Systematic review on the diagnosis, treatment, care and prevention of tuberculosis in prison settings

Prevention and control of communicable diseases in prison settings

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This report was commissioned by the European Centre for Disease Prevention and Control (ECDC), coordinated by Lara Tavoschi with the support of Netta Beer, Helena de Carvalho Gomes, the ECDC Library; and Dagmar Hedrich from EMCDDA.

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## Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>AGREE</td>
<td>Appraisal of guidelines for research and evaluation</td>
</tr>
<tr>
<td>CXR</td>
<td>Chest X-ray</td>
</tr>
<tr>
<td>DOT</td>
<td>Directly observed therapy</td>
</tr>
<tr>
<td>ECDC</td>
<td>European Centre for Disease Prevention and Control</td>
</tr>
<tr>
<td>EEA</td>
<td>European Economic Area</td>
</tr>
<tr>
<td>EFTA</td>
<td>European Free Trade Association</td>
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<tr>
<td>EMCDDA</td>
<td>European Monitoring Centre for Drug and Drug Addiction</td>
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<tr>
<td>GRADE</td>
<td>Grading of recommendations assessment, development and evaluation</td>
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<tr>
<td>HIV</td>
<td>Human immunodeficiency virus</td>
</tr>
<tr>
<td>HWBs</td>
<td>Health Without Barriers</td>
</tr>
<tr>
<td>IGRA</td>
<td>Interferon gamma release assay</td>
</tr>
<tr>
<td>IPT</td>
<td>Isoniazid preventive therapy</td>
</tr>
<tr>
<td>LTBI</td>
<td>Latent tuberculosis infection</td>
</tr>
<tr>
<td>NICE</td>
<td>National Institute for Health and Clinical Excellence, UK</td>
</tr>
<tr>
<td>MSM</td>
<td>Men who have sex with men</td>
</tr>
<tr>
<td>NR</td>
<td>Not reported</td>
</tr>
<tr>
<td>PICO</td>
<td>Population-Intervention-Comparison-Outcome</td>
</tr>
<tr>
<td>PWID</td>
<td>People who inject drugs</td>
</tr>
<tr>
<td>PRISMA</td>
<td>Preferred reporting items for systematic reviews and meta-analyses</td>
</tr>
<tr>
<td>RCT</td>
<td>Randomised controlled trial</td>
</tr>
<tr>
<td>TB</td>
<td>Tuberculosis</td>
</tr>
<tr>
<td>TST</td>
<td>Tuberculin skin test</td>
</tr>
<tr>
<td>UNISS</td>
<td>Università degli Studi di Sassari, Italy</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
</tbody>
</table>
Glossary

Acceptability How acceptable a given intervention is to the target population in relation to the effect of the intervention

Accessibility How accessible a given intervention is to the target population (availability of good health services within reasonable reach and when needed) [1]

Active case finding (macro area 1) Interventions aimed at promoting early diagnosis by means of provider-initiated systematic offer for testing, at entry and/or during stay (which includes at release)

Active TB Active tuberculosis (TB) refers to disease that occurs in someone infected with *Mycobacterium tuberculosis*. It is characterized by signs or symptoms of active disease, or both, and is distinct from latent TB infection, which occurs without signs or symptoms of active disease [2].

Adherence intervention Interventions aimed at increasing individual adherence to TB treatment to achieve treatment completion.

Correctional facility All institutions where a state holds people deprived of their liberty (e.g. prison or jail), excluding migrant centres and police detention rooms

Diagnosis, treatment, care and prevention of TB (macro area 3) All public health measures to prevent TB and minimise TB transmission within the prison environment and in the community

Directly observed therapy (DOT) An approach which seeks to improve treatment adherence by active monitoring and recording of the consumption of each and every drug dose by an ‘observer’ acceptable to the patient and the health system [3]

Feasibility Whether it is feasible to implement an intervention in terms of time, money, or other circumstances

Incentives Rewards that encourage patients with both suspected and confirmed TB to attend TB screening, out-patient follow-up or DOT appointments, which may include money, vouchers or other ‘in kind’ rewards [4]

Jail Locally-operated, short term facilities that hold people awaiting trial or sentencing or both, and people sentenced mostly to a term of less than one year

Latent tuberculosis infection The presence of *Mycobacterium tuberculosis* bacteria in the body without causing symptoms or infectiousness [5]

Prison All penal institutions for the detention of adult individuals with the exclusion of police security rooms and migrant detention centres, unless otherwise specified

Prison population Adult individuals aged 18 years or older in detention¹ (i.e. people in remand custody, people awaiting sentence, people serving sentence) or ‘going through the gate’ (i.e. all prison staff, including healthcare workers, guards and other staff)

Prison setting Prisons, jails and other custodial settings, for the confinement of convicted criminals and accused persons remanded in custody and awaiting trial; excluding migrant centres and police detention rooms

Service model An operational approach to deliver an intervention, defined by descriptors such as time (e.g. at entry, during stay, at release), modality of the offer (e.g. voluntary, mandatory), etc.

Vaccination (macro area 2) Vaccination interventions to prevent infection and minimise the transmission of selected vaccine-preventable diseases, provided at entry and/or during stay (including outbreak situations) in prison.

¹ This population includes vulnerable groups, i.e. MSM, transgender, PWID, foreign-born persons, homeless, other.
Executive summary

People in prisons have a higher prevalence of several communicable diseases than the general population, a fact which affects both the prison and the general population.

The objective of this report is to systematically review data on diagnosis, treatment, care and prevention of tuberculosis (TB) in prison settings, with a focus on the countries of the European Union and the European Economic Area.

A systematic literature review was performed in PubMed and Embase (1990 and newer) and in the Cochrane Library (publications from 1980 and newer). No language or geographical limits were applied. In addition, the following sources were searched through a predefined website list search and a call for papers: conference abstracts (2010 or newer), unpublished research reports, protocols and guidelines (2005 and newer).

From the peer-reviewed literature, 34 primary articles were included: four articles on TB diagnosis, 18 articles on TB care/treatment, and 12 articles on TB prevention. Furthermore, a total of eight conference abstracts/unpublished research reports and 15 guidelines were included.

**Diagnosis:** No studies were found about active TB diagnosis. Four studies (two from EU/EEA countries, two from the USA) reported on the diagnosis of latent tuberculosis infection (LTBI); all studies compared the tuberculin skin test (TST) with the interferon gamma release assay (IGRA). As no gold standard for the diagnosis of LTBI exists, no conclusions could be drawn from these studies.

**Treatment and care:** Five studies and six grey literature documents investigated active TB treatment and care. Two studies (one from an EU/EEA country, one from the USA) compared directly observed therapy (DOT) with self-administered treatment. Both studies concluded that the use of DOT resulted in higher active TB treatment completion rates. One EU/EEA study looking at the effect of the place of treatment concluded that being treated entirely during prison stay increased the chance of active TB treatment completion. When comparing the results of the individual studies, no clear trends were seen regarding treatment duration or adherence intervention.

Two studies from EU/EEA countries and eleven studies from the USA reported on LTBI treatment in correctional facilities. Within-study comparisons revealed that: 1) the use of DOT increased LTBI treatment completion compared to self-administered treatment (one study from the EU/EEA, one from the USA); 2) interventions such as education, incentives, or active referral after release increased LTBI treatment completion compared to usual care (two studies from the USA); 3) short-course LTBI therapies resulted in higher completion rates compared to long-course therapies (one study from the EU/EEA, one from the USA). However, in the latter US study this difference was no longer found when only looking at those incarcerated during the entire treatment. Another US study found no difference in completion rates between both LTBI treatment durations; and 4) those treated in jails were less likely to complete LTBI treatment than those in prisons2 (one study from the USA). When comparing the results of individual studies, DOT and adherence interventions showed a generally similar effect.

The most frequently reported reasons for non-completion of active TB treatment were death, transfer, and loss to follow-up. The most frequently reported reasons for non-completion of LTBI treatment were adverse events, being transferred/released, refusal of treatment continuation, or loss to follow-up.

**Prevention:** Twelve studies and two grey literature documents reported on contact tracing during a TB outbreak in a correctional facility (one from the EU/EEA, the remainder from the US). Different strategies were used and different populations were tested. All studies showed that contact tracing led to the identification of new LTBI and/or active TB cases, a large part of which received treatment.

No (major) cost-effectiveness studies were found on the diagnosis, treatment, care, or prevention of TB.

Both peer-reviewed and grey literature studies show a high level of heterogeneity in the evidence they present, which makes comparisons difficult. A large portion of the studies were conducted in US prison settings, which raises concerns whether these results can be applied to the situation in the EU/EEA. Overall, the level of evidence derived from the included studies is quite low; most studies had a descriptive and observational design, were conducted in single institutions and with relatively small sample sizes, and study characteristics, interventions and outcomes were often poorly described.

The evidence for TB control interventions in correctional facilities is limited, especially with regard to diagnosis and, to a lesser extent, prevention. Results in peer-reviewed and grey literature studies were heterogeneous, making it difficult to arrive at meaningful conclusions. More comparative studies are needed on the effectiveness and impact of different TB strategies in correctional facilities in the EU/EEA. Nevertheless, as part of the effort to eliminate TB,

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2 See Glossary (p. vii) for definitions of ‘jail’ and ‘prison’.
especially in low and intermediate-incidence countries, it is important to identify and treat TB and LTBI in selected at-risk groups, including people in prisons.
1. Background

1.1 Introduction

Worldwide, more than 10 million people are held in correctional facilities, either as pre-trial detainees/remand prisoners or as convicted and sentenced inmates. In 2014, 613 655 people were detained in EU/EEA correctional facilities, with considerable variation between countries [3]. The median imprisonment rate in 2014 was 108.6 persons per 100 000 population, varying from 21.5 per 100 000 in Liechtenstein to 305.0 per 100 000 in Lithuania [3].

Compared with the general public, people in jails or prisons1 have a higher prevalence of infection with human immunodeficiency virus (HIV), hepatitis B, hepatitis C, syphilis, gonorrhoea, chlamydia and tuberculosis (TB) [4]. Those who are healthy on entry are at a higher risk of exposure to communicable diseases such as HIV or TB and are more likely to develop drug addiction problems or mental illnesses than the general population [5,6].

Most people in European prisons are from poor communities and vulnerable social groups, with an increasing proportion of immigrants or people from minority ethnic backgrounds [6]. Drug users form a large part of the imprisoned population. Studies show that a majority of people in prisons have used illicit drugs at some point in their lives, and many have chronic and problematic drug use patterns [7].

People in prisons have a higher prevalence of several communicable diseases than the general population, a fact which affects both the prison and the general population [6]. The main risk factors linked with increased transmission rates in prison settings seem to be proximity (aggravated by overcrowding), diet, and hygiene. The problem can be aggravated by lack of awareness of infection status, and possibly substandard healthcare. Primary, secondary and tertiary prevention offered in prison settings, especially if coupled to adequate linkage to care, could be effective to lower infection rates [5,6].

1.1.1 Guidance on communicable diseases in prison settings

In 2015, ECDC launched a project to develop evidence-based guidance on the prevention and control of communicable diseases in prisons, jails and other custodial settings, with a special focus on EU/EEA countries. ECDC collaborated closely with the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) in order to explore drug use as a risk factor for the transmission of communicable diseases in prison settings and to take into account the high prevalence of people who inject drugs (PWID) among prisoners in the EU/EEA. This collaborative ECDC/EMCDDA project marks the first time that two EU agencies develop a joint evidence-based guidance for the control of communicable diseases in prison settings in the EU.

During a scoping phase, available evidence published from 2000 to 2014 on the burden of communicable diseases, preventive measures and associated costs in prison settings in the EU was assessed, and knowledge gaps on communicable diseases in prison settings were identified. An evidence mapping tool was developed, and findings were supplemented with information from EU/EEA experts in order to define thematic areas to be addressed by the guidance document. This guidance document will be developed as a series of guidance modules on specific thematic areas (macro areas). The following macro areas will be covered:

- Macro area 1: Active case finding for selected communicable diseases at admission and during prison stay
- Macro area 2: Vaccination strategy, including vaccination at entry and vaccination in outbreak situation
- Macro area 3: Diagnosis, treatment, care and prevention of TB
- Macro area 4: Prevention, treatment and care of HIV including prevention of mother-to-child transmission and post-exposure prophylaxis
- Macro area 5: Prevention, treatment and care of viral hepatitis, with a focus on hepatitis C treatment
- Macro area 6: Prevention and control of injecting-related infections among current or former drug users

This systematic review report focuses on macro area 3: diagnosis, treatment, care and prevention of TB.

1.1.2 Active TB and LTBI

TB is an infectious disease caused by Mycobacterium tuberculosis. Following the initial infection, the immune system will most often clear or contain the infection. If the pathogen is not eliminated, it will persist in a dormant state without causing symptoms. This is called latent TB infection (LTBI). Active TB, where the bacterium is no longer controlled by the immune system, can occur at any time following infection and most commonly affects the lungs, causing a chronic cough, loss of weight, loss of appetite, and general malaise [8].

---

1 We use the term ‘prison’ as synonymous with all types of detention and custodial facilities, with the exception of migrant detention centers and police security rooms.
About one quarter of the world’s population is estimated to be infected with *M. tuberculosis* [9]. The lifetime risk of reactivation TB for a person with documented LTBI is estimated to be 5 to 10%, with the majority developing TB disease within the first five years after initial infection. The risk of developing TB disease following infection depends on several factors, the most important one being the immunological status of the infected person. When the infected person’s immune response weakens (e.g. through HIV infection, malnutrition, the use of steroids/other immunosuppressive medications, or advanced age), reactivation of LTBI may occur [10].

Correctional facilities are often high-risk environments for TB transmission because of severe overcrowding, poor nutrition, poor ventilation, and in most cases limited access to insufficient healthcare. Moreover, people in prisons do not represent a mere cross-section of society in general. They are overwhelmingly male, are typically aged 15–45 years, and come predominantly from poorly educated and socioeconomically deprived sectors of the population where TB infection rates are higher and transmission is more frequent. High-risk groups for TB such as drug-users and homeless persons are often overrepresented among offenders. Additionally, they may belong to minority or migrant groups from high-TB burden countries, who have a greater risk of being infected with LTBI. Prisoners are often admitted to cells without being given a health check, which increases the risk for spreading diseases [11].

### 1.1.3 Diagnosis of LTBI and TB

There are currently two types of tests for LTBI diagnosis: the tuberculin skin test (TST) and the interferon gamma release assay (IGRA). There is, however, no gold standard test available to diagnose LTBI [12].

The TST is an intradermal injection of purified protein derivative (PPD), a crude antigenic mixture, shared among *M. tuberculosis*, *M. bovis*, and other non-tuberculous mycobacteria. The test measures in vivo a delayed-type hypersensitivity reaction based on immunological recognition of mycobacterial antigens in exposed individuals. This inflammatory reaction results in the characteristic indurated area at the site of injection. In order to obtain the test result, it needs to be examined by a qualified healthcare provider two days after injection. A negative result can be repeated some weeks later for confirmation.

IGRAs measure cell-mediated immune responses to peptide antigens that simulate mycobacterial proteins. The test involves obtaining a blood sample. There are currently four IGRA tests commercially available: the QuantiFERON-TB Gold, Gold Plus and Gold in Tube (Qiagen GmbH, Hilden, Germany) and the T-SPOT (Oxford Immunotec Limited, Abingdon, UK) [13-15].

A chest X-ray is frequently used as the first step in active pulmonary TB diagnosis. It is also used to rule out active TB in persons who have a positive TST or IGRA and no symptoms of TB disease (i.e. confirmation of LTBI by ruling out active TB). A posterior-anterior chest radiograph detects lesions, which may appear anywhere in the lungs. However, these abnormalities cannot be used to definitively diagnose TB, and therefore the sputum should also be examined. The presence of acid-fast-bacilli on a sputum smear often indicates active TB disease. However, acid-fast microscopy cannot be used to confirm a TB diagnosis because not all acid-fast-bacilli are *M. tuberculosis*. To properly confirm a TB diagnosis, a culture is necessary [16]. Newer diagnostic technologies include the Xpert MTB/RIF test, which is used for both detection of active TB and resistance to rifampicin [17].

### 1.1.4 Treatment and care of LTBI and TB

There are five anti-TB first line drugs to cure active TB: rifampicin, isoniazid, ethambutol, pyrazinamide and streptomycin [6]. Anti-TB medicines have two primary properties: bactericidal activity, and bacteriostatic activity. The first line anti-TB medicines possess these properties to different extents and are used in combination during treatment. Isoniazid and rifampicin are the most powerful bactericidal medicines active against all populations of TB bacilli. Rifampicin is the most potent sterilising medicine available. TB treatment with an adequate regimen for an adequate duration will prevent the development of drug resistance [18].

Progression to active TB, once LTBI has been confirmed, can be averted by preventive treatment. The same drugs as for active TB are used for the treatment of LTBI. However, where in the case of active TB a combination of several drugs is prescribed for a long duration (generally six months), standard therapy for LTBI is frequently a single drug or a combination of two or more drugs but then for a shorter duration (generally three to four months) [10, 19].

Although the same drugs are used for the treatment of active TB as are used for the treatment of LTBI, the principles of treatment of LTBI differ from that of active TB. People with active TB require treatment with a combination of drugs for a long duration and treatment with a single drug is not recommended to treat active TB due to the risk of developing resistance. The current internationally recommended regimen for the treatment of active TB is a combination of four drugs: isoniazid (INH), rifampicin, pyrazinamide, and ethambutol for the first two months; followed by two drugs: INH and rifampicin for the next four months (WHO 2007; WHO 2010b; CDC 2011; NICE 2011). By contrast, standard therapy for people with LTBI, with much lower mycobacterial loads, is a single drug (monotherapy) or a combination of two or more drugs (combination chemotheraphy) for shorter durations (Jasmer 2002a).
Effective treatment for both active and latent TB requires regular medication to be taken for several months [8]. Regardless of which regimen is in place, patients often find it difficult to complete their course of drug treatment. Contributing factors to non-adherence are feeling well while the treatment course has not been finished (active TB) or being healthy while on treatment (LTBI), personal factors (e.g. poor understanding of the disease or treatment requirements), drug side effects, drug resistance leading to protracted treatment periods, social and economic factors (e.g. stigma, lack of support, and poverty), and health system factors (e.g. inconvenient treatment arrangements, poor patient-provider relationships, and no availability of drugs) [20]. Directly observed therapy (DOT) is frequently used in an attempt to improve treatment adherence by active monitoring and recording of the consumption of each and every drug dose [3]. Other measures undertaken to improve treatment adherence are patient education, incentives or enablers [8].

1.1.5 Prevention of TB
Transmission of TB occurs from a person with active pulmonary TB by airborne droplets produced by coughing, sneezing or talking that are subsequently inhaled by contact people [6]. These droplets float in the air and penetrate in the alveoli of the host after inhalation. In moist warm air, the bacteria can survive for hours [21]. Interventions to interrupt transmission can be directed at two pathways: 1) preventing transmission of TB from people with infectious TB to their contacts, and 2) preventing the disease from developing once any contacts have become infected. To prevent transmission, early case detection, immediate and adequate treatment and infection control interventions are needed. To prevent infected contacts from developing active disease, preventive treatment can be administered [6]. As LTBI treatment is covered in the treatment and care section of this report, the prevention section in this report covers the first type of interventions only.

In prison settings, these preventive measures can be targeted as follows [18]:
- Preventing spread of infection from the community to the correctional facility, e.g. active case finding at entry
- Preventing infection among people within the correctional facilities (those imprisoned and/or staff), e.g. active case finding during imprisonment, contact investigation, outbreak control, respiratory isolation
- Preventing infection of community members by those released from the correctional facility or by correctional facility staff, e.g. active case finding at release, regular examination of staff

1.2 Scope and objectives
The objective of this systematic review on diagnosis, treatment, care and prevention of TB in prison settings was to gain insight in the evidence base (peer-reviewed as well as grey literature) for the diagnosis, treatment, care and prevention of TB in prisons, jails and other custodial settings.

This systematic review aims at collating and synthesising all relevant evidence with regard to diagnosis, treatment, care and prevention of TB in prison settings (see specific research questions in the methodology section). It does not include active case finding and vaccination as these topics are covered by separate systematic reviews.
2. Review methods

This systematic review applies a rigorous high-quality methodology, adhering to international methodological standards as established by Cochrane [22] and PRISMA [23]; it also uses the same methodology employed by ECDC during the scoping phase of the project. The screening and selection phases of the systematic review were carried out jointly for the first three macro areas (active case finding, vaccination, and TB prevention and care). This section refers only to the methodology relevant to macro area 3. For a detailed overview of the overall process, please see Appendix 1.

2.1 Review questions

The following objectives, questions, populations and settings were defined for the systematic review on TB:

Review objective:

To gain insights about the evidence base (peer-reviewed and grey literature) for the diagnosis, treatment, care and prevention of TB in prisons, jails and other custodial settings. The objective does not include active case finding and vaccination as these topics are covered by separate systematic reviews.

The PICO method was used to develop specific research questions from these review objectives (Table 1).

**Table 1. PICO method**

<table>
<thead>
<tr>
<th>Prevention, diagnosis, treatment and care of TB</th>
</tr>
</thead>
<tbody>
<tr>
<td>P Adult individuals (≥18 years) in prison settings (i.e. both those detained and those who work in prison settings ('going through the gate'))</td>
</tr>
<tr>
<td>I Diagnosis, treatment, care and prevention of TB</td>
</tr>
</tbody>
</table>
| C ● Comparison with no intervention  
   ● Comparison with alternative intervention  
   ● No comparison  
   ● Comparison between populations in prison settings (e.g. between different prison types, risk groups, etc.)  
   ● Comparison with community setting. |
| O Qualitative outcomes:  
   ● Accessibility  
   ● Feasibility and acceptability of interventions  
   ● Qualitative description of interventions/modes of service delivery  
Quantitative outcomes:  
   ● Uptake (number of persons using a certain intervention or number of persons reached by a certain intervention)  
   ● Measures of effectiveness (e.g. change in TB incidence or prevalence, number of people who have completed treatment, number of people who are linked to care – including community care after release)  
   ● Cost-effectiveness |
| S Prisons, jails and other custodial settings (excluding migrant centres and police detention rooms) |

Review questions:

- Which prevention interventions for TB are effective?
- Which care and/or treatment interventions aimed at control of TB are effective?
- Which service models for prevention, diagnosis, care and/or treatment of TB are effective?
- Which prevention interventions for TB are cost-effective?
- Which diagnosis, care and/or treatment interventions aimed at control of TB are cost-effective?
- Which service models for prevention, diagnosis, care and/or treatment of TB are cost-effective?
- What is the acceptance/uptake/coverage of prevention, diagnosis, care and/or treatment of TB?
- How can the acceptance/uptake/coverage of prevention, diagnosis, care and/or treatment of TB be improved?
- Who should be targeted for prevention, diagnosis, care and/or treatment of TB?
2.2 Search and selection strategy

The search and selection phases for the first three macro areas were combined; see Appendix 1 for a detailed description of the process. A brief description of the strategies and specific issues relevant for macro area 3 can be found below.

Search strategies for peer-reviewed articles

A peer-reviewed literature search was carried out on 4 February 2016 (PubMed, Embase and Cochrane Library). The search included search strings relevant for all three macro areas (Appendix 1). The only search limit was a time limit for macro area 3: literature published from 1990 onwards was searched in PubMed and Embase, while literature published in 1980 or later was searched in the Cochrane Library.

Selection of peer-reviewed articles

Articles were screened by title and abstract, and if considered possibly relevant, in full text. Further scrutiny of the article during the extraction phase could have led to exclusion from the review. Inclusion and exclusion criteria by study design/type, study quality, study population, geographical area, comparison and specific outcomes are described in Appendix 1. High-quality meta-analyses or systematic reviews were included if they matched the review objectives. If a meta-analysis/systematic review was excluded, all relevant articles mentioned in the excluded study were examined individually.

Critical appraisal for peer-reviewed articles

During the selection process, the methodological quality of the articles that appeared to present relevant data for the review were critically appraised using standardised evidence-based medicine checklists in order to identify quality problems.

For this review, the National Institute for Health and Clinical Excellence (NICE) checklists were used for selection purposes because they offer tools for both quantitative and qualitative studies. NICE checklists⁸ are available for the following study designs: systematic reviews and meta-analyses, randomised controlled trials (RCTs), cohort studies, case-control studies, diagnostic accuracy studies, economic evaluations, and qualitative studies. Each study is awarded an overall study quality grading for internal validity and a separate one for external validity:

+++: All or most of the checklist criteria have been fulfilled, where they have not been fulfilled the conclusions are very unlikely to alter

++: Some of the checklist criteria have been fulfilled, where they have not been fulfilled, or not adequately described, the conclusions are unlikely to alter

+: Few or no checklist criteria have been fulfilled and the conclusions are likely or very likely to alter.

If an article received a score of ‘−’ for both the internal and external validity, the article was excluded (exclusion reason ‘insufficient methodology’, see Appendix 4). If methods and/or results were unclear, articles were excluded. Otherwise, articles were included and limitations, if present, were described in the data extraction tables.

Relevant publications in the field of infectious disease also include outbreak investigations, surveillance studies or other observational studies. For these types of studies no standardised checklists are available, and therefore its quality was assessed based on relevant aspects of the existing NICE checklists, supplemented with questions concerning the study design (e.g. whether – in a cross-sectional study – the study population is a representative sample of the source population). See Appendix 2 for a complete list of questions on study design.

Predefined aspects of a study were qualitatively scored using - - or −, +/-, + or ++. The checklist was not designed to calculate a total quality score to assess quality differences between studies. The final decision on whether the quality of a study was sufficient for inclusion was taken by the reviewer, based on his/her expertise and knowledge.

Search strategies for grey literature documents

A grey literature search with a focus on EU/EEA countries was performed to complement the peer-reviewed literature. Articles, abstracts, research reports, case studies, service models, guidelines and protocols which focused on prisons and people in prisons were recovered. The search was conducted through a pre-defined list of websites and a call for papers/experts input. More details can be found in Appendices 1 and 6.

