands. *Eur Respir J* 2008;**32**:419-25.

45. Borraccino A, Migliore E, Piccioni P, Baussano I, Carosso A, Bugiani M. Yield of tuberculosis contact investigation in a low-incidence country. *J Infect* 2014;**68**:448-54.

46. Borrell S, Espanol M, Orcau A, Tudo G, March F, Cayla JA, *et al.* Factors associated with differences between conventional contact tracing and molecular epidemiology in study of tuberculosis transmission and analysis in the city of Barcelona, Spain. *J Clin Microbiol* 2009;**47**:198-204.

47. Carbonne A, Poirier C, Antoniotti G, Burnat C, Delacourt C, Orzechowski C, *et al.* Investigation of patient contacts of health care workers with infectious tuberculosis: 6 cases in the Paris area. *Int J Tuberc Lung Dis* 2005;**9**:848-52.

48. Castilla J, Palmera R, Navascues A, Abeti M, Guillermo A, Irisarri F, *et al.* Population-based contact investigation of a cluster of tuberculosis cases in a small village. *Epidemiol Infect* 2009;**137**:1426-35.

49. Coleman MS, Marienau KJ, Marano N, Marks SM, Cetron MS. Economics of United States tuberculosis airline contact investigation policies: a return on investment analysis. *Travel Med Infect Dis* 2014;**12**:63-71.

50. Collins J, Schlager S, Brasher E. Contact investigation of a case of active tuberculosis. *Am J Infect Control* 2004;**32**:38-43.

51. Cook VJ, Shah L, Gardy J, Bourgeois AC. Recommendations on modern contact investigation methods for enhancing tuberculosis control. *Int J Tuberc Lung Dis* 2011;**16**:297-305.

52. Cook VJ, Sun SJ, Tapia J, Muth SQ, Argueello DF, Lewis BL, *et al.* Transmission network analysis in tuberculosis contact investigations. *J Infect Dis* 2007;**196**:1517-27.

53. Davidow AL, Mangura BT, Wolman MS, Bur S, Reves R, Thompson V, *et al.* Workplace contact investigations in the United States. *Int J Tuberc Lung Dis* 2003;**7**:S446-52.

54. Diel R, Loddenkemper R, Meywald-Walter K, Gottschalk R, Nienhaus A. Comparative performance of tuberculin skin test, QuantiFERON-TB-Gold In Tube assay, and T-Spot.TB test in contact investigations for tuberculosis. *Chest* 2009;**135**:1010-8.

55. Diel R, Meywald-Walter K, Gottschalk R, Rusch-Gerdes S, Niemann S. Ongoing outbreak of tuberculosis in a low-incidence community: a molecular-epidemiological evaluation. *Int J Tuberc Lung Dis* 2004;**8**:855-61.

56. Diel R, Nienhaus A, Lange C, Meywald-Walter K, Forssbohm M, Schaberg T. Tuberculosis contact investigation with a new, specific blood test in a low-incidence population containing a high proportion of BCG-vaccinated persons. *Respir Res* 2006;**7**:77.

57. Driver CR, Balcewicz-Sablinska MK, Kim Z, Scholten J, Munsiff SS. Contact investigations in congregate settings, New York City. *Int J Tuberc Lung Dis* 2003;**7**:S432-8.

58. Duarte R, Neto M, Carvalho A, Barros H. Improving tuberculosis contact tracing: the role of evaluations in the home and workplace. *Int J Tuberc Lung Dis* 2012;**16**:55-9.

59. Edelson PJ, Phypers M. TB transmission on public transportation: a review of published studies and recommendations for contact tracing. *Travel Med Infect Dis* 2011;**9**:27-31.

60. Erkens C, Kamphorst M, Abubakar I, Bothamley G, Chemtob D, Haas W, *et al.* Tuberculosis contact investigation in low prevalence countries: a European consensus. *Eur Respir J* 2010;**36**:925-49.

61. Faccini M, Cantoni S, Ciconali G, Filipponi MT, Mainardi G, Marino AF, *et al.* Tuberculosis-related stigma leading to an incomplete contact investigation in a low-incidence country. *Epidemiol Infect* 2015;**143**:2841-8.

62. Forssman B, Gupta L, Mills K. A tuberculosis contact investigation involving two private nursing homes in inner western Sydney in 2004. *New South Wales Pub Health Bull* 2006;**17**:44-7.

63. Funayama K, Tsujimoto A, Mori M, Yamamoto H, Fujiwara K, Nishimura T, *et al.* Usefulness of QuantiFERON TB-2G in contact investigation of a tuberculosis outbreak in a university. *Kekkaku* 2005;**80**:527-34.

64. Funk EA. Tuberculosis contact investigations in rural Alaska: a unique challenge. *Int J Tuberc Lung Dis* 2003;**7**:S349-52.

65. Gaber KA, Maggs A, Thould G, Goldman JM. An outbreak of tuberculosis in the South West of England related to a public house. *Prim Care Respir J* 2005;**14**:51-5.

66. Gardy JL, Johnston JC, Ho Sui SJ, Cook VJ, Shah L, Brodkin E, *et al.* Whole-genome sequencing and social-network analysis of a tuberculosis outbreak. *New Eng J Med* 2011;**364**:730-9.

67. Gerald LB, Bruce F, Brooks CM, Brook N, Kimerling ME, Windsor RA, *et al.* Standardizing contact investigation protocols. *Int J Tuberc Lung Dis* 2003;**7**:S369-74.

68. Gerald LB, Tang S, Bruce F, Redden D, Kimerling ME, Brook N, *et al.* A decision tree for tuberculosis contact investigation. *Am J Respir Crit Care Med* 2002;**166**:1122-7.

69. Greenaway C, Palayew M, Menzies D. Yield of casual contact investigation by the hour. *Int J Tuberc Lung Dis* 2003;**7**:S479-85.

70. Gulati M, Liss DJ, Sparer JA, Slade MD, Holt EW, Rabinowitz PM. Risk factors for tuberculin skin test positivity in an industrial workforce results of a contact investigation. *J Occup Envir Med* 2005;**47**:1190-9.

71. Guzzetta G, Ajelli M, Yang Z, Mukasa LN, Patil N, Bates JH, *et al.* Effectiveness of contact investigations for tuberculosis control in Arkansas. *J Theoret Biol* 2015;**380**:238-46.

72. Higuchi K, Harada N, Mori T, Sekiya Y. Use of QuantiFERON-TB Gold to investigate tuberculosis contacts in a high school. *Respirol* 2007;**12**:88-92.

73. Jereb J, Etkind SC, Joglar OT, Moore M, Taylor Z. Tuberculosis contact investigations: outcomes in selected areas of the United States, 1999. *Int J Tuberc Lung Dis* 2003;**7**:S384-90.

74. Josaphat J, Gomes Dias, J., Salvador, S., Resende, V., Duarte, R. Tuberculosis: which patients do not identify their contacts? *Pneumologia* 2014;**20**:242-7.

75. Kasaie P, Andrews JR, Kelton WD, Dowdy DW. Timing of tuberculosis transmission and the impact of household contact tracing. An agent-based simulation model. *Am J Respir Crit Care Med* 2014;**189**:845-52.

76. Kawatsu L, Izumi K, Uchimura K, Urakawa M, Ohkado A, Takahashi I. Can social network analysis assist in the prioritisation of contacts in a tuberculosis contact investigation? *Int J Tuberc Lung Dis* 2015;**19**:1293-9.

77. Kettunen CM, Sunmonu Y, Hodgkinson AL, Verzumo M, Belding-Braun K, Vaccariello P, *et al.* Contact investigation of a case of active tuberculosis in the community. *Am J Infect Control* 2007;**35**:421-4.

78. Klovdahl AS, Graviss EA, Yaganehdoost A, Ross MW, Wanger A, Adams GJ, *et al.* Networks and tuberculosis: an undetected community outbreak involving public places. *Soc Sci Med* 2001;**52**:681-94.

79. Kowada A. Cost effectiveness of high resolution computed tomography with interferon-gamma release assay for tuberculosis contact investigation. *Eur J Radiol* 2013;**82**:1353-8.

80. Lambregts-van Weezenbeek CS, Sebek MM, van Gerven PJ, de Vries G, Verver S, Kalisvaart NA, *et al.* Tuberculosis contact investigation and DNA fingerprint surveillance in The Netherlands: 6 years' experience with nation-wide cluster feedback and cluster monitoring. *Int J Tuberc Lung Dis* 2003;**7**:S463-70.

81. Langenskiold E, Herrmann FR, Luong BL, Rochat T, Janssens J-P. Contact tracing for tuberculosis and treatment for latent infection in a low incidence country. *Swiss Med Wkly* 2008;**138**:78-84.

82. Lobato MN, Royce SE, Mohle-Boetani JC. Yield of source-case and contact investigations in identifying previously undiagnosed childhood tuberculosis *Int J Tuberc Lung Dis*. 2003;**7**:S391-6.

83. Logan S, Boutotte J, Wilce M, Etkind S. Using the CDC framework for program evaluation in public health to assess tuberculosis contact investigation programs. *Int J Tuberc Lung Dis* 2003;**7**:S375-83.

84. MacIntyre CR, Plant AJ. Impact of policy and practice on the effectiveness of contact screening for tuberculosis. *Prev Med* 1998;**27**:830-7.

85. Macintyre CR, Plant AJ, Hendrie D. The cost-effectiveness of evidence-based guidelines and practice for screening and prevention of tuberculosis. *Health Econom* 2000;**9**:411-21.

86. MacLellan J, Wallace K, Vacchelli E, Roe J, Davidson R, Abubakar I, *et al.* A multi-perspective service evaluation exploring tuberculosis contact screening attendance among adults at a North London hospital. *J Pub Health* 2015; September, 1-6.

87. Mandal P, Craxton R, Chalmers JD, Gilhooley S, Laurenson IF, McSparron C, *et al.* Contact tracing in pulmonary and non-pulmonary tuberculosis. *Q J Med* 2012;**105**:741-7.

88. Marienau KJ, Cramer EH, Coleman MS, Marano N, Cetron MS. Flight related tuberculosis contact investigations in the United States: comparative risk and economic analysis of alternate protocols. *Travel Med Infect Dis* 2014; **12**: 54-62.

89. Marks SM, Taylor Z, Qualls NL, Shrestha-Kuwahara RJ, Wilce MA, Nguyen CH. Outcomes of contact investigations of infectious tuberculosis patients. *Am J Respir Crit Care Med* 2000;**162**:2033-8.

90. Marra F, Marra CA, Sadatsafavi M, Moran-Mendoza O, Cook V, Elwood RK, *et al.* Cost-effectiveness of a new interferon-based blood assay, QuantiFERON-TB Gold, in screening tuberculosis contacts *Int J Tuberc Lung Dis*. 2008; **12**: 1414-24

91. McKenzie A, Ijaz K, Tillinghast JD, Krebs VE, Diem LA, Metchock B, *et al.* Transmission network analysis to complement routine tuberculosis contact investigations. *Am J Pub Health* 2007;**97**:470-7.

92. Mohr O, Hermes J, Schink SB, Askar M, Menucci D, Swaan C, *et al.* Development of a risk assessment tool for contact tracing people after contact with infectious patients while

travelling by bus or other public ground transport: a Delphi consensus approach. *BMJ Open* 2013;**3**:e002939.

93. Muecke C, Isler M, Menzies D, Allard R, Tannenbaum TN, Brassard P. The use of environmental factors as adjuncts to traditional tuberculosis contact investigation. *Int J Tuberc Lung Dis* 2006;**10**:530-5.

94. Mulder C, Erkens CG, Kouw PM, Huisman EM, Meijer-Veldman W, Borgdorff MW, *et al.* Missed opportunities in tuberculosis control in The Netherlands due to prioritization of contact investigations. *Eur J Pub Health* 2012;**22**:177-82.

95. Mulder C, Harting J, Jansen N, Borgdorff MW, van Leth F. Adherence by Dutch Public Health Nurses to the National Guidelines for Tuberculosis Contact Investigation. *Plos One* 2012;**7**.

96. Munk E, Maltas G, Dorman S, Johnson B, Johnson S, Taylor K, *et al.* Workplace-based investigation of contacts of a patient with highly infectious tuberculosis - Maryland, District of Columbia, and Virginia, 2006. *J Am Med Assoc* 2008;**300**:276-8.

97. Pettit S, Black A, Stenton C, Black N. Outbreak of tuberculosis at a Newcastle public house: the role and effectiveness of contact screening. *Commun Dis Pub Health* 2002;**5**:48-53.

98. Pisu M, Gerald J, Shamiyeh JE, Bailey WC, Gerald LB. Targeted tuberculosis contact investigation saves money without sacrificing health. *J Pub Health Man Pract* 2009;**15**:319-27.

99. Reichler MR, Reves R, Bur S, Thompson V, Mangura BT, Ford J, *et al.* Evaluation of investigations conducted to detect and prevent transmission of tuberculosis. *J Am Med Assoc* 2002;**287**:991-5.

100. Rodriguez EM, Steinbart S, Shaulis G, Bur S, Dwyer DM. Pulmonary tuberculosis in a high school student and a broad contact investigation: lessons relearned. *Maryland Med J* 1996; **45**: 1019-22

101. Ruben FL, Lynch DC. Tuberculosis control through contact investigation. *Pennsyl J Med* 1996;**99:** 22-3.

102. Rubilar M, Brochwicz-Lewinski MJ, Anderson M, Leitch AG. The outcome of contact procedures for tuberculosis in Edinburgh, Scotland 1982-1991. *Respir Med* 1995;**89**:113-20.

103. Sanderson JM, Proops DC, Trieu L, Santos E, Polsky B, Ahuja SD. Increasing the efficiency and yield of a tuberculosis contact investigation through electronic data systems matching. *J Am Med InformAssoc* 2015;**22**:1089-93.

104. Saunders M, J., Koh, G.C., Small, A.D., Dedicoat, M. Predictors of contact tracing completion and outcomes in tuberculosis: a 21-year retrospective cohort study. *Int J Tuberc Lung Dis* 2014;**18**:640-6.

105. Shah NS, Yuen CM, Heo M, Tolman AW, Becerra MC. Yield of contact investigations in households of patients with drug-resistant tuberculosis: systematic review and meta-analysis. *Clin Infect Dis*2014;**58**:381-91.

106. Shrestha-Kuwahara R, Wilce M, DeLuca N, Taylor Z. Factors associated with identifying tuberculosis contacts. *Int J Tuberc Lung Dis* 2003;**7**:S510-6.

107. Sprinson JE, Flood J, Fan CS, Shaw TA, Pascopella L, Young JA, *et al.* Evaluation of tuberculosis contact investigations in California. *Int J Tuberc Lung Dis* 2003;**7**:S363-8.

108. Stoddart H, Noah N. Usefulness of screening large numbers of contacts for tuberculosis: questionnaire based review. *BMJ* 1997;**315**:651.

109. Tian Y, Osgood ND, Al-Azem A, Hoeppner VH. Evaluating the effectiveness of contact tracing on tuberculosis outcomes in Saskatchewan using individual-based modeling. *Health Educ Behav*2013;**40**:98S-110S.

110. Trieu L, Proops DC, Ahuja SD. Using QuantiFERON-TB Gold In-Tube for field-based tuberculosis contact investigations in congregate settings. *J Pub Health Manag Pract* 2013;**19**:E11-3.

111. Underwood BR, White VL, Baker T, Law M, Moore-Gillon JC. Contact tracing and population screening for tuberculosis--who should be assessed? *J Pub Health Med* 2003;**25**:59-61.

112. Ward LJ, Hughes SE, Grabau JC. The evaluation of school-based contact investigations in New York State, exclusive of New York City, 1997-2001. *J Pub Health Manag Pract* 2004;**10**:308-15.

113. Wilce M, Shrestha-Kuwahara R, Taylor Z, Qualls N, Marks S. Tuberculosis contact investigation policies, practices, and challenges in 11 U.S. communities. *J Pub Health Manag Pract* 2002;**8**:69-78.

114. Yeo IK, Tannenbaum T, Scott AN, Kozak R, Behr MA, Thibert L, *et al.* Contact investigation and genotyping to identify tuberculosis transmission to children. *Ped Infect Dis J* 2006;**25**:1037-43.

115. Zangger E, Gehri M, Krahenbuhl JD, Zuberbuhler D, Zellweger JP. Epidemiological and economical impact of tuberculosis in an adolescent girl in Lausanne (Switzerland). *Swiss Med Wkly* 2001;**131**:418-21.

CHAPTER SEVEN: APPENDICES

Appendix 1. Sample Medline search and results by database

1. contact tracing.ti,ab.

2. contact investigation*.ti,ab.

3. (case finding or case finding).ti,ab.

4. case detect*.ti,ab.

5. contact examin*.ti,ab.

6. contact screen*.ti,ab.

7. contact procedur*.ti,ab.

8. close contact*.ti,ab.

9. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8

10. Tuberculosis/

11. TB.ti,ab.

12. tuberculosis.ti,ab.

