



SCIENTIFIC ADVICE

Guidance on tuberculosis control in vulnerable and hard-to-reach populations

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This guidance was coordinated by the ECDC project manager Andreas Sandgren, and produced by an ECDC editorial team consisting of Andreas Sandgren, Marieke J. van der Werf, Netta Beer and the ad hoc scientific panel.

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Abbreviations

CXR	Chest radiography
DOT	Directly observed treatment
ESTC	European Union Standards for Tuberculosis Care
ETHOS	European Typology of Homelessness and housing exclusion
EU/EEA	European Union and European Economic Area
HRDU	High-risk drug users
IDU	Injecting drug users
MXU	Mobile chest X-ray unit
NICE	National Institute for Health and Care Excellence
TB	Tuberculosis
LTBI	Latent TB infection
VOT/VDOT	Video observed treatment/video directly observed treatment

Glossary

Community worker

Community health workers, community health promoters, lay health advisors etc. are members of a community that provide basic health and medical care to their community. In some countries the term 'community worker' is used to indicate a professional who, through training, has the knowledge to work in promoting the welfare of individuals and communities.

Directly observed treatment

An approach which seeks to improve the adherence of people to tuberculosis treatment by having health workers, family members, or community members directly observing them taking their anti-tuberculous drugs [1].

Incentives

Financial or material rewards that patients and/or providers receive, conditional on their explicitly-measured performance or behaviour [2,3]. Rewards that encourage patients with both suspected and confirmed TB to attend TB screening, out-patient follow-up and DOT appointments must meet patients' interests and needs [4], and may include money, vouchers or other 'in kind' rewards.

Enablers

Things or measures which assist patients to adhere to diagnosis and treatment by overcoming barriers to completing investigations and TB treatment [3,4]. Economic constraints due to absences from work to attend appointments, or the direct and indirect costs of accessing treatment, were commonly cited by patients as important barriers to completing TB treatment [5]. Other barriers that are likely to impact on outcomes include housing, nutrition, immigration status and transport [4]. Possible enablers could be, for example, a mobile telephone or public transport tickets.

Intervention

Any measure to improve the success of TB prevention, diagnosis and treatment.

Service models

Any organisational-level intervention aimed at improving TB diagnosis or treatment. This may include:

- specific services, such as outreach clinics
- types of service delivery or accessibility to reduce barriers to accessing TB services; the provision of services in new settings or by different providers
- the way in which information or knowledge management schemes are used to facilitate service delivery
- professional development and education
- other interventions to raise clinicians' and other professionals' awareness of TB [6-8].

Case management

The comprehensive follow-up of a suspected or confirmed TB case, the investigation of and, if needed, treatment, of their contacts. Case management will usually be provided by a specialist TB nurse or a nurse with responsibilities that include TB. Dependent upon the patient's particular circumstances and needs, case management can also be provided by appropriately trained and supported non-clinical members of a TB multidisciplinary team [4].

Standard case management

Co-ordinated by a named case manager and is appropriate for any patient without complicated clinical disease or psychosocial problems, who is able to self-administer treatment and come for regular follow-up to a hospital or community setting. Self-administered treatment is where the patient takes responsibility to collect, organise and administer their medication [4].

Enhanced case management

Co-ordinated by a named case manager working alongside a specialist multidisciplinary TB team able to provide expert clinical and psychosocial care and to engage effectively with the client and the community. Patient centred care which includes Directly Observed Treatment (DOT) or other means of supporting TB treatment adherence should be considered the standard of care from the start of treatment for all TB patients who require enhanced case management [4].

Vulnerable and hard-to-reach populations

Those whose socioeconomic conditions or lifestyle makes it difficult to recognise TB symptoms, access health services, self-administer treatment and attend regular healthcare appointments [9]. Other terminology which has been used to describe these populations include 'under-served' [10] or 'poorly reached' populations.