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Selection of grey literature documents

Documents were included if the reported information was relevant and of sufficient quality. Inclusion and exclusion criteria by period of publication, type of document, document quality, document population, subject of the document, geographical area, specific outcomes of interest are described in Appendix 1. If prison-focused guidelines could not be retrieved/were not available, guidelines with complimentary information on prisons and prisoners were searched to supplement the data. If no additional information could be found, general guidelines were reviewed (i.e. those without a section on prisoners).

Critical appraisal for grey literature

Only grey literature documents with clearly stated methods for compiling data and/or with data sources/references were included. The following document types were identified (in order of quality, highest quality first):

Conference abstracts and unpublished research reports
Conference abstracts were checked against included peer-reviewed literature in order to avoid duplication; if duplication was found, the full-text article from the peer-reviewed literature was preferred. Conference abstracts and unpublished research reports focussing on prison settings were included if they contained information relevant to the review objectives. They were screened using the same inclusion/exclusion criteria as the peer-reviewed literature.

Guidelines
The following types of guidelines were identified (highest quality first):

- Evidence-based: largely based on the scientific literature. Good clinical practices or expert opinions could be used to supplement the scientific literature
- Practice-based: reflects expert opinion or information derived from good clinical practices; some literature references (not systematic) might be included.

Relevant guidelines were critically appraised with a selection of criteria derived from the AGREE instrument:

- The overall objectives of the guidelines are described in detail
- Systematic/clearly stated methods were used to compile the data, and/or data sources/references were given
- The recommendations are specific and unambiguous.

Each of the three criteria were qualitatively scored on a 5-tier scale: –, –, 0, +, and ++. The final decision whether the quality of a guideline was sufficient for inclusion in the evidence base was taken by the reviewer, based on his/her expertise and knowledge.

Case studies/service models
Case studies/service models were included to provide insights in the way specific interventions are implemented in a given setting. Case studies/service models were only included if the below criteria were met:

- Clearly described accounts of interventions/service models related to the relevant macro area
- Elements of monitoring or evidence of success (e.g. pre- and post-intervention testing positivity rate for case finding interventions).
2.3 Data extraction

Data extraction for peer-reviewed articles

All relevant information from included articles was summarised in a standardised evidence table. For articles on the diagnosis, treatment, care and prevention of TB, the evidence tables contain the following information:

- Bibliographic reference: author, year, journal, country
- Study characteristics: study design, study period, follow-up, prison setting, study objective
- Study population: population description, inclusion and exclusion criteria, sample description: sample size, gender, age, risk groups
- Data sources and definitions: description of data source/s and relevant definitions
- TB prevention and care: methods for diagnosis, treatment, care and prevention
- Outcome results: diagnosis, treatment, care and prevention
- Reviewer comments, limitations, and level of evidence: any additional information which was relevant for interpreting the study results, major issues with regard to the critical appraisal, and the final level of evidence based on these considerations.

Data extraction for grey literature documents

Included documents were collated into evidence tables. The evidence tables contain information on the following topics:

- Bibliographic references: e.g. title, year, place of publication
- Source: institute/company, etc. that prepared the document
- Type of document, e.g. conference abstract, guideline, etc.
- Setting and population: country, prison setting, risk groups, etc. to which the results apply
- Intervention: type of intervention and brief description
- Results: relevant results on the objectives given in the document, by objective
- Comments: any additional information which is relevant for interpreting the results.

Level of evidence peer-reviewed literature

The included studies showed a large degree of heterogeneity, therefore the strength of evidence was not assessed beyond individual studies. For the studies included in the review, the level of evidence per individual article was determined based on the study design and the risk of bias, following the GRADE approach criteria (grading of recommendations assessment, development and evaluation).

For randomised controlled trials (RCTs), the following aspects were included to assess the risk of bias:

- Randomisation
- Allocation concealment
- Blinding
- Loss to follow-up
- Intention to treat
- Other limitations (e.g. non-validated method to assess the outcome).

For observational studies, the following aspects were included to assess the risk of bias:

- Appropriateness of eligibility criteria (e.g. the study population is not a representative sample of the source population; selection of exposed and unexposed individuals in cohort studies from different populations)
- Measurement of exposure and outcome (e.g. not measured in a standardised, valid and reliable way or not clearly described; differences in measurement in exposed and non-exposed populations or measurement of the outcome while not blinded for/with knowledge of the exposure)
- Control for confounding (e.g. degree of accuracy when measuring relevant confounders or adjustment in statistical analyses)
- Follow-up (e.g. no or short follow-up or different follow-up for exposed and non-exposed populations)
- Other limitations (e.g. participants and non-participants differ regarding relevant characteristics).

For cost-effectiveness studies, the following aspects were included to assess the risk of bias:

- Nature of health condition reflected by the model
- Time horizon
- Perspective
- Discount rate
- Relevant health outcomes and costs
- Sources used for model input
• Incremental cost-effectiveness ratio
• Sensitivity analyses
• Other limitations.

In general, this led to the following levels of evidence for individual studies (based on the study design and its methodological quality; see risk of bias criteria above):

• High (i.e. high-quality RCTs)
• Moderate (i.e. lower quality RCTs, high-quality cohort/case-control studies, and cost-effectiveness studies)
• Low (i.e. lower quality cohort/case-control studies and cost-effectiveness studies with comparison, high-quality surveillance studies)
• Very low (i.e. low-quality surveillance or other observational studies, outbreak studies, cross-sectional studies without comparison).

2.4 Evidence summary

Separate summary tables were created for diagnosis, treatment and care and prevention (Appendices 7–10). These summary tables contain the following information:

• Bibliographic reference, country, study design
• Setting (e.g. jail, prison), sample (size, age, gender, etc.)
• Methods:
  – Diagnosis: testing method (e.g. chest X-ray, tuberculin skin test), type of offer (e.g. voluntary), who, when (e.g. at entry)
  – Treatment and care: treatment (medicines and dosage), duration, DOT, who, adherence improvement methods (e.g. active referral, education)
  – Prevention: contact tracing method (e.g. stepwise contact investigations), testing method (e.g. tuberculin skin test), who (contacts screened; e.g. other people in prison, staff, etc.), index case patient (main characteristics).
• Results:
  – Diagnosis: uptake, positivity rate, agreement
  – Treatment and care: treatment initiation, treatment completion, effectiveness, other
  – Prevention: contacts screened, TST positives/converters, TB positivity rate, treatment initiation.
• Level of evidence

Cost-effectiveness results, qualitative outcomes (acceptability, feasibility and accessibility), guidelines, protocols and service models were summarised in text only.

Summaries of the peer-reviewed literature and grey literature were separately presented, as were results from the EU/EEA and from other high-income countries.

2.5 Quality control

During the review process, the following quality control measures were used to search and select peer-reviewed literature:

• Peer-review of the search strings by ECDC librarians and expert panel members
• Selection based on title and abstract was performed by two independent researchers. All hits that could be excluded for clearly explicable reasons (inclusion/exclusion criteria) were excluded. When in doubt, the title and abstract were assessed by two researchers and discussed. All articles cited by these two researchers (including articles where doubts remain) were checked by another researcher with expertise in the field of prison health, who then took the final decision on inclusion or exclusion.
• Duplicate screening and critical appraisal of 50% of the full-text articles was performed by two independent reviewers to avoid errors in the selection of articles for data extraction. The results were compared and discussed early in the review process, and any disagreements were adjudicated by a third reviewer. Any doubts arising during the screening of the remainder of the full-text articles were discussed in the project team.
• Evidence tables were compiled by two researchers (not in duplicate), and all evidence tables were reviewed by an independent researcher.
The following quality control measures were applied to search and select grey literature:

- Evidence tables were compiled by a researcher and reviewed by a second researcher.
- Early in the process, a senior researcher also checked a sample of 10% of the articles included in the evidence tables to allow for refinement of data extraction.
- Critical appraisal of the guidelines was performed by a researcher and reviewed by a second researcher.

**Role of the ad-hoc scientific panel**

As part of the project, a multi-disciplinary expert panel was consulted. The panel members were selected based on their expertise in prison health, prevention and control of communicable diseases, and evidence-based public health. The experts came from a variety of organisations, such as clinical professional associations, public health institutions, ministries, EU-funded initiatives, international agencies, and civil society organisations. Experts were based in the Czech Republic, Estonia, France, Germany, Italy, Romania, Spain, Switzerland, and the UK. ECDC staff members were also on the expert panel, adding further areas of expertise (e.g. disease-specific knowledge, preparedness, social sciences, health determinants). See Appendix 3 for a complete list of expert panel members. The panel members were involved in the prioritisation of the systematic review topics, methodology, and evidence gathering.
3. Review results

In the peer-reviewed article search, the PubMed search returned 4,705 hits, the Embase search 5,867 hits, and the Cochrane Library search 59 hits. After the removal of duplicates and the addition of five items after a hand search, 7,041 unique hits remained. After screening the titles and abstracts, a total of 566 articles were selected. Main reasons for the exclusion of articles during the title and abstract screening were:

- Incorrect setting (not a prison setting)
- Ineligible health outcomes (cancer, mental disease, etc.)
- Non-pertinent publication types (e.g. news, letter to the editor, editorial)

After reviewing the full text of the selected articles, 421 articles were excluded. Articles excluded and reasons for exclusion during the full-text selection step can be found in Appendix 4. Additionally, a total of 33 articles could not be retrieved and could therefore not be assessed (see Appendix 5).

In total, 112 articles were included, 34 of them were relevant for macro area 3. Of the 34 articles, four reported on diagnosis, 18 were on treatment and care, and 12 dealt with prevention. Figure 1 shows a flowchart of the selection process. Please note that a combined search for the three macro areas was conducted, and therefore no complete macro area-specific flowchart can be given. The majority of the studies was conducted in the USA; only seven came from the EU/EEA.

The grey literature search focused exclusively on the EU/EEA; a pre-defined websites search returned 22 documents, and a call for papers yielded 127 documents.

Documents received from field researchers were screened based on title and content, and a total of 80 articles were excluded. Exclusion reasons were:

- Outside of date range (i.e. not published in the last five years)
- Not relevant for the review objectives (mental disorders, addiction management, etc.)
- Prevalence/incidence studies
- No country of interest
- More recent documents available
- Insufficient description of the methodology

Articles excluded during this selection step can be found in Appendix 7.

Overall, a total of 69 documents met the predefined inclusion criteria, 23 of which were relevant to macro area 3 and thus included. Of those 23 documents, eight were conference abstracts/unpublished research reports and 15 were guidelines. None of these conference abstracts/unpublished research reports reported on diagnosis, six reported on treatment and care, and two reported on prevention. Six of the guideline documents reported on diagnosis, ten of them were on treatment and care, and nine presented guidelines on prevention. Several guideline documents reported on more than one topic.

The grey literature search focused exclusively on the EU/EEA. Figure 2 presents a flowchart of the selection process. Please note that the searches were conducted for all the three macro areas, and therefore no complete macro area-specific flowchart can be given.
Figure 1. Flowchart: selection process, peer-reviewed literature

PubMed search
n=4 705

Embase search
n=5 867

Cochrane Library
search
n=59

Unique hits
n=7 036

Via references
systematic reviews
n=5

Selected based
on title and abstract
n=566

Included: n=112*
- Macro area 1, active case finding: n=64
- Macro area 2, vaccination: n=19
- Macro area 3, TB prevention and care: n=34

- Diagnosis: n=4
- Treatment and care: n=18
- Prevention: n=12

Excluded, based on title and abstracts
n=6 475

Excluded: n=421
- No/limited data on objectives: n=137
- Non-pertinent publication types: n=81
- Narrative reviews: n=74
- Prevalence/incidence studies: n=35
- Insufficient methodology: n=35
- Duplicate articles: n=18
- Included in other systematic review: n=15
- Incorrect setting: n=15
- No country of interest: n=7
- Modelling studies: n=2
- Children: n=1
- More recent data available: n=1
- Not available: n=33

* Five articles contained relevant data for two macro areas
Figure 2. Flowchart: selection process, grey literature

- Websites search: n=22
- Call for papers: n=127
- Selection based on in-/exclusion reasons
  - Included: n=47
    - Macro area 1, active case finding: n=36
    - Macro area 2, vaccination: n=7
    - Macro area 3, TB prevention and care: n=12
  - Excluded: n=80
    - Outside date range=35
    - Not relevant for the review objectives: n=25
    - Prevalence/incidence studies: n=13
    - No country of interest: n=4
    - More recent documents available: n=2
    - Insufficient description methodology: n=1

- Conference abstracts: n=4
  - Macro area 1, active case finding: n=1
  - Macro area 2, vaccination: n=0
  - Macro area 3, TB prevention and care: n=3
- Guidelines: n=18
  - Macro area 1, active case finding: n=8
  - Macro area 2, vaccination: n=4
  - Macro area 3, TB prevention and care: n=8
- Guidelines: n=17
  - Macro area 1, active case finding: n=11
  - Macro area 2, vaccination: n=5
  - Macro area 3, TB prevention and care: n=7
- Unpublished research reports: n=6
  - Macro area 1, active case finding: n=3
  - Macro area 2, vaccination: n=2
  - Macro area 3, TB prevention and care: n=1
- Conference abstracts: n=22
  - Macro area 1, active case finding: n=2
  - Macro area 2, vaccination: n=0
  - Macro area 3, TB prevention and care: n=0
- Guidelines: n=15
  - Diagnosis: n=6
  - Treatment and care: n=10
  - Prevention: n=9
- Conference abstracts/unpublished research reports: n=8
  - Diagnosis: n=0
  - Treatment and care: n=6
  - Prevention: n=2

* 'Other documents' includes two scientific papers
# Some documents included data on more than one macro area
& Some documents included data on more than one disease
3.1 Diagnosis

The results of the searches on the diagnosis of active TB and LTBI (peer-reviewed and grey literature) are summarised below. See Appendix 8 for a more detailed summary of relevant information.

3.1.1 Active TB

Peer-reviewed literature

No studies in the peer-reviewed literature were found that reported on diagnostic tests for active TB in correctional settings.

Grey literature: conference abstracts and unpublished research reports

No grey literature conference abstracts or unpublished research reports were found that reported on diagnostic tests for active TB in correctional settings.

3.1.2 LTBI

Peer-reviewed literature

Uptake and positivity rate of, and agreement between, diagnostic tests in EU/EEA countries:

Two studies were found that compared TST (Mantoux) with IGRA (QuantiFERON TB-Gold). In one study from Germany, both tests were performed in 91% of the participating male inmates recently admitted to prison and in 62% of the participating employees who might have had contact with a TB index case (Scharlach 2008 [24], very low level of evidence). TST-positivity among inmates was 29.5%, IGRA-positivity was reported at 18.1%. For employees, the positivity rate was not reported. Concordance between both tests was 79.2% (kappa = 0.44, moderate agreement). A similar study was conducted in Spain, with both tests conducted in 82% of the participating male prison population (Marco Mouriño 2011 [25], very low level of evidence). TST and IGRA positivity were 24% and 26%, respectively, and in 33.6% of the inmates one of the tests was positive (kappa = 0.6, good agreement).

Cost-effectiveness

No studies in the peer-reviewed literature were found that reported on the cost-effectiveness of diagnostic tests for LTBI in correctional facilities.

Acceptability, feasibility and accessibility

No studies in the peer-reviewed literature were found that reported on the accessibility, feasibility, or acceptability of diagnostic tests for LTBI in correctional facilities.

Grey literature: conference abstracts and unpublished research reports

No grey literature conference abstracts or unpublished research reports were found that reported on diagnostic tests for LTBI in correctional settings.

3.1.3 Guidelines on active TB and LTBI

Seven practice-based guidelines [6, 11, 18, 28-31] and one evidence-based guideline [32] that reported on diagnosis of TB were included, five of which were specific to the prison setting (four supranational guidelines and one national guideline), while the other two were not (both supranational guidelines).

These guidelines formulated the following relevant recommendations:

Table 1. Summary of guidelines on TB diagnosis

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Active TB</th>
<th>LTBI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specific to prison setting – supranational guidelines</td>
<td>A pulmonary TB suspect should submit at least two sputum samples (preferably early-morning samples, supervised by staff) for microscopy, to be transported to the lab on the same day or otherwise refrigerated. Direct smear microscopy examination of sputum is the most commonly used method for diagnosing TB. The isolation of TB bacilli in</td>
<td></td>
</tr>
</tbody>
</table>
3.2 Treatment and care

Results of the peer-reviewed and grey literature searches on treatment and care of active TB and LTBI are summarised below. See Appendix 9 for a more detailed summary.

3.2.1 Active TB

Peer-reviewed literature

Treatment initiation, treatment completion and effectiveness in EU/EEA countries

One study from Spain was retrieved (Marco 1998 [33], very low level of evidence) which reported on 62 male TB inmates who started treatment consisting of two months of isoniazid, rifampicin, pyrazinamide and ethambutol, followed by four or six months of isoniazid and rifampicin (depending on HIV status). Several incentives were used: a maintenance methadone programme (in and out of prison), economic aids for those released, and referral to sociosanitary centres for former prisoners that are homeless and/or alcoholic. Overall, 75.8% completed treatment, and 45.2% did so while still in jail. Continuous supervision by directly observed therapy (DOT) was significantly
associated with better treatment completion, and having the entire treatment administered during prison stay was borderline significantly associated with better treatment completion.

Another survey study evaluated TB control in pre-trial detention centres and prisons in 22 of the 52 countries of the WHO Regional Office for European region (Aerts 2006 [34], very low level of evidence). This study presents somewhat different outcomes compared to the other studies (i.e. more background information) and is therefore not summarised in the appendix. Prison inmates with TB were treated according to WHO recommendations in 90.9% of the responding countries, 77.3% of the countries applied DOT systematically, and almost all countries provided anti-TB drugs free of charge. The average completion rate amongst the responding countries was 25%, ranging from 0% in Belarus and Latvia to 58% in Romania. 40.9% of countries reported that less than half of patient prison left the correctional system before completing treatment (for 50% of countries this information was not available). The percentage of patients continuing TB treatment after release was 100% in two and 50% in five countries. The average cure rate was 32.9%, ranging from 0% in Belgium to 65.6% in Azerbaijan. Completion and cure rates were unavailable for 12 of the 22 responding countries. Sixteen (72.7%) countries reported that the continuation of TB treatment for released inmates was organised by the public health services (public dispensaries), six by the health sector in which TB care is integrated (private practitioners, hospitals, outpatient clinics), and two by the prison staff themselves.

**Treatment initiation, treatment completion, and treatment effectiveness in non-EU/EEA countries**

Four studies outside the EU/EEA reported on active TB treatment. Overall treatment completion ranged from 82% to 100%, treatment completion in the correctional facility was 65% and 100% (reported in two studies only), and treatment completion among those continuing treatment outside the correctional facility ranged from 38.5% to 100%. Below, each study is summarised in some more detail, because the results should be viewed in light of different study settings, treatment regimens, countries, and populations.

In a study from Turkey, 13 active TB cases found through screening in prison were described (Kiter 2003 [35], very low level of evidence). All TB cases initiated treatment consisting of two to three months of isoniazid, rifampicin, morphazinamide and ethambutol, followed by six to seven months of isoniazid and rifampicin. The treatment was initiated and completed by all inmates, and 54% were cured.

In a US study by Kim et al., 441 TB cases were studied whose treatment (not specified) was initiated in jail and continued after their release (Kim 2007 [36], very low level of evidence). Completion of treatment outside jail was established in 38.5% of study participants. DOT users were significantly more likely to complete treatment than those who self-administered treatment, with field DOT being more effective than clinic DOT. Another US study reported a 100% treatment completion among 13 HIV-infected prison inmates that developed TB after an outbreak (Spradling 2002 [37], very low level of evidence). Treatment consisted of a rifabutin-containing regimen (rifabutin was substituted for rifampin; duration NR) and was under DOT. A further US study described 142 inmates transferred to the prison hospital for evaluation and treatment of TB (not specified, DOT) (Bock 1998 [38], very low level of evidence). Overall treatment completion was 82%; the completion rate for inmates treated in prison only was 65%; it was 59% for inmates who completed treatment after release.

**Cost-effectiveness**

No studies were found in the peer-reviewed literature on cost-effectiveness of active TB treatment and care in correctional facilities.

**Acceptability, feasibility and accessibility in EU/EEA countries**

The reasons for non-completion of active TB treatment with isoniazid, rifampicin, pyrazinamide and ethambutol under DOT conditions were reported in one Spanish study (Marco 1998 [33], very low level of evidence): 9.7% of those starting treatment defaulted (reason not given), 9.7% died, and 4.8% transferred out.

Acceptability, feasibility and accessibility in non-EU/EEA countries: The reasons for non-completion of active TB treatment under DOT conditions (medications not specified) were reported in one US study (Bock 1998 [38], very low level of evidence): 8% died and 11% were lost to follow-up due to release.

**Grey literature: conference abstracts and unpublished research reports**

**Treatment initiation, treatment completion, and treatment effectiveness in EU/EEA countries**

Six conference abstracts reporting on TB treatment (treatment scheme not specified) were included, three from Spain and one each from Germany, Romania and Bulgaria. In summary, the results show initiation rates of 100% in the two studies which reported this information and completion rates of 53.8%–78%. Only two conference abstracts reported the use of DOT [39, 40].

A study by Marco et al. reported on active TB cases from prisons in Catalonia [41]. All patients received treatment, and 72.8% were cured. Another study from Spain reported that among 40 patients who started treatment between 1998 and 2009 (100% treatment initiation rate), 62.8% received DOT in 1998; in 2000, 100% received DOT [39]. Ruiz-Rodriguez et al. reported that 77.9% of active TB patients completed their treatment, and in 2.3% of the patients their treatment failed [40]. In a study from Germany, a diagnosis upon prison entry was significantly associated with unsuccessful or unknown treatment outcomes (OR 5.9, CI 4.9–7.2) compared to passive case
finding [42]. In a Romanian study among 477 active TB cases registered in prison, the treatment success rate in new pulmonary smear positive TB cases was 82.1% in 2009, 68.4% in 2010, and 55.8% in 2011 (no reason for this decline was reported in the conference abstract) [43]. Milanov et al. found that among 735 inmates who started TB treatment between 2004 and 2012 (100% treatment initiation rate), 72.8% completed treatment successfully [44].

Cost-effectiveness

No grey literature documents were found on cost-effectiveness of active TB treatment and care in correctional facilities.

Acceptability, feasibility and accessibility in EU/EEA countries

In a conference abstract from Spain, 19.8% of inmates were released before treatment completion [40]. In another conference abstract from Spain, 27.2% were released before treatment completion [41]. In a conference abstract from Germany, 12% of inmates defaulted treatment, 26% were reported as lost to follow-up, and 8.2% had an unknown treatment outcome (not further specified) [42]. Lastly, in a conference abstract from Bulgaria, 1.8% of inmates died, and 24.5% did not complete treatment because of interruption, transfer, or unknown outcome [44].

3.2.2 LTBI

Peer-reviewed literature

Treatment initiation, treatment completion and treatment effectiveness in EU/EEA countries

Two Spanish studies investigated LTBI treatment in a correctional facility. In one study, different LTBI treatment regimens were compared under DOT: nine months isoniazid, two months rifampicin and pyrazinamide, three months rifampicin and isoniazid, and four months rifampicin (Lopez 2011 [45], low level of evidence). Overall, 89.9% of the inmates started treatment. Treatment with isoniazid only was significantly more often discontinued and voluntarily stopped compared to short-course therapies, but not due to adverse events. Treatment with rifampicin and pyrazinamide combined was significantly more often discontinued compared to treatment with rifampicin and isoniazid combined. Withdrawals due to adverse reactions were also higher with rifampicin and pyrazinamide combined compared to the other therapies, and resulted in more dropouts due to rash compared with isoniazid only and in combination with rifampicin. No significant differences between the treatment regimens were found regarding development of TB. In another study, 113 inmates with an indication for LTBI treatment were offered 6- or 12-month treatment with isoniazid (Martin 2000 [46], very low level of evidence). Treatment was under DOT or medication was delivered weekly. Overall, 74.3% started treatment, and 46.4% completed treatment. Of those who received treatment, 27.4% were still on treatment at the end of the study. Using the Eidus-Hamilton test, it was estimated that 95.7% of patients still on treatment were adherent, while one patient not on DOT was not adherent.

Treatment initiation, treatment completion and treatment effectiveness in non-EU/EEA countries

Eleven studies from the USA were found that reported on LTBI treatment in correctional facilities. These studies investigated different drugs, treatment regimens, treatment timing (during and/or after imprisonment), with or without adherence interventions, and with or without DOT. It is difficult to determine the effect of each of these treatment factors due to the fact that they were often investigated only in combination and could therefore not be examined separately. In a few studies within-study comparisons were made which showed that the use of DOT increases LTBI treatment completion compared to self-administered treatment (one study), that interventions such as education or active referral after release from jail increase LTBI treatment completion compared to usual care (two studies), and that those treated in jails were less likely to complete LTBI treatment than those in prisons (one study). Two studies compared short-course with long-course LTBI therapy. One of the two studies reported a significantly higher completion rate among those on short-course therapy, while the other one did not find a significant difference.

The EU/EEA studies mentioned above are described below in more detail because the results should be viewed in light of different study settings, treatment factors (medication, dosage, duration, DOT and other methods used to improve treatment adherence), and populations. The study results are categorised by: 1) comparison inside versus outside correctional facility, 2) inside correctional facility only, 3) outside correctional facility only, 4) no adherence intervention (excluding DOT).

1) In two of the eleven studies, an LTBI treatment adherence intervention inside jail was compared with one outside jail. In one study, inmates receiving six months of isoniazid under DOT received one informational one-to-one TB session in addition to either TB education in jail (education group), incentives after release (voucher for food/transportation received at TB clinic; incentive group), or nothing else (usual care group) (White 2002 [47], moderate level of evidence). Treatment completion rates outside jail were 23%, 12%, and 12%, respectively. The treatment completion rate was significantly higher for the education group versus the usual care group, but not significantly different for the incentive group versus the usual care group. The pooled rates of patients (education group plus incentive group) who, after their release, visited a TB clinic were significantly higher than the rate in the
usual care group. Another study was a follow-up study of the above study (White 2005 [48], low level of evidence). Inmates who received six months isoniazid in jail and were released before completion were divided in two groups: group 1 received an additional informational one-to-one TB session in 1998–1999, and attempts were made to contact them >30 days after release; group 2 received a course of TB treatment in 2002–2003, with no attempts to contact them (usual care). The completion rates outside jail were significantly higher for the first group compared with the second group (16.3% and 7.9%, respectively).