13. 10 or 11 or 12

14. 9 and 13

15. limit 14 to (English language and humans and yr="1995 -Current"

Results by database

First stage	*Second stage*
CINAHL 332	CINAHL 39
Web of Science 581	Web of Science 32
Cochrane Library 33	Cochrane Library 8
Ovid Medline 1929	Ovid Medline 189
EMBASE 2341	EMBASE 175
PsycINFO 35	PsycINFO 37
EconLIT 3	EconLIT 0
Social Policy and Practice 1	Social Policy and Practice 1

Appendix 2. Extraction table for specific population studies

Details of study	Methods	Results	Conclusions
Ashgar et al. 2009[19] Type of document: Journal article Study design: Describes interviews with patients during a contact tracing investigation, together with providing other routine data collected during the investigation Country: USA Population: 18 patients with TB living in low income area of Miami, Black non-Hispanic, frequented "crack house", mostly HIV positive Quality comments: The data relates to number of contacts	Research methods: Review of medical records and patient interviews Staff involved: n/a Measures used: Tuberculosis skin test (TST) Genotyping	Results/data: Patients were reluctant to name contacts. One patient attended a church and a dialysis centre. Genotyping suggested more than one chain of transmission. Repeated interviews resulted in an average of 5 names per person. Skin tests were offered to observed persons at the crack house and at the named locations. 9% of named contacts had positive TST results. 68% of observed contacts had positive TST results, 10-12% from the named locations had positive results. Observed contacts were 7.8% more likely than named contacts to have positive results. There was no difference in likelihood of a positive result between named locations versus named contacts.	Main conclusions: Site visits and identification of observed contacts are likely to lead to a higher yield of contacts at risk of future TB than named contacts in this population.

identified and test results, rather than providing qualitative data in the form of interview text.			
Bur et al. 2003[5] Type of document: Journal article Study design: Report of a contact investigation Country: USA Setting: Urban community with high rate of drug abuse and prison. An inmate who had spent time in prison and in the community. Quality comments: The study provides general narrative about how the investigation was carried out, with the main data relating to	Research methods: Description of process and outcomes. Staff involved: Prison staff (required around 250 hours of staff time), and health department staff. Measures used: TST DNA fingerprinting	Results/data: Investigation used a "concentric circle approach" whereby evaluation performed among closest contacts and those most at risk of progression to active disease. If the inner circle infection rate exceeds that expected for the population then investigation proceeds to wider circle (less exposure). All inmates housed with case were initially screened, this widened to all inmates. Contact interviews elicited 10 names of the 67 contacts ultimately identified. Other community contacts identified by observation of health staff while present in location carrying out screening. Community screening for a subset of inmates released resulted in only a 5% yield and was abandoned for other released inmates. A high proportion of infected contacts did not complete treatment (more than half community and less than a third of inmates). Eighteen cases identified, 11 in the community and 6 in prison. All named community contacts were TST positive. 41% of inmates housed with case were TST positive, 20% of all inmates. Collaboration between health department and	Main conclusions: Observation in the community was an important means of identifying contacts. There was a large proportion of infected contacts who did not complete treatment.

numbers screened and test results.		prison described as key to the success. Also access to accurate records for inmates.	
Cook et al. 2012[25] Type of document: Journal article Study design: Descriptive Country: Canada Population: Aboriginal communities Quality comments: Little data to support a general description	Research methods: Descriptive only Staff involved: Nurses/healthcare workers Measures used: Description	Results/data: Describes limitations of conventional contact investigation which relies on a person knowing all their contacts and their willingness to share names. Issues with highly mobile persons, non-household environments, casual contacts, level of experience of workers in taking histories, resource shortages, and long lists of contacts. In particular in aboriginal communities issues of community isolation, language, cultural barriers and social stigma. Describes use of social network analysis (identifies how cases are connected to each other), geographic information systems (to visualise data involving distance and location), and genomics (such as DNA fingerprinting) to identify transmission events, individuals acting as spreaders and confirm relations between outbreaks).	Main conclusions: Describes the limitations of interviewing and naming contact methods, suggests the potential of alternative/supplementary approaches.
Curtis et al. 2000[24] Type of document: Journal article Study design: Describes a contact investigation in a homeless shelter Country: USA Population: resident men of a homeless	Research methods: Description of the investigation around 10 cases of TB Staff involved: Unclear Measures used: TST DNA fingerprinting Chest radiography Clinical assessment	Results/data: 70% of shelter users and staff had a positive TST. Seven of the 10 cases had identical DNA fingerprints, eight cases were considered related. The believed source case was a long-term resident who had a previous history of TB, had been referred to hospital for a severe cough but had refused to go. Environmental assessment revealed minimal ventilation, with the air handling unit and exhaust	Main conclusions: A high degree of suspicion of TB should be maintained. Shelter users should be screened prior to admission. Prompt screening should be implemented when cases are detected. Efficient ventilation systems should be in place.

shelter, visitors and staff n=257 Quality comments: The study provides general narrative about how the investigation was carried out, with the main data relating to numbers screened and test results.		fans working poorly. Smoke tube testing showed that air at bed level moved little or travelled horizontally between beds.	Additional effort should be made to treat the population.
Dasgupta et al. 2005[18] Type of document: Journal article Study design: Review and cost effectiveness analysis Country: Canada Population: Low incidence countries immigrants and refugees Quality comments: A reasonably robust review although only one database searched	Research methods: Search of Medline and reference list screening Staff involved: N/A Measures used: Any reported	Results/data: In low incidence countries the public health impact of TB in foreign born persons is modest (estimates of 2%, 11% or 17% of active TB cases in general population that can be attributed to transmission from the foreign born). Reports evidence of cost-effectiveness of contact tracing programmes with $815 saving on hospital care per active case detected, and $600 of saving per active case prevented due to detection of latent infection.	Main conclusions: Global TB control would reduce the risk of TB among human migrants. Contact tracing, particularly in ethnic communities appears to be more effective than screening and less intrusive.
de Vries and van	Research methods: Description	Results/data: 20% of those examined using TST (staff and visitors to 3 homeless shelters and staff	Main conclusions: The authors recommend the use of

Hest, 2005[30] Type of document: Journal article Study design: Describes a contact investigation for a single case Country: Netherlands Population: Drug addicts and homeless persons/ frequenters of homeless shelters, staff of mental health service Quality comments: The study provides general narrative about how the investigation was carried out, with the main data relating to numbers screened and test results.	of the process and outcomes Staff involved: TB physician for mobile X ray, others unclear. Measures used: TST Chest radiography DNA fingerprinting	of mental health service) in first round had latent TB. A second round checked residents at the homeless shelters using TST or a mobile digital X ray. 507 persons were assessed. 127 using TST, with 28 (18 staff members and 10 shelter residents) found to have latent TB. 380 were examined by X ray, with 6 found to have active TB and 4 latent. Testing with DNA fingerprinting indicated that none of the other TB cases had the same DNA fingerprint as the original case. This finding underpinned the decision to re-introduce a screening programme for drug user/methadone user/homeless persons.	mobile X rays for difficult to reach TB groups. They describe the value of molecular technologies for recognising patterns. The overlap between contact investigation and screening was highlighted.
Fitzpatrick et al. 2001[22] Type of document:	Research methods: Describes the process and outcomes of the contact investigation during an outbreak using social network	Results/data: No source patient was identified who accounted for all the outbreak cases. One potentially accounted for 71% (22).	Main conclusions: The authors conclude that a social network approach would have been beneficial to identify

Journal article Study design: Description of an investigation Country: USA Population: A community in Indiana, described as a difficult-to-reach population. 31 patients with TB. Quality comments: The study provides general narrative about how the investigation was carried out, with the main data relating to numbers screened and test results. While some interviews were carried out there are no qualitative data.	methods. Retrospective review of records and interviews with patients who were still available. Staff involved: Public health nurses. Measures used: TST Chest radiography	Only 8 individuals initially provided names of contacts with TB. Retrospective questioning revealed that 29 of known outbreak cases knew either indirectly or directly another case. Transmission seemed to have occurred in congregate social settings (an apartment complex, a junkyard, a local bar, a liquor store). These were named by patients as locations of frequent social gathering to take drugs and alcohol. 6 persons with symptoms were not correctly diagnosed with TB. Health department personnel were not trained in TB control resulting in persons being screened (named contacts and workplace colleagues) not being those at highest risk.	contacts in similar social settings and halt the outbreak earlier, as there was a failure to consider unnamed contacts.
Kline et al. 1995[16] Type of document: Journal article	Research methods: Describes the contact investigation Staff involved: Unclear	Results/data: The index patient supplied a few named contacts, but reported that most time while he had been unwell had been spent at a bar and nearby rooming house. The investigation therefore	Main conclusions: The authors suggested that initial infection may progress to active disease more

Study design: Descriptive Country: USA Population: Frequenters of a bar, the index patient was a homeless person, n=97 contacts, including 4 staff and 93 customers. Most of the participants "used alcohol excessively" Quality comments: The study provides general narrative about how the investigation was carried out, with the main data relating to numbers screened and test results.	Measures used: TST Chest X ray Clinical examination RFLPs	targeted bar staff and customers. 14 cases of active TB and 27 latent infection were detected. In most cases the bar was the only site where there was any contact with the index patient. Four people were later identified with active TB who had been missed by the investigation (they had been unwilling/unable to take part), and 2 further cases of active TB linked to bar frequenters were later identified. RFLP fingerprinting proved useful to supplement the investigation by proving linkages between cases. 19 of the 39 people with positive TSTs attended follow up appointments. Of these, 13 contacts refused prophylaxis or did not complete their treatment. Three of these progressed to active TB. In addition 13 other TST positive contacts did not attend for follow up appointments for chest X ray, and of these 2 cases progressed to active TB	frequently in heavy alcohol users, although the high infectivity of the index patient may have been a significant factor. Chronic alcoholism is a high-risk factor for progression to active disease and major efforts to ensure completion of six months of isoniazid therapy are worthwhile.
Li et al. 2003[12] Type of document: Journal article Study design: Retrospective analysis	Research methods: TB cases identified from surveillance data 1997-1999 Staff involved: Not reported Measures used:	Results/data: 48.8% of patients had four or more contacts identified, 38.7% had one to three contacts, and 12.5% had no contacts. The median number of contacts per patient was 3 (range 0-64). Homeless	Main conclusions: Strategies for contact elicitation among homeless patients should be different from those applied to non-

of data Country: USA Population: Homeless persons n=152 patients of 2988 patients investigated Quality comments: The study provides general narrative about how the investigation was carried out, with the main data relating to numbers screened, contacts identified and test results.	Bacteriologically confirmed cases of pulmonary tuberculosis	patients were more likely to be male, non-Hispanic Black, US-born, unemployed, alcohol or drug abusers, be infected with HIV, and have mental illness. Homeless patients were more likely to have been lost to follow-up prior to treatment completion. The number of contacts identified per homeless patient was significantly lower than for non-homeless patients (median 1 vs. 4, P< 0.001; mean 2.7 vs. 4.8, P<0.001). Homeless patients were four times more likely to have no contacts identified P<0.001.	homeless patients. Greater knowledge of the barriers to contact identification and better approaches to contact investigation among homeless patients are needed. Strategies focused on identifying the location of exposure rather than on eliciting names of contacts is one approach that may be useful among homeless patients. Being homeless at the time of diagnosis should be used as an indicator for prioritizing prompt contact evaluation.
Lofy et al. 2006[13] Type of document: Journal article Study design: Descriptive Country: USA Population: Residents of homeless shelters n=1000 contacts at 10 shelters Quality comments:: The study provides general narrative	Research methods: Describes the outbreak in 2002 and the contact investigation surrounding patients Staff involved: Health department staff Measures used: TST Chest X Ray	Results/data: Transmission occurred over a short duration, in multiple settings, rather than in a single homeless facility. A questionnaire was used to elicit names of contacts and places where patients slept, worked, travelled, sought health care, ate, used drugs, and spent time during their infectious period. Intake logs from facilities frequented by infectious patients were reviewed to quantify the time they spent in each facility while infectious. Facilities visited by infectious patients were prioritised for TB screening based on the number of infectious patients who visited the facilities and	Main conclusions: A comprehensive, resource-intensive approach is needed to control transmission of large TB outbreaks

about how the investigation was carried out, with the main data relating to numbers screened and test results.		the prevalence of positive TST results compared with other homeless sites. Where attendance records were available, these were used to identify clients who were in that location. If no records were available, then staff were asked for names of contacts. Contacts were prioritized for screening based on their cumulative number of exposed visits. Screening contacts with one sputum culture was as sensitive as chest X ray in detecting TB disease (77% vs. 62%). Network analysis and genotyping were used to explore and map clusters. The median number of named contacts was 3.5 (mean 4.8) per patient. Six (14%) of index patients named no contacts. 69% of contacts began treatment for latent infection.	
Malakmadze et al. 2005[17] Type of document: Journal article Study design: Country: USA Population: Wisconsin, n=26 patients n=292 contacts. Described as "hard to reach" and having risk factors of alcohol abuse, crack	Research methods: Patients were re-interviewed and places frequented by the patients while they were infectious were visited to identify contacts. Genotyping was used and findings compared to the original investigation. Staff involved: Unclear Measures used: TST Chest radiograph Genotyping – spoligotyping,	Results/data: The new investigation revealed several previously unrecognized locations of transmission: a single-room occupancy hotel, 2 homeless shelters, a bar, and 2 crack houses. Prior to the further investigation, epidemiologic links were known for 8 of the 26 patients. The investigation revealed 29 previously unsuspected epidemiologic links among 17 other patients. Epidemiologic links were identified for all but one case. Using genotyping methods an additional 98 contacts which had been missed during routine contact investigation were identified. 95% of previously identified contacts had been tested, 16% of these were TST positive and 90%	Main conclusions: Universal genotyping revealed unsuspected TB transmission and previously unrecognised sites of transmission. A policy of genotyping isolates from all (not just some) patients with culture-positive TB is required in order to successfully identify clusters. Genotyping should be used alongside other methods of

cocaine use, homelessness, and unemployment	MIRU, and IS6110 RFLP Epidemiological links	completed treatment. Of the 98 additional contacts identified 31% were tested, 17% (5) were TST positive and 2 began treatment (3 refused).	contact tracing, and can aid detection of unapparent transmission before an increase in incidence, and thus will help identify clusters earlier.
McElroy et al. 2003[14] Type of document: Journal article Study design: Description of an investigation Country: USA Population: An area with low incidence of TB however, drug use and drug sharing common among cases and contacts Quality comments: The main data relates to a description of how the network was established.	Research methods: Describes the process and outcomes of the contact investigation during an outbreak using social network methods including network questionnaire interviews Staff involved: Unclear Measures used: TST Network questionnaire DNA fingerprinting	Results/data: Network visualization illustrated the complexity of interactions among the cases and contacts. The graph established (with 2 exceptions) the potential for contact between each case and at least one other case, a link to strip clubs was established as a connection among all cases.	Main conclusions: The authors conclude that network analysis can clarify connections among cases and people with latent TB that would not be identified by traditional methods. Also that network analysis can identify patterns in behaviours in a group that may help identify sub-groups.
McElroy et al. 2003[7] Type of document:	Research methods: Homeless shelter attendance and	Results/data: Duration of exposure was significantly associated	Main conclusions: Earlier recognition

Journal article Study design: Retrospective review of data Country: USA Population: Homeless shelter residents n=620 shelter employees n=26 Quality comments: The study provides general narrative about how the investigation was carried out, with the main data relating to numbers screened and test results.	medical records 1999-2000 reviewed. Shelter attendance records, collected at nightly check-in included name, age, ethnicity, and specific dates of overnight stays. Dates spent in prison were obtained, and employment records from labour agencies examined. Staff involved: radiologists, nurse, others unclear Measures used: TST On site chest radiography DNA fingerprinting	with likelihood of infection. Those spending 115–153 nights in the shelter had a 3.5 times greater risk of having a positive TST result than those spending less than 38 nights. Of the 119 individuals identified with latent infection 22% began the treatment course and 14% successfully completed it. HIV co-infection is an important factor contributing to the clustering of TB cases. At least half of the outbreak patients either had spent time in prison or had visited the local Sexually Transmitted Diseases Clinic in the prior two year period. If testing had been carried out at these, infection may have been detected. DNA fingerprinting may be useful to detect previously unrecognised links among cases. It may be a useful impetus to further question a patient regarding routine, contacts, and places frequented to uncover social networks. There is a need for improved strategies for ensuring the initiation and successful completion of treatment for latent infection among the homeless.	of the homeless shelter as a main site of transmission might have been facilitated by the use of DNA fingerprinting
Mulder et al. 2009[29] Type of document: Journal article Study design: Systematic review Country:	Research methods: Review of effectiveness of contact tracing for foreign born versus natives exposed to a foreign born case. Staff involved: Not reported Measures used: Effectiveness measures included were	Results/data: No papers using randomised design were found, 18 reported yield or coverage and were included in the review (6 EU). The strategies and context of contact tracing across studies differed considerably. The setting, infectiousness of the source case, media interest were influential factors. Six studies used stone in the pond principle, three used workplace contacts	Main conclusions: Foreign born contacts have a higher median latent TB infection yield than local-born exposed to the same foreign born case. This may be due to higher background rates in this population. Contact tracing may therefore be considered

Netherlands/Sweden Population: Migrants and those born abroad Quality comments: This systematic review was carried out to a reasonable standard	coverage, TB yield, latent TB yield and contacts/index case ratio. The study considered transmission rates and outcomes for foreign born compared to native, European versus non-European studies, and whether closeness of contact affected effectiveness.	only, two studies screened only close contacts, one only household contacts, and for the remaining six the approach was unclear.	as a form of screening. Large variation between studies, and no difference in yield of infected contacts from foreign born index cases, versus whole population index cases. Different strategies are needed for different circumstances.
Mulder et al. 2011[28] Type of document: Journal article Study design: Analysis of records Country: The Netherlands Population: Immigrants Quality comments: The main data relate to test results of those screened.	Research methods: Data extracted from patient records Staff involved: N/A Measures used: Number of contacts investigated	Results/data: Close contacts of immigrant patients were significantly less likely than Dutch patients to be screened for TB (89% versus 93%) or infection (50% versus 75%) although the yield for infection and disease was higher (1.5% versus 0.4% and 13% versus 10% respectively).	Main conclusions: The effectiveness of contact tracing could be optimised by ensuring complete investigation in the immigrant population.