Executive summary

As tuberculosis (TB) incidence drops in most EU/EEA countries, the disease becomes concentrated in those who are at the lower end of the socio-economic scale and especially among vulnerable and socially excluded populations. Tailored approaches are needed to facilitate effective prevention and control of active TB among these groups, whose socioeconomic conditions or lifestyle make it difficult to recognise TB symptoms, access health services, self-administer treatment and attend regular healthcare appointments. Vulnerable and hard-to-reach populations include: homeless people or people with a history of homelessness, high-risk drug users, people with problematic alcohol use, people in prison or in enforced segregation, some vulnerable migrant populations who are excluded from health and social care services and other marginalised, poor and remote groups.

The purpose of the guidance is to provide support, in the form of scientific advice on the options available, to national policymakers, entities responsible for the planning of healthcare and social support systems, national TB programmes, and civil society/non-governmental organisations with an interest in TB, as well as those working with vulnerable groups, when considering strengthening TB prevention and control among vulnerable populations. This guidance provides an overview of interventions to improve early diagnosis of TB and treatment completion in these populations, as well as factors to consider when developing programmes for health communication, awareness and education, and programme monitoring and evaluation.

Several interventions were identified through systematic reviews of published literature for improving early diagnosis and treatment completion. These interventions addressed access to health services and health service providers, the promotion of understanding, communication and trust between patients and health providers, and the enhancement of treatment adherence by enabling, motivating and simplifying completion of diagnosis and treatment. The evidence reviewed indicates that improving access can be achieved through outreach programs using outreach teams and mobile units. Outreach teams included community health workers, street teams, peers and non-clinical professionals who establish a close contact with the patients to facilitate screening, contact tracing and treatment completion through enhanced case management.

Ways of ensuring timely interaction between patients and TB clinics, for both screening and follow-up attendance, included facilitation of contact and use of active referrals. Improving service models and strengthening collaboration between healthcare services, as well as other institutions, have also been shown to improve uptake of screening and treatment by vulnerable populations. Integration of diagnosis and treatment services for different diseases might also lead to improvements. Monetary and material incentives were found to motivate and enable diagnosis and treatment completion, and the use of mobile phones and computers were also identified as a means for reminding patients to attend clinics or for ensuring they have taken their treatment.

Factors to consider when developing health communication, awareness and education programs include potential facilitators and barriers to diagnosis and treatment. Barriers include personal perceptions and social barriers such as stigma and fear, as well as service organisation-related barriers such as lack of access to services or lack of understanding or trust between patients and health providers. Facilitators may include support networks for the patient and culturally-sensitive care.

The range of interventions identified in this guidance document is not exhaustive, and the quality of the evidence is not always very strong. Therefore, existing interventions would benefit from being properly assessed for feasibility and effectiveness, including cost-effectiveness, in different vulnerable populations, contexts and settings. As Europe is targeting TB elimination, the development, implementation and evaluation of additional interventions to improve TB diagnosis and treatment in vulnerable populations would greatly benefit TB control.

Introduction

Objective of guidance

To provide an expert opinion on systematically reviewed evidence on targeted interventions, aimed at facilitating the effective prevention and control of tuberculosis (TB) among vulnerable and hard-to-reach populations, through addressing socio-behavioural determinants and other factors that increase risk of delayed diagnosis, onward transmission, treatment interruption, drug resistance, treatment failure and preventable death.

Scope of guidance

This document aims to provide guidance on interventions and service models for TB prevention and control in vulnerable and hard-to-reach populations in the European Union and European Economic Area (EU/EEA). The topic of TB in vulnerable populations has been identified as relevant for action in the Framework Action Plan to Fight Tuberculosis in the European Union [11], the European Union Standards for Tuberculosis Care (ESTC) [12], the action framework for tuberculosis elimination in low-incidence countries [13], and the concept papers on how to address tuberculosis control in urban risk groups [14,15].