2) In one outbreak study from the USA, an LTBI treatment adherence intervention was used inside prison only (Spradling 2002 [37], very low level of evidence). HIV-infected inmates, for whom active TB was excluded, but who were exposed to a source case, received two months of rifabutin–pyrazinamide under DOT after a TB educational session. Overall, 70.2% completed therapy in prison, and 1.3% developed TB (of whom 67% did not complete/adhere to treatment).

3) Five US studies reported on treatment initiation, completion and/or effectiveness of LTBI treatment using adherence interventions outside the correctional facility. In one study, treatment adherence was compared between inmates receiving either nine months isoniazid or four months rifampicin, both under DOT (White 2012 [49], moderate level of evidence). Incentives after release for both groups were food/transportation vouchers and the availability of a case management team throughout the treatment course. Overall treatment completion rates for isoniazid and rifampicin were 25.5% and 33.3%, respectively (no significant difference). In a survival analysis evaluating time to non-adherence, the following completion rates for isoniazid and rifampicin were found among those remaining in jail for the duration of therapy: 79% and 83%, respectively (no significant difference). This rate was 0% in both treatment groups for those deported or transferred, and 44% and 51% among those who continued treatment after release (no significant difference). In another study, inmates received two months rifampicin + pyrazinamide or 6–12 months isoniazid, depending on the expected incarceration, not using DOT (Lincoln 2004 [50], low level of evidence). Follow-up arrangements were made for inmates still on treatment at release. Overall, 6.8% initiated treatment, of whom 52.4% received rifampicin + pyrazinamide; 47.6% were treated with isoniazid. Overall completion rates were 88.2% for rifampicin + pyrazinamide and 73.9% for isoniazid (significant difference). For those incarcerated during the entire treatment, no significant difference in completion was found between both groups. In a study by Nolan et al., DOT after release was compared with self-administered treatment after release (Nolan 1997 [51], low level of evidence). Inmates with LTBI received isoniazid for 14 days while in jail and for six months outside jail. Patients who were on DOT after their release were visited at least once a week to establish a trusting relationship and to begin to plan for continuing therapy after release. Those on self-administered treatment were instructed to report to the clinic for follow-up of treatment after release. The initiation rate in jail was 64.9%, and after release 40.1% were assigned to DOT, while 19.8% started self-administered therapy. The completion rate outside jail was 60% for the DOT group and 28.8% for the self-administered group, which is a significant difference (rates are overestimated as those directly lost to follow-up after release were not included in the denominator). Bandyopadhyay et al. investigated the completion rate of self-administered isoniazid therapy among inmates with LTBI who were referred to a clinic after release (Bandyopadhyay 2002 [52], very low level of evidence). The completion rate outside prison was 55%. In another study, inmates with LTBI received two months pyrazinamide, under DOT conditions, and were actively referred after release (Bock 2001 [53], very low level of evidence). Treatment completion rates were 48% in those who were in jail for the duration of the treatment and 0% for those released while still on treatment.

4) Three studies used no LTBI treatment adherence interventions. Completion rates ranged from 31.6% among those receiving six months isoniazid not using DOT to 55.9% among those receiving 6 or 12 months isoniazid (depending on HIV status) under DOT conditions. The latter study found that patients treated in jail were significantly less likely than those treated in prison to complete treatment (33.6% versus 57.7%).

In one study, inmates with LTBI received six months isoniazid therapy, not using DOT (White 2005 [54], low level of evidence). Overall completion was 31.6% (inside and outside jail), with 18.9% completion in those only treated in jail. In another study, all jail entrants with LTBI received rifampicin and pyrazinamide using DOT (Lobato 2005 [55], very low level of evidence). Overall, 47.5% completed therapy (inside and outside jail), with 20.9% completion in those that continued treatment after release. In another study by the same author, inmates with LTBI received 6–12 months isoniazid, under DOT conditions; 89.6% initiated treatment, and 55.9% completed treatment (Lobato 2003 [56], very low level of evidence). Patients treated in jail were significantly less likely than those treated in prison to complete treatment (33.6% versus 57.7%), due to the high turnover and shorter stay of inmates in jails.

Cost-effectiveness
One study reported that giving inmates a two-week supply of isoniazid preventive therapy (IPT) at the time of release, with the instruction to follow-up in the community clinic, where six months of self-administered IPT was prescribed for HIV-negative persons and 12 months for HIV-positive persons, would yield a cost savings of USD 9,227 over 4.5 years in addition to the public health benefit (USA, Bandyopadhyay 2002 [52], very low level of evidence).
Acceptability, feasibility and accessibility in EU/EEA countries

In a Spanish study, the most common reasons for non-completion were voluntary withdrawal and adverse reactions (15.8% and 8.8% for isoniazid therapy, and 8.8% and 13.2% for short-course therapies) (Lopez 2011 [45], low level of evidence). In another Spanish study it was reported that of those who did not complete treatment (26.2% of total sample), 90% did so due to discomfort (Martin 2000 [46], very low level of evidence).

Acceptability, feasibility and accessibility in non-EU/EEA countries

Reasons for not initiating LTBI treatment were reported in four US studies (Lincoln 2004 [50] and Nolan 1997 [51], both low level of evidence; Lobato 2003 [56] and Lobato 2005 [55], both very low level of evidence): LTBI treatment was not recommended because patients were older than 35 years (two studies: 90.8% and 40.3%), treatment refusal (two studies: 7.8% and 12.9%), release/transfer of patients (two studies: 16.1% and not reported, but indicated as the main reason), and incomplete evaluation (one study: 17.5%). (Percentages given above refer to people who did not take up treatment as the denominator.)

Reasons for non-completion of LTBI treatment were reported in seven US studies (White 2002 [47], moderate level of evidence; Lincoln 2004 [50] and Nolan 1997 [51], both low level of evidence; Lobato 2005 [55], Lobato 2003 [56], Spradling 2002 [37], Bock 2001 [53], all very low level of evidence). Reasons included adverse events (six studies, range 0.4–14.4%), transferred/moved/pardoned/released inmates (six studies, range 0–44%), people who refused treatment continuation (three studies, range 1.3–6.7%), patients who were lost to follow-up (three studies, range 5.3–59.6%), people still on treatment (one study: 8.8%), patients who did not adhere to treatment despite DOT (one study: 5.8%), change of treatment (one study: 4.9%), and other/unknown factors (one study: 9.5%). (Percentages given above refer to people who did not complete treatment as the denominator.)

Grey literature: conference abstracts and unpublished research reports

No grey literature documents were found that reported on LTBI treatment and care in correctional facilities.

3.2.3 Guidelines on active TB and LTBI

Nine guidelines that reported on the treatment and care of TB were included, six of which were specific to prison settings (three practice-based supranational guidelines [6, 18, 31] and three national guidelines: one evidence-based [57] and two practice-based [30, 58]). The remaining three were not specific to prison settings (all supranational guidelines, one practice-based [29] and two evidence-based [59, 60]).

The table below summarises the relevant recommendations given in these nine documents.

Table 2. Summary of guidelines on TB treatment and care

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Active TB</th>
<th>LTBI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specific to prison setting – supranational guidelines</td>
<td></td>
<td></td>
</tr>
<tr>
<td>USAID, 2009 [18]</td>
<td>The use of fixed-dose combinations is recommended for treatment of all TB cases. The standard treatment regimen recommended for new cases with either pulmonary or extrapulmonary TB consists of two phases: 1) four medicines: rifampicin, isoniazid, pyrazinamide, and ethambutol administered for two months, 2) followed by two medicines: rifampicin and isoniazid for four months. Supervised or DOT for the daily administration of medicines for treatment of all new cases is imperative in prison settings. Previously treated people in prison should be assessed for drug susceptibility as early as possible. Services providing TB care in prisons should offer support to patients to ensure that treatment will be completed. Discharge planning for soon-to-be-released persons is an important part of TB case management to ensure continuity of care. See Appendix 9 for recommendations depending on the availability of types of DSTs.</td>
<td>HIV-infected individuals with LTBI can receive IPT to prevent them from developing active forms of TB. The lack of DST should not preclude programs from implementing IPT. It is crucial, prior to initiating IPT, to rule out active TB. IPT is given daily through self-administration for six to nine months. Discharge planning for soon-to-be-released people in prison is an important part of TB case management. It is essential in ensuring the continuity of TB management and therapy among persons with TB or LTBI.</td>
</tr>
<tr>
<td>WHO, 2014 [6]</td>
<td>In prison settings, a daily treatment is recommended, and the whole process should be under the direct supervision of a healthcare worker. WHO recommends the use of fixed-dose combination drugs as they are thought to improve adherence, errors in prescribing are avoided and the number of tablets to be ingested is reduced. New patients (who have no history of previous TB treatment or who have received anti-TB drugs for less than one month) with pulmonary TB should receive a regimen including six months of rifampicin. In the intensive phase the patient receives isoniazid, rifampicin, pyrazinamide and ethambutol daily for two months, and in the continuation phase isoniazid and rifampicin for four months, it is highly recommended that the resistant pattern of the strains the patient is infected with is documented and the appropriate treatment administered accordingly.</td>
<td></td>
</tr>
<tr>
<td>WHO, 2007 [31]</td>
<td>To ensure that the treatment takes place without interruption, most tuberculosis control programmes have introduced DOT. The progress of treatment is measured after the initial phase at the end of the second month by microscopy of sputum and then again in the continuation phase and at the end of treatment. Treatment is needed for a minimum of six months and often longer, with an initial phase in which four to five drugs are used and a continuation phase in which two to three drugs are used. Second-line drugs, in large quantities and for a very long duration (18 to 24 months), must be administered to people with multidrug-resistant tuberculosis.</td>
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</tbody>
</table>
3.3 Prevention

Results of the peer-reviewed and grey literature searches on the prevention of active TB and LTBI are summarised below (see Appendix 10 for a detailed summary of relevant information). Peer-reviewed literature, conference abstracts and unpublished research reports were only found on the topic of contact tracing during TB outbreaks. No literature on other prevention measures used in prison settings were found, but some of the included guidelines reported on other preventive measures.

**Peer-reviewed literature**

**Coverage, effectiveness and treatment initiation in EU/EEA countries**

Only one study was found that reported on contact tracing after a TB outbreak in the UK (Ahmed 2007 [61], very low level of evidence). In this study, 90.9% of contacts exposed to the index case patient from a training prison initiated treatment. No literature on other prevention measures used in prison settings were found, but some of the included guidelines reported on other preventive measures.

**Coverage, effectiveness and treatment initiation in non-EU/EEA countries**

Eleven US studies reported on contact tracing after a TB outbreak (all very low level of evidence). In five studies, both inmates and employees were screened (Sosa 2008 [62], Bur 2003 [63], Prendergast 1999 [64], Bergmire-Sweat 1996 [65], Schwartz 1992 [66]); in two studies community contacts were also screened (Griffin 2004 [67], McLaughlin 2003 [68]), while in four studies only inmates were screened (Mohle-Boetani 2002 [69], Patterson 2000 [70], Valway 1994 [71], Johnsen 1993 [72]). The percentage of persons screened ranged from 59.3% to 100% [63-68, 70, 71]. TST positivity in tested inmates ranged from 1.6% to 30.1% [62-64, 66, 67, 71], while TST positivity in correctional facility employees ranged from 0% to 10.7% [62, 63, 67, 72]. In one outbreak study, 24.3% of all inmates and prison employees combined had a positive TST [65]. TST conversion in prior TST-negative inmates was reported in six studies; TST conversion rates ranged from 6.7% to 46.6% [63, 66-68, 70, 71].
The TST conversion rate among prison employees was 2.3% [68] and 2.8–4.9% [64], 0% among nursing and medical staff [72], 7.4% among community hospital employees, 25.0% among emergency department employees, and 3.6% among other hospital employees [68]. The positivity rate for active TB determined through contact tracing was reported in seven studies, with a range from 0% to 13.9% among inmates [64, 65, 67, 68, 70-72]. Two studies reported the overall positivity rate for active TB, both for inmates and employees, which was 0% in one study [62] and 2.7% in the second study [63]. For correctional facility employees, the rate was 0% in two studies [64, 67]; the rate could not be calculated in two other studies (one active TB case in each study, percentage not reported; both studies were somewhat dated [65, 71]). The range of LTBI treatment initiation was 25% to 100% [63-65].

**Cost-effectiveness**

No studies in the peer-reviewed literature were found that reported on the cost-effectiveness of TB prevention in correctional facilities.

**Acceptability, feasibility and accessibility**

No studies in the peer-reviewed literature were found that reported on the accessibility, feasibility or acceptability of TB prevention in correctional facilities.

**Grey literature: conference abstracts and unpublished research reports**

**Coverage, effectiveness and treatment initiation in EU/EEA countries**

A study conducted in a prison in Italy reported on TB contact tracing after a case of TB disease was diagnosed [73]. Nine cellmates were tested with TST, seven of whom were positive and received prophylaxis; four completed the treatment. Among the 125 screened section contacts, 55.2% were positive. At 60-day follow-up after identification of the first active TB case, 19.7% of previously negative section contacts tested positive. A study from Bristol, United Kingdom, reported on an outbreak investigation after the diagnosis of active TB in a recently (within four weeks) released person [74]. The contact tracing included 78 individuals from the Bristol prison (30 staff members and 48 inmates). Other contacts outside the prison (n=78) were also screened. The screening method included a questionnaire and IGRA tests. None of the tested contacts were positive and no converters were identified (25 contacts had not completed the follow-up period at the time of the report).

**Cost-effectiveness**

No grey literature documents were found that reported on the cost-effectiveness of TB prevention in correctional facilities.

**Acceptability, feasibility and accessibility**

EU/EEA countries: In the Italian study described above [73], 6% of section contacts refused to be tested and 0.6% were released before testing. At 60-day follow-up, 10.7% refused to be tested, 21.4% were lost to follow up after release, and for 1.8% no information was available. Of the seven TST-positive cellmates who were prescribed prophylaxis, one was lost to follow up, two were released, and one refused the treatment.

**Guidelines**

Nine guideline documents were included that reported on TB prevention, eight of which were specific to prison settings (four supranational practice-based guidelines [6, 18, 31, 75] and four national guidelines, three practice-based [30, 76, 77] and one evidence-based [57]). The remaining guideline was a general guideline document (a supranational practice-based guideline [29]). In contrast to the peer-reviewed and grey literature, the guidelines also reported on preventive measures other than contact tracing.

The table below summarises the relevant recommendations given in these nine documents.

**Table 3. Summary of guidelines on TB prevention**

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Specific to prison setting – supranational guidelines</th>
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</thead>
<tbody>
<tr>
<td>WHO, 2014 [6]</td>
<td>Policy and service delivery areas related to TB infection control may be studied at four levels: 1) programmatic (organisational) control measures, including TB infection control policy development, strategic planning, advocacy, human resource development, monitoring and evaluation, and operational research, 2) administrative control measures, including early TB case detection, TB screening, separation or isolation of patients, and cough etiquette and hygiene, 3) environmental control measures, including natural and mechanical ventilation and ultraviolet germicidal irradiation, personal protection control measures, including respirators and respiratory fit testing. Several infection control measures can be conducted in prisons: intensified TB screening for new or transferred people in prison; preparing special quarantine blocks or cells for new or transferred people in prison; conducting contact investigations for TB suspects and cases; improving infection control by carrying out organisational, administrative and environmental interventions in prisons by using information, education and communication for people in prison; examining people in prison before release; examining prison staff regularly; instituting early TB case detection; and using effective treatment.</td>
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<tr>
<td>Guideline</td>
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<tr>
<td><strong>WHO, 2009 [75]</strong></td>
<td>Prompt identification of people with TB symptoms (i.e. triage) is crucial. People suspected of having TB must be separated from other patients, placed in adequately ventilated areas, educated on cough etiquette and respiratory hygiene, and be diagnosed as a matter of priority. It is also crucial to separate infectious patients after triage. In particular, patients living with HIV, other forms of immunosuppression, or with (or being suspected of having) drug-resistant TB should be separated from those with suspected or confirmed infectious TB.</td>
</tr>
<tr>
<td><strong>WHO, 2007 [31]</strong></td>
<td>Institutional measures to prevent the spread of TB include schedules for ventilating living areas, measures to ensure good heating (while avoiding sealing windows) and allowing people in prison to spend enough time outside. Support for case finding can be an efficient measure for controlling TB.</td>
</tr>
<tr>
<td><strong>USAID, 2009 [18]</strong></td>
<td>Exact same recommendations as WHO, 2014/Dara, 2009, see above.</td>
</tr>
<tr>
<td><strong>Specific to prison setting – national guidelines</strong></td>
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</tr>
<tr>
<td><strong>NICE, 2016 [57]</strong></td>
<td>Any person in prison with high clinical suspicion of pulmonary TB or abnormal chest X-ray with suspicion of TB (both pending the outcome of diagnostic tests), or with confirmed pulmonary smear-positive TB in the first two weeks of treatment (or if non-compliant, for as long as deemed necessary) should be isolated in a single cell as soon as possible (preferably in the healthcare unit if available) and should have a medical assessment as soon as possible. Patients with pulmonary smear-positive TB should be asked to wear a surgical mask when leaving isolation during the infectious period.</td>
</tr>
<tr>
<td><strong>Public Health England, 2013 [30]</strong></td>
<td>Everyone with X-ray changes indicative of active TB, as well as those with symptoms who are awaiting X-ray, should be isolated in an adequately ventilated individual room or cell. People in prison should be retained on medical hold until they have proven smear-negative and had an X-ray that does not suggest active TB, or had a negative risk assessment for MDR-TB and completed two weeks of the standard treatment regimen.</td>
</tr>
<tr>
<td><strong>Spanish government, 2009 [77]</strong></td>
<td>Thirteen recommendations for isolation room conditions are listed, such as that the patient should always be isolated in a single cell, the ventilation system must permit the complete air renewal at least six times per hour, and surgical masks for the patients in isolation must also be available. See Appendix 10 for a complete list of recommendations.</td>
</tr>
<tr>
<td><strong>Dutch Tuberculosis Foundation, 2013 [76]</strong></td>
<td>Measures that should be undertaken before consulting the physician in case of a suspected active TB case are: do not place the person suspected of TB in a cell with others, and approach the person suspected of TB with an appropriate nose and mouth mask. When the physician strongly suspects active TB, direct isolation should take place and further diagnostics should be performed as soon as possible. The person suspected of active TB should be transported wearing a nose and mouth mask. When active infectious TB is confirmed, the patient stays in isolation. Staff directly contacting the patients should wear a nose and mouth mask when entering the cell.</td>
</tr>
<tr>
<td><strong>Other guidelines – supranational guidelines</strong></td>
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<tr>
<td><strong>Migliori, 2012 [29]</strong></td>
<td>All providers of care for patients with TB should ensure that persons who are in close contact with patients who have infectious TB (e.g. in families, congregate settings like migrant shelters, schools and prisons), are evaluated and managed in line with international recommendations. The determination of priorities for contact investigation is based on the likelihood that a contact: 1) has undiagnosed TB; 2) is at high risk of having been infected by the index case; 3) is at high risk of developing TB if infected; and 4) is at risk of having severe TB if the disease develops. Persons of any age with HIV infection who are close contacts of an infectious index patient and who, after careful evaluation, do not have active TB should be treated for presumed latent TB infection with isoniazid.</td>
</tr>
</tbody>
</table>
4. Discussion

4.1 Main findings

This systematic review provides an overview of the best available evidence in the peer-reviewed and grey literature on the diagnosis, care/treatment and prevention of TB in correctional facilities. Below, the main findings from the peer-reviewed literature and grey literature are summarised. The results will be combined with findings from guidelines and expert opinions and will be used to inform an upcoming ECDC guidance document.

4.1.1 Diagnosis

Active TB

No conclusions can be drawn about active TB diagnosis in correctional facilities (no studies were found).

LTBI

Four studies from the peer-reviewed literature (two from the EU/EEA, two from the USA; all four had a very low level of evidence) were found reporting on LTBI diagnosis in correctional facilities. In all four studies, TST and IGRA were compared. As no gold standard for the diagnosis of LTBI exists, no conclusions could be drawn from these studies. No grey literature studies were found.

4.1.2 Treatment and care

Active TB

Treatment initiation, treatment completion and effectiveness

Five studies were included from the peer-reviewed literature and six from the grey literature. Within-study comparisons revealed the following:

- DOT: two studies (one from the EU/EEA, one from the USA; both with a very low level of evidence) compared DOT with self-administered treatment; both concluded that the use of DOT resulted in higher treatment completion rates for active TB.
- Treatment during and/or after imprisonment: one EU/EEA study (very low level of evidence) assessed the effect of the place of treatment and concluded that being treated entirely during a prison stay increased the chance of treatment completion for active TB.

No further within-study comparisons were found. When comparing the results of the individual studies, no clear trends were seen regarding treatment duration or adherence intervention. The included studies investigated diverse sets of factors associated with treatment uptake, adherence, completion and outcome (e.g. different treatment regiments, adherence interventions). It is challenging to determine the relative effect of each single factor, as they were often investigated in combination, were used among different populations, and applied in different settings. It is difficult to determine the effect of each of these treatment factors due to the fact that they were often investigated in combination, were used among different populations, and applied in different settings.

Cost-effectiveness

No cost-effectiveness studies found.

Acceptability, feasibility and accessibility

The most frequently reported reasons for non-completion of active TB treatment were death, transfer/loss to follow-up, and refusal of treatment.

LTBI

Treatment initiation, treatment completion and effectiveness

Two studies from the EU/EEA and eleven studies from the USA were found in the peer-reviewed literature that reported on LTBI treatment in correctional facilities. No grey literature studies were found. Below, the main findings from within-study comparisons are presented:

- DOT: the use of DOT increased completion of LTBI treatment compared with self-administered treatment (one EU/EEA study with a very low level of evidence, one US study with a low level of evidence)
- Adherence intervention: interventions such as education, incentives, or active referral after release increased LTBI treatment completion compared with usual care (two US studies, one with a moderate and one with a low level of evidence)
- Duration of treatment: in two studies, short-course LTBI therapies resulted in higher completion rates compared with long-course therapies (one EU/EEA study, one US study; both with a low level of evidence). In the latter study, this difference was no longer found when only looking at those imprisoned during the
entire treatment. Another US study found no difference in completion rates between short- and long-course LTBI treatment options (moderate level of evidence).

- Type of correctional facility: those treated in jails were less likely to complete LTBI treatment than those in prisons (one US study with a very low level of evidence).

When comparing the results of individual studies, a generally similar effect of DOT and adherence interventions appears to be present. However, due to the heterogeneity of the studies, no conclusions can be drawn based on such between-study comparisons.

**Cost-effectiveness**

No cost-effectiveness results were found.

**Acceptability, feasibility and accessibility**

The most frequently reported reasons for non-completion of LTBI treatment were the occurrence of adverse events, being transferred/moved/paroled/released, refusal of treatment, and loss to follow-up.

### 4.1.3 Prevention

Twelve peer-reviewed literature studies were found reporting on contact tracing during a TB outbreak in a correctional facility (one study from the EU/EEA, the remainder from the USA, all with a very low level of evidence). Moreover, two studies were found in the grey literature reporting on this topic. These were all observational studies, not designed to investigate contact tracing as an intervention. Different strategies were used, and different populations were tested. In all studies, contact tracing led to the identification of new LTBI and/or active TB cases, a large part of which started treatment. Based on these descriptive studies, no conclusions can be drawn regarding whether contact tracing is effective, and who should be tested and when.

### 4.2 Knowledge gaps

#### 4.2.1 General gaps

This systematic review identified a large heterogeneity between studies in both the peer-reviewed and grey literature, making comparisons difficult. More comparative studies are needed on the effectiveness and impact of the different diagnosis, care/treatment and prevention strategies in the EU/EEA. A large part of research comes from the USA, which is not representative of the EU/EEA situation, as the healthcare system, correctional system and population are different. Overall, the level of evidence of the included peer-reviewed literature is quite low. Studies of higher quality and with conclusive evidence are needed as a basis for guidance development.

Topic-specific knowledge gaps are outlined below.

#### 4.2.2 Topic-specific gaps

**Diagnosis**

No studies were found that reported on diagnostic tests for active TB in correctional settings. For LTBI, only four studies were found, half of which from the EU/EEA. As no diagnostic gold standard exists for LTBI, no conclusions can be based on these results. No evidence was retrieved on cost-effectiveness of diagnostic tests for active TB or LTBI in correctional settings. Moreover, no evidence was retrieved on the acceptability, feasibility or accessibility of diagnostic tests for active TB or LTBI in correctional settings.

**Treatment and care**

Hardly any data were available on the effectiveness of active TB treatment and care in prison settings in the EU/EEA. No cost-effectiveness data were available for active TB treatment and care, and for LTBI only one study with limited data on cost-effectiveness was found (not considered a main finding). More comparative studies are needed on DOT versus self-administered treatment or on different adherence interventions.

**Prevention**

No peer-reviewed literature, conference abstracts or unpublished research reports were found on respiratory isolation in correctional facilities. Despite the lack of literature on respiratory isolation in correctional facilities, this measure might still be relevant and is therefore included in several guidelines, despite the lack of documented evidence. No studies were found on the cost-effectiveness of contact tracing. Moreover, no evidence was retrieved on the acceptability, feasibility or accessibility of preventive measures for TB in correctional settings.

### 4.3 Strengths and limitations

The strengths of this systematic review include the use of three peer-reviewed literature databases. A broad search over a long period of time was conducted, not limited by outcomes of interest or language. Additional searches for grey literature, such as guidelines, protocols, conference abstracts and unpublished research reports were
conducted to counterbalance the fact that research on the topic of prisons and health is generally underrepresented in peer-reviewed literature databases. Multiple grey literature sources were searched. Supplemental documents were retrieved by experts (including documents in languages other than English). Four field researchers performed extensive literature searches in their countries.

A rigorous methodology was applied to identify, critically appraise, analyse and summarise the relevant evidence in order to minimise selection and confirmation bias due to preconceived notions. Researchers adhered to international methodological standards such as Cochrane [22] and PRISMA [23]; it also uses the same methodology employed by ECDC during the scoping phase of the project. A multi-sectoral expert panel in the field of prison health, prevention and control of communicable diseases, and guidance development was closely involved during all steps of the review process.