National Institute for Health and Care Excellence, 2012[31] Type of document: Guidance Study design: Guidance based on evidence reviews Country: UK Population: Hard to reach groups Quality comments: Guidelines based on commissioned high quality reviews of the literature	Research methods: Based on reviews of evidence and expert consultation. Draws on Matrix Evidence report Staff involved: TB Teams, public health units Measures used: Any	Results/data: The guidance recommends that teams should co-ordinate investigations at places where the index case spends a significant amount of time. There should be partnership working between health and social care, voluntary, community, and statutory organisations. Peer educators should be involved when possible. Digital mobile radiography units should be considered in places where there are large numbers of at risk people. Strain typing and social network analysis should be used to explore where transmission is occurring with a focus on active case finding in these settings. People in contact with children who have active TB (close and wider contacts) should be traced to identify the source.	Main conclusions: Investigation of locations is important. Partnership working is required. Use of peer educators can be valuable.
Oeltmann et al. 2006[15] Type of document: Journal article Study design: Descriptive Country: USA Population: Illicit	Research methods: Describes the investigation Staff involved: Outreach workers Measures used: TST	Results/data: All reported frequent “hotboxing,” the practice of smoking marijuana with others in a vehicle with the windows closed so that exhaled smoke is repeatedly inhaled. The risk for a positive TST result was 2.8× greater among friends than among other contacts (95% CI	Main conclusions: Alternative strategies to name-based contact investigations are important

drug users mean age 22 years, n=11 patients n=22 contacts Quality comments: The study provides general narrative about how the investigation was carried out, with the main data relating to test results	Chest radiography	1.3–6.0). There was a reluctance to name contacts at risk and the location that were frequented. Workers had to arrange meetings at times and locations convenient to the group. Outreach workers needed to establish trust in order to gain co-operation. Screenings could place in varying locations including street corners and in car parks. Often outreach workers were successful only after spending hours driving throughout the community searching for patients and contacts.	
Ospina et al. 2012[26] Type of document: Journal article Study design: Evaluation of an intervention Country: Spain Population: Immigrant communities Quality comments: This is the only study which endeavours to evaluate an	Research methods: Compared the 2 year intervention period with 2 year pre-intervention period. Staff involved: Community health workers trained in TB and psycho-social skills. Measures used: Number of TB cases detected	Results/data: The increase in contact tracing coverage during the intervention period was statistically significant. Pre-intervention contact tracing was performed on 65%, compared to 81.6% during the intervention period ($p<0.001$). Factors which were associated with contact tracing not being performed were: being diagnosed in a hospital without contact tracing; being born in India/Pakistan/North Africa; having an unknown residence; being HIV infected; or being homeless.	Main conclusions: The authors recommend the use of community health workers as improving the effectiveness of contact tracing. They describe the key elements of the role as being interpreters, inter-cultural mediators, and undertaking community actions to reinforce patient response.

intervention using an uncontrolled "before and after" design. The main data relate to numbers screened and test results. There is little data regarding the precise nature of the community worker intervention			
Rizzo et al, 2011[9] Type of document: Report Study design: Systematic review Country: UK Population: Hard to reach groups Quality comments: Systematic review which underpinned the NICE guidelines.[31]	Research methods: Review of effectiveness and cost effectiveness of identification and management of TB in hard to reach groups Staff involved: N/A Measures used: Any	Results/data: Included 32 studies. Tracing household contacts of foreign born cases appeared to be cost-effective but not for those who are not household contacts (evidence from two studies). The cost effectiveness of active screening compared to passive case detection is uncertain. Using incentives to increase take up of TST and further investigation is effective and cost effective in drug users and homeless populations. Use of peers can help identify contacts among drug users and improve screening rates among homeless populations. Concerns about death and stigma prevent many people being tested.	Main conclusions: In hard to reach or at risk populations an active approach to case finding is recommended. The use of monetary incentives is recommended.

Sterling et al. 2000[23] Type of document: Journal article Study design: Description Country: USA Population: Described as being highly mobile, predominantly young (median age 24 years), black, male, infected with the human immunodeficiency virus (HIV), and gay, transvestite or transsexual. Quality comments: The study provides general narrative about how the investigation was carried out, with the main data relating to numbers screened and test results.	Research methods: Describes the management of a TB outbreak Staff involved: Community workers, nurses Measures used: Contacts identified, numbers tested	Results/data: Combined naming contacts with visits to the home of the source case. Also, work-site screenings. Also included location-based screening at a nightclub frequented by source cases. A community outreach worker was used to facilitate contacts with members of the community. Community awareness was enhanced by distributing letters to clinics, and placing flyers in clubs.	Main conclusions: Only 14 of the 114 contacts (12%) were named by cases. Others were identified via location-based Screening or observation, or referrals from HIV clinics or community workers.

Van Loenhout-Rooyackers et al. 2002[27] Type of document: Journal article Study design: Analysis of data Country: The Netherlands Population: Asylum seekers. Contacts of a person found to have TB on entry compulsory TB screening. Quality comments: Data from an ongoing longitudinal study relating to numbers screened and test results.	Research methods: Data from the DNA Fingerprinting Surveillance Project Staff involved: TB nurse Measures used: Chest X ray Clinical symptoms	Results/data: Conventional tracing uses the ring principle (close contacts from same facilities or same procedures from native country screened first, if high infection rate then screen shelter employees/visitors/those moved to other shelters). Infection rate of 60% in first ring (5 people), 10.5% in second (among staff/visitors). Four cases among asylum seekers were later identified as originating from the index case. Over a two year period regular contact tracing identified a suspected link between patients in 22% of cases. Using DNA fingerprinting techniques a definite link was made in 26% of cases and probable in a further 21%.	Main conclusions: DNA fingerprinting may detect late transmission of infection after conventional contact tracing has been completed, and identifies links that are not found by regular contact tracing.
Wallace et al. 2003[20] Type of document: Journal article Study design:	Research methods: Qualitative Staff involved: Unclear Measures used: None	Results/data: Aspects such as culture, language, risk factors and different settings may lead to a requirement for different approaches to conventional contact tracing. Reports use of different assessments in USA versus Mexico (TST versus symptom screening). Highlights	Main conclusions: Need for customised approach for different population groups.

Description Country: USA Population: Describes how practices may be customised to different populations including foreign born, prisoners, homeless. Quality comments: The authors report carrying out interviews and group discussions with field workers and programme managers, although the data are purely descriptive.		investigations carried out by different agencies for inmates versus their contacts outside the prison. Describes the use of photographs for contact investigation among the homeless as nicknames and aliases may be used. Importance of registers in homeless shelters. Describes use of TST screening of all residents in homeless shelters.	
Yun et al. 2003[21] Type of document: Journal article Study design: Description	Research methods: Retrospective review of notes on investigations. Staff involved: Unclear Measures used: Numbers screened and/or completed	Results/data: Only 27 (44%) of 61 contacts completed treatment for latent TB infection. Contacts living in shelters were less likely to be contacted than non-shelter. 18% of contacts were not evaluated.	Main conclusions: There was a failure to identify contacts in some cases, although a large number of contacts were traced.

Country: USA Population: Homeless Quality comments: The study provides general narrative about how the investigation was carried out, with the main data relating to numbers screened and test results.	treatment		

Appendix 3. Extraction table for wider population studies

Detail of study	Methods	Results	Conclusions
Aissa et al. 2008[36] Type of document: Journal article Study design: Cohort study Country: France Population: Individuals over 15	Research methods: Participants enrolled over an 18 month period for first cohort, over a 12 month period for second cohort. Aim to develop and evaluate a model for TB contact screening. Staff involved: N/A Measures used: Physical examination, TST, chest	Results/data: Mean number of contacts per case was 6 (1-122). 98% were BCG vaccinated. Overall infection rate for contacts who completed screening was 27%, 1% active and 26% latent infection. Risk of TB infection in a contact was significantly related to receiving free health care (p=0.005 OR 2 95% CI 1.2-3.2) and also the contact being a smoker (p=0.021 OR 1.6 95% CI 1.1-2.4). High	Main conclusions: A number of risk factors are associated with likelihood of infection. A significant proportion of infections may not be due to recent exposure.

living in the environment of a patient with pulmonary TB and who were culture-positive. Mean age 41.5 years. N=325 index cases and 2009 contacts (1575 completed screening). Quality notes: Provides statistical analysis to support conclusions	radiograph	incidence of TB in country of birth was significantly associated with risk of infection (p<0.0001 OR 2.2 95% CI 1.5-3.2). Risk of infection strongly associated with number of hours spent with index case, closeness of contact (at night p=0.0009 OR 2.1 95% CI 1.3-3.3), and being a first degree relative (p=0.001 OR 2.1 95% CI 1.3-3.3). Infectiousness of index case also important.	
Anger et al. 2012[37] Type of document: Journal article Study design: Cohort Country: USA Population: N=30,561 contacts diagnosed as having active TB who had been identified during previous investigations of 5182 TB cases. Aged over 5 years. 1% HIV infected, 56% non-	Research methods: TB registry in New York used to identify contacts during previous investigations over a 6 year period. Followed up, up to 4 years later. Staff involved: N/A Measures used: TST Chest radiograph for contacts with symptoms or positive TST results	Results/data: 48% completion rate for chemoprophylaxis. Latent TB infection was diagnosed in 79% of contacts who initiated chemoprophylaxis, and 61% who later completed treatment, and 39% who did not complete treatment. Highlights the limitations of using the TST to diagnose LTBI (TST can produce false-positive results for individuals who have received the BCG vaccine). Interferon-c release assays (IGRAs),	Main conclusions: Estimate of 102 contacts need to be evaluated per prevalent case diagnosed (95% CI 90–115). Contacts who completed chemoprophylaxis had the lowest incidence, although those who initiated and did not complete also had decreased incidence compared to contacts who did not initiate treatment. Contact screening is therefore

household exposure. 39% not USA born. Quality notes: Provides statistical analysis to support conclusions		IGRAs may better prioritize chemoprophylaxis for those with greater risk of tuberculosis. Also, uptake and completion of chemoprophylaxis may be higher when LTBI is diagnosed with IGRAs. The absolute risk reduction afforded by chemoprophylaxis initiation was estimated to be 1.1% (95% CI, .6%–1.9%). This equates to approximately 88 contacts needing to be treated, in order to prevent one case of TB (95% CI, 53–164).	effective, even when completion rates are below ideal levels.
Ansari et al. 1998[38] Type of document: Journal article Study design: Before and after Comparative Country: UK Population: Residents of South Glamorgan n=103 + n=103 index cases, n= 611 + n=732 close contacts Quality notes: Provides descriptive statistics only to	Research methods: Compared data from the TB contact tracing clinic, the Public Health Service Mycobacterium Reference Unit, and the Consultant in Communicable Diseases Control, South Glamorgan Health Authority at two time points: before and after a change to the contact tracing protocol. Staff involved: Chest clinic staff Measures used: Heaf test Chest X ray	Results/data: Previously close contacts had been invited for follow up annual radiological surveillance. In the changed policy close contacts were either discharged or referred to the chest clinic following their initial screening with no annual follow up. Close contacts defined as members of the same household sharing bathroom and kitchen facilities, and very close associates such as boy/ girlfriend or frequent visitors to the home of the index case. 97% of contacts screened under both protocols, old protocol 23% considered unnecessary, new protocol 14% considered unnecessary. 1% of contacts screened were found to have disease and treated. 3% were given chemo- prophylaxis and 22% were vaccinated with BCG. Some lapses in adherence to the protocol were found: out of 707 contacts screened, 181 were	Main conclusions: The revised protocol seemed to be as effective as the previous, more complex protocol. Screening of casual contacts and contacts of extra-pulmonary TB cases is not cost-effective.

support conclusions		casual contacts, who need not have been screened. Compared with the results of the previous protocol fewer contacts were unnecessarily screened. However, referrals to the chest clinic increased, and the number given chemoprophylaxis.	
Bailey et al. 2002[39] Type of document: Journal article Study design: Retrospective analysis of data Country: USA Population: Oklahoma, n=294 contacts for the index patient, a 23 year old HIV positive male who had been in prison 5 times. N=1019 contacts for secondary cases. Quality notes: Some statistical analysis	Research methods: Reviewed available hospital admission charts, health department records, chest radiographs, and prison records. Contact investigation data were taken from paper records. Used network visualisation and metrics to investigate the outbreak. Staff involved: TB control staff Measures used: TST Genotyping Closeness of relationship - reach, degree, and betweenness	Results/data: The strength of each patient–contact relationship was defined by the local TB control staff as close (>4-hour exposure indoors or in a confined space), casual (exposure other than close), or undetermined (relationship strength not able to be characterised). 42% of contacts had a positive TST. With the exception of hospital, work and school contacts, all categories of contacts had positive TST rates exceeding 40%. The network diagram indicated that the index patient was directly linked to 56% and indirectly linked to 18% of secondary cases. Reach, degree, and betweenness scores were calculated for relationships between the index case and contacts. The highest 20 scores and lowest 5 scores for each metric were used to prioritisation. Contacts prioritised using network analysis were more likely to have latent infection than non-prioritised contacts (odds ratio=7.8 95% CI=1.6-36.6).	Main conclusions: Network analysis is useful in earlier detection of tuberculosis transmission and for prioritisation of contacts to complement standard contact investigation. It can be useful while awaiting genotyping results which can take many months. Data required to perform network analyses is already routinely collected and needs to be organised into the proper format for analysis. While the costs may be beyond some programmes, principles such as pursuing repeatedly named contacts could be adopted. Decisions need to be made regarding how frequently network analysis should be used.

Banner, 2013[40] Type of document: Journal article Study design: Descriptive Country: Australia Population: Primary school children/staff, n=260 contacts. Quality notes: Narrative description of the investigation	Research methods: Describes the methods used for investigation of one case (a teacher at the school) and outcomes Staff involved: TB Co-ordinator at a chest clinic, Public Health Unit Director, Head of local Health Service Measures used: TST Chest radiography	Results/data: The children and staff that the teacher had most contact with were screened initially. Information sent to parents of these children, and an information session given to staff by the co-ordinator. A second round of screening was carried out for those judged to be at medium risk. Media involvement and parental pressure led to screening of a further low risk group. 260 contacts screened, with 18 students and 7 teachers infected (12% of high risk group, 5,5% of medium and 1.5% of low). None developed active disease.	Main conclusions: Highlights the importance of holding information session for teachers, sending letters and factsheets to all parents, and holding an open parent evening. Also, the need for a central point of communication and for media departments to be alerted and updated.
Bargman et al. 2013[41] Type of document: Report Study design: Descriptive Country: USA Population: High school pupils and staff. N=1249 contacts screened Quality notes: Narrative description	Research methods: Describes the investigation around one index case. Staff involved: 81 staff from county and state health departments, two county medical reserve corps members, representatives from two schools of nursing, one school district representative, five nurses from four health departments, a clerk, two people from the Centre for Disease Control. More than 885 person hours for the screening	Results/data: The investigation initially conducted in members of the household and teachers/students who shared at least two classes. It was later extended to all students and school personnel. Evaluation of all contacts with IGRA at the local laboratory was not feasible. A combined strategy using IGRA and TST was adopted. Those who were BCG (bacilli Calmette-Guerin) vaccinated or who reported a positive TST were IGRA tested. Local news media and internet social media reported the story and false information. Public meetings and meetings with news reporters were held to address concerns and perceptions about	Main conclusions: The investigation was complex and labour-intensive and required immediate availability of a large workforce. It is important to counter public fears by providing simple, credible, accurate, consistent and timely information about an event, and to let the public know what action they can take.

of the investigation	and 890 hours for the treatment. Measures used: TST IGRA (interferon gamma release assay) blood test	TB. The index case later disclosed a number of non-school social contacts.	
Behr et al. 1998[42] Type of document: Journal article Study design: Retrospective analysis of cases Country: USA Population: Cases of tuberculosis in San Francisco between 1991-1996 with positive cultures who had been previously identified as contacts to active cases n=11,211 contacts Quality notes: Detailed description	Research methods: Used DNA fingerprinting to further examine links between contacts and active cases. Routinely collected data from the TB registry was analysed. Staff involved: Disease control investigators Measures used: TST Chest radiograph for those with positive TST	Results/data: People who spent an estimated total of at least 40 to 100 hours with the index cases in the 3 months prior to diagnosis or during the infectious period were considered to be "close contacts" and those who shared the same front door with the index case were considered to be "household contacts." For index cases with positive sputum smears, evaluation of extended family members and contacts at the school, place of work, or social setting was initiated immediately with further expansion dependent on numbers found with positive TSTs. For index cases having negative smears but positive cultures, the initial investigation focused on close and household contacts, and the investigation was extended only if there was a higher-than-expected prevalence of positive TSTs in the inner circle. For culture-negative index cases, investigation was limited to close and household contacts. For index cases younger than 15 years of age, investigation was directed towards finding a possible source.	Main conclusions: DNA fingerprinting demonstrated that 30% of contacts with tuberculosis developed the disease at nearly the same time as, but not as a result of transmission from the index case. Contacts may have other risk factors for TB so the infection may have come from a source other than the index case. Contact tracing may be a useful way of identifying individuals at risk.

of links between cases, and role of DNA fingerprinting.		The study found that index and contact cases were infected with the same strain of TB in 38 instances (70%; 95% CI: 56-82%); and 16 pairs (30%) were infected with unrelated strains. Unrelated infections were more common among foreign-born (risk ratio =5.22, p<0.001), particularly Asian (RR =3.89, p= 0.002).	
Bock et al. 1998[43] Type of document: Journal article Study design: Descriptive Country: USA Population: Residents of a rural low income county, n=9 cases Quality notes: Narrative description of the investigation	Research methods: Describes an investigation surrounding an outbreak in 1996 Staff involved: Measures used: TST Chest radiography for those with symptoms	Results/data: Initially 61 contacts were named by patients. When an outbreak was suspected patients were re-interviewed by "experienced interviewers" and patients, family and contacts were all interviewed resulting in an additional 282 contacts, 19% of these had positive TSTs. Re-interview also established an illegal gambling group and other potential sites of infection such as bars and school. Some contacts were missed, because the normal daily connections between them were not recognized by investigators and social settings that were frequented were missed.	Main conclusions: Illicit social connections were not identified as contacts. As TB rates were low in the area there was no specialised/experienced team. The follow up investigation was delayed by 19 months as an outbreak was not initially suspected.
Borgen et al. 2008[44] Type of document:	Research methods: Describes the methods used for investigation of one case (an employee), and	Results/data: Contacts approached via letter to all households,	Main conclusions: The investigation could have