This guidance provides the results of systematic reviews and ad hoc scientific panel opinions based on these results. This is followed by an ECDC assessment.

Vulnerable and hard-to-reach populations are defined as those whose socioeconomic conditions or lifestyle make it difficult to recognise TB symptoms, access health services, self-administer treatment and attend regular healthcare appointments [9]. Targeted interventions of relevance to these populations fall into two groups: TB-specific interventions and interventions that aim to address broader structural and intermediate determinants that increase vulnerability.

Interventions addressing broader structural determinants may address issues such as poverty and overcrowding, while TB specific interventions aim to detect cases early in order to interrupt transmission and prevent severe complications of late diagnosis, limit progression of infection to disease, and ensure TB treatment completion and cure. In this document we mainly focus on the TB-specific interventions, however, the importance of simultaneously addressing broader structural determinants as part of a comprehensive strategy to achieve TB elimination cannot be overstated.

Since the target populations for interventions in this guideline are defined as vulnerable due to their social circumstances and lifestyle, the guidance covers interventions that address the socio-behavioural determinants of TB in these populations. It does not include interventions that are primarily targeted at individuals whose risk for TB exposure, infection and disease is increased solely due to specific co-morbidities that compromise their immunity (such as HIV positive individuals) or as a function of their place of birth. For example, it does not cover interventions among entire migrant populations more generally. It does, however, include interventions that are relevant to specific vulnerable migrant populations. Screening and managing TB among migrant populations will be covered in future ECDC documents. The populations covered in this guidance are more specifically defined in the Background chapter of this document.

The guidance does not cover interventions directly related to detection and management of latent TB infection (LTBI), as this will be comprehensively covered in future ECDC work.

Aim of guidance and target audience

The purpose of this guidance is to provide Member States with support, in the form of scientific advice on the options available, when considering measures for strengthening TB prevention and control among vulnerable populations in national TB programmes and/or to aid in the development of national guidance or TB control strategies.

Target audiences for the document are national policymakers, entities responsible for the planning of healthcare and social support systems, national TB programmes, civil society organisations and non-governmental organisations with an interest in TB, as well as those working with vulnerable groups.

Background

Tuberculosis as a public health priority for EU/EEA

Tuberculosis is prevalent in all EU/EEA Member States, both in high and middle-income countries and remains a public health priority irrespective of local incidence rates. In 2014, there were 58 008 cases of TB reported in the EU/EEA, with an incidence rate of 12.8 cases per 100 000 population [16]. The epidemiology of TB differs across the EU/EEA and depends, among other things, on where a Member State is in the path towards TB elimination. Countries that still have a moderate or high incidence of TB (more than 20 cases per 100 000 population) have different priorities compared with countries that have entered the elimination phase (less than 10 cases per 100 000 population). Overall, there is a declining trend in TB incidence across most EU/EEA countries.

As TB incidence drops, the disease becomes concentrated in populations at the lower end of the socio-economic scale and especially among vulnerable and socially excluded populations. Thus, the epidemiology of TB across EU/EEA Member States is characterised by a shift in burden of disease from the general population to specific population sub-groups. In general, TB cannot be controlled at national population level unless specific efforts are made to find and treat cases occurring among those most socio-economically disadvantaged and vulnerable.

The main pillars of TB prevention and control are early diagnosis and case management, which are essential not only for the successful treatment of TB patients, but also for controlling TB as a public health problem. There is no simple linear relationship between the costs related to TB prevention and control and the case load, and there is an immediate and well documented danger in cutting public spending on TB based on a decline in TB cases. This is related to the fact that the resources required to run enhanced diagnosis and case management interventions in vulnerable populations are often higher compared to standard TB control interventions.