Limitations exist in the area of identified literature. A large number of studies had a descriptive and observational design, which cannot be used to assess effectiveness or causality because of the lack of control groups. Moreover, descriptive studies are subject to certain biases, e.g. a risk of confounding, poor sampling procedures, and loss to follow-up. Only a small number of direct comparative studies were found. Drawing conclusions based on indirect comparisons between studies has serious limitations, as differences in population characteristics, settings, countries, diagnostic methods, treatment regimens, etc. can influence study outcomes. In addition, study characteristics, interventions and outcomes were often poorly described, hampering comparisons. Most studies did not take confounding or modifying factors into account, and making corrections for such factors can substantially influence the results of a study. Many studies were also conducted in only one institution and had relatively small sample sizes, which limits their generalisability. These limitations resulted in the inclusion of studies of mostly low or very low quality. Limitations of each study were added to the evidence tables (see Annexes).

The focus of this report was on EU/EEA countries. Unfortunately, few studies were retrieved from these countries, while the majority of studies came from the USA. While studies from non-EU/EEA countries may be valuable sources of data on TB prevention, care and control interventions, their findings may not be simply extrapolated to the EU/EEA context due to differences in population structure, healthcare delivery, and correctional systems.

Although this review focused on adults, the researchers did not reject studies that included people below 18 years of age. Studies focusing solely on young populations were not included.

As no gold standard for the diagnosis of LTBI exists, no conclusions could be drawn on the accuracy of LTBI diagnostic methods based on the included studies.

It was difficult to determine the factors responsible for the observed treatment outcomes in several studies on TB/LTBI treatment because interventions were often part of a bundle of measures which were not examined separately (i.e. different drugs, different regimens, use of DOT, and different adherence interventions).

Lastly, some studies did not clearly describe whether the focus of the study was on active TB or on LTBI. This meant that it was not always clear whether the population under study had active TB or LTBI, or at which types of TB conditions the therapy was directed.

Study settings varied widely between included studies. In jails, in which persons are generally incarcerated for shorter periods, treatment completion, diagnosis or contact tracing participation is often hampered by the fact that inmates are released or transferred soon after entry. This is less of a problem in prisons, where inmates are incarcerated for longer periods of time. Moreover, jails or prisons tend to be different in different countries (e.g. prison setting, composition of the prison population). Similar settings are therefore not directly comparable between countries. This also applies to healthcare settings, which can differ widely between countries, even within the EU/EEA.

Outcome definitions varied between studies, and were lacking in some studies. This mostly concerned the denominators used for various rates, such as the acceptance rate or treatment completion rate. Where possible, outcome values were recalculated to prevent incorrect comparisons.
5. Conclusions

The overall objective of this project is to develop a series of evidence-based guidance on prevention and control of communicable diseases in prisons. This systematic review focused on the diagnosis, treatment, care and prevention of TB and LTBI, and is meant to inform the production of a guidance document on TB prevention and control in prison settings. This systematic review found a weak evidence base, with few comparative studies and wide variation between studies, but was also able to identify diagnostic methods, treatment regimens, adherence interventions, and contact tracing methods used within the prison setting.

A small number of studies that investigated treatment and care relied on within-study comparisons, providing evidence that DOT results in higher treatment completion rates for both active TB and LTBI in prison settings. Other factors that increased treatment completion were: treatment completed during a prison stay (active TB), short-course therapies (LTBI), and type of correctional facility (LTBI). Education, incentives, or active referral after release also increased LTBI treatment completion.

This systematic review highlights important knowledge gaps. More operational research is needed to assess the (cost) effectiveness of diagnostics, treatment options, adherence to interventions, and prevention strategies. Ideally, future studies should compare different strategies and interventions so that differences in the results can be easily traced back to specific elements of a strategy or intervention. This review also showed the value of grey literature as a source of evidence on TB prevention, care and control interventions in prison settings in the EU/EEA. Sharing knowledge and experiences between EU/EEA countries may be a useful approach to stimulate research on this topic and to promote good practices in the region.

6. Next steps

The findings of this systematic review will serve as the evidence base for the development of an ECDC public health guidance document on the diagnosis, treatment, care and prevention of TB in prison settings. This guidance will be part of a broader set of guidance documents on the prevention and control of communicable diseases in prison settings, which will also encompass other interventions such as active case finding, vaccination, and specific methods for disease prevention and control.
References


Appendix 1. Search and selection strategy for MA1, MA2 and MA3

This appendix covers the general methodology used for all three macro areas (MA). It is important to get an overview of this overall process since the search and selection phases were carried out jointly for all three MAs. This appendix is attached to each one of the systematic review reports of each individual MA, while in the methods section of the systematic review reports only information relevant to a specific MA, and a summary of the process is presented.

1. Review objectives and questions

The following three review objectives were defined:

**Macro area 1: Active case finding**

To gain insight in the evidence base (peer-reviewed as well as grey literature) for active case finding (i.e. at admission and during stay) for communicable diseases in prisons, jails and other custodial settings which function as prisons.

**Macro area 2: Vaccination**

To gain insight in the evidence base (peer-reviewed as well as grey literature) for vaccination (i.e. at admission and during stay) against communicable diseases in prisons, jails and other custodial settings which function as prisons.

**Macro area 3: TB prevention and care**

To gain insight in the evidence base (peer-reviewed as well as grey literature) for diagnosis, treatment, care and prevention of TB in prisons, jails and other custodial settings which function as prisons.

The PICO method was used to develop specific research questions from these review objectives.

### 1. Active case finding for selected communicable diseases at entry and during prison stay

<table>
<thead>
<tr>
<th>P</th>
<th>Adult individuals (≥18 years) in prison settings (i.e. those detained and those who work in prison settings (‘going through the gate’))</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Active case finding for communicable diseases at entry and during prison stay</td>
</tr>
</tbody>
</table>
| C | • Comparison with no intervention;  
  • Comparison with alternative intervention;  
  • No comparison;  
  • Comparison between populations in prison settings (e.g. between different prison types, risk groups, etc.);  
  • Comparison with community setting |
| O | Qualitative outcomes:  
  • Accessibility  
  • Feasibility and acceptability of active case finding at entry and during prison stay  
  • Qualitative description of interventions/modes of service delivery  
  Quantitative outcomes:  
  • Uptake (number of persons screened)  
  • Positivity rate  
  • Measures of effectiveness (e.g. change in communicable disease incidence or prevalence)  
  • Cost-effectiveness |
| S | Prisons, jails and other custodial settings with a function as prison (excluding migrant centres and police detention rooms) |

### 2. Vaccination interventions, including vaccination at entry and in outbreak situations

<table>
<thead>
<tr>
<th>P</th>
<th>Adult individuals (≥18 years) in prison settings (i.e. those detained and those who work in prison settings (‘going through the gate’))</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Vaccination against communicable diseases at entry and during prison stay (including outbreak situations)</td>
</tr>
</tbody>
</table>
| C | • Comparison with no intervention;  
  • Comparison with alternative intervention;  
  • No comparison;  
  • Comparison between populations in prison settings (e.g. between different prison types, risk groups, etc.);  
  • Comparison with community setting |
| O | Qualitative outcomes:  
  • Accessibility  
  • Feasibility and acceptability of vaccination at entry and during prison stay  
  • Qualitative description of interventions/modes of service delivery  
  Quantitative outcomes:  
  • Acceptance/uptake (number of persons vaccinated) |
For each of these macro areas specific review questions were defined and formulated:

**Macro area 1: Active case finding**
1. What are the communicable diseases that should be covered by active case finding?
2. Which types of active case finding methods are effective?
3. Which service models of active case finding are effective?
4. Which types of active case finding methods are cost-effective?
5. Which service models of active case finding are cost-effective?
6. What is the uptake of active case finding?
7. How to improve the uptake of active case finding testing?
8. Who should be targeted for active case finding, when and how often?

**Macro area 2: Vaccination**
9. What are the communicable diseases that should be covered by vaccination?
10. Which vaccination interventions are effective?
11. Which service models of vaccination are effective?
12. Which vaccination interventions are cost-effective?
13. Which service models of vaccination are cost-effective?
14. What is the acceptance/uptake of vaccination?
15. How to improve the acceptance/uptake of vaccination?
16. Who should be targeted for vaccination?

**Macro area 3: TB prevention and care**
17. Which prevention interventions for TB are effective?
18. Which care and/or treatment interventions aimed at control of TB are effective?
19. Which service models for prevention, diagnosis, care and/or treatment of TB are effective?
20. Which prevention interventions for TB are cost-effective?
21. Which diagnosis, care and/or treatment interventions aimed at control of TB are cost-effective?
22. Which service models for prevention, diagnosis, care and/or treatment of TB are cost-effective?
23. What is the uptake of prevention, diagnosis, care and/or treatment of TB?
24. How to improve the uptake of prevention, diagnosis, care and/or treatment of TB?
25. Who should be targeted for prevention, diagnosis, care and/or treatment of TB?

2. Peer reviewed literature search

The search strategy was developed building on the scoping phase by ECDC with respect to using PubMed and Embase as peer-reviewed data sources. Additionally, the Cochrane Library database was searched for systematic reviews and economic evaluations.

Search strings

In order to find relevant articles for the macro areas in PubMed and Embase, search strings were developed for each of the following concepts:

- Prisons, jails and other custodial settings
- Active case finding
- Vaccination
- TB prevention and care

It was decided not to add a search string on outcomes, to prevent missing relevant articles. In PubMed and Embase search string #1 was combined using ‘AND’ with each of the macro area specific search strings (i.e. #1 AND (#2 OR #3 OR #4)).

For Cochrane Library one generic search using the terms for prisons was used to search for all relevant systematic reviews and economic evaluations.

**PubMed**

#1 Prisons and other custodial settings


#2 Active case finding


#3 Vaccination


#4 TB prevention and care


**Embase**

#1 Prisons and other custodial settings

'prison'/exp OR 'prisoner'/exp OR prison*:ti,ab OR penal:ti,ab OR jail*:ti,ab OR reformator*:ti,ab OR custodial:ti,ab OR custody:ti,ab OR gaol*:ti,ab OR remand*:ti,ab OR penitentiary*:ti,ab OR detention*:ti,ab OR correctional*:ti,ab OR detainee*:ti,ab OR inmate*:ti,ab OR imprison*:ti,ab OR confinement:ti,ab OR incarcerate*:ti,ab OR cellmate*:ti,ab

#2 Active case finding

'mass screening'/exp OR 'screening test'/exp OR 'screening'/de OR 'mandatory testing'/exp OR screen*:ti,ab OR 'case finding'/exp OR 'case finding':ti,ab OR 'case-finding':ti,ab OR casefinding:ti,ab OR 'cases finding':ti,ab OR 'cases identification':ti,ab OR 'cases identification':ti,ab OR testing:ti,ab OR 'rapid test':ti,ab OR 'rapid tests':ti,ab OR
Systematic review on the diagnosis, treatment, care and prevention of tuberculosis in prison settings

'Systematic review on the diagnosis, treatment, care and prevention of tuberculosis in prison settings'

From the articles retrieved from PubMed, Embase

Reference lists of good quality systematic review articles were checked for further potential relevant articles. The only search limit that was applied for this systematic review is a time limit: literature was searched in PubMed and Embase from 1990 onwards for macro area I (active case finding) and III (TB prevention and care), and from 1980 for macro area II (vaccination). In Cochrane Library, systematic reviews and economic evaluations were searched from 1980 onwards for all three macro areas.

Language limits were not applied. Additionally, age and geographical limits were not applied in the search phase. Moreover, only articles that were performed in EU/EEA (candidate) countries or in the United States of America (USA), Canada, Australia or New Zealand were included (see section 2.4.6). Articles from these non-EU/EEA high-income countries were included to broaden the evidence base.

Running the literature search

The final searches in PubMed, Embase and Cochrane Library were run on 4 February 2016. Due to overlap between the three macro areas, the search strings were combined in a single search. The relevant full text publications were subdivided into the three separate macro areas during the screening of full article phase.

PubMed, Embase, and Cochrane Library output, including all indexed fields per hit (e.g. title, authors, abstract), were exported to Endnote version X7.4 and saved in separate folders per database. Duplicate articles were removed through automatic and manual duplicate removal.

Hand search

Reference lists of good quality systematic review articles were checked for further potentially relevant articles.

3. Peer reviewed literature selection

From the articles retrieved from PubMed, Embase, and Cochrane Library the relevant references were selected by a three-phase selection procedure, based on:

- Screening of title and abstract (first selection phase): in this phase, titles of publications were screened based on the inclusion and exclusion criteria (see section 2.4.7). If the title was inconclusive, the abstract was read. Articles with titles and abstracts that suggest that they did not contain information relevant to the review objectives were not selected for full text assessment (no reason for exclusion documented per article). In case of doubt, the article was checked full-text in the second selection step. Articles that were excluded during screening of title and abstract were stored in an indexed folder in Endnote.
- Screening of full article (second selection phase): the articles selected during the first phase were assessed in full text. PDF-files of the original articles were downloaded and stored. Articles were included if the reported information was relevant (based on the inclusion and exclusion criteria, see section 2.4.7) and of sufficient quality (see section 2.4.8). The reasons for exclusion of full text papers were documented per article and summarised in an exclusion table.
• Screening during data-extraction phase: further scrutiny of the article during the data-extraction phase could have led to exclusion. For example, when articles make use of the same dataset and present identical outcome measures, the most recent or the most extensive article was included.

The process of selection and inclusion and exclusion of articles was registered in an Excel file and an Endnote library.

**Inclusion and exclusion criteria**

The inclusion and exclusion criteria are listed in Table 1 below.

**Table A-1. Inclusion and exclusion criteria peer-reviewed literature**

<table>
<thead>
<tr>
<th>Inclusion</th>
<th>Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Study design/type</strong></td>
<td></td>
</tr>
<tr>
<td>Meta-analysis or systematic review⁴</td>
<td>Narrative review</td>
</tr>
<tr>
<td>Randomised controlled trials (RCTs)</td>
<td>Case reports</td>
</tr>
<tr>
<td>Non-randomised, prospective comparative studies</td>
<td>Non-pertinent publication types (e.g. expert opinions, letters to the editor, editorials, comments, conference abstract/poster, news, consensus document, chapter)</td>
</tr>
<tr>
<td>Prospective observational studies (e.g. cohort studies)</td>
<td>Animal studies</td>
</tr>
<tr>
<td>Retrospective observational studies (e.g. case-control studies)</td>
<td>Genetic studies, biochemistry or molecular studies</td>
</tr>
<tr>
<td>Cross-sectional studies</td>
<td>Modelling studies (i.e. this did not apply to economic evaluation studies)</td>
</tr>
<tr>
<td><strong>Study quality</strong></td>
<td></td>
</tr>
<tr>
<td>Study duration (no minimum)</td>
<td>Insufficient methodological quality (both inherent methodology as well as insufficient description of inherent methodology provided; based on quality checklists)</td>
</tr>
<tr>
<td>Number of subjects (no minimum)</td>
<td></td>
</tr>
<tr>
<td><strong>Study population</strong></td>
<td></td>
</tr>
<tr>
<td>Adults in prisons, jails and other custodial settings that function as a prison</td>
<td>Children (&lt;18 years)</td>
</tr>
<tr>
<td>Detained persons, including persons in remand custody</td>
<td>Persons in police custody</td>
</tr>
<tr>
<td>Persons ‘going through the gate’ (e.g. prison guards, healthcare workers, etc.)</td>
<td>Persons in migrant detention centres</td>
</tr>
<tr>
<td><strong>Geographical area</strong></td>
<td></td>
</tr>
<tr>
<td>EU/EEA + candidate countries, EFTA and other high-income countries (i.e. USA, Canada, Australia, New Zealand)</td>
<td></td>
</tr>
<tr>
<td><strong>Study comparison</strong></td>
<td></td>
</tr>
<tr>
<td>Comparison appropriate for a specific outcome</td>
<td>Clinical studies on efficacy or effectiveness of vaccination with other comparisons than no vaccination as control (e.g. vaccines for other diseases)</td>
</tr>
<tr>
<td>Clinical studies on efficacy or effectiveness of vaccination with no vaccination as control</td>
<td></td>
</tr>
<tr>
<td><strong>Specific outcomes of interest</strong></td>
<td></td>
</tr>
<tr>
<td>Quantitative outcomes</td>
<td>No exclusion based on outcomes</td>
</tr>
<tr>
<td>Qualitative outcomes</td>
<td></td>
</tr>
</tbody>
</table>

⁴High-quality meta-analyses or systematic reviews were included in case they matched the review objectives. If not, the relevant individual articles from these meta-analyses/systematic reviews were checked. If an individual article reported new and relevant data and the study was of sufficient quality, it was included.

**4. Grey literature search**

A grey literature search with a focus on EU/EEA countries was performed to complement the evidence from the peer-reviewed literature. Reports and documents focusing on prisons and people in prisons were searched for.

The following types of documents were searched for:

- Articles, abstracts, research reports
- Guidelines and protocols
- Case studies, service models

This grey literature search comprised the following sources:

- A pre-defined list of websites
- Call for papers/experts input

**Search on websites of conference abstracts**

In order to capture studies not published yet in peer-reviewed literature, conference abstracts published in the last five years (i.e. from 2010 onwards) were searched for on all the following websites of relevant congresses:

- International Union for Tuberculosis and Lung Disease (http://www.theunion.org/)
- European Respiratory Society (http://www.ersnet.org/)
Search on other websites

The following sources were searched for other grey literature documents published in the last ten years (i.e. from 2005 onwards):

Guidelines:
• Guidelines International Network (http://www.g-i-n.net/)
• NICE guidelines (https://www.evidence.nhs.uk/)

Organisations and institutes:
• WHO – Health in prisons programme (HIPP) (http://www.euro.who.int/prisons)
• WHO – EU (http://www.euro.who.int/en/home)
• WHO – IRIS (http://apps.who.int/iris/)
• Council of Europe/POMPIDOU Group (http://www.coe.int/T/DG3/Pompidou/AboutUs/default_en.asp), and other Council of Europe documents
• UNODC (http://www.unodc.org/)
• ECDC (http://ecdc.europa.eu/en/Pages/home.aspx)
• Public Health England (PHE) – (http://www.gov.uk)
• European Monitoring Centre for Drugs and Drug Addition (EMCDDA) (http://www.emcdda.europa.eu/)
• International Corrections and Prisons Association (ICPA, http://icpa.ca/)

Bibliographies
• Campbell Collaboration (http://www.campbellcollaboration.org/)
• Bibliography on HIV/AIDS and Hepatitis C in prisons (http://www.aidslaw.ca/)
• IDEAS (https://ideas.repec.org/)
• Evidence in Health and Social Care (NHS Evidence, https://www.evidence.nhs.uk/)
• Open grey (http://www.opengrey.eu)

Conduct of the main search on pre-defined websites and corresponding search terms

The main search for grey literature on the pre-defined websites was performed by two senior researchers. The main search was performed in English. On each website, a more general search was conducted at first using only terms for prisons (i.e. prison, jail, correctional, incarcerated). If this resulted in many hits, a more specific search was performed by combining the prison terms with ‘infectious diseases’, ‘screening’/’case finding’, ‘vaccination’ and ‘tuberculosis’. In case a website was only focused on prison populations, only this latter search was performed.

Expert input

In addition to the search on pre-defined websites, expert input was used in the form of:
• A search for documents conducted by field researchers of the HWBs Federation Network
• A ‘call for paper’ issued to experts contacted via the HWBs Federation Network and members of the ECDC expert panel

See Appendix 6 for more details.

Activities of field researchers

Five national field researchers and infectious diseases specialists were identified within the HwBs network, one for each of the EU/EEA countries represented in the Federation, namely France, Germany, Italy, the Netherlands and Spain. The field researchers conducted a search for national guidelines, protocols (clinical/intervention), and unpublished research reports relevant to the objectives (based on the inclusion and exclusion criteria, Section 2.5.4); documents written in English or in other EU/EEA languages were searched. This was done by searching the national websites of HWBs member organisations:
• SIMSPe-Onlus: Italian Society for Prison Health and Medicine (http://www.sanitapenitenziaria.org/);
• APSEEP: Association des Professionnels de Santé Exerçant en Prison (http://www.sante-prison.com/fr/);
• NAPDUK: National Association of Prison Dentistry UK (http://www.napduk.org/);
Call for paper

A 'call for paper' was issued to stakeholders in the field by the selected national field researchers, via e-mail. The grey literature search officially started on 18 April 2016, with an official letter and call to the researchers sent by HWBs' Secretariat. After two weeks from the start, an e-mail reminder was sent out. If clarifications or additional details were needed, the respective national contact point was contacted. The call was also shared with the ECDC expert panel members.

The initial deadline was set on 2 May 2016. However, due to the low number of contributions received in particular on MA 2, the replacement of some field researchers and the possibility to collect further documents by the panel members, the definitive deadline for the collection of documents was extended to 30 June 2016.

The call targeted stakeholders, service providers or technical experts working in the field to submit additional documents including abstracts, national guidelines, protocols, unpublished research reports and/or intervention case studies/service models regarding the three macro areas. For the latter, a short pre-defined format was provided to collect clearly described accounts of their intervention/service model related to the relevant macro areas.

5. Grey literature selection

All retrieved documents were reviewed by two researchers. Documents were included if the reported information was relevant and of sufficient quality (see inclusion and exclusion criteria below). A record was kept of the reasons for exclusion of documents screened in full text.

Inclusion and exclusion criteria

Table A-2. Inclusion and exclusion criteria grey literature

<table>
<thead>
<tr>
<th>Period of publication</th>
<th>Inclusion</th>
<th>Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conference abstracts: from 2005 onwards</td>
<td>Document without a clear source/reference for the relevant information</td>
<td></td>
</tr>
<tr>
<td>Other documents: from 2010 onwards</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Type of document</th>
<th>Inclusion</th>
<th>Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guidelines</td>
<td>Published article</td>
<td></td>
</tr>
<tr>
<td>Intervention or clinical protocols</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unpublished research results</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Case studies/service models, including measures of effectiveness</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Document quality</th>
<th>Inclusion</th>
<th>Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Only grey literature documents with a methods section or an overview of sources.</td>
<td>Children (&lt;18 years)</td>
<td></td>
</tr>
<tr>
<td>Document without a clear source/reference for the relevant information</td>
<td>Persons in police custody</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Persons in migrant centres</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Document population</th>
<th>Inclusion</th>
<th>Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults in prisons, jails and other custodial settings that function as a prison</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Detained persons, including persons in remand</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Persons ‘going through the gate’ (e.g. prison guards, healthcare workers, etc.)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subject of the document</td>
<td>Inclusion</td>
<td>Exclusion</td>
</tr>
<tr>
<td>Active case finding for communicable diseases at entry and during prison stay</td>
<td>No exclusion based on outcomes</td>
<td></td>
</tr>
<tr>
<td>Vaccination against relevant communicable diseases at entry and during prison stay (including outbreak situations)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prevention, diagnosis, treatment and care of TB</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Geographical area</th>
<th>Inclusion</th>
<th>Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>EU/EEA</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Specific outcomes of interest</th>
<th>Inclusion</th>
<th>Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quantitative outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Qualitative outcomes</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Guidelines selection

Guidelines were selected in a three-step approach. First, only prison-focused guidelines were searched for relevant information. However, when there was not sufficient information on certain review objectives coming from these prison-focused guidelines, guidelines that have a relevant section on prisoners were searched for relevant information. To include such guidelines, multiple transparent sources should have been stated for the prisoner group and a recommendation for this specific group should have been made. In case there was still a lack of information on a certain topic, general population guidelines were reviewed for relevant information.
### Appendix 2. Quality appraisal checklists other than NICE

#### Cross-sectional study

<table>
<thead>
<tr>
<th>Author</th>
<th>Countries</th>
</tr>
</thead>
</table>

**Internal validity**

- The study addresses an appropriate and clearly focused question
- The study population is clearly described
- The population is a representative sample of the source population
- The outcome measures are described
- The assessment of outcome is made blind to exposure status
- Where blinding was not possible, there is some recognition that knowledge of exposure status could have influenced the outcome assessment
- Exposure status is measured in a standardised, valid and reliable way
- The measurement of outcome is clearly described (e.g., written questionnaire, face-to-face interview, internet survey)
- The main potential confounders are identified and taken into account in the design and analysis
- Comparison is made between participants and non-participants to establish their similarities/ differences
- Confidence intervals are provided
- If study is carried out at more than one site, results are comparable for all site

**Overall assessment of the study**

- How well was study done to minimize confounding/ bias, and to establish a causal relationship?
- If coded + or -, what is the likely direction in which bias might affect the study results?
- Was the likelihood of bias due to measuring exposure and outcome at the same moment, taken into account by the authors?
- Are you certain that the overall effect is due to the exposure being investigated?
- Are the results of the study applicable to the patient group targeted in the search question?

**Comments**

- Include or exclude?
- If exclusion, give reason

#### Surveillance study

<table>
<thead>
<tr>
<th>Author</th>
<th>Countries</th>
</tr>
</thead>
</table>

**Internal validity**

- The study addresses an appropriate and clearly focused question
- The population being studied is selected from a data source that is representative for the overall population of interest
- The outcomes are clearly defined
- The outcomes are clearly defined
- The main potential confounders are identified and taken into account in the design and analysis

**Additional questions**

- Are epidemiological outcomes described that can be used in this review, e.g. incidences or rates per 100,000 or proportion of cases?
- Is the study population large enough to be a representative sample of the source population?
- Is the disease of interest the main subject of the paper?
- Are the outcomes of the study based on observed cases (and not on assumptions or models?)
- The surveillance period is long enough to detect new cases and to accurately calculate prevalence/ incidence rates

**Overall assessment of the study**

- Are the results valid?
<table>
<thead>
<tr>
<th>Are the results applicable to the population targeted in the search question?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comments</td>
</tr>
<tr>
<td>Include or exclude?</td>
</tr>
<tr>
<td>If exclusion, give reason</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other research (applied to outbreak studies)</th>
<th>Code as - - / - / + - / + / ++ or NA if not applicable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Author</td>
<td></td>
</tr>
<tr>
<td>Countries</td>
<td></td>
</tr>
</tbody>
</table>

**Internal validity**
- The study addresses an appropriate and clearly focused question
- The study population is clearly described
- The population is representative of the source population
- Exposure status is measured in a standardised, valid and reliable way
- The outcomes are clearly defined
- Variation (e.g. range, SD) in outcome of interest is provided
- The diagnosis of interest is the main subject of the paper

**Overall assessment of the study**
- Are the results valid?
- Are the results applicable to the population targeted in the search question?