Journal article Study design: Descriptive Country: Netherlands Population: Supermarket employees and customers, 80 co-workers and estimated 23,700 inhabitants of the area around the supermarket (4.4 km^2) Quality notes: Narrative description of the investigation	outcomes, Staff involved: Measures used: TST – Mantoux method Chest radiography for older adults, those with BCG vaccination, TB or a positive TST.	locally distributed flyers, the internet and press releases. Invited to attend a local sports hall. A questionnaire was completed including demographics and frequency of visits. 21326 customers registered for screening, all but 56 of these were tested. In total 15 cases of TB disease were identified by the contact investigation (12 of these were thought to be directly from the source case). 359 cases of latent infection were identified (34% of these were thought to be due to recent exposure). 114 individuals needed to be skin tested in order to identify one case.	been improved by limiting testing to TST only and restricting it to frequent (at least once a week) customers. Use of IGRA instead of or in addition to TST could have improved positive predictive value of testing and enables TST for those with BCG vaccination. The optimal size of a contact investigation is setting specific, and depends not only on resources and logistics but also on background prevalence of LTBI.
Borraccino et al. 2014[45] Type of document: Journal article Study design: Retrospective data analysis Country: Italy Population: N=833 TB cases, n=4441	Research methods: Analysis of registry data over a 6 year period Staff involved: N/A Measures used: TST – Mantoux method Those with symptoms or positive test also clinical and radiographic examination	Results/data: Median number of contacts per case was 3, highest number 150. Those living in congregate settings showed a significantly higher number of contacts (RR = 1.38 95% CI 1.30-1.46). Homeless and those not born in Italy had fewer contacts. Contacts aged over 35 were more likely to be evaluated than those aged less than 25 (OR 1.45 95% CI 1.05-1.94). Regular and household contacts were more easily evaluated.	Main conclusions: More effort should be focused on younger TB contacts and those with results of sputum smear negative but sputum culture positive.

contacts in one region Quality notes: Provides numbers investigated but no links with investigation method			
Borrell et al. 2009[46] Type of document: Journal article Study design: Retrospective data analysis. Compares conventional contact tracing with molecular epidemiology methods Country: Spain Population: Residents of one city n=892 cases (contact tracing carried out for 613), 5087 contacts.	Research methods: Analysed cases reported to the programme over a 2 year period. Staff involved: N/A Measures used: Smear positivity IS6110-based restriction fragment length polymorphism ananlysis Myobacterial interspersed repetitive unit 12 typing	Results/data: 30% of contacts were household. Contact tracing not performed in 31% of cases – 3.5% lack of consent, 4.5% logistic difficulties, 11.6% patient living alone, 11.6% lack of referral to study by GP. A household link, and individuals under aged 15 were most frequently identified by conventional contact tracing (predominantly mother-son). Molecular epidemiological methods tended to identify non-household links and identified more individuals from precarious economic circumstances and social difficulties (p-=0.002).	Main conclusions: Contacts identified via conventional tracing methods may differ to those identified using molecular epidemiological methods. While household relationships are important other links such as neighbourhood and leisure settings are relevant. In a sizeable proportion of cases identified the link with the source case was unknown.

Quality notes: Some statistical analysis comparing the methods			
Canadian Agency for Drugs and Technologies, 2014[1] Type of document: Report Study design: Review and guidelines Country: Canada Population: Staff and patients in hospital Quality notes: Systematic review under-pinnined the guidelines	Research methods: Systematic review Staff involved: Unclear Measures used: TST	Results/data: In one trial identified - age was the only predictor of latent TB infection (mean age 40 +/- 9 versus mean age 36 +/- 9 years p=0.036). There was a low contagiousness of the index case to staff members. The review found little evidence relating to contact investigation in hospital settings.	Main conclusions: Guidelines regarding contact investigation in other settings may be applicable to a hospital setting, although recommendations are based on a low level of evidence.
Carbonne et al. 2005[47] Type of document: Journal article	Research methods: Describes the methods used for investigation of 6 cases of health care workers	Results/data: Testing of patients was based on the degree of infectiousness of the worker, patient characteristics (lowered immunity, young children, those not BCG vaccinated), length of	Main conclusions: The overall response rate was low. The use of a Freephone

Study design: Descriptive Country: France Population: Health care workers and patients in Paris hospitals Quality notes: Narrative description of the investigation	with infectious TB Staff involved: Crisis team including members of a hygiene unit, clinical wards, laboratories, occupational health service, risk management staff, Regional Centre, health authorities, trained staff for helpline. Measures used: TST for children Chest X ray and medical observation	exposure and proximity. Patients notified by letter and GP notified. Telephone help-line set up. A press release and media campaign were used in some cases. Number of contacts varied widely between cases. No TB disease was identified, two potential latent cases had unclear links to the source case. The methods used for the TST did not enable latent cases to be identified.	number was very valuable. Different screening practices used made analysis of information difficult.
Castilla et al. 2009[48] Type of document: Journal article Study design: Descriptive Country: Spain Population: Residents of a small village. N=751. Quality notes: Narrative description of the investigation	Research methods: Describes the investigation procedures for 8 index cases. Staff involved: Measures used: TST Medical consultation Chest radiography for those with positive TST	Results/data: Initial contacts - family/friends/workmate or schoolmate. Investigation expanded to others living in the village in same age group (19-23 years). Summoned to medical consultation, interviewed and completed survey form including socio-demographics, health and disease, and public places frequented. Close contact defined as exposure for more than 6 hours per week, occasional contact as less than 6 hours per week. Close contact (friends/lived/work together) explained 24.7% of the cases detected. Sporadic contact explained 37.9%. Frequenting the same	Main conclusions: The cases in the cluster appeared to have no close relationship but frequented some of the same bars.

		bars explained 33.3% of infections.	
Coleman et al. 2014[49] Type of document: Journal article Study design: Cost-effectiveness evaluation Country: USA Population: Flight-related contacts Quality notes: Economic model	Research methods: A return on investment model was used Staff involved: N/A Measures used: Treatment costs	Results/data: The costs calculated included that for contact tracing and also for testing/treating TB disease and latent TB infection. Average cost-per-contact used in the model was $16.76. Different states have different contact investigation processes therefore a range of expenditures per contact was developed - $28, $47, $134 and $164. The model indicated that every $1 spent on investigations and treatment resulted in more than $1 of saving at moderate/high rates of infection and disease. Low rates of infection and disease resulted in negative returns.	Main conclusions: At moderate/high rates of infection contact investigation and treatment was cost effective for flight-related contact. A modified contact investigation procedure with sputum culture and smear positive *or* cavitation on chest x ray (instead of *and* chest x ray) was more cost-effective.
Collins et al. 2004[50] Type of document: Journal article Study design: Descriptive Country: USA Population: Staff and patients of a veterans administration facility and local hospitals Quality notes: Narrative description	Research methods: Describes the methods used for investigation for one case Staff involved: Infection Control Professional, three investigators, Regional Public Health Service Administrator, two additional investigators from the department of public health. Measures used: TST	Results/data: Used the concentric circles approach to contact tracing. Skin testing performed at workplace of co-employees to facilitate compliance. Patients of the facility and ex-patients were sent letters requesting they report for testing. The circle of contacts was expanded due to potential contacts being comprised by additional health conditions. Initial testing and 3 month follow-up. Latent infection in 2% of co-workers, 2.4% of fellow patients, 46% of family members, 13% of closest contacts, 5% of contacts in congregate housing facility. Situation complicated by another family member identified with active TB.	Main conclusions: The extent of cross facility contact complicated the investigation, and the importance of good communication among services was highlighted. TB should be considered as a potential co-morbidity in patients being treated for other diseases such as cancer.

of the investigation		Challenge in identifying symptoms of many contacts due to side effects of treatment for cancer. Changes in staffing rotas complicated identifying contacts.	
Cook et al. 2007[52] Type of document: Journal article Study design: Analysis of existing patient data together with a questionnaire Country: USA/Canada Population: Patients and contacts in three counties. N=87 TB patients, n=440 contacts mean age 29 years. Quality notes: Predominantly narrative description of the investigation	Research methods: Used social network analysis methods. Supplemented routine investigation procedures with an interview to collect data on places of social aggregation over a 6 month period Staff involved: Unclear Measures used: TST Molecular genotyping – spoligotyping, multiple interspersed repetitive units variable number tandem repeats, IS6110-based restriction fragmentation length polymorphism analysis	Results/data: Interviews with TB patients and contacts elicited 1056 places of social aggregation. TB patients not linked via conventional contact tracing were linked by mutual contacts or places of social aggregation. For two of the Counties few interconnections or common places were found, or groups connected by SNA were found not to be the same strain on genotyping. For the third County no association between TST positivity and densely connected contacts was found however, places of social aggregation revealed a connected network. For this investigation an association between TST results and being in the denser area of a person-place network was found ($p<0.01$).	Main conclusions: Network visualisations can provide evidence of the presence or absence of case clustering before genotype results are available in some instances (one of three investigations examined).

Cook et al. 2011[51] Type of document: Journal article Study design: Descriptive review Country: Canada Population: Any Quality notes: Narrative review	Research methods: Provides an overview of the literature Staff involved: N/A Measures used: N/A	Results/data: Strategies for prioritisation have given priority to household contacts, and those at greatest risk. Closeness of contact based on amount of time rather than environmental or social factors. Extension of contact tracing often depends on number of TST positives compared to background rate. The influence of the infectious period, and contact risk factors is unknown. Guidelines and recommendations vary. Limitations of contact tracing in high risk or vulnerable groups highlighted, with importance of casual contacts and locations not always recognised. The completion of treatment remains a significant barrier. There are currently no guidelines for use of social network analysis, geographic information systems genomics, geno-typing. These may be of particular use in high risk communities.	Main conclusions: Focus needs to be on development of questionnaires, electronic data management, local capability and expertise, co-ordinated approaches, strategies and evaluation.
Davidow et al. 2003[53] Type of document: Journal article Study design: Retrospective review of data Country: USA Population: Employees of 5 workplace study sites	Research methods: Analysis of case and contact records, including TB interview records, clinic charts, and TB case reports Staff involved: Unclear Measures used: TST	Results/data: Subset of data from the Reichler et al. study. For smear-positive cases, workplace investigations were carried out alongside household and social contact investigations at all sites. For smear-negative cases, however, two sites conducted [53] investigations conditional on the results of household and social investigations. Over 30% of the investigations involved 20 or more contacts. The median number of contacts	Main conclusions: The potential for transmission of TB in the workplace needs further recognition. There was inconsistent and limited recording of data collected during the investigations. There were also differences between the locations in regard to who was selected for screening and who was used as the primary source of

n=349 cases, n=724 contacts Quality notes: Narrative description of the investigation		identified differed between smear-positive cases (9 contacts) and smear negative cases (7 contacts p<0.04). 68% of cases were fully screened, of these 29% had a positive TST.	information. Standard guidelines for workplace investigations, written workplace investigation policies, and standard data collection practices are needed.
Diel et al. 2004[55] Type of document: Journal article Study design: Examination of a cluster of cases during the study period Country: Germany Population: Customers of a bar close to a red light district, next door to a hostel for homeless people n=38 patients (12 of no fixed abode) with 4 index cases, n=421 contacts Quality notes:	Research methods: Further examined the contact tracing investigation using DNA fingerprinting Staff involved: Public health staff Measures used: TST DNA fingerprint	Results/data: Average 12.8 contacts per patient, five reported none. Ten patients were not originally included in the investigation and were only identified as linked by DNA fingerprinting. There were reports of a fear of social discrimination and intentionally antisocial behaviour due to irritation over the contact tracing procedure, which was perceived to be intrusive. Some of these cases reported trying to shield drinking partners from "bullying methods" of the "health police" by naming only contacts in more distant bars, or by naming their more transient contacts, such as neighbours. Persons who were presumed to be in close contact with eight of the patients showed no disease during the initial contact investigation, with some becoming ill after the investigation. Tracing of contacts was relevant for reaching a	Main conclusions: Only 40% of the 20 cases with epidemiologically confirmed recent transmission were included in the contact investigation. Conventional contact tracing is insufficient for the detection of chains of transmission in some harder to reach communities. DNA fingerprinting can not only provide important information regarding recent infection of one patient by another; it also allows structural weaknesses in an investigation to be identified. Contact investigation should examine the location itself and not focus on personal

Narrative description of the investigation		diagnosis only in two cases. 40.1% of close contacts had positive TST results, 1.9% became ill. Twelve of 20 cases with confirmed recent transmission could only be determined by DNA fingerprinting.	contacts and inflexible X-ray screening schedules. There should be a focus on informing the persons concerned about symptoms of disease and, if appropriate, conducting rapid screening by chest X-ray or sputum analysis.
Diel et al. 2006[56] Type of document: Journal article Study design: Testing of contacts Country: Germany Population: N=309 contacts Quality notes: Limited relevant data	Research methods: Compared the effectiveness of the two tests Staff involved: N/A Measures used: TST and QFT-G	Results/data QFT-G was unaffected by BCG vaccination status, unlike the TST.	Main conclusions: In close contacts who were BCG-vaccinated, the QFT-G assay appeared to be a more specific indicator of latent tuberculosis infection than the TST
Diel et al. 2009[54] Type of document: Journal article Study design: Testing of close contacts	Research methods: Carried out testing using IGRAS Staff involved: N/A Measures used: QuantiFERON-TB-Gold In Tube assay (QFT) and the T-	Results/data Use of either IGRA as a replacement for the TST would decrease the number of LTBI suspects to be investigated by approximately 70%. .	Main conclusions IGRAs are more accurate than TST

Country: Germany Population: n=182 close contacts Quality notes: Limited relevant data	Spot.TB test (T-Spot)		
Driver et al. 2003[57] Type of document: Journal article Study design: Retrospective analysis of investigations Country: USA Population: People in "congregate settings" (schools (37% of investigations), workplaces (45% of investigations), drug treatment centres, single room hostels, other locations) n=2740 contacts	Research methods: Analysed 100 investigations over a 5 year period Staff involved: Outreach staff Epidemiologist, screening, education and training staff, co-ordinator Measures used: TST Genetic testing Symptomatic contacts referred for chest radiography	Results/data: Testing carried out for high risk groups as soon as possible and again 10-12 weeks later. For other testing was performed once (10-12 weeks after exposure). Decision to perform testing at a congregate setting (not just household) based on: infectiousness of source case; size, crowding; windows of setting; characteristics of contacts such as age and immune status; case clusters. Use of written protocols, checklists, site-specific questionnaires. Contacts notified by letter with plans for testing and educational materials included. Telephone reminders were used by schools. A health educator conducted group sessions on TB at sites. Transmission classified as likely, possible, unlikely or unknown. Exposure defined as number of hours per week the	Main conclusions: Transmission at congregate sites was uncommon (22% of investigations) and is resource intensive. TST testing after most contacts would have converted should be considered in low risk groups. Treatment completion rates were poor.

Quality notes: Narrative description of the investigation		source case was at the site in the prior three months. Close contacts defined generally as those spending more than 8 hours per week with the source case. 83% of contacts were tested, 20% were infected, 52% completed treatment. Sites with likely infection compared to those unlikely tended to be those where the source case had a longer duration of cough (median 13 versus 6 weeks p=0.01) cavitary lesions (84% versus 44% p=0.01) Transmission defined as likely in 16%, possible in 7%, unlikely in 72% and could not be assessed in 5%.	
Duarte et al. 2012[58] Type of document: Journal article Study design: Comparison of data from two time periods (different strategies in use) Country: Portugal Population: Residents	Research methods: Data on prevalence of infection among contacts compared 2001-3 and 2004-6. Staff involved: Public health professionals Family doctors Measures used: TST	Results/data: During the first period the investigation interview targeted close contacts, during the second period visits to home and workplace were also included. 67% of eligible contacts screened in first period, 3% with active TB and 27% with latent. 83% completed therapy. Estimate 0.75 cases of infection per index patient identified. In second period 87% of contacts were screened. Interviews identified 950 contacts, home and	Main conclusions: Expanding contact investigations to home and [58] visits increased the number of individuals screened and identified further patients with active and latent TB.

of a metropolitan area. N=809 contacts in first period, n=683 in second period Quality notes: Narrative description of the investigation	Evaluation of symptoms Chest X radiography	workplace visits helped identify 2629 contacts. Estimate 1.4 cases of infection per index patient. While there was an increase in workload resources did not change between the study periods.	
Edelson et al. 2011[59] Type of document: Journal article Study design: Systematic review Country: Canada Population: Travellers on public transport Quality notes: Systematic review	Research methods: Systematic review of literature on TB transmission among bus or train travellers Staff involved: N/A Measures used: Evidence of infection	Results/data: Twelve documents were included. There was support for the possibility of TB transmission from active TB cases to co-travellers. In most reports exposure occurred daily over weeks or months. Ventilation was frequently reported to be poor. The reports did not provide evidence regarding the precise risk to co-travellers or identify which may be at greatest risk.	Main conclusions: Contact tracing decisions should be based on proximity to index case, duration of exposure, and other risk factors such as infectiousness of index case or susceptibility of contact
Erkens et al. 2010[60] Type of document: Journal article Study design: Narrative review Country: The Netherlands	Research methods: Descriptive overview of the literature, expert consultation and recommendations Staff involved: N/A Measures used: N/A	Results/data: Key importance of establishing infectiousness of source case, the likelihood of infection among contacts, and the risk of them developing TB. Outdoors transmission is highly improbable. Room size, air circulation and ventilation are important factors in dispersal of bacteria. Visits to potential transmission locations to estimate risk	Main conclusions: A risk assessment approach is needed. Tests to identify latent TB have variable predictive value.