Interventions such as screening programmes, outreach work, increased social support are more human resource intensive and have higher costs per TB case. Thus, a shift in TB epidemiology will most likely necessitate a shift in public health spending and investment towards reaching the last pockets of TB in the society. This would allow for reaching elimination earlier than otherwise would be feasible and will, in the long term, achieve economic savings in respect to TB prevention and control, as well as save people from having to suffer from TB disease in the future.

Vulnerabilities and socio-behavioural determinants on the path towards tuberculosis elimination

Income levels per capita and income inequality are important predictors for TB epidemiology in European countries [17,18], and investments in social protection programmes for vulnerable groups are likely to be a crucial complement to the whole package of TB prevention and control [19].

Data from both specific surveys and routine surveillance across individual Member States demonstrate that as TB incidence falls, cases among the most vulnerable and socio-economically disadvantaged groups become an increasing proportion of the total burden, often associated with pockets of high incidence in urban settings [14]. Poverty, social exclusion and marginalisation of population groups play an important role in shaping the epidemiology of TB in rural areas as well, where efforts to control TB can be undermined by limited access to specialist health services and a low index of clinical suspicion of TB among health professionals.

The increased risk of TB observed in vulnerable populations stems from multiple socio-behavioural determinants that act at different levels and commonly exacerbate one another. These include structural determinants such as legal, economic, cultural and language barriers, and social factors that may put individuals in a vulnerable position.

Additional determinants are related to physical factors such as:

- poor housing and living conditions or homelessness
- lack of access to healthcare, high cost and delays to receiving care, and discrimination by health workers
- individual behaviours such as drug and alcohol abuse, and individual attitudes resulting from stigma and lack of awareness
- biological factors such as age, sex, HIV status and co-morbidities
- life events such as imprisonment and exclusion resulting from voluntary or forced migration.

The interaction and overlap of all of these factors can increase individual vulnerability to TB [13,15,20-22].

Similarly, the natural history of TB is influenced by the same range of socio-behavioural determinants, affecting the whole chain through risk of exposure, risk of consequent infection, risk of developing TB disease, treatment adherence, to cure. Vulnerabilities associated with higher risk of infection and progression to TB disease are often linked to higher risks of exposure to infectious peers due to, for example, living in overcrowded and congregated housing conditions or correctional facilities with infectious individuals.

Factors linked with weakened immunity may pose an increased vulnerability to progress from infection to disease. Vulnerabilities such as lack of awareness of signs and symptoms, difficulties in recognising symptoms, and poor access to healthcare are associated with delayed or missed diagnosis and onward transmission of the disease.

Vulnerability is further increased among diagnosed cases through poor adherence to treatment, loss to follow-up, and as a consequence increased risk of the development of drug resistance and relapse [23,24]. Many may also suffer from other distressing illnesses and may be confronted with pressing economic or social issues influencing adherence to treatment. In addition, healthcare staff may lack the necessary awareness and skills for the prompt identification of vulnerabilities in order to adequately address their specific needs. Some groups may find the healthcare services hard-to-reach because TB clinics and procedures are too static/rigid and even reluctant to adapt themselves to new patients' conditions.

Standard models of care reliant on passive presentation of symptomatic individuals and self-administrated treatment are in general not sufficient to control TB among vulnerable populations. An outreach approach including active case finding and enhanced case management is an option that can support the timely diagnosis and successful completion of treatment. As mentioned above, effectively delivering the enhanced interventions relevant to vulnerable populations is more resource-intensive than standard approaches to TB control.

Target populations and definitions

As mentioned in the introduction, the target population for this guidance is vulnerable and hard-to-reach individuals (herein referred to as vulnerable populations). These are defined as adults, young people and children, whose social circumstances or lifestyle, or those of their parents or carers, make it difficult to:

- recognise the clinical onset of TB
- access diagnostic and treatment services
- self-administer treatment (or in the case of children and young people, have treatment administered by a parent or carer)
- attend regular appointments for clinical follow-up [6-8].