**Comments**
- Include or exclude?
- If exclusion, give reason
Appendix 3. Expert panel members and ECDC/EMCDDA staff

Expert panel members

<table>
<thead>
<tr>
<th>Name</th>
<th>Organisation</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barbara Janíková</td>
<td>Government of Czech Republic</td>
<td>Czech Republic</td>
</tr>
<tr>
<td>Kristel Kivimets</td>
<td>Ministry of Justice</td>
<td>Estonia</td>
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<tr>
<td>Fadi Meroueh</td>
<td>Association des Professionnels de Santé Exerçant en Prison</td>
<td>France</td>
</tr>
<tr>
<td>Heino Stöver</td>
<td>HA-REACT</td>
<td>Germany</td>
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<tr>
<td>Peter Wiessner</td>
<td>Action Against AIDS and EATG</td>
<td>Germany</td>
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<tr>
<td>Ruth Zimmerman</td>
<td>Robert Koch Institute</td>
<td>Germany</td>
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<tr>
<td>Roberto Ranieri</td>
<td>Società Italiana di Medicina e Sanità Penitenziaria</td>
<td>Italy</td>
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<tr>
<td>Lucia Mihaiescu</td>
<td>Formerly with Romanian National Administration of Penitentiaries</td>
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<td>Jose-Manuel Royo</td>
<td>General Secretariat of Penitentiary Institutions</td>
<td>Spain</td>
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<tr>
<td>Stefan Enggist</td>
<td>Federal Office of Public Health</td>
<td>Switzerland</td>
</tr>
<tr>
<td>Eamonn O’Moore</td>
<td>Public Health England</td>
<td>UK</td>
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<td>Alison Hannah</td>
<td>Penal Reform International</td>
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<td>Jan Malinowski</td>
<td>Council of Europe</td>
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<tr>
<td>Lars Moller</td>
<td>WHO</td>
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</tr>
<tr>
<td>Ehab Salah</td>
<td>United Nations on Drugs and Crime</td>
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ECDC and EMCDDA staff who attended expert panel meetings

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<thead>
<tr>
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<tr>
<td>Dagmar Hedrich</td>
<td>EMCDDA</td>
</tr>
<tr>
<td>Andrew Amato</td>
<td>ECDC</td>
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<tr>
<td>Netta Beer</td>
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<td>Ida Czumbel</td>
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<tr>
<td>Erika Duffell</td>
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<td>Teymur Noori</td>
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<td>Kate Olsson</td>
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<tr>
<td>Anastasia Pharris</td>
<td>ECDC</td>
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<td>Pasi Penttinen</td>
<td>ECDC</td>
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<td>Jan Semenza</td>
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<td>Ettore Severi</td>
<td>ECDC</td>
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<tr>
<td>Gianfranco Spiteri</td>
<td>ECDC</td>
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<tr>
<td>Judit Takas</td>
<td>ECDC</td>
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<tr>
<td>Lara Tavoschi</td>
<td>ECDC</td>
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<tr>
<td>Marieke van der Werf</td>
<td>ECDC</td>
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Appendix 4. Exclusion table peer-reviewed literature and corresponding reference list

Exclusion table second selection step

<table>
<thead>
<tr>
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<td>[1-137]</td>
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<tr>
<td>Non-pertinent publication types (n=81)</td>
<td>[138-218]</td>
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<td>Narrative reviews (n=74)</td>
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<td>[293-327]</td>
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<tr>
<td>Insufficient (description of) methodology (n=35)</td>
<td>[328-362]</td>
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<tr>
<td>Duplicate articles (n=18)</td>
<td>[363-380]</td>
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<tr>
<td>Already included in another systematic review (n=15)</td>
<td>[381-395]</td>
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<tr>
<td>Incorrect setting (n=15) (e.g. police detention centre, or juvenile detention centre)</td>
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<tr>
<td>Not country of interest (n=7)</td>
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<tr>
<td>Modelling studies (n=2)</td>
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<tr>
<td>Children (n=1)</td>
<td>[420]</td>
</tr>
<tr>
<td>More recent data available (n=1)</td>
<td>[421]</td>
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</table>

Reference list of excluded articles during second selection step

17. Bellin EY, Fletcher DD, Safyer SM. Association of tuberculosis infection with increased time in or admission to the New York City jail system. JAMA. 1993;269(17):2228-31.

41


142. Improving TB control in prisons may lead to better national programmes. BMJ (clinical research ed). 2000;320(7232):G.


146. Prevention and control of tuberculosis in correctional and detention facilities: recommendations from CDC. Endorsed by the Advisory Council for the Elimination of Tuberculosis. MMWR Recommendations and reports : Morbidity and mortality weekly report Recommendations and reports / Centers for Disease Control. 2006;55(Rr9):1-44.


Systematic review on the diagnosis, treatment, care and prevention of tuberculosis in prison settings


190. Linas BP, Wong AY, Freedberg KA, Horsburgh CR. The cost effectiveness of tuberculin skin test and interferon gamma release assay screening for latent tuberculosis infection in the U.S. American Journal of Respiratory and Critical Care Medicine. 2011;183(1).


211. Strike C, Watson TM, Gohil H, Miskovic M, Robinson S, Arkell G, et al. Best practice recommendations for Canadian harm reduction programs that provide service to people who use drugs and are at risk for HIV, HCV, and other harms-part 2: Service models, referrals for services, and emerging areas of practice. Canadian Journal of Infectious Diseases and Medical Microbiology. 2015;26:92B.


220. [The role of institutions for the prevention of tuberculosis: organization, relation with the DDASS (Regional Public Health System), and physicians]. Medecine et maladies infectieuses. 2004;34(8-9):354-7.


Appendix 5. Peer-reviewed literature references that could not be retrieved in full text


Appendix 6. Report on field search for grey literature

Field researchers

A field researcher was appointed through Health Without Barriers in each of the following countries where the federation is active, namely UK, Germany, Spain, France and Italy. Several attempts have been made to find a field researcher for the Netherlands, through an e-mail exchange with Dr Michel Westra (member of HWBs) and Dr Kim van Rooy.

The European field researchers appointed as responsible for each country were:

- Ruth Gray, United Kingdom
- Sofia Victoria Casado Hoces, Spain
- Leon Weichert, Germany
- Deborah Iwanikow, France
- Giordano Madeddu, Italy

Materials

The grey literature research officially started on 18th April 2016, with an official letter and call to the researchers sent by HWBs’ Secretariat. The definitive deadline for the collection of materials regarding the first three macro areas (active case finding, vaccination and TB) was settled on 30th June 2016. A call for paper (see below) was issued by HwB and translated in the relevant language by the field researcher. It was up to the field researcher whether to work in team with any other expert they wished to involve, or to perform the research on their own.

Results

The following are the results concerning the first three selected Macro areas:

1. UK
The batch of documents has been received on 10th May 2016. A total of 37 documents have been sent to HWBs.

2. Spain
The batch of documents has been received on 28th April 2016. A total of 93 documents have been sent to HWBs.

3. Germany
The batch of documents has been received on 24th May 2016. A total of 18 documents have been sent to HWBs. The fact that the prison healthcare system in Germany is not managed by central headquarters, instead is handled by the single Länder, has affected negatively the research.

4. France
The batch of documents has been received on 6th June 2016. A total of five documents have been sent to HWBs.

5. Italy
The batch of documents has been received on 24th April 2016. A total of 62 documents have been sent to HWBs.

Call for papers

This guidance will support Field Researchers work in researching and collecting relevant Grey Literature documents in the following prioritized macro areas:

- Active case finding for selected communicable diseases at entry and during prison stay;
- Vaccination strategy, including vaccination for selected communicable diseases at entry and in outbreak situations;
- Prevention, diagnosis, care and treatment of TB.

Who is the focus?

Prison population: adult people aged 18 years or older in prison settings (i.e. those detained or in remand and those ‘going through the gate’).
Systematic review on the diagnosis, treatment, care and prevention of tuberculosis in prison settings

**Which is the setting?**

Prison setting: prisons and other custodial settings which function as prison excluding migrant centers and police detention rooms.

**Key issues and scoping questions**

The key issues and scoping questions will be useful to guide the systematic review of the grey literature.

Macro area 1

Key issue: Active case finding: routine and provider initiated offer for testing, at entry and during stay in prison settings.

Scoping questions
- What are the diseases you actively screen for in prison?
- When do you screen for these diseases (at entry, during detention)?
- What types of active case finding do you use (i.e. universal screening, opt-out or opt-in strategy, high risk group screening, provider-directed)?
- Which types of interventions do you use to increase the rate of active care finding?
- What interventions do you use to increase staff competency for active case finding?
- What methods do you use to evaluate your institution active case finding program?

Macro area 2

Key issue: Vaccination at entry and during outbreak situations in prison settings.

Scoping questions
- What are the diseases you cover by vaccination?
- Which vaccination strategies do you use (i.e. universal, high risk-targeted interventions?)
- What is the acceptance/uptake of vaccination?
- How do you improve the acceptance/uptake of vaccination?
- What methods do you use to evaluate your institution vaccination program?

Macro area 3

Key issue: Prevention, diagnosis, care and treatment of TB: all measures to prevent TB and minimise TB spread within prison environment and in the community.

Scoping questions:
- Which prevention interventions for TB do you use?
- Who do you target for prevention, diagnosis, care and/or treatment of TB?
- Which care and/or treatment interventions aimed at control of TB do you use?
- Which service models for prevention, diagnosis, care and/or treatment of TB are used in your institution?
- Which strategy to improve the acceptance/uptake/coverage of prevention, diagnosis, care and/or treatment of TB do you use?

**What kind of papers?**

National Field Researchers will be asked to collect and summarise (in a short pre-defined format):

Existing documents describing:
- National guidelines
- Institutional protocols
- Unpublished research reports/national conference abstracts

Summaries of:
- Intervention case studies
- Service models

regarding the macro areas of this specific contract (active case finding/vaccination for communicable diseases, and prevention, diagnosis, care and treatment of TB in prisons and other custodial settings).

**Inclusion and exclusion criteria**

The following inclusion and exclusion criteria will be applied for the grey literature search:
Table: Inclusion and exclusion criteria

<table>
<thead>
<tr>
<th>Period of publication</th>
<th>Inclusion</th>
<th>Exclusion</th>
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</thead>
<tbody>
<tr>
<td>Conference abstracts: last five years</td>
<td>Case-finding/vaccination/tuberculosis in prisons and other custodial settings that function as prisons</td>
<td>Case-finding/vaccination/tuberculosis in studies in which prisoners are only mentioned briefly as one of the risk groups</td>
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<tr>
<td>Other documents: last ten years</td>
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<td>Case-finding/vaccination/tuberculosis in migrant centers and police detention rooms</td>
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</table>

<table>
<thead>
<tr>
<th>Main focus of document</th>
<th>Inclusion</th>
<th>Exclusion</th>
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<tr>
<td></td>
<td>Guidelines</td>
<td>Case-finding/vaccination/tuberculosis in studies in which prisoners are only mentioned briefly as one of the risk groups</td>
</tr>
<tr>
<td></td>
<td>Intervention or clinical protocols</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Unpublished research results</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Case studies/service models, including measures of effectiveness</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Content of document</th>
<th>Inclusion</th>
<th>Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Document without a clear source/reference for the relevant information</td>
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</table>

<table>
<thead>
<tr>
<th>Document quality</th>
<th>Inclusion</th>
<th>Exclusion</th>
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<tbody>
<tr>
<td>Only grey literature documents with a methods section or an overview of sources. This means that when information relevant to our objectives is retrieved from a grey literature document, it must be clear what the source of this information is</td>
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</table>

<table>
<thead>
<tr>
<th>Document population</th>
<th>Inclusion</th>
<th>Exclusion</th>
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<tbody>
<tr>
<td>Adults in prisons and other custodial settings that function as a prison</td>
<td>Children (&lt;18 years)</td>
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<tr>
<td>Detained persons, including persons in remand</td>
<td>Persons in police custody</td>
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</tr>
<tr>
<td>Persons ‘going through the gate’ (e.g. prison guards, healthcare workers, etc.)</td>
<td>Persons in migrant centres</td>
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</table>

<table>
<thead>
<tr>
<th>Subject of the document</th>
<th>Inclusion</th>
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<tr>
<td></td>
<td>Active case finding for communicable diseases at entry and during prison stay</td>
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</tr>
<tr>
<td></td>
<td>Vaccination against relevant communicable diseases at entry and in outbreak situations</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Prevention, diagnosis, care and treatment of TB</td>
<td></td>
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</table>

<table>
<thead>
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<td>EU/EEA</td>
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<th>Specific outcomes of interest</th>
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<td>Quantitative outcomes</td>
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<tr>
<td></td>
<td>Qualitative outcomes</td>
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Data extraction and summary

Relevant data will be extracted from included documents in order to create evidence tables, or case studies/service models are summarized according to the template described below. The tables/summaries will be compiled by each Field Researcher and reviewed by the HWBS Responsible for the Grey Literature Researcher.

Ad 1. Existing national guidelines, institutional protocols and unpublished research reports/conference abstracts

The included documents will be summarised by collecting, per individual record, relevant information in a standardised data extraction format (Evidence table; see Appendix below).

Ad 2. Intervention case studies and service models

Case studies and service models can be summarised according to pre-defined format, including:

- Source
- Setting
- Target population(s) (country, prison setting, risk groups)
- Clearly described accounts of their intervention/service model related to the relevant macro area (see also scoping questions above).
- Elements of evaluation/monitoring or evidence of success (e.g. if case finding intervention, pre- and post-intervention testing positivity rate).
- Resource requirements
- Linkage to care

Case studies/service models can be included when at least the third and fourth item on the list are met.
### Table: Evidence table for national guidelines, institutional protocols and unpublished research reports/conference abstracts

<table>
<thead>
<tr>
<th>Reference</th>
<th>Source</th>
<th>Type of document</th>
<th>Setting, population</th>
<th>Intervention</th>
<th>Results</th>
<th>Comments</th>
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</thead>
<tbody>
<tr>
<td>Author, title, year, web link (when available)</td>
<td>Institute/company, etc.) that prepared the document</td>
<td>National guideline, institutional protocol, unpublished research report/conference abstract</td>
<td>Country, prison setting, risk groups, etc. to which the results apply</td>
<td>Type of intervention or service model; brief description</td>
<td>Relevant results on the objectives given in the document; per objective</td>
<td>Additional information that is relevant for interpreting the results</td>
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## Appendix 7. Exclusion table grey literature and corresponding reference list

Exclusion table second selection step

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<tr>
<th>Exclusion reason (number of articles)</th>
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<tr>
<td>Insufficient description methodology (n=1)</td>
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Reference list of excluded articles during second selection step

40. Libro bianco malattie infettive. 2015.
41. Aprea L. Linee guida per le procedure di isolamento del paziente affetto da tubercolo. 2007.
42. Babudieri S. Studi in ambito penitenziario: ultime acquisizioni. 2009. Presented at X Congresso Nazionale S.I.M.S.Pe.
68. Gabbuti A. Misure per la terapia dell’ infezione cronica HBV. Collegamento con i SerT, Comunità terapeutiche. Attivazione assistenza domiciliare per i pazienti a gli arresti domiciliari. 2015.
71. Rodríguez Martínez A. Patología infecciosa en reclusos extranjeros de una prisión andaluza. Revista espanola de sanidad penitenciaria. 2010;S12:83. Presented at del VIII Congreso de Sanidad Penitenciaria y XIV Jornada de la SESP.
Appendix 8. Summary tables and guideline summaries – diagnosis

Active TB

Peer-reviewed literature
No studies were found that reported on diagnostic tests for active TB in correctional settings.

Grey literature
No grey literature documents were found that reported on diagnostic tests for active TB in correctional settings.

LTBI

Peer-reviewed literature

Uptake, positivity rate and agreement
The included articles are summarised in tables below. Please keep in mind that the agreement between *M. tuberculosis* detection tests should be interpreted with caution as there is currently no gold standard.

**EU/EEA countries**

<table>
<thead>
<tr>
<th>Reference, country, study design</th>
<th>Prison setting, sample</th>
<th>Testing method, offer</th>
<th>Who, when</th>
<th>Uptake</th>
<th>Positivity rate</th>
<th>Agreement</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scharlach, 2008 [24] Germany Diagnostic accuracy study</td>
<td>One prison n=149 inmates n=45 prison employees</td>
<td>- TST: Mantoux - IGRA: QuantiFERON TB-Gold Voluntary</td>
<td>Male inmates and prison employees who might have had contact with TB index case, until 3 months after diagnosis of index case</td>
<td>Participation rate: 57% Tests performed: - Inmates: both tests 91% - Prison employees: both tests 62%</td>
<td>Inmates: - TST: 29.5% - IGRA: 18.1% Prison employees: NR</td>
<td>Concordance: 79.2% (95% CI NR) Kappa: 0.44 (95% CI NR)</td>
<td>Very low</td>
</tr>
<tr>
<td>Marco Mouriño, 2011 [25] Spain Diagnostic accuracy study</td>
<td>One preventive male prison n=181 inmates</td>
<td>- TST: Mantoux - IGRA: QuantiFERON TB-Gold NR</td>
<td>Persons recently admitted to prison After intake (timing NR)</td>
<td>Participation rate: 89% Tests performed: - Both tests: 82%</td>
<td></td>
<td>Concordance: NR Kappa: 0.6 (95% CI 0.4-0.7)</td>
<td>Very low</td>
</tr>
<tr>
<td>Porsa, 2007 [26] USA Diagnostic accuracy study</td>
<td>One prison n=300 inmates</td>
<td>- TST - IGRA: T-SPOT.TB TST NR, T-SPOT.TB voluntary</td>
<td>Adult inmates NR (TST directly after T-SPOT.TB)</td>
<td>Participation rate: NR Tests performed: - Both tests: 100%</td>
<td>TST: 8.5% IGRA: 19%</td>
<td>Concordance: 82.8% (95% CI 79-87%) Kappa: 0.29 (95% CI 0.17-0.41)</td>
<td>Very low</td>
</tr>
<tr>
<td>Porsa, 2006 [27] USA Diagnostic accuracy study</td>
<td>One prison n=409 inmates</td>
<td>- TST - IGRA: QuantiFERON TB-Gold TST NR, QuantiFERON TB-Gold voluntary</td>
<td>Adult inmates NR (TST directly after QuantiFERON TB-Gold)</td>
<td>Participation rate: 89% Tests performed: - Both tests: 100%</td>
<td>TST: 9% IGRA: 5.4%</td>
<td>Concordance: 90% (95% CI 87-93%) Kappa: 0.25 (95% CI 0.10-0.41)</td>
<td>Very low</td>
</tr>
</tbody>
</table>

CI=confidence interval, IGRA=interferon gamma release assay, NR=not reported, PPV=positive predictive value, TST=tuberculin skin test

*Agreement should be interpreted with caution as there is currently no gold standard for detection of *M. tuberculosis*

**Other countries**

<table>
<thead>
<tr>
<th>Reference, country, study design</th>
<th>Prison setting, sample</th>
<th>Testing method, offer</th>
<th>Who, when</th>
<th>Uptake</th>
<th>Positivity rate</th>
<th>Agreement</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Porsa, 2007 [26] USA Diagnostic accuracy study</td>
<td>One prison n=300 inmates</td>
<td>- TST - IGRA: T-SPOT.TB TST NR, T-SPOT.TB voluntary</td>
<td>Adult inmates NR (TST directly after T-SPOT.TB)</td>
<td>Participation rate: NR Tests performed: - Both tests: 100%</td>
<td>TST: 8.5% IGRA: 19%</td>
<td>Concordance: 82.8% (95% CI 79-87%) Kappa: 0.29 (95% CI 0.17-0.41)</td>
<td>Very low</td>
</tr>
<tr>
<td>Porsa, 2006 [27] USA Diagnostic accuracy study</td>
<td>One prison n=409 inmates</td>
<td>- TST - IGRA: QuantiFERON TB-Gold TST NR, QuantiFERON TB-Gold voluntary</td>
<td>Adult inmates NR (TST directly after QuantiFERON TB-Gold)</td>
<td>Participation rate: 89% Tests performed: - Both tests: 100%</td>
<td>TST: 9% IGRA: 5.4%</td>
<td>Concordance: 90% (95% CI 87-93%) Kappa: 0.25 (95% CI 0.10-0.41)</td>
<td>Very low</td>
</tr>
</tbody>
</table>
CI=confidence interval, IDU=injecting drug use, IGRA=interferon gamma release assay, NR=not reported, T-SPOT.TB=enzyme-linked immunospot assay for IFN-γ, TST=tuberculin skin test, USA=United States of America

Agreement should be interpreted with caution as there is currently no gold standard for detection of M. tuberculosis

Cost-effectiveness

No studies were found that reported on the cost-effectiveness of detection tests for M. tuberculosis in correctional facilities.

Grey literature

No grey literature documents were found that reported on diagnostic tests for active TB in correctional settings.

Guidelines on active TB and LTBI

Guidelines specific to the prison setting - supranational guidelines


A flowchart presenting how to establish a diagnosis of TB can be found in Figure 1 on page 47 of the guideline.

The most common symptom of pulmonary TB (PTB) is a persistent, productive cough, often accompanied by other nonspecific symptoms. The physical signs in patients with PTB are nonspecific. They do not help to distinguish PTB from other chest diseases. A pulmonary TB suspect should submit at least two sputum samples for microscopy. Secretions build up in the airways overnight, so an early morning sputum sample is more likely to contain tubercle bacilli than a sample taken later in the day.

TB suspects should submit sputum samples under supervision by health or security staff. Samples should be collected in a well-ventilated area, and staff observing need to take adequate precautions to avoid contagion by standing away from or behind the suspect and by using a respirator (e.g. FFP II or III or N95 respirator), if available. Samples should be transported the same day to the designated laboratory for processing. If not, sputum specimens should be refrigerated.

'TDirect smear microscopy examination of sputum is the most commonly used method for diagnosing TB. ‘The isolation of TB bacilli in sputum (and other clinical specimens) through culture, with further biochemical or molecular tests for identification, constitutes the definitive diagnosis of TB.’

Sensitivity of culture is substantially higher than that of smear microscopy; sputum smear microscopy detects only up to 50 percent of culture confirmed pulmonary TB cases. Therefore, the importance of its use to confirm disease should be emphasized, especially among HIV-infected individuals, who are frequently smear-negative. Additionally, this method allows for identification of drug-susceptibility patterns, crucial for guiding therapeutic management. Therefore culture and drug susceptibility testing (DST) shall be considered for all TB patients who are suspected to be infected with multidrug resistant strains. Culture is part of the routine work-up when evaluating TB suspects in industrialized countries.

‘All pulmonary TB suspects must submit sputum samples for diagnostic smear microscopy. In some instances, however, chest radiography is required to establish the diagnosis of pulmonary TB. The most important indication is when there is clinical suspicion of tuberculosis despite negative sputum smears. The diagnosis of bacteriologically negative (two or more negative smears, at least one culture negative, or both) TB is therefore always presumptive and must be based on other clinical and epidemiological information, including failure to respond to broad-spectrum antibiotics and exclusion of other pathology. Chest radiography is necessary to document cases of smear-negative pulmonary TB when culture is not available or reliable’ (Table 3 on page 45 of the guideline highlights the indications for chest radiography during diagnostic evaluation of TB).

Source: USAID, Tuberculosis Coalition for Technical Assistance, International Committee of the Red Cross. Guidelines for control of tuberculosis in prisons. 2009 (Type of guideline: practice-based; level of evidence: ++, –) [18]

5 Relevant guidelines were critically appraised with a selection of criteria derived from the AGREE instrument (1. The overall objective/objectives of the guideline is/are specifically described; 2. Systematic/clear methods were used to search for evidence for compiling the data and/or clear data sources/references; 3. The recommendations are specific and unambiguous). The criteria were qualitatively scored using - - or -, 0, + or ++; no total quality score of summed + and – was calculated.
**WHO. Prisons and Health.**

Direct smear microscopy is comparatively inexpensive and fast, does not require sophisticated equipment and can be carried out by trained technicians in primary care settings. Consequently, it is the method of choice for early identification of TB cases in low-resource settings.

'Prisoners suspected of having pulmonary TB should submit two samples to establish a diagnosis of TB. It is preferable to obtain early morning sputum as this is more likely to contain tubercle bacilli. The way sputum is produced is also very important. Sputum samples should be submitted following instructions from and under the supervision of a health care worker to ensure sampling with the right technique and from the right person. Samples should be collected in a well-ventilated area (better outdoors). In some prison settings, inmates may exchange their sputum samples or use other practices to get positive results from the sputum smear, so staff need to observe the production of the sample, using personal protective measures (filter face-piece 2 or N95 respirators) and/or other infection control measures.'

'Culturing a specimen means growing the bacilli on media, which are substances that contain nutrients, in the laboratory. Löwenstein Jensen is the most frequently used solid media. Not all TB patients have positive smears. If there are only a few bacilli in the sputum (around 10–20) the smear will appear negative but the culture will usually be positive. A positive culture is proof of TB. The isolation of TB bacilli in sputum (and other clinical specimens) through culture, with further biochemical or molecular tests for identification, constitutes a definitive diagnosis of TB. The sensitivity of the culture is substantially higher than that of smear microscopy; sputum-smear microscopy detects only up to 50% of culture-confirmed pulmonary TB cases.'


The recommendations apply to the:

- use of Xpert MTB/RIF in sputum specimens (including pellets from decontaminated specimens) (data on the utility of Xpert MTB/RIF in extrapulmonary specimens are still limited);
- TB prevention and control care in prisons
- use of one sputum specimen for diagnostic testing, acknowledging that multiple specimens increase the sensitivity of Xpert MTB/RIF but have major resource implications;
- use in children, based on the generalization of data from adults and acknowledging the limitations of microbiological diagnosis of TB (including MDR-TB) in children.

Access to conventional microscopy, culture and DST is still needed for monitoring therapy, for prevalence surveys and/or surveillance, and for recovering isolates for drug susceptibility testing other than rifampicin (including second-line anti-TB drugs).'