Population: N/A Quality notes: Descriptive overview of the literature		are recommended. Children under 5 years are a main target for investigation. IGRA tests more sensitive in detecting TB infection than TST. A positive TST should be followed by IGRA. While neither are able to distinguish latent from active TB, some studies suggest IGRAs superior to TST in predicting latent infection becoming disease, although this finding not consistent. Chest X rays are usually normal in persons with latent infection. The degree of exposure depends on intensity and duration. Contacts are classified into circles of priority groupings. Where only a TST is used, a cut-off point for positivity must be decided with decisions regarding sensitivity versus specificity. Likelihood of infection and BCG status should be considered.	
Faccini et al. 2015[61] Type of document: Journal article Study design: Descriptive	Research methods: Describes methods used in an investigation for one case Staff involved: Unclear Measures used:	Results/data: Concentric methods approach used. A source case had been identified several years earlier however, no contact investigation had been performed beyond family members. Perceived stigma had led the case to claim they were unemployed.	Main conclusions: TB related stigma has major implications on TB control programmes as it can lead to incomplete identification of contacts. Establishing trust and rapport between public

Country: Italy Population: Workers at a call centre n=107 Quality notes: Narrative description of the investigation	TST Clinical examination Chest X ray, pulmonary assessment, interferon gamma release assay if positive TST Genotyping		and patients is important, with training in interviewing staff important. Genotyping was important to establish linkages.
Forssman et al. 2006[62] Type of document: Journal article Study design: Descriptive Country: Australia Population: Residents and staff of a nursing home Quality notes: Narrative description of the investigation	Research methods: Description of an investigation for one case Staff involved: Unclear Measures used: TST Chest X ray and clinical assessment if positive TST	Results/data: No further cases of infection were found. The investigation highlighted that there was no policy in place regarding screening of residents or staff in the district. Many staff were from TB endemic countries and were TST positive.	Main conclusions: Highlights the need for TB screening.
Fox et al. 2013[32] Type of document: Journal article Study design: Systematic review	Research methods: Systematic review of studies reporting the prevalence of TB and annual incidence of TB among contacts of patients with	Results/data: 108 studies included from high-income countries. There were an average of 5.1 contacts per index case in high income studies (95% CI 2.3-5). The definitions of household contact and close	Main conclusions: Contacts of TB are at a high risk of developing infection, particularly in the first year although there is

and meta-analysis Country: Australia Population: Any Quality notes: Systematic review including a large number of studies	TB Staff involved: N/A Measures used: Any	contact varied considerably. In high income settings the prevalence of TB amongst contacts was 3.3% (95% CI 27.6-42.7) and of latent infection was 34.8% (95% CI 27.6-42.7). The incidence is highest in the first year after contact, and remains above background incidence for at least five years after exposure. Children under five years of age and people living with HIV were particularly at risk. Foreign born contacts were significantly more likely to have latent infection than locally born contacts in high-income countries (OR 3.39 95% CI 3.10-3.71 p<0.0001).	heterogeneity in reported prevalence. Many of the patterns of infection in contacts reflect that of the whole population. There is a need to demonstrate that contact tracing is more effective than case-finding alone.
Funayama et al 2005[63] Type of document: Journal article Study design: Analysis of test results Country: Japan Population: n=462 University students Quality notes: Limited data of	Research methods: Compared QFT to TST Staff involved: N/A Measures used: QFT TST	Results/data: In the non-close-contact group, the QFT-positive rate was only 0.8 %. In the TST group strong tuberculin reactions with erythema of 30 mm or larger were seen in 18.2% in the (most likely due to the previous history of BCG vaccination).	Main conclusions: QFT is a useful method for diagnosing tuberculosis infection, especially among individuals who show tuberculin reactivity due to past BCG vaccination.

relevance			
Funk, 2003[64] Type of document: Journal article Study design: Descriptive Country: USA Population: Alaska natives Quality notes: Narrative description of the investigation	Research methods: Describes the investigation of an outbreak in one region. Staff involved: Public health nurses Measures used: TST	Results/data: Describes the challenges of investigation in remote areas including the interviewer being unfamiliar with the culture and a non-native language speaker. Named contacts collected are not always screened. A workshop for health providers may be beneficial to improve investigations.	Main conclusions: Contact investigations are challenging and labour intensive.
Gaber et al. 2005[65] Type of document: Journal article Study design: Descriptive Country: UK Population: Locals who attended a house South West England including children (the public house had	Research methods: Description of the investigation Staff involved: Consultant in Communicable Disease Control, Respiratory physician, Microbiologist, TB nurse, Communicable Disease Control Nurse, hospital and ward managers Measures used: Chest X ray	Results/data: The investigation centred on three avenues for contact tracing: the local public house; close-contacts; and inpatient hospital staff and patients (as the index case was currently a patient). Staff and regular visitors to the public house were sent letters to attend screening, and all children were screened. Other potential contacts were also offered screening, and letters were made available at the public house. The letter included education about TB symptoms, mode of transmission, the availability of effective treatment and a telephone help line. Local GPs were kept informed. An open	Main conclusions: Despite identifying few conventional close household contacts, a significant number of secondary cases were detected from tracing contacts at a single location. Multidisciplinary team working is essential for effective management of an investigation.

a playroom attached) n=184 contacts Quality notes: Narrative description of the investigation	Contacts who had symptoms or an abnormal X ray were screened by the Respiratory unit of the local district general hospital.	access radiology service carried out the screening. At the hospital patients who had more than 8 hours contact and other close contacts with the index case were screened. The first seven patients who had undergone anaesthesia using the same ventilator after the index patient were also screened. In total 15 contacts were treated for active TB and 13 were given chemoprophylaxis. DNA fingerprinting indicated all infections originated from a single source	
Gardy et al. 2011[66] Type of document: Journal article Study design: Further analysis of a previous investigation using additional methods Country: Canada Population: Residents of a community in British Columbia n=41 cases (included two children)	Research methods: Compares data and conclusions drawn from contact tracing, social network investigation, DNA fingerprinting and whole-genome sequencing approaches. Staff involved: Nurses Trained interviewers Measures used: Social Network Questionnaire Laboratory confirmed TB	Results/data: The Social Network Questionnaire was used subsequent to contact tracing interviews with the cases. The "name generator" questions related to: drug and alcohol use; residential and travel history; places of social aggregation; and identification of contacts in the context of high-risk behaviours and locations. A single social network diagram was developed using software to characterise relationships between contacts. During the contact investigation there was an emphasis on contacts of a paediatric case, in an effort to find the source of the child's infection however, a single source case could not be clearly	Main conclusions: Genotyping and contact tracing alone did not capture the true dynamics of the outbreak. Social network analysis outperformed contact tracing in identifying a probable source case as well as several locations and persons who could be subsequently targeted for follow-up. DNA fingerprinting had

Quality notes: Narrative description of re-examination of the investigation		identified. A social network approach using the SNQ added to the investigation by revealing previously unreported social interactions and several locations frequented by infectious patients (two hotels, meal/community centres, and crack houses). Restriction-fragment–length polymorphism (RFLP) and 24 loci mycobacterial interspersed repetitive units variable number of tandem repeats (MIRO-NNTR) whole-genome sequencing was carried out. This revealed two distinct TB lineages with 80% of contacts having both lineages. Social transmission networks were constructed to further examine relationships. Genome sequencing allowed the social network to be divided into sub-networks associated with specific genetic lineages of the disease. It was also valuable in enabling removal of social relationships that could not have led to transmission according to the genomic data. This greatly reduced the complexity of the network, and aided identification of index patients.	suggested that the outbreak had a single TB lineage, whereas more in-depth whole sequence molecular epidemiology revealed two lineages.
Gerald et al. 2002[68] Type of document: Journal article Study design: Describes the	Research methods: Generalised estimating equations and classification and regression trees were used to develop a decision tree for predicting a positive TST result in contacts.	Results/data: The decision tree developed had a 9% sensitivity and 22% specificity. It had a false-negative rate of 7-10%. It was estimated that use of the decision tree could enable around a 20% reduction in	Main conclusions: Decision trees can be developed to assist in prioritising contacts for investigation.

development and testing of a decision-support tool Country: USA Population: State of Alabama Quality notes: Describes development and testing of the tool rather than usage	The tree was tested in a set of 3162 contacts. Staff involved: N/A Measures used: TST	number of contacts investigated. Priorities for contacts to be investigated are: 1. if the index case has cavitary disease, or 2. the total exposure per month was more than 120 hours, or 3. the contact is below age 15. If none of these criteria are met than a case should only be investigated if: 1. the contact was exposed to a smear positive case in their home, or 2. the contact was exposed in a place where the ventilation was minimal.	
Gerald et al. 2003[67] Type of document: Journal article Study design: Development of protocols, standardised recording system, and evaluation of an intervention for field workers Country: USA Population: TB Field	Research methods: Examination of existing protocols and development of revised versions via focus groups, also new sheet to record information. The intervention was underpinned by Social Cognitive Theory and the Health Belief Model. It consisted of a workshop and computer-based module with individual supervisors allocated. It focused on interviewing skills and	Results/data: Existing protocols required investigation of those with close and prolonged contact however, there was considerable variance among field workers regarding the meaning of these terms. There was also variance in understanding of methods for eliciting information and the use of concentric circle analysis were apparent. There was a need to quantify information and standardise definitions using a new Contact Exposure and Assessment Worksheet. The quality of the training sessions was rated at mean 4.61 and overall value of training rated 4.71	Main conclusions: Attention should be paid to precisely defining terms, protocols should be standardised, and resources devoted to training to improve adherence to protocols.

Workers n= 6x small groups of 8-10 individuals. Quality notes: An evaluative study, although very limited data regarding effectiveness	behaviour to improve efficiency and effectiveness, including skills work, use of motivational strategies during interviewing, training on new protocols and forms, and case scenarios. Follow up monthly meetings in addition to workshops. The training took place over a 6 month period. The protocols had been piloted in two areas. Staff involved: Staff involved: TB field workers (registered nurses and disease intervention specialists who are college graduates with training in TB). Measures used: Feedback from managers and staff Review of records	(scale 1-5 5-excellent). Some further training was required when data entry errors and misunderstandings were identified.	
Greenaway et al. 2003[69] Type of document: Journal article Study design: Review	Research methods: Reviewed published data relating to the likelihood of tuberculin reactions in casual contacts. Staff involved: N/A	Results/data: Casual contact defined as "persons sharing the same air, but having no direct contact with the index cases". The hourly risk of infection reported among casual contacts ranged from 0.18% to 0.53%, and averaged 0.28% per hour. Individuals exposed early in the course of the disease were less likely to have TB conversion	Main conclusions: The decision to extend a contact investigation to a group of casual contacts in a work place or school should be based on

Country: Canada Population: Divided into 4 groups (low/high background prevalence of TB) Quality notes: review of available data	Measures used: TST	than those exposed later in the course of disease. Those with lower previous exposure to TB are more likely to be newly infected following a short duration of exposure (5 hours exposure for contacts from areas with low prevalence of TB will result in almost 50% likelihood of new infection versus 200 hours of exposure for individuals from countries with higher prevalence will result in 40% likelihood of new infection). Casual contacts with a high likelihood of previous exposure should undergo TST only if the initial index case was heavily contagious and/or the duration of contact was prolonged. Casual contacts with a low likelihood of prior mycobacterial exposure should be tested following as little as 5-10 hours of exposure.	1) evidence of transmission from the index case to closer contacts, 2) the number of hours of exposure, 3) the likelihood, in the population to be screened, of previous exposure to mycobacteria.
Gulati et al. 2005[70] Type of document: Journal article Study design: Descriptive Country: USA Population: Employees of an industrial company	Research methods: Examined a contact investigation for one index case to identify levels of infection and factors associated with transmission Staff involved: Occupational health medicine team – physician and industrial hygienist	Results/data: Investigation included individual interviews and assessment of buildings and ventilation systems. The contact investigation was part of evaluation of the workplace for solvent and noise. All 104 employees were recommended to be screened as the index case had worked in various areas, n=97 completed screening. A screening questionnaire was developed and pilot tested which asked for information regarding risk factors	Main conclusions: The workplace can be an important site for transmission, screening should be considered for workplaces with large number of employees from high prevalence countries.

described as having many foreign workers n=104. Index case an immigrant from El Salvador who lived alone. Quality notes: Narrative description of the investigation	Measures used: TST	for TB and symptoms. Possible risk factors for transmission at the workplace were identified and odds ratios calculated for an association with having a positive TST for each. Workplace risk factors included spending time in the lunchroom (OR 4.45 95% CI =1.32-23.25 p=0.004) and carpooling with the case (OR 5.54 95% CI =1.32-23.24 p=0.004). 37% were TST positive.	
Guzzetta et al. 2015[71] Type of document: Journal article Study design: Development of epidemiological model Country: USA Population: Residents of one County Quality notes: Modelling of data	Research methods: Development of a computational model using notification data during a 10 year period. Staff involved: N/A Measures used: N/A	Results/data: The model indicated that the contact tracing programme (using a household contact then school/work contact then wider contact approach) significantly reduced TB incidence (by 18.6%) and deaths (23.7%) compared to passive diagnosis only. The model indicated that around one fifth of recently transmitted cases are identified by contact tracing. Consideration of smear-positive cases only has a negative impact on effectiveness rather than also including smear-negative cases (reduces incidence avoidance to 10.4% and deaths to 13.2%)	Main conclusions: A key aspect in success of the programme was investigation of contacts of smear-negative cases which nearly doubled the effectiveness. While these cases have a lower rate of infectiousness they contribute a substantial share to transmission rates.

Higuchi et al. 2007[72] Type of document: Journal article Study design: Cohort study Country: Japan Population: High school students n=349 Quality notes: Limited data regarding accuracy of testing rather than other elements of an investigation	Research methods: Compared results from different testing methods and followed up participants over time Staff involved: N/A Measures used: TST QFT-G Chest X-ray	Results/data: QFT-G appears more specific than TST as contacts with positive TST and negative QFT-G responses were not offered prophylaxis, and none developed tuberculosis during 3.5 years of follow up.	Main conclusions The replacement of TST with QFT-G, or combined use of TST and QFT-G, may be more useful in diagnosing true infection
Jackson et al. 2008[3] Type of document: Journal article Study design: Qualitative Country: UK Population: Residents of Greater Glasgow N=21 patients and n=3 next of kin, age 7 to 73 years.	Research methods: Interviews Staff involved: N/A Measures used: N/A	Results/data: Patients with TB understood the cause of TB as a pathogen which was spread by person-to-person contact and could be influenced by level of immunity, social and environmental factors. Most patients believed that they had acquired TB from an unknown infected person, and from a short period of contact time. Often public places were suggested as infection locations, particularly confined or crowded locations. Known TB contacts or stereotypical patients were always male, with female participants often described poor, "tramp" individuals. Infection was often perceived to be a matter of bad luck or to have occurred when the	Main conclusions: Most patients understood the concept of airborne transmission, and contact, but prolonged contact was not thought to be required. Modes of transmission described included airborne, sharing utensils, consumption of infected foods/drink, and exchange of bodily fluids. Aligning contact tracing with

Quality notes: Provides some qualitative data to underpin conclusions		immune system was weakened (such as being ill).	these lay beliefs may improve the approach.
Jackson et al. 2009[2] Type of document: Journal article Study design: Retrospective examination of surveillance data, interviews with nurses and patients Country: UK Population: Most residents of one Health Board area, Social connections of 64 patients investigated, n=26 patients interviewed Quality notes: Mostly describes number of links. Interview aimed to uncover this information rather	Research methods: Social network enquiry approach using molecular epidemiology and staff/patient interviews to further analyse social connections in contact investigations over a previous 10 year period Staff involved: Nurse specialists Measures used: IS6110 restriction fragment length polymorphism Spoligotyping	Results/data: 43 epidemiological links between patients were identified, with 14 of these newly uncovered by interviewing patients. Associations detected by previous surveillance review were family-friend relationships, while over half of associations reported during the new interviews related to friends and socialising in public houses. 16 sites of exposure were identified, 54% of patients frequented more than one of these sites. 14 previously unidentified links were found. Associations were not discernible for 45% of patients.	Main conclusions: Use of a standardised interview schedule including social activities prior to diagnosis enables detection of time, place or person characteristics that link individuals.

than providing qualitative data			
Jereb et al. 2003[73] Type of document: Journal article Study design: Retrospective data analysis Country: USA Population: Data from 29 States Quality notes: Limited data presented	Research methods: Data from the Centers for Disease Control and Prevention Measures used: Number of cases Number of contacts Number evaluated Number completed treatment	Results/data: The number of cases, number of contacts, and incidence varied widely between areas. Evaluation was carried out for 83% of contacts, 44% completed treatment. 10% of cases had no contacts listed.	Main conclusions: Impact on prevention is limited by low number of infected contacts completing treatment.
Joint Tuberculosis Committee of the British Thoracic Society, 2000[33] Type of document: Journal article Study design: Review and guidelines Country: UK	Research methods: Review of literature Staff involved: N/A Measures used: Any	Results/data: Contact tracing may be a method of assessing and screening a local population with a high incidence of tuberculosis. Cases of tuberculosis occurring as part of an outbreak can be linked using molecular epidemiological or DNA fingerprinting techniques, provided that they are bacteriologically proven. Close contacts - people from the same household	Main conclusions: Importance of location and period of exposure

Population: Any Quality notes: Review of literature to underpin recommendations		sharing kitchen facilities and very close associates such as boyfriend/girlfriend or frequent visitors to the home. A contact at work or in a hospital ward may be as close as a household contact. It is important to examine lifestyle to identify locations of contact. Examination of casual contacts is only necessary if the index case is smear positive, highlight infectiousness (more than 10% of household contacts infected) or contacts are unusually susceptible. Contacts should be investigated for the period of time that the patient has had respiratory symptoms (if unknown for 3 months preceding the first positive sputum smear or culture. For airline passengers the risk to fellow travellers is small. World Health Organisation guidance recommends that contact tracing should be taken when (1) the diagnosis has been confirmed; (2) the index case is smear positive and was symptomatic with cough at the time of the flight; (3) the duration of exposure was more than eight hours; and (4) it is less than three months since the flight. For children, if the index case is smear positive (a) all children, irrespective of BCG history, who have been close contacts should be tested and any children who have not received BCG vaccination who have had casual contact.	