Individuals' increased vulnerability to TB stems from a unique set of different and commonly overlapping socio-behavioural determinants that can be addressed by a package of care tailored to the specific needs of each patient. In general, with an increasing number of vulnerabilities, the risk of TB or of an unfavourable treatment outcome becomes higher and there will be increasing challenges to early case detection and successful management. Many of the factors that compound individual risk are well described in the literature, but the following factors, such as homelessness, drugs and alcohol and imprisonment, are often not systematically defined. This lack of clear definitions potentially restricts the ability of TB services to identify and focus on vulnerable groups.

Individuals who fulfil the criteria for being considered vulnerable include: homeless people or people with a history of homelessness, high-risk drug users, people with problematic alcohol use, people in prison or in enforced segregation, some vulnerable migrant populations who are excluded from health and social care services (for example, undocumented migrants and those with no access to social protection programmes), and other marginalised, poor and remote groups determined locally, such as Roma populations. Where the term 'people' is used, it refers to every one (of all ages, ethnic background and migration status) who belongs to a vulnerable group.

The following section provides more detailed definitions of the target vulnerable populations. For the purpose of this guidance we aimed to be inclusive and used a broad concept for each of the populations, in contrast to using a very specific case definition that would be needed for the purpose of collecting surveillance data on these populations.

Homeless people or people with a history of homelessness

There is no widely accepted common EU definition of homelessness. The European Federation of National Organisations working with the Homeless argues for a broad definition of homelessness. This is captured in the European Typology of Homelessness and housing exclusion (ETHOS) definition, which includes not only people who are roofless, but also people who are houseless and people who live in temporary, insecure and inadequate poor-quality housing. Roofless people are those without a shelter of any kind and sleeping rough; houseless are those who have a place to sleep, but it is of temporary nature such as in institutions or shelters; living in insecure housing encompasses those who are threatened with severe exclusion due to insecure tenancies, eviction or domestic violence; and, living in inadequate housing are those in caravans on illegal campsites, in unfit housing, or in extreme overcrowding.

The ETHOS definition also acknowledges that homelessness is a process (rather than a static phenomenon) that affects many vulnerable households and individuals at different points in their lives. Therefore, people with a history of homelessness are also of interest for the purpose of this guidance [25].

High-risk drug users

The European Monitoring Centre for Drugs and Drug Addiction defines high-risk drug use as 'recurrent drug use that is causing actual harms (negative consequences) to the person (including dependence, but also other health, psychological or social problems) or is placing the person at a high probability/risk of suffering such harms'. This definition encompasses the use of various psychoactive substances (excluding alcohol, tobacco and caffeine) in a high-risk pattern, irrespective of the drugs administration route i.e. injecting or inhaling [26].

The systematic literature reviews undertaken as part of developing this guidance primarily concerned evidence on people who inject drugs. However, the ad hoc scientific panel was of the opinion that the evidence presented on people who inject drugs is applicable and can be reliably extrapolated to the broader definition of high-risk drug users.

People with problematic alcohol use

There is no universally accepted definition for individuals who experience hazardous and harmful effects from alcohol use. The definitions used depend on the culture and belief related to alcohol use. Thus the amount and frequency of alcohol consumption that is considered problematic depends on the setting. Common terms used for people who face a problem with alcohol use are alcoholics, people with alcohol use disorders, people with alcohol dependence syndrome, people who abuse alcohol, people with problematic alcohol use, etc. 'People with problematic alcohol use', was the preferred term by the ad hoc scientific panel for the purpose of this document.

The term problematic alcohol use puts the focus on the problematic consequences for the person drinking alcohol, irrespective of whether the person is alcohol dependent or uses alcohol in an abusive manner. The problematic consequences may be expressed as either behaviours or physical harms that become a determinant of increased TB vulnerability either through increased risk of exposure and/or immune suppression, or other morbidities that increase risk of progression to active disease.