Source: WHO Regional Office for Europe. Prison and Health. 2014 (Type of guideline: practice-based; level of evidence: ++, γ,0)

**WHO Regional Office for Europe. Health in prisons**

'The diagnosis is based on staining and direct microscopy of sputum. Mass X-ray screening is justified in the prison population, but it needs to be complemented with screening for symptoms and with passive case-finding.'

'The case definitions are determined by the site of tuberculosis, the result of sputum smear microscopy, the severity of tuberculosis and the history of previous treatment for tuberculosis.'

Source: WHO. Health in prisons. 2007 (Type of guideline: practice-based; level of evidence: ++, γ,0) [31]

**WHO. Status paper on Prisons and TB**

'The basis for diagnosis of infectious TB is microscopy examination of sputum, since it immediately identifies the most infectious patients who can be isolated and started on treatment. Smear microscopy is not done or is of unacceptable quality in many settings. The staff are sometimes inadequately trained, microscopes may be of low quality and poorly maintained, the staining may be inadequate, there may be little staff retraining and few supervisory visits, and quality assurance through exchange of slides is rarely done. This is currently a major problem in TB programmes worldwide, including those in prisons. An adequate network of smear microscopy sites should be set up inside the prison system, so that peripheral prisons/colonies have easy and rapid access and the number of performed tests is still sufficient to ensure adequate quality. The network in the prison system should be coordinated with the network outside, so that collaboration at local level may be achieved.

A special challenge in smear microscopy is that in some prisons there is a market for selling sputum positive for TB, because it leads to transfer to a hospital unit and better conditions. Reliable prison staff must receive training about this issue, and know how to supervise the production of sputum adequately and directly. The ultimate way to counter this problem will be to increase living and working conditions in all prison facilities.'
Ideally, all TB suspects should be tested by sputum culture and drug susceptibility testing (DST) in addition to sputum smear microscopy, if the budget allows it. This is currently done in several countries, but does not provide reliable results in many settings since not all laboratories are part of the Supranational Reference Laboratory Network set up by WHO. Laboratories carrying out sputum culture and DST also need strict safety measures to prevent infection of the staff, and such facilities are expensive to build and to run. Such laboratories should therefore be centralized as much as possible and coordinated with the system in the civil sector.'

Source: WHO. Status paper on Prisons and TB. 2007 (Type of guideline: practice-based; level of evidence: +,+,0) [11]

**Guidelines specific to the prison setting – national guidelines**

**United Kingdom: Management of tuberculosis in prisons: Guidance for prison healthcare teams.**

'Any prisoner with a productive cough for more than three weeks who also has any other TB symptom (fever, night sweats, coughing blood, weight loss or generally feeling unwell) should be isolated in a single cell as soon as possible (preferably in the healthcare unit if available) and should have a medical assessment as soon as possible.'

'Sputum specimens should be taken from the patient (if they are able to produce good quality specimens) and sent for TB microscopy and culture to the local laboratory as soon as possible. The case should be reported to the local Health Protection Team promptly.'

- Chest x-rays should be done in the prison (where available) as soon as possible (see Appendix 2 of the guideline on page 15, Pathway A).
- Chest x-rays should be reported urgently and reports given to the prison doctor.

'Sputum samples for microscopy and culture:

- Three consecutive sputum samples should be obtained over three days. One of these should be an early morning specimen. Poor quality specimens may delay diagnosis.
- The three samples should be accurately labelled and sent individually with the request form to the local microbiology department. The specimens can be kept in the specimen fridge if they are being collected over the weekend.'
- The prison doctor must liaise with the microbiology department to obtain sputum results. If possible, a second member of the healthcare team should also be allocated to follow up results.

Appendix 2 on page 15 of the guideline provides an algorithm for the management of TB in prisons.


**Other guidelines**

**European Union Standards for Tuberculosis Care – Standard for TB diagnosis**

'Standard 1: All persons presenting with signs, symptoms, history or risk factors compatible with TB should be evaluated for pulmonary and/or extrapulmonary TB.

Standard 2: All patients (adults, adolescents and children who are capable of producing sputum) suspected of having pulmonary TB should have at least two sputum specimens submitted for microscopic examination, culture and drug susceptibility testing (DST) in a quality-assured laboratory. In countries, settings or populations in which MDR-TB is suspected in a patient, rapid testing for the identification of rifampicin- and isoniazid-resistance, using validated tools in a quality assured laboratory should be performed.

Standard 3: For all patients (adults, adolescents and children) suspected of having extrapulmonary TB, appropriate specimens from the suspected sites of involvement should be obtained for microscopy, culture, DST and histopathological examination in a quality-assured laboratory.

Standard 4: All persons with chest radiographic findings suggestive of pulmonary TB should have sputum specimens submitted for microscopic examination, culture and DST in a quality-assured laboratory.

Standard 5: The diagnosis of culture-negative pulmonary TB should be based on the following criteria: all bacteriological tests are negative (including direct sputum smear examinations, cultures and rapid molecular testing); chest radiographic findings are compatible with TB; and there is a lack of response to trial of broad spectrum antimicrobial agents (because the fluoroquinolones are active against *M. tuberculosis* complex and, thus, may cause transient improvement in persons with TB, they should be avoided). In persons who are seriously ill or have known or suspected HIV infection or have any immune compromising conditions, the diagnostic evaluation should be expedited and, if clinical evidence strongly suggests TB, a course of anti-TB treatment should be initiated.'

ECDC. Handbook on TB laboratory diagnostic methods for the European Union

Many national guidelines for LTBI diagnosis now include IGRAs although most countries continue to recommend and use TST. A review of current guidelines indicated that guidelines are predominantly available in high-income countries with established LTBI screening programmes. Four approaches are generally adopted:

- two-step approach of TST first, followed by IGRA, either when the TST is negative (to increase sensitivity, mainly in immunocompromised individuals), or when the TST is positive (to increase specificity, mainly in BCG-vaccinated individuals);
- either TST or IGRA, but not both;
- IGRA and TST together (to increase sensitivity); or
- IGRA only, replacing the TST.

Information included in the different national guidelines and recommendations suggests that IGRAs are increasingly being recommended, primarily in low-incidence settings, as they offer a higher specificity combined with logistical advantages. TST is still favoured in high-incidence and low-resource settings.

In high-incidence settings, the ECDC suggests not to use IGRAs to diagnose LTBI since the focus of prevention and control is on identifying and treating active TB cases. In low-incidence settings a two-step approach is suggested. For active TB diagnosis, ECDC suggests that IGRAs should not be a replacement for standard diagnostic methods and generally do not have an added value in most clinical situations, when combined with standard methods for diagnosing active TB. However, in certain clinical situations (e.g. patients with extrapulmonary TB, patients who test negative for acid-fast bacilli in sputum and/or negative for M. tuberculosis after culture, TB diagnosis in children, or in the differential diagnosis of infection with non-tuberculous mycobacteria), ECDC suggests that IGRAs could contribute supplementary information as part of the diagnostic process and laboratory management.

Appendix 9. Summary tables and guideline summaries – treatment and care

**Active TB**

**Treatment-reviewed literature**

**EU/EEA countries**

<table>
<thead>
<tr>
<th>Reference, country, study design</th>
<th>Prison setting, sample</th>
<th>Treatment, duration, DOT</th>
<th>Who, adherence improvement methods</th>
<th>Treatment initiation</th>
<th>Treatment completion</th>
<th>Effectiveness</th>
<th>Cured</th>
<th>Other</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marco, 1998 [33] Spain Longitudinal study</td>
<td>Men’s Penitentiary Centre n=62</td>
<td>2HRZE + (4RH or 6RH) HIV+ nine months, HIV- six months DOT</td>
<td>All TB inmates diagnosed in 1995 after systemic screening at entry/during stay Incentives: municipal MMP, economic aid, sociosanitary centres for homeless/alcoholic ex-prisoners</td>
<td>NR</td>
<td>75.8% completion - In prison: 45.2% - Outside prison: not possible to calculate Non-completion: - 9.7% defaulted from treatment - 9.7% died - 4.8% transferred out</td>
<td>Continuous supervision on DOT was associated with better completion (OR 16.8, 95% CI 2.4-116.2, ( p=0.004 )) Entire treatment administered during prison stay associated with better completion (OR=7.35, 95% CI 0.79-68.16, ( p=0.07 ))</td>
<td>NR</td>
<td>75.8% completion (according to WHO criteria)</td>
<td>Very low</td>
</tr>
<tr>
<td>Kiter, 2003 [35] Turkey Longitudinal study</td>
<td>One district prison n=13</td>
<td>INH, RIF, morphamidium and ethambutol for 2-3 months + RH 6-7 months nine months Oberved by prison staff, under supervision of the dispensary</td>
<td>Inmates with active TB found through active yearly screening and passive screening NR</td>
<td>NR</td>
<td>100%</td>
<td>100% completion (according to WHO criteria)</td>
<td>NR</td>
<td>75.8% completion</td>
<td>Very low</td>
</tr>
<tr>
<td>Kim, 2007 [36] USA Longitudinal study</td>
<td>One large urban jail n=441</td>
<td>NR NR Self-administration (30.3%) or DOT (49.7%)</td>
<td>All TB cases whose treatment was initiated in jail and was continued after their release to the community NR</td>
<td>NR</td>
<td>38.5% completion outside jail</td>
<td>DOT users more likely to complete treatment than those who self-administered (OR 8.48, 95% CI 4.43-16.2, ( p&lt;0.01 )) Inmates on field DOT more likely to complete treatment than those on clinic DOT (OR 6.89, ( p&lt;0.01 ))</td>
<td>NR</td>
<td>38.5% completion</td>
<td>Very low</td>
</tr>
</tbody>
</table>

CI=confidence interval, DOT=directly observed therapy, HIV=human immunodeficiency virus, HRZE=isoniazid, rifampicin, pyrazinamide and ethambutol, INH=isoniazid, MMP=maintenance methadone programme, NR=not reported, OR=odds ratio, RH=rifampicin, isoniazid, RIF=rifampicin, TB=tuberculosis, WHO=World Health Organisation

1 Treatment completion: number of persons that completed treatment/persons that initiated treatment

2 Those that died or transferred out were not included in the denominator of the completion rates used in the OR calculations

Other countries

<table>
<thead>
<tr>
<th>Reference, country, study design</th>
<th>Prison setting, sample</th>
<th>Treatment, duration, DOT</th>
<th>Who, adherence improvement methods</th>
<th>Treatment initiation</th>
<th>Treatment completion</th>
<th>Effectiveness</th>
<th>Cured</th>
<th>Other</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tbody>
</table>

\( p<0.01 \)
### Cost-effectiveness

No studies were found that reported on the cost-effectiveness of TB treatment and care in correctional facilities.

### Grey literature

#### Treatment initiation, completion and effectiveness

<table>
<thead>
<tr>
<th>Reference, country, study design</th>
<th>Prison setting, sample</th>
<th>Treatment, duration, DOT</th>
<th>Who, adherence improvement methods</th>
<th>Treatment initiation</th>
<th>Treatment completion</th>
<th>Cured</th>
<th>Other</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spradling, 2002 USA Longitudinal / outbreak study</td>
<td>One HIV-dedicated dormitory in a state prison n=13</td>
<td>Rifabutin-containing regimen (rifabutin substituted for rifampin) NR DOT</td>
<td>HIV-infected inmates, exposed to the source case patient, on treatment for TB NR</td>
<td>NR</td>
<td>100% completion  - In prison: 100%  - Outside prison: 100%  Non-completion: NR</td>
<td>NR</td>
<td>NR</td>
<td>Very low</td>
</tr>
<tr>
<td>Bock, 1998 USA Longitudinal study</td>
<td>One state prison system n=142</td>
<td>All inmates with suspected or confirmed TB, transferred to central prison hospital for evaluation and treatment until prison term ended  Follow-up arrangement for inmates still on treatment at release</td>
<td>NR</td>
<td>82% completion  - In prison: 65%  - Outside prison: 59%  Non-completion:  - 8% died  - 11% lost to follow-up due to release prior to completing treatment</td>
<td>NR</td>
<td>NR</td>
<td>Very low</td>
<td></td>
</tr>
</tbody>
</table>

**CDC=** Centers for Disease Control and Prevention, **CI=** confidence interval, **DOT=** directly observed therapy, **HIV=** human immunodeficiency virus, **NR=** not reported, **TB=** tuberculosis, **USA=** United States of America

1. Treatment completion: number of persons that completed treatment/persons that initiated treatment
2. In prison: number of persons that completed treatment while in prison/persons that initiated treatment in prison
3. Outside prison: number of persons that completed treatment outside prison/persons that initiated treatment in prison and continued treatment outside prison
4. DOT monitoring: can be performed in the community (field) where the patients live, or in a health care clinic, in which case patients have to come in to a designated clinic each time they take medications
### Cost-effectiveness

No studies on cost-effectiveness have been found from the grey literature search.

### LTBI

#### Peer-reviewed literature

**Treatment initiation, completion and effectiveness**

The included articles are summarised in tables below. As many studies from non-European countries were found that reported on LTBI treatment, this table was further split up by place of adherence intervention (i.e. inside and/or outside correctional facility).

#### EU/EEA countries

<table>
<thead>
<tr>
<th>Reference, country, study design</th>
<th>Prison setting, sample</th>
<th>Treatment, duration, DOT</th>
<th>Who, adherence improvement methods</th>
<th>Treatment initiation</th>
<th>Treatment completion</th>
<th>Effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lopez, 2011 [45] Spain Longitudinal study</td>
<td>A medium-sized prison for convicts n=902</td>
<td>- 2000-2004: choice between INH or RZ - 2004-2008: INH - After 2008: choice between INH, R, or Rif</td>
<td>Inmates with an indication for treatment of LTBI or primary chemoprophylaxis Health education to all inmates and staff</td>
<td>INH: 67.8% Short-course therapies: 76.6% - RZ: 73.4% - RH: 85.4% - RIF: 100% Non-completion: INH:</td>
<td>- INH more often discontinued compared to short course therapies (OR 1.56, 95% CI: 1.30-1.85; p=0.002). No voluntary withdrawals higher in INH compared to short course treatment (OR 2.03, 95% CI: 1.30-3.15; p&lt;0.001).</td>
<td>Low</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Reference, country, study design</th>
<th>Prison setting, sample</th>
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<th>Treatment initiation</th>
<th>Treatment completion</th>
<th>Effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retrospective study</td>
<td>as initial regimen in 65.7% of cases NR DOT in most cases</td>
<td>Prisons with active TB identified at prison entry NR</td>
<td></td>
<td>-77.9% completed treatment Reasons for non-completion: -19.8% returned to freedom before completion -2.3% failed treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fiebig L 2013 [42] Germany Longitudinal study</td>
<td>German prisons N=472</td>
<td>NR NR NR</td>
<td>NR</td>
<td>53.8% Reasons for non-completion: -12% defaulted treatment -26% reported as lost to follow up -8.2% with unknown treatment outcomes</td>
<td>NR In multivariable analysis prison entry screening was found to be associated with unsuccessful or unknown outcomes with odds ratio = 5.9 (CI 4.9-7.2)</td>
<td>Conference abstract</td>
</tr>
<tr>
<td>Cioran N 2013 [43] Romania Retrospective, longitudinal study</td>
<td>Romanian prisons N = 477 between 2009-2011: 174 in 2009, 155 in 2010 and 148 in 2011</td>
<td>NR NR NR</td>
<td>NR</td>
<td>The success rate among new pulmonary smear positive cases was 82.1% in 2009, 68.4% in 2010 and 55.8% in 2011</td>
<td>NR Conference abstract</td>
<td></td>
</tr>
<tr>
<td>Milanov V 2014 [44] Bulgaria Retrospective</td>
<td>Bulgarian prisons N=783</td>
<td>NR NR NR</td>
<td>NR</td>
<td>72.8% Reasons for non-completion: -13 (1.8%) died -180 (24.5%) did not complete their treatment because of interruption, transfer or unknown outcome</td>
<td>NR Conference abstract</td>
<td></td>
</tr>
</tbody>
</table>
### Other countries: Comparison LTBI treatment adherence intervention inside and outside correctional facility

<table>
<thead>
<tr>
<th>Reference, country, study design</th>
<th>Prison setting, sample</th>
<th>Treatment, duration, DOT</th>
<th>Who, adherence improvement methods</th>
<th>Treatment initiation</th>
<th>Treatment completion$^2$</th>
<th>Cured</th>
<th>Other</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>White, 2002 [47] USA Open-label randomised trial</td>
<td>One county jail n=325</td>
<td>INH six months DOT</td>
<td>Inmates with LTBI, who started therapy while still undergoing therapy One informational one-to-one TB session, then TB education every 2 weeks while in jail</td>
<td>NR</td>
<td>23% completion outside jail Non-completion: 2.8% discontinued due to adverse events</td>
<td>NR</td>
<td>- Education group was more than twice as likely to complete therapy as was the usual care group (OR 2.2, 95% CI 1.04-4.72; p=0.04). Those in the incentive group did not differ from those in the usual care group (OR 1.07, 95% CI 0.47-2.4, p=0.05) - Pooled rates of completing a first visit to the TB clinic after release for the education and incentive groups tod</td>
<td>Moderate</td>
</tr>
<tr>
<td>Martin, 2000 [46] Spain Longitudinal study</td>
<td>One penitentary n=113</td>
<td>INH HIV- with normal CXR: six months; HIV+ or abnormal CXR2: 12 months DOT or weekly delivery of medication</td>
<td>Inmates with an indication for treatment of LTBI NR</td>
<td>74.3%</td>
<td>46.4% completion Non-completion: 27.4% still on treatment 26.2% treatment interrupted (90% due to discomfort)</td>
<td>NR</td>
<td>95.7% of inmates still on treatment</td>
<td>Very low</td>
</tr>
</tbody>
</table>

CI=confidence interval, CXR=chest X-ray, DOT=directly observed therapy, INH=isoniazid, LTBI=latent tuberculosis infection, NR=not reported, OR=odds ratio, RIF=rifampicin, RZ=rifampicin, pyrazinamide, RH=rifampicin, isoniazid, WHO=World Health Organisation

$^1$ Treatment completion: number of persons that completed treatment/persons that initiated treatment

In prison: number of persons that completed treatment while in prison/persons that initiated treatment in prison

Outside prison: number of persons that completed treatment outside prison/persons that initiated treatment in prison and continued treatment outside prison

$^2$ The authors were not consistent with the term TB/LTBI. However, active disease was ruled out and we therefore assumed that all the results are applicable to LTBI
### Systematic review on the diagnosis, treatment, care and prevention of tuberculosis in prison settings

#### LTBI treatment adherence intervention inside correctional facility

<table>
<thead>
<tr>
<th>Reference, country, study design</th>
<th>Prison setting, sample</th>
<th>Treatment, duration, DOT</th>
<th>Who, adherence improvement methods</th>
<th>Treatment initiation</th>
<th>Treatment completion</th>
<th>Cured</th>
<th>Other</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spradling, 2002 [37] USA</td>
<td>One HIV-dedicated dormitory in a state prison n=225</td>
<td>Rifabutin-pyrazinamide, rifabutin dosage ranging from 150 mg twice a week to 450 mg/day two months DOT</td>
<td>HIV-infected inmates exposed to source case patient in which a TB diagnosis was excluded TB educational session about potential adverse effects</td>
<td>NR</td>
<td>70.2% completion in prison Non-completion: 8.4% released before completion 10.7% discontinued due to adverse events 4.9% changed treatment 5.8% did not adhere despite DOT (putting it in cheek/under tongue while under supervision and discarding it later)</td>
<td>1.3% developed TB disease (of which 67% did not complete/ adhere to treatment)</td>
<td>NR</td>
<td>Very low</td>
</tr>
</tbody>
</table>

**CI=confidence interval, DOT=directly observed therapy, INH=isoniazid, LTBI=latent tuberculosis infection, NR=not reported, OR=odds ratio, RCT=randomised controlled trial, RR=relative risk, TB=tuberculosis, USA=United States of America**

1. Treatment completion: number of persons that completed treatment/persons that initiated treatment
2. Treatment initiation: number of persons that completed treatment/persons that initiated treatment

#### Treatment completion outside prison

<table>
<thead>
<tr>
<th>Reference, country, study design</th>
<th>Prison setting, sample</th>
<th>Treatment, duration, DOT</th>
<th>Who, adherence improvement methods</th>
<th>Treatment initiation</th>
<th>Treatment completion</th>
<th>Cured</th>
<th>Other</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>White, 2005 [48] USA Cohort study following open-label randomised trial</td>
<td>One county jail n=268</td>
<td>INH six months NR</td>
<td>Inmates with LTBI in jail who were released before completion of therapy One TB session in 1998-1999 (from RCT), attempts to find all subjects from &gt;30 days after release</td>
<td>NR</td>
<td>16.3% completion outside jail Non-completion: 1.0% still on therapy 2.9% taken off – side-effects 12.5% self-stopped, lost to follow-up after visiting TB clinic at least once 67.3% lost to follow-up (no TB clinic visit at all)</td>
<td>7.9% completion outside jail Non-completion: 0.6% moved/referred 6.7% self-stopped/lost to follow-up after visiting TB clinic at least once 84.8% lost to follow-up (no TB clinic visit at all)</td>
<td>NR</td>
<td>Low</td>
</tr>
</tbody>
</table>

- Subjects in the usual care period remained less likely to go to clinic (RR: 0.37, 95% CI: 0.18-0.75; p=0.006) after correction for variables

**CI=confidence interval, DOT=directly observed therapy, INH=isoniazid, LTBI=latent tuberculosis infection, NR=not reported, OR=odds ratio, RCT=randomised controlled trial, RR=relative risk, TB=tuberculosis, USA=United States of America**

- Usual care group significantly less likely to go to clinic, at the 30-day period after release (unadjusted RR 0.84, 95% CI 0.75-0.95; p=0.002) or any time after release (unadjusted RR 0.79, 95% CI 0.68-0.92; p=0.001)
1 Treatment completion: number of persons that completed treatment/persons that initiated treatment
In prison: number of persons that completed treatment while in prison/persons that initiated treatment in prison
Outside prison: number of persons that completed treatment outside prison/persons that initiated treatment in prison and continued treatment outside prison

LTBI treatment adherence intervention outside correctional facility

<table>
<thead>
<tr>
<th>Reference, country, study design</th>
<th>Prison setting, sample</th>
<th>Treatment, duration, DOT</th>
<th>Who, adherence improvement methods</th>
<th>Treatment initiation</th>
<th>Treatment completion(^1)</th>
<th>Effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>White, 2012 [49] USA</td>
<td>One county jail, n=364</td>
<td>INH (900 mg, 76 doses)(^2) nine months, twice weekly DOT</td>
<td>Inmates diagnosed with LTBI at entry Incentives after release: lunch, restaurant coupon, bus token; case management team throughout treatment course</td>
<td>NR</td>
<td>25.5% completion</td>
<td>- No significant difference in treatment completion between INH and RIF (p=0.10) - No significant difference in treatment completion in jail and after release between INH and RIF in the survival analysis (p=0.72 and 0.49)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RIF (600 mg, 120 doses)(^2) four months, once daily DOT</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Nolan, 1997 [50] USA Retrospective cohort study</td>
<td>One county correctional facility (awaiting trial or sentenced (&lt;2.5) years) n=2,127</td>
<td>- Expected incarceration six-months: choice between RZ (600 mg/d) or INH (300 mg/day) - Expected incarceration 2-six months: RZ only (same dosage) RZ two months daily, INH 6–12 months daily</td>
<td>Inmates with LTBI Follow-up arrangement for inmates still on treatment at release</td>
<td>6.8% - RZ: 52.4% - INH: 47.6%</td>
<td>33.3% completion Survival analysis: - In jail during entire therapy: 83% - Deported/transferred: 0% - Continue treatment after release: 44% Non-completion: NR</td>
<td>- Higher completion rate with RZ than with INH (RR 1.19, 95% CI 1.01-1.40; p=0.03) - For those incarcerated during entire treatment, no significant difference in completion between both regimens (RR 1.10, 95% CI 0.94-1.28; p=0.22)</td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Nolan, 1997 [51] USA Longitudinal study</td>
<td>One county jail (80% released within 2 weeks) n=744</td>
<td>Community-based DOT INH While in jail: 14 days, daily; once released: 52 twice weekly doses of 900 mg While in jail: self-administration, DOT only when proven unable to manage own medication; once released: DOT</td>
<td>Inmates with LTBI Clients were visited at least once a week to establish a trusting relationship, and to begin to plan for continuing INH therapy after the client's release from jail</td>
<td>Total while in jail: 64.9% Once released: 40.1%</td>
<td>Total while in jail: 7.6% completion Non-completion: - 0.4% side effects - 37.7% transferred to other facility/other health department upon release - 54.2% still on treatment once released Total once released: 29.8% Once released DOT: 60%(^3) Non-completion: - Lost to follow-up: 32.4% - Refused to continue: 6.7% - Stopped on medical advice: 1.0%</td>
<td>Treatment completion higher among those on DOT than on self-administered therapy (p=0.0002)</td>
</tr>
</tbody>
</table>

\(^1\) Treatment completion: number of persons that completed treatment/persons that initiated treatment
\(^2\) For those incarcerated during entire treatment
\(^3\) Non-completion
No LTBI treatment adherence intervention

ALT=alanine aminotransferase, CI=confidence interval, DOT=directly observed therapy, HIV=human immunodeficiency virus, INH=isoniazid, LTBI=latent tuberculosis infection, NR=not reported, RIF=rifampicin, RR=relative risk, RZ=rifampicin and pyrazinamide, USA=United States of America

1 Treatment completion: number of persons that completed treatment/persons that initiated treatment
In prison: number of persons that completed treatment while in prison/persons that initiated treatment in prison
Outside prison: number of persons that completed treatment outside prison/persons that initiated treatment in prison and continued treatment outside prison

2 Reincarcerated participants were continued on treatment, but if lost to follow-up restarted twice, allowing a maximum of three regimen attempts, per jail protocol

3 Those lost to follow-up directly after release are not included in the denominator, therefore the completion rate is overestimated

No LTBI treatment adherence intervention
Table 1

<table>
<thead>
<tr>
<th>Reference, country, study design</th>
<th>Prison setting, sample</th>
<th>Treatment, duration, DOT</th>
<th>Who, adherence improvement methods</th>
<th>Treatment initiation</th>
<th>Treatment completiona</th>
<th>Cured</th>
<th>Other</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lobato, 2003 [56] USA Longitudinal study</td>
<td>49 correctional facilities and systems n=23,965</td>
<td>INH Biweekly; HIV-six months, HIV+ or inadequately treated old pulmonary TB 12 months DOT</td>
<td>Inmates with LTBI NR</td>
<td>89.6%</td>
<td>55.9% completion Non-completion: - 8.8% still on treatment - 14.2% moved/pardoned/transferred - 5.2% lost to follow-up - 3.6% refused treatment - 2.9% adverse drug event - 0.6% other - 8.8% unknown</td>
<td>NR</td>
<td>Patients treated in jails were less likely than those treated in prisons (33.6% vs. 57.7%) to complete treatment (OR 0.29, 95% CI 0.26-0.32; p&lt;0.001)</td>
<td>Very low</td>
</tr>
</tbody>
</table>

CI=confidence interval, DOT=directly observed therapy, HIV=human immunodeficiency virus, INH=isoniazid, LTBI=latent tuberculosis infection, NR=not reported, OR=odds ratio, RZ=rifampicin and pyrazinamide, TB=tuberculosis, TST=tuberculin skin test, USA=United States of America

aTreatment completion: number of persons that completed treatment/persons that initiated treatment

In prison: number of persons that completed treatment while in prison/persons that initiated treatment in prison

Outside prison: number of persons that completed treatment outside prison/persons that initiated treatment in prison and continued treatment outside prison

If an inmate that begun therapy did not follow-up with TB clinic after release, INH was restarted at second jail term, however if this cycle repeated, INH was not prescribed again in the third jail term

Cost-effectiveness

EU/EEA countries: No data

Other countries: One longitudinal study from the USA (Bandyopadhyay 2002 [52], very low level of evidence) estimated the cost-effectiveness of giving inmates at the time of release a 2-week supply of isoniazid preventive therapy (IPT) with the instruction to follow-up in the community clinic. At the clinic, six months of self-administered IPT was prescribed for HIV-negative persons and 12 months for HIV-positive persons. A biweekly regimen (300 mg/day) was used and patients were generally seen monthly to assess adherence and tolerance. Inmates with documented prior adequate prophylaxis, those >35 years old with no other risk factors, and those with a history of side effects from isoniazid treatment were not offered IPT. The economic evaluation estimated that the program would prevent 2.68 cases of TB reactivation, with a projected cost to the healthcare system of $42,093, yielding a cost savings of $9,227 over 4.5 years in addition to the public health benefit.