		If there is evidence of transmission screening of casual contacts with BCG vaccination be initiated.	
Josaphat et al. 2014[74] Type of document: Journal article Study design: Retrospective data analysis Country: Portugal Population: Cases and contacts from one disease centre, n=61 cases. Quality notes: Identifies factors associated with being identified, some statistical analysis	Research methods: Review of case records over a one year period Staff involved: N/A Measures used: Individual characteristics Numbers identified as contacts	Results/data: 67% of cases identified all their contacts, 32% did not. 23% of contacts were identified by the Public Health Unit, and 76% by the index case. Being employed, and not being a relative or co-habitant were risk factors for not being identified by the index case (OR=4.82 95% CI 1.71-13.54; and OR-0.22 95% CI 0.10-0.47 respectively). Contacts identified by the index case tended to be younger (mean age 33 versus mean age 40 p=0.001). Being a drug user was not a risk factor for not being identified.	Main conclusions: Employed contacts may not be identified as readily as relatives and co-habitants by index cases.
Kasaie et al. 2014[75] Type of document: Journal article Study design: Simulation modelling Country: USA	Research methods: developed an agent-based simulation model of a TB epidemic. Compared household contact tracing to active case finding in the community. Staff involved: N/A	Results/data: The model indicated that the maximum 5-year reduction in TB incidence achievable by household contact tracing was 10 to 15% (2–3% per year), although impact would be lower with imperfect coverage or reduced sensitivity. The model suggested that TB incidence might continue to decline for 2 years and would remain	Main conclusions: Contact tracing can have substantial epidemiologic impact (up to 7% reduction in incidence per year) but only if it achieves relatively complete population coverage, is sustained over

Population: 2000 households Quality notes: Development of a epidemiological model	Measures used: Incidence	below baseline levels for more than 15 years after a 5-year contact tracing intervention. The addition of preventive therapy nearly doubled the estimated impact.	time, and includes preventive therapy. Short-term evaluations of contact tracing are likely to underestimate their long-term impact therefore contact tracing evaluation should encompass longer-term evaluation of latently infected contacts.
Kawatsu et al. 2015[76] Type of document: Journal article Study design: Retrospective review of data Country: Japan Population: Residents of Tokyo n=8 patients and 376 contacts Quality notes: Calculates degree of relationship scores used for network analysis	Research methods: Reviews data relating to an investigation for a TB outbreak surrounding one index case. Developed a social network analysis matrices Staff involved: Primary health centre nurse Measures used: TST	Results/data: Relationship score was calculated based on nature of contact (household, work [same room, same floor, same building, shares smoking room]). Two values for degree of contact and one value for betweenness centrality were calculated. The odds ratio was calculated for association between the likelihood of latent TB being diagnosed and contact relationship score at each percentile rank. The odds ratio was not significant for degree of contact score and the likelihood of latent TB at any percentile rank. There was a significant association for contacts with higher betweenness score and latent TB infection (OR 2,12 p=0.020 95% CI 1.14-3.96 at the 40th percentile). For contacts with betweenness scores equal to or greater than 90th percentile they were 3.66 times more likely to have latent TB infection diagnosed.	Main conclusions: Betweenness scores (but not centrality scores) were useful to identify contacts who may be at greater risk of latent TB infection. Social network analysis matrices can be useful during contact investigations however, the complexity and time-consuming nature of the method at present reduces the potential for it to be incorporated into routine contact investigations.
Kettunen et al. 2007[77]	Research methods: Describes the approach used for investigation	Results/data: family members, friends and co-workers tested. Only people who had spent time in	Main conclusions:

Type of document: Journal article Study design: Descriptive Country: USA Population: Residents of one State, n=87 Quality notes: Narrative description of the investigation	of one case Staff involved: Public health nurse, infection control practitioner Measures used: TST	the same residence on a routine basis were infected. The source case was believed to have had TB for some time before diagnosis. A pre-employment TST had been carried out but the patient denied symptoms of TB and a co-existing condition blurred the symptoms.	Contact tracing requires diligence and effective communication.
Klovdahl et al. 2001[78] Type of document: Journal article Study design: Descriptive, further examination of contact investigations Country: USA Population: Houston, Texas, study focuses on n=37 patients with active TB associated with an outbreak 1993-6 having	Research methods: Describes an initiative to DNA fingerprint all new cases of TB during a five year period. Fingerprints were obtained and stored in a database and pattern matching software used. Newly diagnosed patients were approached and interviewed using the Houston Myobacteria Active Surveillance Form Staff involved: Research staff Measures used: DNA fingerprint	Results/data: Contact investigation had identified only 12 links among these 27 cases. The index case could not be linked to any other, half (51%) of cases could not be linked to another case. 33/34 of the cases could be linked however by location (44 bars/restaurants/cafes). A network diagram was constructed and centrality scores calculated. About 80% of the patients were linked by other people or places, individuals were often linked by multiple places providing several opportunities for infection. Based on the centrality scores, six of the top 10 most significant people/place elements in the network were locations, in particular bars.	Main conclusions: DNA fingerprinting identified the size of the outbreak and recognition of the importance of location (bars) was central to understanding of the outbreak. Contact naming investigation had been unable to identify links in the transmission network.

identical DNA finger prints. 70% identified themselves as gay, 10% as bisexual, 70% reported that they had a positive HIV test. Quality notes: Narrative description of links between contacts			
Kowada, 2013[79] Type of document: Journal article Study design: Cost effectiveness analysis Country: Japan Population: 20 year old contacts in developed countries Quality notes: Economic modelling	Research methods: Assessed the cost effectiveness of the different assessment methods using Markov modelling Staff involved: N/A Measures used High resolution computed tomography Chest X ray QuantiFERON TB Gold In-Tube TST Cost effectiveness	Results/data: QFT followed by high resolution computed tomography yielded the greatest benefit at the lowest cost ($US 6308.65; 27.56045 quality-adjusted life-years). Cost-effectiveness was sensitive to BCG vaccination rate.	Main conclusions: A strategy with QFT followed by high resolution computed tomography strategy yielded the greatest benefits at the lowest cost. High resolution computed tomography instead of CXR, is recommended
Lambregts et al. 2003[80] Type of document:	Research methods: Retrospective analysis of clusters to establish the impact	Results/data: DNA fingerprinting established an epidemiological link in 31% of clustered cases	Main conclusions: DNA fingerprinting and cluster monitoring can be

Journal article Study design: Investigation of the role of DNA fingerprinting and cluster monitoring to TB control Country: The Netherlands Population: National data Quality notes: Outlines links established by using the method	of establishing cluster links via DNA fingerprinting on contact investigations 1995-2000 Staff involved: Project nurse Measures used: Number of cases	where no link had been assumed or documented. Cluster feedback significantly improved the confirmation of documented epidemiological links ($p<0.001$). The additional information regarding cluster links seemed to have limited impact on contact investigations however, with only 1% extended as a result of receiving cluster feedback.	useful to confirm suspected epidemiological links, and to identify new links where transmission is not suspected. It may be useful where links between cases of TB are vague or with long periods in between. It may be regarded as a complimentary strategy to contact tracing, with both approaches required.
Langenskiold et al. 2008[81] Type of document: Journal article Study design: Retrospective analysis of data Country: Switzerland Population: Patients and contacts from one hospital in Geneva,	Research methods: Medical record data examined from a 10 year period. Staff involved: N/A Measures used: TST Chest X-ray	Results/data: There was an average of 4.3 contacts per index case. Being of foreign origin, level of exposure and contagiousness of the index case were predictive of latent infection. Treatment completion rate was 67%. 0.2% of those screened were found to have active disease, 36% latent TB.	Main conclusions: Contact tracing effectiveness relies on improving therapy acceptance and completion rates.

excluding those HIV-infected or children, n=3582 Quality notes: Describes brief characteristics of the data			
Lobato et al. 2003[82] Type of document: Journal article Study design: Retrospective review of data Country: USA Population: Children under age 5 resident in California n=164 Quality notes: Brief description of characteristics of the data	Research methods: Review of patient records from 38 contact investigations Staff involved: TB programme staff Measures used: TST	Results/data: 61% of contacts with a positive TST were started on treatment, no data for completion. Almost half of the investigations found two or more previously undiagnosed TB cases.	Main conclusions: Improved strategies are required for identifying young children with latent TB.
Logan et al. 2003[83] Type of document: Journal article Study design:	Research methods: Used discussion and stakeholder engagement to develop tools and logic models based on the Centre for Disease Control	Results/data: The logic model outlines resources required, activities and outputs detailing the processes and required standards of a contact investigation. A self-evaluation questionnaire was developed from the models. The questionnaire	Main conclusions: The paper refers to a number of tools that were developed however, they are not

Development of a tool for self-evaluation of investigations Country: USA Population: Any Quality comments: Describes the process of development but no evaluative data	framework for developing evaluation tools. Staff involved: Nurse care managers, public health nurses Measures used: Tool developed	was piloted to refine the questions. A transmission risk assessment checklist was also developed to be used at initial visits to the TB case/ suspect's home, work or school, and other places. A decision tree was also developed which illustrates the contact investigation process at the patient level, from determining the infectiousness of the TB case/suspect to screening close contacts for TB infection and disease. The checklist and decision tree were intended to be piloted although no suitable investigations were started during the period of the study.	provided within it. The focus of the paper is on using the framework for developing evaluation tools.
Macintyre et al. 1998[84] Type of document: Journal article Study design: Retrospective analysis of data Country: Australia Population: Victoria, n=1,142 contacts screened in 1991	Research methods: Further examination of a contact investigation in 1991 Staff involved: Unclear Measures used: TST Chest radiography	Results/data: Chest radiography was overused and was the sole screening tool for nearly 40% of contacts. 80% of repeat x rays were done following a normal initial study. TST was underused, and had only been carried out for 60% of contacts. 22% of contacts had received preventive therapy.	Main conclusions: Under-use of guidelines led to inefficiencies in the investigation

Quality notes: Narrative description of the investigation			
MacIntyre et al. 2000[85] Type of document: Journal article Study design: Cost effectiveness analysis Country: Australia Population: All Quality notes: Used modelling methods to investigate a hypothetical scenario	Research methods: Compared contact tracing as it had been carried out, if guidelines had been followed, and a hypothetical model. Staff involved: N/A Measures used: Costs in terms of cases prevented, cases found and contacts traced	Results/data: The cost for contact investigation during 1991 was estimated at $309,065 per case prevented. It was found that during this period prevention was not considered a priority, and few infected contacts identified received preventive therapy. The authors estimated that if guidelines had been correctly followed, that the cost would have been $58,742 per case prevented. The cost of the hypothetical evidence-based model was estimated at $3,881 per additional case prevented, although this would be impacted by lower referral rates, lower rates of preventive therapy, and lower efficacy of preventive therapy than the rates used during the calculations.	Main conclusions: Case finding is expensive in all three models. Clear programme aims, adherence to guidelines and high rates of preventive therapy are essential in order to achieve cost-effectiveness.
Maclellan et al. 2015[86] Type of document: Journal article Study design: Qualitative	Research methods: Questionnaires to contacts (half who attended half who did not), interviews with clinic nurses Staff involved: Specialist TB nurses and one nurse from the	Results/data: People reported attending due to concern regarding the severity of the disease and worry regarding other vulnerable people. TB reportedly kept a secret. Good working relationships with GPs were reported as important to prompt non-attenders to attend, although it was recognised that people in	Main conclusions: Three core areas of awareness, hospital service delivery, and leadership in the service were identified.

Country: UK Population: Contacts referred to a TB screening clinic in North London. N=30 contacts, n=8 nurses Quality notes: Includes qualitative data to underpin conclusions	Health Protection Unit Measures used: N/A	hard to reach populations may not have GPs. Importance of working with a community to allay fears, educate and reduce the stigma. The need for contact screening could cause fears of eviction in shared housing. Sending letters to the patient to distribute could be helpful. Most non-attenders reported they were unaware of their missed appointment. Contact details could be inaccurate, shared houses with muddled incoming post, limited understanding of the need for screening, being unable to take time off work, childcare issues were all given as reasons for not attending. Importance of outreach workers to trace contacts via home visits/telephone calls highlighted by nurses. Walk in appointments could be inconvenient for people with limited time available, mornings and different days reported best. A GP surgery location was more convenient than a hospital. Use of SMS reminders recommended. Need for TB services to raise their profile, for leadership and resources for administration, community outreach, and core nursing staff.	
Mandal et al. 2012[87] Type of document: Journal article Study design:	Research methods: Analysed data on screening episodes over a 3 year period. Staff involved:	Results/data: The programme screens close contacts, household contacts, and casual contacts (mostly workplace). 14.7% of contacts declined screening.	Main conclusions: Contact tracing should be carried out for non-pulmonary as well as

Retrospective data analysis Country: UK Population: Patients of a clinic in Edinburgh aged over 18. N=275 index cases and n=24 contacts. Quality notes: Limited data	Measures used: TST QuantiFERON Gold	Contact tracing for non-pulmonary TB is as important as for pulmonary. Active TB identified in 4.3% and latent in 21.7% of contacts of non-pulmonary patients. The number of casual contacts in the study was small, difficult to conclude if this group should be routinely screened or not. 21.2% of casual contacts were found to have active or latent disease.	pulmonary. Screening of casual contacts could be limited to certain circumstances
Marienau et al. 2014[88] *Same study as Coleman et al. 2014* Type of document: Journal article Study design: Cost effectiveness analysis Country: USA Population: Flight-related contacts n=9284 contacts Quality notes: Cost-effectiveness	Research methods: Economic analysis comparing a previous to a modified protocol for contact investigation for in-flight exposure. Data from 2007-2009. Staff involved: N/A Measures used: Transmission risk Cost	Results/data: The modified protocol changes the criteria for a contact investigation from within 6 months to within 3 months of the flight. Also the criteria is changed to require sputum positive for TB by culture or nucleic acid amplification test and sputum smear positive for acid-fast bacilli and cavitation on chest X-ray. Applying the new protocol estimate that 81 fewer potential cases and 409 fewer contacts would be investigated (half the investigations), of whom 115 might test positive (3 with active disease). Risk for new protocol 1.4-19%, and for old protocol 1.1-24%. Estimated cost under old protocol $222,000 to $1,300,000, under new protocol $99,449 to	Main conclusions: The new protocol is more cost efficient while retaining an acceptable level of public health risk.

analysis		$584,824	
Marks et al. 2000[89] Type of document: Journal article Study design: Retrospective data analysis Country: USA Population: Data from metropolitan areas of more than 5000,000 residents. Sample of n=1080 index cases and n=6225 close contacts Quality notes: Describes characteristics of the data	Research methods: Data reported to the Centres for Disease Control and Prevention Staff involved: Public health nurses Outreach workers TB programme personnel Health department staff Measures used: TST	Results/data: Median 6 days to patient interview (mean 22). Procedures differed between sites including who supervised workers and what screening contacts received. All sites defined household contacts as close. 68% of patients identified household contacts, 24% non-household relatives, 21% leisure contacts, 5% co-workers, 17% other types of close contacts. One third of patients only identified household contacts. The amount and type of data on contacts varied. Risk factors for disease often not recorded. Median of 4 (mean 6) close contacts per patient. A home visit led to average two additional contacts (likely to be young children). Fewer close contacts identified by homeless, males and Asian/Pacific islanders. No contacts identified for 8% (88), Homelessness was significantly correlated with having no identified contacts (RR 1.3 95% CI 1-1.5). High TST conversion rates among foreign born contacts may be the result of prior infection or boosting rather than recent infection. This should be considered before expanding investigations.	Main conclusions: Contact investigation could be improved by consistently defining a close contact and ensure patients list non-household as well as household close contacts. Provision of targeted TB screening and access to care is needed for high risk contacts.
Marra et al. 2008[90] Type of document:	Research methods: Economic modelling using Markov model	Results/data: The most cost effective strategy was to administer QFT-G in BCG-vaccinated only contacts, and to	Main conclusions: QFT-G should be used in a

Journal article Study design: Cost effectiveness analysis Country: Canada Population: drew data from a provincial population-based database, and published literature Quality notes: Cost effectiveness analysis	Staff involved: N/A Measures used: Cost effectiveness	reserve TST for all others. Incremental net monetary benefit CA$3.70 per contact for BCG vaccinated only. The least cost-effective strategy was QFT-G for all contacts, incremental net monetary benefit of CA$11.50 per contact.	targeted fashion.
McKenzie et al. 2007[91] Type of document: Journal article Study design: Examination of records relating to a cluster of cases, further interviewing of patients Country: USA Population: N=251 contacts from community, prison,	Research methods: Describes use of network analysis to produce visualisations and calculate measures of importance in the transmission network. Staff involved: TB control staff Measures used: TST Clinical observation	Results/data: Examined "reach" "degree" and "betweenness" between the contacts in the network. 42% of contacts had a positive TST. The diagram helped to link secondary cases with TB who were not named by the index patient. The majority of contacts could be linked to the index case, those who could not were investigated further. The metrics calculated enabled contacts with higher scores to be prioritised. Three contacts with high ranking "betweenness" scores were links to the overall network.	Main conclusions: Network analysis provides a means to identify linkages among cases, quantify the magnitude of an outbreak, and to begin control measures before genotyping results are available. It also can assist prioritisation of contacts to screen.

hospital, school, total of 1039 contacts visualised Quality notes: Calculated scores for relationship used in network analysis			
Mohr et al. 2013[92] Type of document: Journal article Study design: Delphi method Country: Germany Population: 23 topic experts involved Quality notes: Describes development but not testing of the instrument	Research methods: Describes development of a decision-making instrument for contact tracing in TB and meningococcal disease after contact on public transport. Staff involved: N/A Measures used: N/A	Results/data: Experts asked to rate elements on a scale of low indication for contact tracing-neutral position-high indication for contact tracing. Nine elements for TB identified. Symptoms of index case Infectiousness of index case Drug resistance pattern of index case Evidence of transmission to other contact person Quality of contact between index case and contact person (face to face/social interaction) Proximity of contact to case during exposure (more/less than 1 metre) Duration of exposure (more/less than 8 hours) Susceptibility of contact (under 5 years of age/HIV/substance abuse/other disease)	Main conclusions: The tool may help rapid decision-making.