There are standardised screening tools, such as the Alcohol Use Disorders Identification Test developed by the World Health Organization to assess alcohol consumption, drinking behaviours, and alcohol-related problems [27].

People in prison or in enforced segregation

In this guidance document, the term 'prison' is used for any place of detention. We include people who are in any form of detention or penitentiary facility, including people in centres for pre-trial, in prison for convicted crimes, in centres for juvenile offenders and in other correctional facilities. We have also included migrants held in congregated secure or closed settings in this category.

Detention may pose an increased risk of being exposed to and infected with TB, due to the clustering of vulnerable groups and the crowded living conditions. Risk groups from the community, especially high-risk drug users and homeless people are often over-represented in detained populations. For the purpose of this guidance we also recognise individuals with a history of imprisonment as a vulnerable group due to their increased risk of TB exposure and infection resulting from a period of detention.

Vulnerable migrant populations

For this guidance document, the most relevant target population are migrants arriving from high TB incidence countries whose current circumstances put them at increased risk of delayed diagnosis, onward transmission, and unfavourable treatment outcome, due to poor access to healthcare and inadequate social support services. For some migrants, challenges arising from their change in social circumstances, language, cultural or lifestyle barriers in the new country can lead them to fulfil the criteria for vulnerability. Examples of vulnerable migrant populations include those who are undocumented, those with no right to access social protection, those who are detained in congregate settings, and some refugees, asylum seekers and new arrivals [6-8,28].

However, not all migrant populations are vulnerable, as many migrants in EU Member States can quickly recognise the clinical onset of TB and readily access diagnostic and treatment services. In many EU Member States, migrant populations are already specifically targeted with screening interventions aimed at detecting either LTBI or active disease.

Other marginalised, poor, and remote populations

Marginalisation is a term used to describe the process of social exclusion and segregation of individuals with low socio-economic status in society. This process, often expressed through laws, policies, structures and societal behaviours and stigmatisation, can systematically prevent entire groups from exercising their human rights. Common examples of marginalisation include exclusion from access to social benefits and resources, housing, employment, healthcare and education.

This broad category of 'other marginalised, poor and remote populations' is highly context-specific and should be locally defined but can include: people in extreme poverty not covered by any of the other defined populations groups, sex workers, individuals in remote areas suffering from social exclusion, Roma populations, indigenous and other ethnic minorities.

Guiding principles when working with vulnerable populations

Prior to the ad hoc scientific panel's deliberation of the evidence, and reflecting their view that TB-specific interventions should ideally be underpinned by interventions targeted at broader structural and intermediate determinants that increase vulnerability, the following set of guiding principles were proposed by the panel. These overarching 'guiding principles' were considered fundamental to assure the effectiveness of interventions and service models.

Reduce poverty and social exclusion

Improved living conditions and nutrition were major factors in the dramatic decline in TB incidence across Europe prior to the advent of effective treatment. Poverty and social exclusion remain directly linked with the risk of TB, onward transmission and treatment outcomes. Political efforts to reduce poverty and work against social exclusion and inequality pay a significant community health dividend across the spectrum of chronic and infectious diseases among which TB offers one of the highest returns on investment for any health condition. Thus, societies that increase the socio-economic profile, by reducing poverty and work against social exclusion, will in the long term reduce the burden of TB among their citizens [19].

Equitable access to healthcare and social services

Early diagnosis and completion of treatment are the most important elements for effective TB prevention and control. Ensuring equitable access to healthcare and social support services, by, for example, providing diagnosis and treatment free of charge, and through instituting the necessary legal, social and economic policies, is fundamental to TB control.

Patient-centred approach

Treatment interruption contributes to the development of drug resistance, to TB transmission, and to poor outcomes for individual patients. A patient-centred approach to administration of drug treatment, based on the patients' needs and mutual respect between the patient and the provider, is valuable for all patients. Supervision and support would ideally be gender-sensitive and should draw on the full range of recommended interventions and available support services.