Grey literature

No grey literature documents were found that reported on LTBI treatment and care in correctional facilities.

Guidelines2 on active TB and LTBI

Guidelines specific to the prison setting – supranational guidelines

Guidelines for control of tuberculosis in prisons. USAID, Tuberculosis Coalition for Technical Assistance, International Committee of the Red Cross. 2009

Aims of treatment

The aims of tuberculosis treatment are as follows:

- Cure the patient of TB
- Prevent death from active TB or its late effects
- Prevent relapse of TB

2 Relevant guidelines were critically appraised with a selection of criteria derived from the AGREE instrument (1. The overall objective/objectives of the guideline is/are specifically described; 2. Systematic/clear methods were used to search for evidence for compiling the data and/or clear data sources/references; 3. The recommendations are specific and unambiguous). The criteria were qualitatively scored using - - or - , 0, + or ++; no total quality score of summed + and – was calculated.
Decrease transmission of TB
Prevent the development and transmission of drug resistance

Anti-TB medicines have three primary properties: bactericidal activity, sterilizing activity, and the ability to prevent resistance. The essential anti-TB medicines possess these properties to different extents. Isoniazid and rifampicin are the most powerful bactericidal medicines active against all populations of TB bacilli. Rifampicin is the most potent sterilizing medicine available. Pyrazinamide and streptomycin are also bactericidal against certain populations of TB bacilli. Pyrazinamide is active only in an acid environment. Streptomycin is bactericidal against rapidly multiplying TB bacilli. Ethambutol is used in association with more powerful medicines to prevent the emergence of resistant bacilli. Daily treatment is recommended in prison settings.

The purpose is to identify MDR among patients with smear-positive pulmonary, smear-negative pulmonary, and extrapulmonary TB. Supervised or directly observed treatment (DOT) for the daily administration of medicines for treatment of all new cases is imperative in prison settings. The preferred continuation phase regimen is four months of rifampicin and isoniazid administered daily. The primary advantage of this regimen is the low rate of treatment failure and relapse for patients with fully susceptible TB or TB with initial isoniazid resistance. The use of rifampicin requires measures to support patients in adhering to treatment and preventing development of rifampicin resistance.

Previously treated cases
Drug resistance is more likely to develop in previously treated patients (i.e., patients who have been treated for longer than one month) who continued to be or who became smear positive (or culture positive). The Global Plan to Stop TB 2006-2015 sets a target that by 2015, all previously treated patients should have access to DST at the beginning of treatment. The purpose is to identify MDR as early as possible so appropriate treatment can be given. The approach to the initiation of retreatment depends on the country's laboratory capacity, specifically when (or if) DST results are routinely available for the individual patient.

Countries using rapid DST will have results available within hours or days, and can use the results to decide which regimen to start for the individual patient.
Countries using conventional methods will have results available within weeks (if using liquid media) or months (if using solid media). Because of this delay in receiving DST results, countries using conventional methods will need to start an empiric regimen while awaiting results of DST.
For countries which do not yet have DST routinely available for individual retreatment patients, an interim approach is described below.

Countries will need to use a mix of approaches if they are in a transition where some areas of the country do not yet have DST results routinely available and others do, or some laboratories use rapid and others use conventional DST methods.

Previously treated patients in settings with rapid DST—With line probe assays, MDR can be essentially confirmed or excluded within hours to days, which allows the results to guide the regimen at the start of therapy.
Previously treated patients in settings where conventional DST results are routinely available for individual patients—Obtaining specimens for conventional culture and DST should not delay the start of therapy. Empiric regimens, often based on drug resistance surveillance data, are used while awaiting the results of conventional DST (liquid or solid media), and should be started promptly. This is especially important if the patient is seriously ill or the disease is progressing rapidly. Placing a patient on an empiric regimen pending DST is done to avoid clinical.
deterioration. Also, once empiric therapy begins to render the patient less infectious, the risk of transmission to contacts decreases.

While awaiting the results of conventional DST, WHO recommends the country's standard, empiric MDR regimen for patient groups with high levels of MDR and the eight-month first-line drug regimen for patient groups with medium or low levels of MDR.

For many countries, drug resistance surveys will show that patients whose prior course of therapy has failed have a high likelihood of MDR so this group will receive a standard MDR regimen. When DST results become available, regimens should be adjusted appropriately. If the patient's DST results show susceptibility to isoniazid and rifampicin, treatment is changed to the six-month rifampicin containing regimen used for new patients.

Often drug resistance surveys show that those relapsing or returning after default will have a medium or low likelihood of MDR, so they will receive the eight-month retreatment regimen of first-line drugs. However, levels of MDR in these patient registration groups vary by setting.

Previously treated patients in settings where DST is not routinely available for individual patients—In many countries, there is not yet laboratory capacity to routinely conduct DST for each previously treated patient (or the results arrive too late to guide therapy). Even though DST is not yet routinely available for individual patient management in these countries, the NTP may be able to collect or access some information on levels of MDR-TB in previously treated patients, by using data from a drug resistance survey, a national or supranational reference laboratory. These data are critical for ascertaining the level of MDR in retreatment patients.

For anti-TB therapy to be effective, appropriate medicines must be used in appropriate doses and ingested correctly for appropriate durations. Adherence to treatment is crucial to achieve cure. Factors that may lead patients to interrupt or stop treatment must be addressed. Services providing TB care in prisons should offer support to patients to ensure that treatment will be completed. Close liaison between the prisons and the NTP is necessary to ensure that prisoners with TB complete treatment after release.

'Response to treatment should be monitored by sputum smear examination. In general, two sputum specimens should be collected for smear examination at each follow-up sputum check. Sample collection should be done without interrupting treatment."

'At the time of a patient's registration to start treatment, setting aside enough time to meet with the patient is important. This initial meeting is a prime opportunity to advise, counsel, and educate the patient on the following

- The importance of cough hygiene (e.g. cover the mouth when coughing and sneezing)
- DOT
- How to recognize potential side effects
- The need for follow-up through sputum smear monitoring
- The use of isolation measures.'

Recommended treatment regimens for previously treated patients (re-treatment regimen) is detailed in Table 7 on page 56 of the guideline.

'Care of patients receiving TB treatment include: Monitoring of TB Patients for Significant Adverse Effects of Anti-TB Medicines (see Table 11 on page 66 of the guideline)

Prevention of adverse effects of medicines

Discharge planning for soon-to-be-released prisoners is an important part of TB case management. It is essential in ensuring the continuity of TB management and therapy among persons with TB and LTBI."

'The success of post-release follow-up relies on two factors:

- A structured system of referral between the prison and the community
- Interventions to increase adherence to TB treatment.

Although these factors should be addressed by the NTP, often they are not.'

**LTBI**

'HIV-infected individuals with LTBI can receive IPT to prevent them from developing active forms of TB. IPT has been demonstrated to reduce the risk of progression from latent infection to active TB by up to 60 percent. Its efficacy on survival and duration of the protection conveyed remains limited [WHO and CDC. 2008. A Revised Framework to Address TB-HIV Co-infection in the Western Pacific. Geneva: WHO].

IPT is part of the package of care for persons living with HIV/AIDS. The benefit of IPT has been studied among patients with a positive tuberculin test (TST). Many countries however, do not use or have access to TST. The lack of TST should not preclude programs from implementing IPT. In such settings, IPT can be started without TST results as part of the package of care for persons living with HIV/AIDS. It is crucial, prior to initiating IPT, to rule out active tuberculosis. IPT is given daily through self-administration for six to nine months.'
WHO. Prison and health. 2014

The aims of treatment for TB are to cure the patient and restore quality of life and productivity, to prevent death from active TB or its late effects, to prevent relapse of TB, to reduce transmission of TB to others and to prevent the development and transmission of drug resistance. There are five anti-TB first line drugs: rifampicin (R), isoniazid (H), ethambutol (E), pyrazinamid (Z) and streptomycin (S). Rifampicin and isoniazid are the most powerful bactericidal medicines active against TB bacilli. In prison settings, a daily treatment is recommended and the whole process should be under the direct supervision of a health-care worker (Rapid implementation of the Xpert MTB/RIF diagnostic test. Technical and operational ‘How to’ practical considerations. Geneva, World Health Organization, 2011 [http://whqlibdoc.who.int/publications/2011/9789241501569_eng.pdf]). WHO recommends the use of fixed-dose combination drugs as they are thought to improve adherence, errors in prescribing are avoided and the number of tablets to be ingested is reduced (Treatment of tuberculosis: guidelines for national programmes. Geneva, World Health Organization, 2003. Available from: http://whqlibdoc.who.int/hq/2003/who_cds_tb_20033313_eng.pdf).

New patients (who have no history of previous TB treatment or who have received anti-TB drugs for less than one month) with pulmonary TB should receive a regimen including six months of rifampicin. In the intensive phase the patient receives isoniazid, rifampicin, pyrazinamide and ethambutol daily for two months, and in the continuation phase isoniazid and rifampicin for four months (2HRZE/4HR).

Since in many settings, particularly prisons, the risk of drug-resistant TB may be high, it is highly recommended that the resistant pattern of the strains the patient is infected with is documented and the appropriate treatment administered accordingly.

The approach to the initiation of retreatment depends on the laboratory capacity of the country/institution, specifically when (or if) DST results are routinely available for the individual patient. Countries using rapid molecular based DST will have results for rifampicin/isoniazid available within one to two days; these results can be used in deciding which regimen to start for the individual patient.

The use of conventional DST methods yields results within weeks (for liquid media) or months (for solid media). Because of this delay, prison health facilities using conventional methods will need to start an empirical regimen while DST results are awaited and then modify the regimen based on the DST results. Alternatively, treatment might be started with the standard re-treatment regimen, which includes streptomycin and lasts for eight months (2HRZES/1HRZE/SHRE), and modified once the DST results are available.'

'The European Region has the highest rate of multi-drug resistant TB (MDR-TB) in the world, which illustrates the failure of health systems to treat the disease effectively. Additionally, the social determinants contributing to the emergence and spread of the disease still prevail in most settings. People living with HIV, migrants, prisoners and other vulnerable populations are at most risk.'

The Consolidated Action Plan to Prevent and Combat Multidrug and Extensively Drug-Resistant Tuberculosis in the WHO Regional Office for Europe Region 2011–2015 has six strategic directions and seven areas of intervention. In view of the high prevalence of M/XDR-TB in prison settings, prison health systems should follow all the steps defined for the civilian sector, as only very close integration between civilian and prison health systems guarantees success countrywide. The Plan includes the following special action to be taken in prison settings:

Strengthen MDR-TB control in prisons

Activity 7.2.1 The Regional Office, using the successful model of its Health in Prison Project, will assist Member States in continuously improving TB control in penitentiary services.

Activity 7.2.2 Member States will ensure that early diagnosis and effective treatment of M/XDR-TB are available in all penitentiary services across the Region by the first quarter of 2013.

Activity 7.2.3 Member States will establish mechanisms for the continuum of care for released prisoners receiving TB treatment by the end of 2012.'

Source: WHO Regional Office for Europe. Prison and health 2014. (Type of guideline: practice-based; level of evidence: ++, ++, 0) [6]

WHO Regional Office for Europe. Health in prisons. 2007

'To ensure that the treatment takes place without interruption, most tuberculosis control programmes have introduced directly observed therapy (DOT). The drugs are thus taken while the health care worker watches the intake.

The progress of treatment is measured after the initial phase at the end of the second month by microscopy of sputum and then again in the continuation phase and at the end of treatment.

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An important managerial feature of the WHO strategy for controlling tuberculosis is that treatment outcomes (see Table 6.1 on page 50 of the guideline) are registered in a way that enables cohort analysis.

‘Five first-line drugs are available for normal tuberculosis treatment. A combination of these drugs has to be taken regularly to prevent the development of resistance. Each drug dose includes several tablets. To prevent mistakes, health care staff should supervise the administration of each dose (direct observed therapy (DOT)).

The usual treatment duration is 6–8 months. Because many tablets have to be taken, ideally under direct observation, and because of the long duration of treatment, achieving treatment success in prisons is quite complicated.’

‘Proper treatment will reduce coughing in two to three weeks and, if the bacilli are sensitive to the drugs used, the majority will be killed within one month. Treatment is needed for a minimum of six months and often longer, with an initial phase in which four to five drugs are used and a continuation phase in which two to three drugs are needed. Because treatment is required over a long period of time and with several drugs, ensuring adherence is often difficult. Another problem in correctional facilities in eastern Europe is that more than half of the people with tuberculosis harbour bacillary strains that are resistant to the commonly used drugs. These people are very difficult to cure and may remain infectious for a long time.’

‘A very serious form of tuberculosis that is resistant to the usual anti-tuberculosis drugs has developed in recent years. Multidrug-resistant tuberculosis is especially prevalent in prisons in eastern Europe, where 30–50% of prisoners with tuberculosis probably have multidrug-resistant tuberculosis. Second-line drugs, in large quantities and for a very long duration (18 to 24 months), must be administered to people with multidrug-resistant tuberculosis. These drugs are weak, are very expensive, create many adverse effects and are not always in sufficient supply on the world market.’

Source: WHO Regional Office for Europe. Health in prisons. 2007 (Type of guideline: practice-based; level of evidence ++, +, 0) [31]

**Guidelines specific to the prison setting – national guidelines**

**United Kingdom: Tuberculosis in prisons or immigration removal centres.**

All prisoners and immigration removal centre detainees having treatment for active TB should have a named TB case manager. The case manager should be responsible for contingency planning for discharge from prison or detention.

Prisons and immigration removal centres should ensure multidisciplinary TB staff have access to prisoners and detainees who need treatment (for example, by being given security clearance).

All prisoners having treatment for active TB should have directly observed therapy.

Prison health services should have contingency, liaison and handover arrangements to ensure continuity of care before any prisoner on TB treatment is transferred between prisons or released. In addition, other agencies working with prisoners or detainees should also be involved in this planning.

Prison and immigration removal centre healthcare services should liaise with the named TB case manager (from the multidisciplinary TB team) to ensure contingency plans for continuation of treatment are drawn up for prisoners and immigration removal centre detainees with TB.

Multidisciplinary TB teams should ensure accommodation is available for the duration of TB treatment after the prisoner or detainee’s release.

Multidisciplinary TB teams should ensure direct observed therapy is arranged for prisoners or detainees being treated for TB after their release. This should be available close to where they will live in the community.

Source: Tuberculosis in prisons or immigration removal centres. National Institute for Health and Care Excellence (NICE). 2016 (Type of guideline: evidence-based; level of evidence: ++, ++, +) [57]

**United Kingdom: Management of tuberculosis in prisons: Guidance for prison healthcare teams.**

Assessment for multi-drug resistant (MDR) TB

All patients with confirmed or suspected pulmonary TB should have a risk assessment carried out in liaison with the local TB service in relation to multi drug resistant TB (MDRTB). The assessment will include:

- History of previous TB treatment
- History of contact with MDRTB
- Previous residence in a country with high incidence of MDRTB
- Known HIV infection
- History of non-compliance with previous medication
All cases at high risk of MDRTB must be isolated appropriately. This will usually mean transfer to an outside hospital.

'Urgent referral is required from the prison doctor/GP to the Consultant respiratory physician or infectious diseases Consultant in the local NHS TB service.'

'Prisoners must be given written and verbal information about their diagnosis and treatment and medical records should be updated as necessary.'

'The prisoner should be placed on medical hold by the prison doctor until s/he is fit to attend court and is no longer considered to be infectious to others.'

'All prisoners with TB (or who are on treatment for latent TB infection) should receive directly observed therapy (DOT) in which a responsible prison officer, nurse or pharmacist supervises, witnesses and records the swallowing of every dose of TB medication.'

'Anti TB drugs must never be given 'in possession'.

The local TB service (TB nurse) should visit the prisoner where possible within one week of the prisoner commencing TB treatment to assess side effects and clinical issues, and advise on compliance. Thereafter, agreed schedule for the TB nurse to visit each patient should be agreed.

Any issues of concern (e.g. compliance or side effects) noted by the prison healthcare team should be reported to the local TB service as soon as possible (same working day). The local TB service should undertake an immediate risk assessment on the telephone and should make a visit to assess the patient based on the risk assessment.

The prison doctor and the local NHS TB service must be informed of any missed dose of medication for any reason as soon as possible.

The prison lead nurse/TB link nurse will liaise weekly with pharmacy regarding prisoners on treatment to identify all TB patients on treatment in the prison.

Treatment cards should be regularly checked by the prison lead nurse/TB link nurse to ensure treatment is being given.

If the patient has to leave the prison for any reason e.g. court appearance, transfer or release, at least one week's medication should accompany him/her.

Prisoners taking methadone who are prescribed rifampicin may require an upward dose adjustment of methadone, as rifampicin decreases the efficacy of methadone. This must be done in liaison with the substance misuse doctor and the local TB service.

Only those who need to be aware of the diagnosis should be informed. Care must be taken to avoid stigmatisation of prisoners who have TB.


Italy: Protocollo operativo per la gestione della tubercolosi nel sistema penitenziario italiano.

'Recommendation 8. In subjects treated for latent or active TB the therapy should always be directly observed (DOT) by healthcare staff during the complete therapeutic course.

For the treatment of TB in special situations such as liver or kidney failure, pregnancy, toxic hepatitis, allergic reactions during treatment, HIV infections etc. the management in referral specialized centers is recommended.'

Source: Protocollo operativo per il controllo della tubercolosi nel sistema penitenziario italiano. Ministero della Giustizia, Dipartimento della amministrazione penitenziaria, Provveditorato regionale per la Puglia, Ufficio per il trattamento intramurale. 2008 (Type of guideline: practice-based; level of evidence: +,−,+) [58]

Other guidelines

European Union standards for tuberculosis care – standards for TB diagnosis

'Standard 7: Any practitioner treating a patient for TB is assuming an important public health responsibility to prevent ongoing transmission of the infection and the development of drug resistance. To fulfil this responsibility, the practitioner must not only prescribe an appropriate regimen, but also utilise local public and/or community health services, agencies and resources when necessary, to perform contact investigation, to assess the adherence of the patient and to address poor adherence when it occurs.

Standard 8: All patients (including those with HIV-infection) who have not been previously treated and without any risk factors for drug resistance should receive an internationally accepted first-line treatment regimen using drugs of known bioavailability. The initial phase should consist of two months of isoniazid, rifampicin, pyrazinamide and
Standard 9: To assess and foster adherence, a patient-centred approach to administration of drug treatment, based on the patient’s needs and mutual respect between the patient and the provider, should be developed for all patients. Supervision and support should be individualised and should draw on the full range of recommended interventions and available support services, including patient counselling and education. A central element of the patient-centred strategy is the use of measures to assess and promote adherence to the treatment regimen and to address poor adherence when it occurs. These measures should be tailored to the individual patient’s circumstances, based on a detailed anamnesis of the patient’s clinical and social history, and be mutually acceptable to the patient and the provider. Such measures may include direct observation of medication ingestion (directly observed treatment) and identification and training of a treatment supporter (for TB and, if appropriate, for HIV-infection) who is acceptable and accountable to the patient and to the health system. Appropriate incentives and enablers, including financial, social and psychosocial supports, may also serve to enhance treatment adherence.

Standard 10: Response to therapy in patients with pulmonary TB should be monitored by follow-up smear microscopy and culture at the time of completion of the initial phase of treatment (two months for drug-susceptible TB). If the sputum smear and culture are positive at completion of the initial phase, sputum smears should be examined again at three months and, if positive, drug susceptibility testing should be performed. In patients with extrapulmonary TB and in children unable to produce sputum, the response to treatment is assessed clinically.

Standard 11: An assessment of the likelihood of drug resistance, based on history of prior treatment, exposure to a possible source case having drug-resistant organisms and the community prevalence of drug resistance, should be obtained for all patients. Rapid testing, including rapid rifampicin and isoniazid resistance testing should be performed for all patients suspected of resistance as defined in standards 2 and 8. Furthermore, patient counselling and education should begin immediately for all TB patients, in order to minimise the potential for transmission. Infection control measures appropriate to the setting should be applied as recommended in ESTC public health standard 20.

Standard 12: Patients with, or highly likely to have, TB caused by drug-resistant (especially MDR/extensively drug-resistant (XDR)-TB) organisms should be treated with specialised regimens containing second-line anti-TB drugs. The regimen chosen may be standardised or based on suspected or confirmed drug susceptibility patterns. At least four drugs to which the organisms are known, or presumed, to be susceptible to, including an injectable agent and pyrazinamide, should be used. Treatment should be given for at least 20 months, the recommended intensive phase of treatment being 8 months (instead of six months as in previous recommendations).

Standard 13: A written record of all medications given, bacteriological response and adverse reactions should be maintained for all patients.


**WHO. Guidelines for the programmatic management of drug-resistant tuberculosis.**

In the treatment of patients with MDR-TB (who had not previously received MDR-TB treatment), it is recommended that there should be an intensive phase of at least 8 months’ duration and total treatment duration of at least 20 months.

Source: WHO. Guidelines for the programmatic management of drug-resistant tuberculosis. 2011 update. (Type of guideline: evidence-based; level of evidence: ++,++,++) [59]

**WHO. Treatment guidelines for drug-resistant tuberculosis, 2016 update**

In patients with rifampicin-resistant or multidrug-resistant TB, a regimen with at least five effective TB medicines during the intensive phase is recommended, including pyrazinamide and four core second-line TB medicines - one chosen from group A, one from group B, and at least two from group C8 (conditional recommendation, very low certainty in the evidence). If the minimum of effective TB medicines cannot be composed as above, an agent from group D2 and other agents from D3 may be added to bring the total to five.

Group A=Levofloxacin; Moxifloxacin; Gatifloxacin; Group B=Amikacin, Capreomycin, Kanamycin, (Streptomycin); Group C= Ethionamide (or Prothionamide), Cycloserine (or Terizidone), Linezolid, Clofazimine; Group D2=Bedaquiline, Delamanid; Group D3=p-aminosalicylic acid, Imipenem-cliaastatin, Meropenem, Amoxicillin-clavulanate, Thioacetazone
In patients with rifampicin-resistant or multidrug-resistant TB, it is recommended that the regimen be further strengthened with high-dose isoniazid and/or ethambutol (conditional recommendation, very low certainty in the evidence).

In patients with rifampicin-resistant or multidrug-resistant TB who have not been previously treated with second-line drugs and in whom resistance to fluoroquinolones and second-line injectable agents has been excluded or is considered highly unlikely, a shorter MDR-TB regimen of 9–12 months may be used instead of a conventional regimen (conditional recommendation, very low certainty in the evidence).

Source: WHO treatment guidelines for drug-resistant tuberculosis, 2016 update (type of guideline: evidence-based; level of evidence: +++, ++, +++) [60].
Appendix 10. Summary tables and guideline summaries – prevention

Peer-reviewed literature

The coverage, effectiveness, treatment initiation and cost-effectiveness of contact tracing after TB outbreaks in correctional facilities is summarised below. No studies were found that reported on respiratory isolation in correctional facilities.