		Environmental factors (external ventilation present or not/with/without circulation)	
Muecke et al. 2006 [93] Type of document: Journal article Study design: Descriptive Country: Canada Population: University students n=1144 Quality notes: Narrative description of the investigation	Research methods: Describes the investigation around one index case and calculates the risk factors for a positive TST Staff involved: Public health unit Occupational health Measures used: TST Observation of symptoms Chest radiography for those with positive TST Genotyping	Results/data: Used the concentric circles approach. Began with family and close social contacts. Close social contact defined as every day or every other day. Regular social contact defined as twice a week. Investigation expanded as high number of positive TSTs to other students and University staff. Local media used to contact people at three rave parties. Duration of exposure based on number of hours of lectures attended with index case. Size, type of ventilation and air changes per hour calculated for lecture rooms. Divided into more then or less than 300m.^{3} 27.5% of students had positive TST results, 3 had active TB. 69% of close social contacts and family had positive TST results, 3 active TB. Majority of students shared only one course with index case. Those who were exposed for 3 hours a week over 12 weeks had an approximately four fold greater risk of infection than lose with less exposure. Main risk factors were more than 35 hours exposure, and smaller classroom (OR 6.6 95% CI 1-44.9 and OR 5 95% CI 1.4-10).)	Main conclusions: The hourly risk of infection together with ventilation measurements can be useful elements of contact investigations
Mulder et al. 2012[94] Type of document:	Research methods: The study analysed factors associated with the likelihood of having contacts	Results/data: Contacts were investigated for 78% of cases.	Main conclusions: Contacts of immigrant index

Journal article Study design: Retrospective analysis of data Country: The Netherlands Population: TB patients from the nationwide surveillance register 2006–07 n=904 patients more than two thirds were immigrant cases (half of these asylum seekers or illegal residents) Quality notes: Describes characteristics of the data	of an infected patient traced Staff involved: Not reported Measures used: Frequency of investigation Characteristics of index patient	Contacts were significantly less often investigated around immigrant index cases (OR: 0.60; 95% CI: 0.40– 0.92) compared to Dutch index cases. Contacts were significantly more often investigated for smear positive index cases (OR: 3.52; 95% CI: 2.23–5.55) and culture positive index cases (OR: 2.71; 95% CI: 1.76– 4.16), compared to smear negative and culture negative index cases, respectively. Contacts were significantly less often investigated around actively found index cases when compared to passively found index cases (OR: 0.38; 95% CI: 0.26–0.57) and around index cases who belonged to a risk group compared with index cases who did not (OR: 0.44; 95% CI: 0.30–0.65).	cases were significantly less often investigated compared to contacts of Dutch index cases. By not investigating the contacts of immigrant patients, there is a risk of missing a significant number of infected and diseased contacts.
Mulder et al. 2012[95] Type of document: Journal article	Research methods: Interviews, each participant was interviewed around the time a contact investigation had commenced,	Results/data: Participants described identification as challenging as index cases were not always able to recall or willing to share information.	Main conclusions: Staff did not always adhere to guidelines and tended to

Study design: Qualitative Country: Holland Population: Public health nurses n=14 from different regions Quality notes: Provides qualitative data to underpin conclusions	and then again after the investigation had been completed. Staff involved: Public health nurses Measures used: N/A	Nurses tended to identify more contacts than just those at substantial risk of infection. There was a perception that as many as possible gave a more comprehensive view of the level of infectiousness of the index case. There were concerns regarding missing contacts and further transmission, those who were anxious or expected to cause conflicts were often classified as contacts even though the risk was low. Immunocompromised individuals were often not prioritised. Assessing the level of infectiousness of immigrants was described as challenging due to the high risk of infection in the country of origin. Native Dutch contacts were often included despite their limited exposure. Half of nurses used the available prioritisation table. It was described as difficult due to limited ability to capture exposure locations, or the appearance of prioritising different groups could be problematic. Terms such as daily, frequent or intensive were often used for level of exposure rather than terms in the guidelines. Nurses who were more experienced tended to use the table less. 6 investigations were appropriately scaled up, one was appropriately not scaled up. Seven were incorrectly scaled up to casual contacts. Guidelines regarding background prevalence in the community were ambiguous therefore were	identify more individuals as contacts than recommended, and there was evidence of scaling up to casual contacts which was not required. The criteria for classification could be perceived as unhelpful/ambiguous and there was difficulty interpreting background population prevalence data. The usefulness of the stone in the pond principle requires accurate data regarding prevalence in specific communities (such as immigrants)

		often not used.	
Munk et al. 2008[96] Type of document: Journal article Study design: Descriptive Country: USA Population: Residents and co-workers in Maryland n=287 contacts Quality notes: Narrative description of the investigation	Research methods: Description of the investigation surrounding one index case Staff involved: TB control staff Measures used: TST Chest radiography Sputum AFB smear for those with symptoms	Results/data: Household contacts, close social contacts, close workplace contacts and co-workers who travelled in a van with the index case were given high priority and evaluated within 7 days. Family and social contacts with less duration of exposure and in more open environments were categorised as medium priority. Co-workers at sites of employment were classified as low priority. High rate of infection in high priority cases (39%) led to expansion to low priority contacts. 15% of these had positive TST. No cases of active TB were found. 71% of the medium or high priority cases with latent infection agreed to begin treatment, and 33% of low priority.	Main conclusions: The workplace can be an important location for contact investigations.
National TB Controllers Association and Centre for Disease Control, 2005[34] Type of document:	Research methods: Outlines guidelines for contact investigation developed by an expert working group Staff involved: Varying by area	Results/data: While guidelines and standards are provided, unusually close exposure (prolonged exposure in a small, poorly ventilated space or a congregate setting) or exposure among particularly vulnerable populations at risk for TB disease such as children or immunocompromised individuals could justify starting an investigation	Main conclusions: Provides a comprehensive overview of contact tracing procedures and decision-making considerations.

Report Study design: Guidelines Country: USA Population: All Quality notes: Guidelines developed by expert concensus	Measures used: Any	that would normally not be conducted. If contacts are likely to become unavailable then the investigation should receive a higher priority. Investigations may be affected by exaggerated concern regarding TB in a community and an investigation being demanded. Outlines factors influencing prioritisation including type of TB, level of infectiousness, age, HIV status. Having written policies and procedures for investigations improves the efficiency and uniformity of investigations. Establishing trust and consistent rapport between public health workers and patients is critical to gain full information and long-term cooperation during treatment. Workers should be trained in interview methods and tutored. Patients should be interviewed by persons who are fluent in their primary language or interpreters provided. Provides recommendations for the content of interviews, a minimum of two is recommended. Sites visits are required as they enable additional contacts to be identified and are the most reliable source of information regarding transmission settings. Details such as room sizes, ventilation systems, and airflow patterns should be considered together with how often and how long the index	

		patient was in each setting. Data from the investigation should be recorded on standardized forms. Priorities should be assigned to contacts, and resources should be allocated to complete all investigative steps for high- and medium-priority contacts. Priorities are based on the likelihood of infection and the potential hazards to the individual contact if infected considering characteristics of the index patient, characteristics of the contact, intensity, frequency and duration of exposure. Provides detail on the contact interview content, decision-making for expanding investigations, involvement of the media, and considerations for specific population settings.	
New York City Department of Health and Mental Hygiene[35] Type of document: Guidance Study design: Guidance Country: USA Population: City population	Research methods: Description Staff involved: Measures used: N/A	Results/data: Provides definitions of terms. Priorities for contact investigation based on both the characteristics of the known or suspected TB index patient and the characteristics of the contact. Provides tables and flow charts for decisions to conduct or continue contact investigation. Provides a table outlining contacts most likely to be infected and contacts at high risk of developing TB once infected.	Main conclusions: Provides flow charts to underpin decision-making during investigations

Quality notes: Details on basis for guidance not provided			
Pettit et al. 2002[97] Type of document: Journal article Study design: Descriptive Country: UK Population: Customers of a public house n=12 cases, n=122 contacts Quality notes: Narrative description of the investigation	Research methods: Describes the investigation carried out Staff involved: Unclear Measures used: TST DNA fingerprinting	Results/data: Initial contact investigation focused on close contacts and revealed no further cases of infection. However, cases who all were customers of a public house where the presumed index case was a regular customer were later identified, and the investigation was extended to all staff/customers. N=85 of n=122 contacts were screened. The identification of regular patrons was extremely difficult. Two cases came to light due to health education/awareness raising. One further case was identified by the investigation and two children were given preventive therapy (1.18% case detection rate)	Main conclusions: Transmission can occur between customers of a public house therefore extended contact screening beyond close contacts must be considered.
Pisu et al. 2009[98] Type of document: Journal article Study design: Cost effectiveness analysis comparing conventional contact tracing with contact	Research methods: A cost-effectiveness analysis using a decision-analytic model comparing traditional concentric circle contact tracing with a contact priority model. Staff involved: N/A Measures used:	Results/data: The contact priority model uses a decision rule (exposure hours, home, poorly ventilated environment) to explicitly categorise contacts as high risk requiring testing or low risk not requiring testing. The analysis used the total cost each model divided by outcomes (number of active TB cases, number of life years attained) to calculate	Main conclusions: Conventional concentric circles contact tracing was found to be more effective, but more costly than a contact priority model.

priority models Country: USA Population: Residents of Alabama Quality notes: Cost effectiveness analysis	TST Costs	incremental cost-effectiveness ratios (ICERs). A decision tree approach was used to model elements such as the likelihood of a TST being performed, and Markov models were used to represent costs and outcomes. Estimated cost of investigating a contact was $250. Conventional concentric circles contact tracing was found to be more effective, but more costly than a contact priority model. Savings would be made on cost of TSTs however, there would be higher costs from active disease in a contact priority model. The concentric circles approach was estimated to prevent one additional case of active disease for a cost of $92,934 and one additional life year $185,920. Estimated cost per 1000 contacts was $339,896 for concentric circles and $294,596 for contact priority. There would be estimated one or two additional cases of active disease per 3000 contacts with a contact priority model.	
Rea & Rivest 2014[6] Type of document: Guidance (grey literature) Standards for contact follow-up and outbreak management in TB control (Chapter 12 of	Research methods: Descriptive Staff involved: Public health/TB control authorities in collaboration with treating clinicians and other providers Measures used:	Results/data: Only respiratory TB is infectiousness in most cases. Contact investigation should be carried out for both smear negative and smear-positive cases. Source case investigation is recommended for children under 5 with a diagnosis of active TB. Contact tracing should identify and treat any secondary cases and identify individuals with	Main conclusions: The concentric circles approach does not take into account contacts who are vulnerable but may have had less exposure, and can be difficult to apply in congregate settings. Level of

Tuberculosis Standards) Study design: Guidance referencing underpinning literature Country: Canada Population: Any Quality notes: No details on process for developing guidance	N/A	latent infection in order to offer preventive treatment. Interviews should include questions about locations/activities of exposure and also specific named contacts. Prioritisation of contacts should be based on infectiousness of the source case, extent of exposure and vulnerability of those exposed. Most effort should be put into contacts who are most at risk of being infected and/or most at risk of developing active TB disease if infected. High priority – household contacts plus non-household who are immunologically vulnerable Medium priority – close non-household contacts with daily or almost daily exposure including those at school or work Low priority – casual contacts with lower amounts of exposure. Initial contact investigation should be carried out for high and medium priority contacts for index cases with smear-positive/cavitary/laryngeal TB. For smear-negative non-cavitary pulmonary TB the initial contact should be for high priority contacts only. Investigation should be expanded if initial testing indicates transmission has occurred. TST and symptom assessment 8 weeks after exposure is recommended for non-household contacts. Household and high priority contacts	priority should be considered. DNA fingerprinting can be useful to confirm or disprove linkages. It can be useful in populations in which contact investigation is challenging (such as the homeless). All cases should be asked about locations where they spend time. Social network analysis may be helpful. School, workplace and other congregate setting investigations including homeless and other marginalised populations are best carried out on site. Need for good organisation, adequate staffing and resources, clearly defined roles and responsibilities.

		should be tested initially and again at 8 weeks. Two step TST is not recommended. A history of BCG vaccination does not alter the interpretation of the TST result. A positive test is 5mm or greater, or an increase of at least 6mm from previous test. Elderly people in long term care should not be tested with TST. In homeless people and those with drug addictions non-judgement and supportive staff, use of incentives may help rates of participation. Interventions on site for a single session are likely to have more success. The primary focus should be on detection of secondary cases rather than assessment and treatment of latent TB.	
Reichler et al. 2002[99] Type of document: Journal article Study design: Retrospective review of records Country: USA Population: Five areas	Research methods: Data analysed from contact investigations carried out in 1996 Staff involved: N/A Measures used: TST converters	Results/data: Close contact defined differently in different areas. Closeness was not recorded in records for many contacts. For analysis "close" defined as members, visitors, or workers in the index case household or were friends or relatives. Number of contacts higher for patients who had both a positive smear and cavitary disease (median 8 $p<0.001$). 13% of patients had no contacts	Main conclusions: Effective investigations require standard definitions of close contact and contact, definition of what constitutes exposure (duration, time, frequency, location), standard criteria for expanding investigations, develop effective data management

of the USA with programmes perceived as the best, and best organised data. Patients aged over 14 n=360, n=3824 contacts Quality notes: Describes characteristics of the data	Numbers screened	identified, an additional 11% had no close contacts identified. Patients with no contacts were more likely to live in a homeless shelter (13% versus 2% p<0.001). Only half of those patients with no contacts were recorded as being interviewed. Less than two thirds of contacts completed screening.	systems, define the extent of investigation needed in different settings.
Rodriguez et al. 1996[100] Type of document: Journal article Study design: Descriptive Country: USA Population: High school students N=122 close contacts N=1804 non-close Quality notes: Narrative description of the investigation	Research methods: Describes the investigation surrounding one case Staff involved: Public health staff Measures used: TST Cost	Results/data: Positive TSTs were found among 2.5% of close contacts, and 1.9% of non-close. No other active TB case was identified. The cost of TST screening was estimated to be $36,507.	Main conclusions: Screening was costly and diverted staff from other duties. Existing guidance regarding expanding investigations should be followed.

Ruben and Lynch, 1996[101] Type of document: Journal article Study design: Descriptive Country: USA Population: Residents of Pittsburgh Quality notes: Narrative description of the investigations	Research methods: Describes the investigations carried out over a one year period. Staff involved: Measures used:	Results/data:	Main conclusions:
Rubilar et al. 1995[102] Type of document: Journal article Study design: Retrospective review of data Country: UK Population: Residents of Edinburgh n=632 cases of TB notified, n=3688 contacts Quality notes:	Research methods: Reviewed records of cases of TB notified 1982-1991 (20% of records had been mislaid) Staff involved: Measures used:	Results/data: 7.9% of those cases notified had been identified by contact tracing. 1.4% of contacts screened had active TB and 1% had latent infection. 54% of contacts with TB were under age 14, 34% were aged 15-44, 8% were aged 45-64 years and 4%) were aged over 65. 84% of the cases among contacts were in contacts of patients with sputum smear-positive respiratory disease, and 98% of TB in contacts was detected within the first 3 months of screening. Infection which may be detected later by ongoing radiography may be the result of infection from	Main conclusions: Screening of close contacts of all index cases other than smear-positive respiratory index cases was not recommended. Screening of young people should be prioritised and carried out within the first three months.

Describes characteristics of the data		another source or re-activation of infection acquired from another source.	
Sanderson et al. 2015[103] Type of document: Journal article Study design: Descriptive Country: USA Population: Patients and staff on a maternity ward n=285 Quality notes: Narrative description of the investigation	Research methods: Describes the contact investigation methods using electronic health data (electronic medical records and an immunisation register) Staff involved: Hospital staff, Department of Health and Mental Hygiene staff Measures used: None	Results/data: The linking of data from different electronic health systems reduced the resource burden required for the investigation. The identification, notification and evaluation of contacts was aided by the systems, and documented evidence of exposure assisted the focusing of those at greatest risk. 100% of those potentially exposed were contacted. The systems also identified current health care providers who were contacted to distribute letters and guidelines.	Main conclusions: Electronic health data is useful for enhancing contact investigations.
Saunders et al. 2014[104] Type of document: Journal article Study design: Retrospective analysis of data Country: UK Population: Data	Research methods: Analysed trends in data over a 20 year period 1990-2010 Staff involved: TB nursing service Measures used: Screening completion rates	Results/data: 40.9% of contacts failed to complete screening. There was no evidence of a trend over the study period. The number of contacts screened for each positive screening outcome was 15 for pulmonary TB and 45 for extra pulmonary TB. Contacts were less likely to complete screening if they were of working age, male, black, from the	Main conclusions: Work is required to increase screening completion rates and to increase screening for working age, Black. and Indian Subcontinent populations.

collected at a Birmingham hospital n=7365 Quality notes: Describes characteristics of the data	Screening outcomes Number of contacts	Indian subcontinent. Contacts tested using IGRAs were more likely to complete screening.	
Shah et al. 2014[105] Type of document: Journal article Study design: Systematic review and meta-analysis Country: USA Population: Patients with drug-resistant TB Quality notes: Systematic review	Research methods: Calculated the reported yield of contact investigations Staff involved: N/A Measures used: Number of household contacts	Results/data: Analysed data from 25 studies. The pooled yield was 7.8% for active TB and 47.2% for latent infection (there was significant heterogeneity $p<0.0001$). The majority of cases were identified in the first year	Main conclusions: There is a high yield of active and latent infection in household contacts of patients with drug-resistant TB
Shrestha-Kuwahara et al. 2003[106] Type of document: Journal article Study design:	Research methods: Focus groups Staff involved: Contact investigation staff Measures used: N/A	Results/data: Patients reported providing contacts easily and willingly. On occasions while they had given a large number of contacts only a few appeared in the records. Homeless people could only give street names of their friends, and acknowledged	Main conclusions: Programmes may be enhanced by staff training in listening, culturally appropriate interviewing techniques, re-interviewing

Qualitative Country: USA Population: Pulmonary TB patients from the USA/Mexico n=54 programme staff n=18 Quality notes: Provides qualitative data to underpin conclusions		finding them was difficult when they had no place of residence. Patients reported preferring to inform contacts themselves prior to the health department. Trust and good rapport were described as important. Also good communication. Using interpreters or interpreters not being available could be challenges. Differences in understanding of the term "contact" and "at risk contact", term could be vague or understood incorrectly. Some patients were unclear about the purpose of needing names, it was not clear that the focus wasn't getting the names it was finding the people who may have been infected. Fears regarding stigma, loss of employment or loss of housing, and alienation or abandonment were described. The timing of the investigation was when patients could be feeling ill and afraid and confused after diagnosis. Re-interviewing patients at a less stressful time could be helpful. Staff reported need for training in counselling, improved systems of co-ordination between service providers, and training in social and economic issues.	patients after initial fears and confusion have reduced. There seemed a mismatch between most patients reportedly giving contacts willingly and the small number of contacts recorded. There may be misconceptions regarding understanding of what a contact means, effective communication is needed.
Sprinson et al. 2003[107]	Research methods:	Results/data:	Main conclusions:

Type of document: Journal article Study design: Retrospective analysis of data Country: USA Population: California n=15,582 contacts Quality notes: Describes the characteristics of the data	Analysis of programme management reports over one year to estimate effectiveness. Staff involved: Measures used: TST Costs Contacts identified	11% of cases had no contacts elicited. Mean number of contacts per case was 10.5 (range 0-170). 88.6% of contacts were evaluated, disease was found in 0.6% and latent infection in 24.1%. 13 of the 42 areas met the performance target of evaluating 95% of contacts. 66% of contacts started treatment, and 64.2% completed. Around half chose to stop, 17% moved, and for 17% the reason was unknown. 31% of areas met the target of 85% treatment completion. Investigations were estimated to have detected 81% of TB cases which might have been identifiable, and estimated to have prevented 34.6% of future TB cases which might have occurred in the following 2 years. Costs were estimated at $4.8 million.	Performance did not meet national objectives. Further data are required to evaluate performance.
Stoddardt & Noah, 1997[108] Type of document: Journal article Study design: Survey of consultants in communicable disease control and medical officers of environmental health	Research methods: Survey sent to 155 districts. It requested information on the number of new cases of TB found in the preceding three years in which more than 100 contacts had been screened. Staff involved: Measures used: TST	Results/data: 46% of districts reported at least one investigation which had screened more than 100 contacts. Forty four cases of TB were found in 18 of the 56 incidents, giving a detection rate of 0.375%.	Main conclusions: The authors question the continued use of large scale screening. Close contacts should be carefully defined, and only they should be screened.