Reach beyond the health sector

In order to successfully address the factors that increase vulnerability to TB in different individuals and whole populations groups, consideration should be given to reaching beyond the traditional health sector and working towards a population health approach. Population health is an approach that aspires to improve the health of the entire population and to reduce health inequities among population groups. In order to reach these objectives, it looks at and acts upon the broad range of factors and conditions that have a strong influence on our health.

Integration of services

An integrated service model encompasses the full range of physical and psycho-social needs associated with vulnerability, and includes initiatives to reach out with services into non-traditional settings, and work in partnership with a range of other health and social care providers as well as civil society organisations to address co-morbidities and other relevant socio-behavioural determinants. For example, TB treatment could be integrated with current HIV treatment initiatives. With vulnerable TB patients it is important to also work towards addressing and resolving the socio-behavioural determinants that put individuals at increased risk of TB in the first place. Outcomes to care may go beyond cure, and also aim to address the predisposing risk factors and seek to reduce risk of relapse and future infection.

Gender and cultural sensitivity

Good communication and trust between the patient and the health providers are necessary for the successful uptake of TB diagnosis and care. In addition to the need to overcome language barriers, good communication requires understanding and respect for the patient's values and beliefs. Miscommunication could delay diagnosis, result in poor treatment support and adherence, and erode overall trust in the healthcare system.

Non-stigmatisation and respect

Tuberculosis patients that experience stigma and discrimination may be reluctant to access health and social care services. It is of paramount importance that frontline TB professionals and other social care providers are aware of the benefits gained when services are non-stigmatising, and where persons are treated with empathy and respect regardless of who they are. Promoting non-judgmental attitudes among all care and support staff is central to creating trust and effectively reaching and treating vulnerable people.

Empowerment and participation

Empowerment and participation of vulnerable individuals and population groups in planning and delivering targeted health interventions is key to their success and overall effectiveness. Vulnerable TB patients have first-hand experience of TB symptoms, and the challenges of accessing diagnostic services and completing a lengthy course of drug treatment. Their insights and contribution are of great value in designing better services, addressing barriers to care and strengthening links with vulnerable communities. The ultimate and most effective means of empowering vulnerable people is to promote their participation in all aspects of TB prevention and control activities and especially in targeted interventions to tackle stigma, raise awareness and improve early case detection [29].

Guidance development

Systematic reviews

In order to assess which interventions targeting hard-to-reach and vulnerable groups are effective, four systematic literature reviews were performed. The reviews aimed to synthesise evidence on facilitators and barriers to TB diagnosis and treatment, and to provide a comprehensive selection of interventions that have been used to strengthen TB prevention and control among vulnerable populations, and summarise their effect.

The systematic reviews were an update and extension of the four evidence reviews on TB interventions in hard-to-reach groups in Europe conducted for the National Institute for Health and Care Excellence (NICE) in 2010 [6-8,28]. The first review is qualitative, examining the barriers and facilitators to the uptake of TB diagnosis and treatment services by people from hard-to-reach groups. The second review examines the effectiveness and cost-effectiveness of interventions that raise awareness of TB and increase the identification of TB cases in hard-to-reach populations. The third review explores the effectiveness and cost-effectiveness of interventions to improve the management of TB cases in hard-to-reach groups. The last review focuses on the effectiveness and cost-effectiveness of service models that manage TB in hard-to-reach populations. The results from both the NICE systematic reviews and the updated systematic reviews commissioned by ECDC are presented in the Conclusions. The updated systematic reviews will be made available through open access publications.

Ad hoc scientific panel

An ad hoc scientific panel was set-up and tasked to review and assess the evidence-base from the systematic literature reviews, and subsequently express consensus opinions on good practices for interventions and service models targeting vulnerable groups.