Coverage, effectiveness and treatment initiation:

**EU/EEA countries**

<table>
<thead>
<tr>
<th>Reference, country, study design</th>
<th>Prison setting, number of contacts</th>
<th>Contact tracing method, testing method</th>
<th>Who, index case patient</th>
<th>Contacts screened, % (n/N)</th>
<th>Effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ahmed, 2007 [61] UK Outbreak study</td>
<td>Training prison n=55</td>
<td>'Stone in the pond' method, cut-off point of 30 hours contact time - HEAF test and QuantiFERON blood test - CXR for positive QuantiFERON and/or HEAF test contacts</td>
<td>Inmates, teachers, family/friends, prison officers and hospital contacts exposed to index case-patient</td>
<td>- Total: 90.9% (50/55) O Inmates: 28.0% (14/50) O Prison officers: 24.0% (12/50) O Teachers: 4.0% (2/50) O Hospital contacts: 32.0% (16/50) O Family: 10.0% (5/50) O Friends: 2.0% (1/50)</td>
<td>NR</td>
</tr>
</tbody>
</table>

CCDC: consultant in communicable disease control; CXR: chest radiograph; LTBI: latent tuberculosis infection; NR: not reported; TB: tuberculosis; UK: United Kingdom

*TST positives: number of persons with a positive TST/total number of persons tested

**Other countries**

<table>
<thead>
<tr>
<th>Reference, country, study design</th>
<th>Prison setting, number of contacts</th>
<th>Contact tracing method, testing method</th>
<th>Who, index case patient</th>
<th>Contacts screened, % (n/N)</th>
<th>Effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sosa, 2008 [62] USA Outbreak study</td>
<td>Correctional facility (state-run jail and prison) n=NR</td>
<td>All inmates who had resided at the prison since 2005 and employee testing - Medical histories - Symptom evaluation and TST - CXR in contacts with new positive TST and inmates with a previous positive TST</td>
<td>Inmates and employees exposed to one of the index case-patients - Case 1: male, M. tuberculosis cultured in mid-January 2006 from one of the sputum specimens - Case 2: male, identified in May 2006</td>
<td>- Inmates: % NR (910/NR) - Prison employees: % NR (485/NR)</td>
<td>TST positives: - Inmates: 5.8% (53/910) - Prison employees: 2.1% (10/485)</td>
</tr>
</tbody>
</table>

Griffin, 2004 [67] USA Outbreak study

3 jails, 1 state prison n=318

6-month contact investigation TST

Inmate contacts, jail/prison employees, household

- Total: 80.5% (256/318): 0

Inmate

TST positives: - Total: 18.4% (47/256)

Inmates: 27.5% (28/102)

- Total: 0.6% (2/256)

Inmate: 2.0% (2/102)

NR

Very low

86
<table>
<thead>
<tr>
<th>Reference, country, study design</th>
<th>Prison setting, number of contacts</th>
<th>Contact tracing method, testing method</th>
<th>Who, index case patient</th>
<th>Contacts screened, % (n/N)</th>
<th>TST positives, % (n/N); converters, % (n/N)</th>
<th>TB positivity rate, % (n/N)</th>
<th>Treatment initiation, % (n/N)</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bur, 2003 [63] USA Outbreak study</td>
<td>Local jail in Baltimore City - n=344 inmates - n=NR jail employees</td>
<td>Stepwise standard contact tracing approach - TST - Individuals with positive TSTs underwent CXR and clinical evaluation</td>
<td>All arrestees processed through one CBIF and jail treatment inmates of dormitory A - Sputum smears and cultures when clinical signs or abnormal CXR</td>
<td>Male index case-patient, smear positive in August 2002, after being held in 3 jails and 6 weeks after arrival in prison</td>
<td>39.8% (102/256) Jail/prison employees: 54.7% (140/256) Household contacts: 2.3% (6/256) Other contacts: 3.1% (8/256)</td>
<td>0 Jail/prison employees 10.7% (15/140) 0 Household contacts: 66.7% (46/69) 0 Other contacts: 0% TST converters in prior TST negatives: - Inmates: 10.0% (6/60)</td>
<td>- 2.7% (6/221) - TB treatment: 100% (6/6) - LTBI treatment: 37.5% (12/32)</td>
<td>Very low</td>
</tr>
<tr>
<td>Mclaughlin, 2003 [68] USA Outbreak study</td>
<td>Prison dormitory HIV-housing unit - n=323 inmates (n=157 right side; n=137 left side) - n=74 inmates released prior to screening - n=398 prison employees</td>
<td>Stepwise contact investigations - TST in all inmates with prior negative TST - Medical evaluation, record review, CBIF, LTBI treatment inmates of dormitory A - Sputum smears and cultures when clinical signs or abnormal CXR</td>
<td>Inmates, prison employees, visitors to case patients, and contacts of released case patients Male index case-patient, blood culture drawn in July 1999 grew M. tuberculosis susceptible to all first-line anti-TB medications, lived on right side of dormitory A</td>
<td>Inmates released prior to screening: 60.8% (45/74) - Prison employees: 77% (307/398)</td>
<td>- TST positives: - Initial screening jail contacts: % NR (17/NR) - Expanded screening jail contacts: 14.5% (32/221) - Jail employee contacts: 0% TST converters in prior TST negatives: - Inmates: 15.6% (38/249)</td>
<td>- TST positives: - Initial screening jail contacts: 41.2% (7/17) - Expanded screening jail contacts: 14.5% (32/221) - Jail employee contacts: 0% TST converters in prior TST negatives: - Inmates: 15.6% (38/249)</td>
<td>- TST positives: - Initial screening jail contacts: 41.2% (7/17) - Expanded screening jail contacts: 14.5% (32/221) - Jail employee contacts: 0% TST converters in prior TST negatives: - Inmates: 15.6% (38/249)</td>
<td>Very low</td>
</tr>
<tr>
<td>Mohle-Boetani, 2002 [69] USA Outbreak study</td>
<td>Correctional facility (HIV housing unit) - n=NR</td>
<td>Stepwise contact investigation within the prison of inmate case patient - Symptom review - TST all inmates - CXR for inmates with symptoms/TST conversion - Sputum samples for AFB detection</td>
<td>All inmates in the HIV housing unit Male index case-patient, smear positive for AFB on 28 August, 1995, isolated and treated</td>
<td>% NR (mid-October &gt;75 inmates screened; mid-November &gt;100 inmates screened; December &gt;450 inmates screened)</td>
<td>- TST converters in prior TST negatives: - Inmates: 46.6% (104/223)</td>
<td>- % NR (n=5) secondary cases before screening, based on symptoms - % NR (n=5) secondary cases in outbreak wing during screening - % NR (n=3) inmates recently paroled after residing in outbreak wing</td>
<td>- TST converters in prior TST negatives: - Inmates: 46.6% (104/223)</td>
<td>Very low</td>
</tr>
<tr>
<td>Patterson, 2000 [70] USA Outbreak study</td>
<td>State correctional facility (housing HIV+)</td>
<td>Contact investigation of dormitory A inmates - Symptom review - TST</td>
<td>All men who had spent 1-152 days in dormitory A during</td>
<td>Inmates: 69.0% (223/323) Left side: 66.7% (108/162)</td>
<td>- TST converters in prior TST negatives: - Inmates: 46.6% (104/223)</td>
<td>- 13.9% (31/232) Left side: 3.7% (4/108) Right side: 23.5% (27/115)</td>
<td>- TST converters in prior TST negatives: - Inmates: 46.6% (104/223)</td>
<td>Very low</td>
</tr>
<tr>
<td>Reference, country, study design</td>
<td>Prison setting, number of contacts</td>
<td>Contact tracing method, testing method</td>
<td>Who, index patient</td>
<td>Contacts screened, % (n/N)</td>
<td>TST positives, % (n/N); converters*, % (n/N)</td>
<td>TB positivity rate, % (n/N)</td>
<td>Treatment initiation, % (n/N)</td>
<td>Level of evidence</td>
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<tr>
<td>Prendergast, 1999 [64] USA Outbreak study</td>
<td>2 state correctional institutions (with HIV housing units) - n=542 inmates (prison A: n=312; prison B: n=140) - n=190 released inmates prison A+B: - n=542 prison employees (prison A: n=319; prison B: n=223)</td>
<td>Screening of all exposed inmates, released inmates and prison employees - Prison A: TST - Prison B: sputum specimen - CXR screening of all the contacts remaining in the housing unit</td>
<td>Inmates who resided at least 1 day on the same wing as case-patients and prison employees - Male index case-patient prison A, late August 1999, isolated and started multidrug TB therapy - Male index case-patient prison B, January 19, 1996, isolated and started multidrug TB therapy</td>
<td>- Prison A: 59.3% (185/312) of the exposed inmates - Prison B: 100% (140/140) of the exposed inmates - Prison A+B released inmates: 44.2% (84/190) - Prison employees prison A+B: NR</td>
<td>- Prison A: 10.0% (17/145)</td>
<td>- Prison A: 7.6% (14/186) inmates (including 3 parolees) - Prison B: 100% (1/1) LTBI treatment - Prison A: NR - Prison B: 100% (23/25)</td>
<td>Very low</td>
<td></td>
</tr>
<tr>
<td>Bergmire-Sweat, 1996 [65] USA Outbreak study</td>
<td>Department of Criminal Justice facility (medium security prison) - n=686 MROP inmates - n=NR prison employees</td>
<td>All inmates were screened - TST - CXR for positive TST results</td>
<td>Inmates or prison employees assigned to the MROP - Male index case-patient, diagnosed with AFB smear and culture positive TB in late April 1994</td>
<td>- 65.5% (449/686) subjects received PPD skin tests - 34.5% (237/686) subjects received CXR</td>
<td>- TST positives: 24.3% (109/449) Abnormal CXR with prior positive PPDs: 4.2% (10/237)</td>
<td>- Inmates: 2.0% (2/101) prison employee: % NR (1/NR)</td>
<td>- Standard 4 drug therapy including INH (INH, rifampin, ethambutol, pyrazinamide): 100% (15/15) - INH: 85.6% (89/104)</td>
<td>Very low</td>
</tr>
<tr>
<td>Valway, 1994 [71] USA Outbreak study</td>
<td>Maximum security prison n=471</td>
<td>Contact investigation was applied during the potentially infectious period - Interviews/medical records - TST - Converters and anergic inmates were examined with CXR</td>
<td>Inmates exposed to the index case patient - Male index case-patient, ill with undiagnosed MDR-TB when he arrived at prison</td>
<td>65.0% (306/471)</td>
<td>- TST positives: 30.1% (92/306)</td>
<td>- Inmates: 2.1% (10/471) - 2 inmates were susceptible to all medications - 1 inmate had already been diagnosed with TB - Prison guard: % NR (1/NR)</td>
<td>NR</td>
<td>Very low</td>
</tr>
<tr>
<td>Johansen, 1993 [72] USA Outbreak study</td>
<td>10 distinct correctional facilities n=NR</td>
<td>Contact investigations - Known TST-negative: baseline TST and TST repeated after 8-12 weeks - TST-positive: CXR</td>
<td>Inmates exposed to an active TB case - 34 contact tracing investigation s in the past 2 years; n=34 index cases of which n=28 had TB, 33 males and 1 female</td>
<td>- % NR (1,306/NR) inmates were skin tested - % NR (34/NR) contact investigations with sputum smear and culture information</td>
<td>- TST converters in prior TST negatives: 6.7% (8/120)</td>
<td>- 0.0%</td>
<td>NR</td>
<td>Very low</td>
</tr>
</tbody>
</table>
AFB: acid-fast bacilli; CBIF: central booking intake facility; CDC: Centers for Disease Control and Prevention; CXR: chest radiograph; HIV: human immunodeficiency virus; INH: isoniazid; LTBI: latent tuberculosis infection; MDR-TB: multi-drug-resistant tuberculosis; MROP: mentally retarded offenders program; NR: not reported; PPD: purified protein derivative; TB: tuberculosis; TST: tuberculosis skin test; USA: United States of America.

* TST positives: number of persons with a positive TST/total number of persons tested

* TST converters are calculated only for those persons with a known baseline negative TST: number of persons who converted to a positive TST/total of persons with known baseline negative TST

1 Of the 119 converters, n=15 were lost to follow-up and n=15 received standard-4 drug therapy.

**Cost-effectiveness**

No studies were found that reported on the cost-effectiveness of TB contact tracing in correctional facilities.

**Grey literature**

The coverage, effectiveness, treatment initiation and cost-effectiveness of contact tracing after TB outbreaks in correctional facilities is summarised below. No studies were found that reported on respiratory isolation in correctional facilities.

**Coverage, effectiveness and treatment initiation**

<table>
<thead>
<tr>
<th>Reference, country, study design</th>
<th>Prison setting, number of contacts</th>
<th>Contact tracing method, testing method</th>
<th>Who, index case patient</th>
<th>Contacts screened, % (n/N)</th>
<th>TST positives*, % (n/N); converters*, % (n/N)</th>
<th>TB positivity rate, % (n/N)</th>
<th>Treatment initiation, % (n/N)</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schwartz, 1992 [66] USA Outbreak study</td>
<td>State correctional institution n=3,070</td>
<td>Contact investigation TST</td>
<td>Inmates and employees exposed to index-case patient 3 index case patients diagnosed between Sept-Oct 1991, in total 7 person-months infectious during 1991</td>
<td>95.9% (2,944/3,070)</td>
<td>TST positives: - Inmates: 29.7% (873/2,944) TST converters in prior TST negatives: - Inmates: 45.7% (148/324) - Employees % NR (2/NR)</td>
<td>NR</td>
<td>NR</td>
<td>Very low</td>
</tr>
<tr>
<td>Gabbuti A 2010 [73] Italy Outbreak study</td>
<td>Single prison (Solicciano, Tuscany) N=156 -9 cellmates -147 section contacts</td>
<td>NR TST</td>
<td>Inmates, contacts exposed to index-case patient 1 case of smear positive pulmonary TB diagnosed on November 2010 - Cellmates: 100% (9/9) - Section contacts: 85.0% (125/147)</td>
<td>TST positives: - Cellmates: 77.8% (7/9) - Section contacts: 55.2% (69/125) Converters: - Cellmates: NR - Section contacts: 19.7% (11/56)</td>
<td>Total: 0.8% (1/125)</td>
<td>- TB treatment for six months: n=1 (100%) - Prophylaxis: n=7/7 (100%) cellmates with positive TST</td>
<td>Outbreak study</td>
<td></td>
</tr>
<tr>
<td>Pankania B 2016 [74] UK Outbreak study</td>
<td>Single prison (Bristol) N=78 (30 members of staff and 48 inmates) Other contacts: -23 prisoners</td>
<td>NR Questionnaire + IGRA</td>
<td>Inmates, prison staff, other contacts exposed to index-case patient A young male, ex recent inmates (released</td>
<td>IGRA positive: 0% Converters: 0% (22 contacts have not completed follow up)</td>
<td>Not applicable</td>
<td>Outbreak study</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Systematic review on the diagnosis, treatment, care and prevention of tuberculosis in prison settings

### Cost-effectiveness

No studies on cost-effectiveness have been found from the grey literature search.

### Guidelines

**Guidelines** specific to prison setting — supranational guidelines

**WHO. Prisons and health**

TB infection control is a combination of measures aimed at minimizing the risk of TB transmission. The basis of such infection control is early and rapid identification of individuals with suspected and known TB and effective treatment of disease. TB infection control, as a component of WHO's revised Stop TB Strategy (Stop TB Partnership. Global Plan to Stop TB 2011– 2015. Geneva, World Health Organization, 2010), is intended to strengthen health systems.

Policy and service delivery areas related to TB infection control (WHO policy on TB infection control in health-care facilities, congregate settings and households. Geneva, World Health Organization, 2009 [http://whqlibdoc.who.int/publications/2009/9789241598323_eng.pdf]) may be studied at four levels:

- managerial (organizational) control measures, including the development of TB infection control policy, strategic planning, advocacy, human resource development, monitoring and evaluation, operational research;
- administrative control measures, including early TB case detection, TB screening, separation or isolation of patients, cough etiquette and hygiene;
- environmental control measures, including natural and mechanical ventilation, ultraviolet germicidal irradiation;
- personal protection control measures, including respirators and respiratory fit testing.


- preventing the spread of infection from community to prison by using intensified TB screening for new or transferred prisoners and preparing special quarantine blocks or cells (to be used for one or two weeks) for new or transferred prisoners;
- preventing the transmission of TB infection from one prisoner to other prisoners or to prison staff by:
  - conducting contact investigations for TB suspects and cases;
  - improving infection control by carrying out organizational, administrative and environmental interventions in prisons;
  - and using information, education and communication for prisoners;
- preventing the infection of family members and the community by released prisoners or prison staff by examining prisoners before release and examining prison staff regularly;

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6 Relevant guidelines were critically appraised with a selection of criteria derived from the AGREE instrument (1. The overall objective/objectives of the guideline is/are specifically described; 2. Systematic/clear methods were used to search for evidence for compiling the data and/or clear data sources/references; 3. The recommendations are specific and unambiguous). The criteria were qualitatively scored using - - or -, 0, + or ++; no total quality score of summed + and – was calculated.
• establishing TB infection control in the community by instituting early TB case detection and using effective treatment.

Source: WHO Regional Office for Europe. Prison and health 2014. (Type of guideline: practice-based; level of evidence: ++,0) [6]

**WHO. Policy on TB infection control in health-care facilities, congregate settings and households.**

'Control 8a – Promptly identify people with TB symptoms (triage)

Prompt identification of people with TB symptoms (i.e. triage) is crucial. [...] people suspected of having TB must be separated from other patients, placed in adequately ventilated areas, educated on cough etiquette and respiratory hygiene, and be diagnosed as a matter of priority (i.e. fast tracked).

Control 8b – Separate infectious patients

It is also crucial to separate infectious patients after triage. The specific criteria (e.g. smear and culture status) for separating patients will depend on the local settings and patient population. In particular, patients living with HIV or with strong clinical evidence of HIV infection, or with other forms of immunosuppression, should be physically separated from those with suspected or confirmed infectious TB. Patients with culture-positive drug-resistant TB – especially MDR and XDR-TB – or people suspected of having drug-resistant TB should be separated (preferably according to the drug resistance profile) or isolated from other patients, including other TB patients.'

Source: WHO policy on TB infection control in health-care facilities, congregate settings and households. WHO. 2009 (Type of guideline: practice-based; level of evidence: ++,++,++) [75]

**WHO Regional Office for Europe. Health in prisons.**

'The individual behavior of people with tuberculosis can significantly reduce the spread of tuberculosis:

• most importantly, tuberculosis drugs must be taken regularly;
• covering the mouth with a tissue when coughing, sneezing or laughing is also important;
• people with active tuberculosis should not go to places where contact with healthy people is possible; and
• windows should be opened frequently so that rooms can be ventilated adequately.'

'The fact that tuberculosis can be cured with correct treatment led to the most potent interventions – the ones that take into account the population perspective. Mathematical modelling has shown that identifying at least 75% of the infectious cases and curing at least 85% of them will sharply reduce the rate of transmission in the population – to the extent that this effectively controls disease.'

'Support for case finding – such as by referring prisoners with symptoms to health care workers – can lead to earlier treatment, reducing the amount of time people who are infectious spend with other prisoners, and can therefore be an efficient measure for controlling tuberculosis.'

Source: WHO Regional Office for Europe. Health in prisons. WHO, 2007 (Type of guideline: practice-based; level of evidence: ++,0) [31]

**Tuberculosis Coalition for Technical Assistance, International Committee of the Red Cross, USAID. Guidelines for control of tuberculosis in prisons.**

'Prison health services are often ill-equipped to respond to the challenge of implementing effective TB control. TB infection control is a combination of measures aimed at minimizing the risk of TB transmission. The foundation of such infection control is early and rapid identification of individuals with suspected and known TB and effective treatment of disease. Developing (TB) infection control capacity should be embedded in broader strategic plans, so that resources are allocated. Clear goals and objectives, activities, and outcomes have to be defined by program managers and prison health authorities.' Policy and service delivery areas related to TB infection control may be studied at four levels:

• Programmatic (organizational) control measures, including TB infection control policy development, strategic planning, advocacy, human resource development, monitoring and evaluation, and operational research
• Administrative control measures, including early TB case detection, TB screening, separation or isolation of patients, and cough etiquette and hygiene
• Environmental control measures, including natural and mechanical ventilation and ultraviolet germicidal irradiation (UVGI)
• Personal protection control measures, including respirators and respiratory fit testing.
Several infection control measures could be conducted based on figure 7:

Preventing spread of infection from community to prison by:
- Using intensified TB screening for new or transferred prisoners
- Preparing adaptation blocks or rooms (to be used for two to four weeks) for new or transferred prisoners

Preventing TB infection among prisoners (from one TB prisoner to other prisoners) or to prison’s staff by:
- Conducting a contact investigation for TB suspects and cases
- Improving infection control (i.e., implementing organizational, administrative, and environmental interventions) in prisons
- Using information, education and for prisoners

Preventing infection of family members and the community by a released prisoner or prison staff by:
- Examining prisoners before release
- Examining prison staff regularly

Establishing TB infection control in the community by:
- Instituting early TB case detection
- Using effective treatment’

Source: Guidelines for control of tuberculosis in prisons. Tuberculosis Coalition for Technical Assistance, International Committee of the Red Cross, USAID. 2009 (Type of guideline: practice-based; level of evidence: ++, ++, 0) [18]

Guidelines specific to prison setting - national guidelines

**United Kingdom: Tuberculosis in prisons or immigration removal centres.**

‘In prisons or immigration removal centres, everyone with X-ray changes indicative of active TB, as well as those with symptoms who are awaiting X-ray, should be isolated in an adequately ventilated individual room or cell. Prisoners and detainees should be retained on medical hold until they have:

- Proven smear-negative and had an X-ray that does not suggest active TB, or
- Had a negative risk assessment for multidrug-resistant TB and completed 2 weeks of the standard treatment regimen.’

Source: Tuberculosis in prisons or immigration removal centres. National Institute for Health and Care Excellence (NICE). 2016 (Type of guideline: evidence-based; level of evidence: ++, ++, ++) [57]

**United Kingdom: Management of tuberculosis in prisons: Guidance for prison healthcare teams.**

‘Any prisoner with a productive cough for more than three weeks who also has any other TB symptom (fever, night sweats, coughing blood, weight loss or generally feeling unwell) should be isolated in a single cell as soon as possible (preferably in the healthcare unit if available) and should have a medical assessment as soon as possible.’

‘Prisoners should be isolated in a single cell in the following circumstances:

- High clinical suspicion of pulmonary TB, pending the outcome of diagnostic tests.
- Abnormal chest x-ray with suspicion of TB, pending the outcome of diagnostic tests.
- With confirmed pulmonary smear positive (sputum microscopy) TB, can only be moved out of the single room if compliant with treatment for at least the first two weeks and have been assessed by the local TB service.
- Confirmed pulmonary TB and non-compliant with treatment, for as long as deemed necessary by the local TB service and Health Protection Team.

Patients with pulmonary smear positive TB should be asked to wear a surgical mask when leaving isolation during the infectious period (usually until two weeks’ treatment is complete).’


**Spain: Prevención de la trasmisión aérea de la tuberculosis en centros penitenciaros.**

‘Conditions of isolation rooms:

1. The patient should be always isolated in a single cell. Isolation cells must be the sunniest and the ones that allow the best ventilation and must be far from person transit and preferably situated in high floors.'
2. The door must be always closed. Windows must be always closed before opening the door.

3. The air coming out from the isolation cell must not enter the general ventilation and an isolated circuit should be in place.

4. The ventilation system must permit the complete air renewal at least 6 times per hour (ideally 12 times).

5. The installation of a common extractor hood (like cooker hoods) could be sufficient to ease air renewal 6 times per day. A negative pressure system between the cell and the aisle must be created.

6. A consultation with a specialized technician is suggested for the choice of the extractor hood.

7. If a forced air system is not available, the air renewal should be assured by opening the window for at least 5 minutes several times per day.

8. Air direction should be monitored in order to confirm the presence of negative pressure in the cell.

9. The existence of an anteroom separating the isolation cells from the aisle could increase the efficacy of the isolation.

10. In all infirmaries an isolation room should be present. However, it is desirable that at least 10% of the rooms could be allocated to this purpose.

11. A sign with basic recommendations should be placed on the isolation cell door.

12. High filtration efficiency masks (0.1 μ) for prison officers and support staff who have direct contacts with the patient must be available.

13. Surgical masks for the patients in isolation must also be available."

Source: Prevención de la transmisión aérea de la tuberculosis en centros penitenciarios. 2ª edición. Gobierno de España, Ministerio del Interior, Ministerio de Sanidad y Consumo. 2009 (Type of guideline: practice-based; level of evidence: +,+,+)[77]

The Netherlands. TB procedure voor arrestantenbewaarders en penitentiair medewerkers

The following steps should be undertaken regarding prevention of TB among staff:

1. Verification of suspicion of/diagnosis of TB: is it infectious? To assess infectiousness, symptoms and complaints should be assessed, mainly cough complaints, and a chest X-ray and sputum investigation are necessary. Measures that should be undertaken before consulting the physician are:
   - Do not place the person suspected of TB in a cell with others
   - Approach the person suspected of TB with an appropriate nose and mouth masks (type FFP2)*

2. When the physician strongly suspects active TB: direct isolation should take place and further diagnostics should be performed as soon as possible. The persons suspected of active TB should be transported for diagnostics wearing a nose and mouth mask (type FFP2)

3. When active infectious TB is confirmed, the patient stays in isolation. Staff directly contacting the patients should wear a nose and mouth mask (type FFP2) when entering the cell.

*A mask that is effective in the prevention of TB should meet the following criteria:

- Cover both the nose and the mouth
- A filtering efficiency of at least 95% for particles >1 μm
- Leakage of 10% or less

The mask should meet the European guideline EN 149-2001 and should be of the type FFP-2.

Source: Tuberculose bij arrestanten en gedetineerden: procedure voor arrestantenbewaarders en penitentiair medewerkers. KNCV Tuberculosefonds (2013) (Type of guideline: practice-based; level of evidence: -,-,0)[76]

Other guidelines – supranational guidelines

European Union standards for tuberculosis care – standard for public health and TB prevention

'Standard 18: All providers of care for patients with TB should ensure that persons who are in close contact with patients who have infectious TB (e.g. in families, congregate settings like migrants shelters, schools and prisons), are evaluated and managed in line with international recommendations. The risk of TB transmission depends on the concentration of the mycobacteria in the air, the duration of the contact and the susceptibility of the contact to infection and disease. The determination of priorities for contact investigation is based on the likelihood that a contact: 1) has undiagnosed TB; 2) is at high risk of having been infected by the index case; 3) is at high risk of developing TB if infected; and 4) is at risk of having severe TB if the disease develops.
Standard 19: Children under five years of age and persons of any age with HIV infection who are close contacts of an infectious index patient and who, after careful evaluation, do not have active TB should be treated for presumed latent TB infection with isoniazid.

Standard 20: Each healthcare facility caring for patients who have, or are suspected of having infectious TB, should develop and implement an appropriate TB infection control plan.

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