Country: UK Population: n=732 contacts Quality notes: Limited relevant data			
Tian et al. 2013[109] Type of document: Journal article Study design: Developed mathematical model of TB dynamics Country: Canada Population: Province of Saskatchewan Quality notes: Mathematical modelling	Research methods: Comparison of scenarios with contact tracing and without Staff involved: N/A Measures used: Risk of infection	Results/data: Comparison of a scenario involving contact tracing and no contact tracing indicated a higher average prevalence of TB infection with no contact tracing. The benefit of tracing the first 45% of contacts was greater than tracing the second 45%, indicating a diminishing return. Prioritising contacts on the basis of number of times that they have been named had adverse outcomes. Increasing the speed of the investigation (90% of contacts are tested within 30 days of diagnosis) did not lead to projected significant improvement in active cases or prevalence of infection. Reducing loss to follow up to a 10% level could lead to significant benefits in infection rates (5.4% prevented p=0.02). Targeting investigations by prioritising by age (children under 9 years old are traced first) and ethnicity (first nation individuals traced first)	Main conclusions: Contact tracing leads to positive outcomes. Reducing loss to follow up and targeting investigations may increase effectiveness.

		could improve the effectiveness compared to non-prioritisation (preventing 11% of cases over 20 years p<0.0001)	
Trieu et al. 2013[110] Type of document: Journal article Study design: Descriptive Country: USA Population: HIV infected index case, hotel resident and work colleague contacts n=31 Quality notes: Narrative description of the investigations	Research methods: Describes two investigations using the IGRA test Staff involved: Unclear Measures used: QuantiFERON-TB Gold In-Tube IGRA	Results/data: The study indicated that the IGRA test can be used in congregate settings. The drawbacks are increased cost compared to TSTs (16 times more) and requires staff trained in taking blood samples. Specimens also need to be received at a laboratory within 16 hours of collection. Positive aspects of IGRA use are only a single encounter with a contact was needed and there were fewer false positive results due to BCG or other bacteria present meaning fewer people given prophylaxis treatment.	Main conclusions: Use of IGRAS in the field is feasible. It may be particularly preferred to TSTs in people hard to follow up and contacts who are BCG vaccinated.
Underwood et al. 2003[111] Type of document: Journal article Study design: Retrospective data analysis to examine	Research methods: Analysis of patient records and a TB data base 1997-1999. Compares new entry screening versus contact tracing. Staff involved: Specialist TB nurses	Results/data: Contact tracing of patients with both smear-negative pulmonary TB and non-pulmonary TB identified individuals with active and latent TB with combined prevalence similar in each group (7%).	Main conclusions: A contact-tracing strategy is more effective than new entrant screening. Contact tracing (even in cases of non-infectious TB) in high

screening versus contact tracing approaches Country: UK Population: Described as living in a socio-economically deprived area (Tower Hamlets London) N=227 cases n=643 contacts, n=332 new UK entrants screened. Quality notes: Compares data from two methods of screening rather than evaluating effectiveness of contact tracing	Measures used: Number of cases detected Number screened	Contact tracing in cases of non-pulmonary disease is not recommended, but the results suggested that it may be at least as productive as the screening of new arrivals to the UK from high-incidence countries.	incidence areas could be seen as a way of screening extended families or communities at particularly high risk.
Verdier et al. 2012[8] Type of document: Journal article Study design: Retrospective analysis of data	Research methods: Analysed data from contact investigations between 2001-2006 to identify risk factors for finding TB latent or active infection	Results/data: Stone in the pond principle followed, close contacts, then regular contacts, then community contacts. Residential or family relationships highest risk of infection, work or education contact resulted in lower chance of transmission. Risk factors	Main conclusions: The risk factors match current guidelines: diagnosis of index patient, closeness of contact relationship, age of patients and contacts, and number of infections of close contacts.

Country: The Netherlands Population: Rotterdam, n=21,540 contacts Quality notes: Provides limited data	Staff involved: Public health nurse Measures used: TST	included older age of the patient, older age of the contact. Greater infection risk in community contacts was present if a large number of close contacts were infected.	
Ward et al. 2004[112] Type of document: Journal article Study design: Retrospective analysis of data Country: USA Population: Schools in New York State n=6990 contacts Quality notes: Describes characteristics of the data	Research methods: Analysed data from a TB registry for children aged 5-19 years old 1997-2001 Staff involved: N/A Measures used: Sputum smear TST	Results/data: Each county used their own cut-off points in measuring millimetres of induration on the TST for determining if a contact was positive. TST positivity amongst close and not-close contacts increased with increasing age of index cases (4.6% age 5-9 years; 5.5% age 15-19 years). The number of contacts tested increased with increasing children's age. In very young children infection suggests recent transmission so the emphasis is on finding the index case. In older children transmission between children becomes more likely so there is greater focus on locating contacts. In the first round of testing the mean number of close contacts per index case tested was 81 (range 0-725), and was significantly more than not-close contacts ($p<0.0001$). Lower SES status of contacts was associated with greater TB risk (assessed by median income).	Main conclusions: Many school investigations test more contacts than might be expected due to parental concern and public pressure (no data presented regarding this). Contact investigations may label close/not close after the investigation has been completed, there may be limited documentation regarding labelling. It was often not recorded whether TST results for contacts were "negative" or "not read"

		Pupils at smaller schools were also at greater risk of being TST positive. In one of the four regions not-close contacts unexpectedly had a higher rate of TST positivity than close contacts across the study as a whole (7.3% versus 5.1%). In two regions close contacts had a higher rate of TST than not-close (20% and 15.2% versus 5.1%). The final region data did not differentiate between levels of contact. 47.1% completed treatment (higher for this investigation than for the State as a whole.	
Wilce et al. 2002[113] Type of document: Journal article Study design: Qualitative and document analysis Country: USA Population: Staff from 11 urban areas. Quality notes: Provides a range of descriptive data to underpin conclusions	Research methods: Interviews with staff and examination of policies and procedures Staff involved: Various Measures used: N/A	Results/data: All areas had policies in the form of documents or checklists. Policies varied widely in their content and comprehensiveness. Most described the main steps involved in a contact investigation, but specific actions within these were often not specified. Review of medical records was only briefly mentioned in some policies, the time after diagnosis for an interview was often unclear, follow up interviews were recommended in 7 areas. The content of the interview was typically left to the discretion of the interviewer. Field visits were not required in 4 areas, policies typically provided few details on the procedure for visits. Checklists for assessing risk of transmission were typically available, although without accompanying instructions or space for recording findings.	Main conclusions: There was generally inconsistency in guidelines, staffing and training across the different services. Comprehensive policies and support are required to improve the standard of contact tracing investigations.

		Sites did not consistently define a "close" contact. Information regarding risk factors such as HIV could be hard to obtain although most sites had policies regarding immunocompromised persons. 5 sites referred to the concentric circles approach (but provided little guidance on how to apply it). At 6 sites decisions regarding expansion were made by the worker responsible, at 4 by a supervisor, and during a meeting at one site. Two sites routinely excluded casual contacts due to limited resources. Staffing models and training varied between sites. Data recording and data managements systems varied. Also monitoring procedures. Challenges reported related to communication barriers, structural barriers, and patient-level barriers.	
Yeo et al. 2006[114] Type of document: Journal article Study design: Retrospective review of data Country: Canada Population: Under age 18 residents of	Research methods: Examined public health data 1996-2000, carried out additional genotyping Staff involved: N/A Measures used: Number of cases and contacts IS6110-based genotyping, and spoligotyping	Results/data: Nineteen children were diagnosed after contact investigations of known adult cases No contact investigation had been carried out for 8 children. For the remaining 39 children, a total of 616 contacts were identified. The median number of contacts per child was 9 (interquartile range, 6-10). Four probable source cases were identified, all involving parents or other relatives. Genotyping by the research team identified up to 14 possible	Main conclusions: The contact investigations were extensive and had mostly been able to identify latent tuberculosis infection, but less successfully identified the source cases. Genotyping indicated a substantial number of further sources of potential transmission.

Montreal n=66 Quality notes: Describes characteristics of the data		additional index cases. From the records available it was possible to identify a link to the children for only one of these additional cases.	
Zangger et al. 2001[115] Type of document: Journal article Study design: Descriptive Country: Switzerland Population: Residents of Lausanne including family and school pupils and staff n=53 Quality notes: Narrative description of the investigation	Research methods: Describes investigation around one source case (a 15 year old girl) Staff involved: Doctor Health officer A nurse from the TB service Measures used: TST Chest X ray for those with positive TST Cost	Results/data: Three proximity groups: 1 people living under same roof and close friends 2 classmates and teachers 3 occasional contacts, other schoolmates Passing from one group to next reduced rate of infection by 4 times. Compliance rate for treatment was 64%. The cost of the investigation was over 24000 Swiss Francs. The index case had arrived from Africa and had a positive test on arrival but no treatment.	Main conclusions: The distribution of cases confirms the importance of duration of contact and proximity of contact with the index case

Appendix 4. Papers excluded at full article stage

Abubakar I, Stagg HR, Cohen T, Mangtani P, Rodrigues LC, Pimpin L, Watson JM, Squire SB, Zumla A: Controversies and unresolved issues in tuberculosis prevention and control: a low-burden-country perspective. Journal of Infectious Diseases 2012, 205(suppl 2):S293-S300.	Review of TB control strategies, does not refer to contact tracing.
Armbruster B, Brandeau ML: Contact tracing to control infectious disease: when enough is enough. Health Care Management Science 2007, 10(4):341-355.	Focus on other conditions
Begun M, Marks GB, Wood JG, Newall AT: Contact Tracing of Tuberculosis: A Systematic Review of Transmission Modelling Studies. PLoS ONE 8(9): e72470. doi: 10.1371/journal.pone.0072470	Review of models, with emphasis on model development methods.
Cardona M, Bek MD, Mills K, Isaacs D, Alperstein G: Transmission of tuberculosis from a seven-year-old child in a Sydney school. J Paediatr Child Health 1999, 35(4):375-378.	Focus on transmission rather than contact tracing.
Chakhaia T, Magee MJ, Kempker RR, Gegia M, Goginashvili L, Nanava U, Blumberg HM: High utility of contact investigation for latent and active tuberculosis case detection among the contacts: a retrospective cohort study in Tbilisi, Georgia, 2010-2011. PLoS ONE [Electronic Resource] 2014, 9(11):e111773.	Non OECD country
Classen CN, Warren R, Richardson M, Hauman JH, Gie RP, Ellis JHP, van Helden PD, Beyers N: Impact of social interactions in the community on the transmission of tuberculosis in a high incidence area. Thorax 1999, 54(2):136-140.	Not OECD country (South Africa)
Cook SA, Blair I, Tyers M: Outbreak of tuberculosis associated with a church. Communicable Disease &	Focus on transmission rather than contact tracing.

Public Health 2000, 3(3):181-183.	
Crawford JT: Genotyping in contact investigations: a CDC perspective. International Journal of Tuberculosis & Lung Disease 2003, 7(12 Suppl 3):S453-457.	Discusses the use of genotyping, no data.
Cronin WA, Golub JE, Lathan MJ, Mukasa LN, Hooper N, Razeq JH, Baruch NG, Mulcahy D, Benjamin WH, Magder LS et al: Molecular epidemiology of tuberculosis in a low- to moderate-incidence state: are contact investigations enough? Emerging Infectious Diseases 2002, 8(11):1271-1279.	Focus on transmission rather than contact tracing.
Dahle UR, Nordtvedt S, Winje BA, Mannsaaker T, Heldal E, Sandven P, Grewal HM, Caugant DA: Tuberculosis in contacts need not indicate disease transmission. Thorax 2005, 60(2):136-137.	Highlights that infection in contacts may be due to reactivation of disease rather than having a focus on contact tracing as an intervention.
Dasgupta K, Schwartzman K, Marchand R, Tennenbaum TN, Brassard P, Menzies D: Comparison of cost-effectiveness of tuberculosis screening of close contacts and foreign-born populations. American Journal of Respiratory & Critical Care Medicine 2000, 162(6):2079-2086.	Although mentions contact tracing, has a focus on screening of immigrants and the evaluation of two screening programmes.
del Castillo Otero D, Penafiel Colas M, Alvarez Gutierrez F, Soto Campos JG, Calderon Osuna E, Toral Marin J, Sanchez Gomez J: Investigation of tuberculosis contacts in a nonhospital pneumology practice. European journal of clinical microbiology & infectious diseases : official publication of the European Society of Clinical Microbiology 1999, 18(11):790-795.	Focus on transmission rather than contact tracing.
Faccini M, Codecasa LR, Ciconali G, Cammarata S, Borriello CR, De Gioia C, Za A, Marino AF, Vighi V, Ferrarese M et al: Tuberculosis Outbreak in a Primary School, Milan, Italy. Emerging Infectious Diseases 2013, 19(3):485-487.	Focus on transmission of infection

Kondo S, Ito M: Efficacy of tuberculosis contacts investigation and treatment, especially of preventive therapy in infants and young children. Tuberculosis 2003, 78(11):677-682.	Focus is on diagnosis and treatment rather than contact tracing.
LoBue PA, LeClair JJ, Moser KS: Contact investigation for cases of pulmonary Mycobacterium bovis. International Journal of Tuberculosis & Lung Disease 2004, 8(7):868-872.	Predominant focus on Mycobacterium Bovis.
Mandeville KL, Harris M, Thomas HL, Chow Y, Seng C: Using social networking sites for communicable disease control: Innovative contact tracing or breach of confidentiality? Public Health Ethics 2014, 7(1):47-50.	Focus on other conditions.
McElnay C, Thornley C, Armstrong R: A community and workplace outbreak of tuberculosis in Hawke's Bay in 2002. New Zealand Medical Journal 2004, 117(1200):U1019.	Refers to delays in contact tracing as a factor in the outbreak however, focus is on infection rates and therapy.
Migliore E, Borraccino A, Baussano I, Piccioni P, Carosso A, Bugiani M: Outcomes of a tuberculosis contact investigation programme in Italy. European Respiratory Journal 2012, 40(5):1291-1293.	Brief report duplicating information in Borraccino et al. paper.
Mohle-Boetani JC, Flood J: Contact investigations and the continued commitment to control tuberculosis. Journal of the American Medical Association 2002, 287(8):1040-1042.	Comment on other papers
Morrison J, Pai M, Hopewell D: Tuberculosis and latent tuberculosis infection in close contacts of people with pulmonary tuberculosis in low-income and middle-income countries: a systematic review and meta-analysis. The Lancet Infectious Diseases 2008, 8(6):359-368.	Focus on the yield of investigations and argues for the need to carry out contact investigations in high incidence countries.
Ohno H, Ikegami Y, Kishida K, Yamamoto Y, Ikeda N, Taniguchi T, Ikeda T, Sato A, Kurasawa T, Miyanomae	Predominant focus on numbers infected and treatment rather than the contact investigation.

K: A contact investigation of the transmission of Mycobacterium tuberculosis from a nurse working in a newborn nursery and maternity ward. Journal of Infection and Chemotherapy 2008, 14(1):66-71.	
Reichler MR, Tapia J, Chavez-Lindell T, McAuley J, Thomas J, Yuan Y, Mangura B: Results of a Prospective Evaluation of Tuberculosis (TB) Contact Investigations Conducted in the United States and Canada. American Journal of Respiratory and Critical Care Medicine 2009, 179.	Conference abstract.
Vella V, Racalbuto V, Guerra R, Marra C, Moll A, Mhlanga Z, Maluleke M, Mhlope H, Margot B, Friedland G et al: Household contact investigation of multidrug-resistant and extensively drug-resistant tuberculosis in a high HIV prevalence setting. International Journal of Tuberculosis & Lung Disease 2011, 15(9):1170-1175.	Non OECD country (South Africa)
Webb RM, Holcombe M, Pearson MM: Tuberculosis contact investigation in a rural state. International Journal of Tuberculosis & Lung Disease 2003, 7(12 Suppl 3):S353-357.	Describes the programme over 10 years in Mississippi.