The panel members were identified by ECDC's TB programme experts, using the ECDC Expert Directory, suggestions from the ECDC Advisory Forum, by searching the literature for experts that publish on related topics, and by professional contacts through the ECDC TB Surveillance and other networks and working groups. The panel was officially appointed by the ECDC Acting Director in June 2015. The experts were selected based on their expertise in: TB prevention and control, interventions and service models targeting hard-to-reach and vulnerable populations, and; integrated health programmes (TB/HIV/hepatitis/other diseases or health service programmes).

The experts were asked to provide opinions based on their professional and scientific experience, and to do so on a personal basis, as an independent expert and not representing the interests of any commercial body, Member State or professional body. All panel members signed a declaration of interest, which was reviewed by the ECDC compliance officer. None of the members of the panel declared any interests that would be considered to be a conflict with regard to the topic and their participation in the panel. The panel was independent from ECDC, which organised, hosted and observed the panel meetingⁱ.

Before the meeting, which took place on 7–8 September 2015, the panel members reviewed the systematic reviews and a draft of the guidance document. Opinions on the evidence from the systematic reviews were collected through a Delphi process. During the meeting, the panel discussed the evidence base and the results of the Delphi process, agreed upon panel opinions and provided input to the draft guidance document produced by ECDC. After the meeting, more rounds of the Delphi process were completed and the panel members reviewed the revised guidance document based on the discussions at the meeting and continuation of work on this topic by ECDC.

ⁱ See Appendix 1 for further details on the members of the ad hoc scientific panel and their declared interests.

Evidence synthesis and grading

Generation of evidence

The evidence base from the systematic reviews was compiled by developing a summary for each specific area identified in the reviews. For each summary of the systematic review results, a statement of the strength of the evidence is provided. To structure the evidence synthesis, we applied the system used in the previous NICE evidence reviews [6-8,28] to promote comparability of previous and current results.

The quality and the risk of bias of all the included studies were assessed by using the modified NICE Quality Assessment Tools for: Quantitative Intervention Studies, Quantitative Studies Reporting Correlations and Associations, Qualitative Studies, and Economic Evaluations. Each study was given a quality rating: high quality [++], medium quality [+] or low quality [-].

In addition to the quality assessment for every study, the overall strength of the evidence extracted from the studies included in the updated reviews, and the reviews conducted by NICE, was assessed. The strength of the evidence was assessed and reported as described in NICE [6-8,28]:

- **no evidence** – no evidence or clear conclusions from any studies;
- **weak evidence** – no clear or strong evidence/conclusions from high quality studies and only tentative evidence/conclusions from moderate quality studies or clear evidence/conclusions from low quality studies;
- **moderate evidence** – tentative evidence/conclusions from multiple high quality studies, or clear evidence/conclusions from one high quality study or multiple medium quality studies, with minimal inconsistencies across all studies;
- **strong evidence** – clear conclusions from multiple high quality studies.

One study may include a combination of intervention activities or elements. Therefore, it was sometimes difficult to estimate the strength of evidence for a specific intervention activity or element, as it was not possible to determine which of these contributed to the study success.

Delphi process

The summarised systematic review results were used to collect the ad hoc scientific panel opinions that are incorporated into this guidance document. To guide this process from evidence to guidance, we designed a modified Delphi process. A Delphi process is a method to collect opinions or views in a way where the members of a group are not influenced by each other. This particular modified Delphi process included four steps:

- Collecting the panel members' opinions on which systematic review results are relevant to include in the guidance document, and to provide suggestions for opinions to be made for each relevant systematic review result.
- Discussions at the panel meeting to agree on options for interventions to be presented in the guidance document. In this step, panel members could also add evidence.
- Scoring of the different options for interventions based on criteria that were developed at and after the panel meeting. Each panel member was invited to provide scores based on their judgement of each criterion for each option for intervention.
- Consolidation of the scoring of the options for interventions and other panel member opinions, and review by the panel members to secure consensus on all elements included.

More details on the methodology of the Delphi process can be found in Appendix 2.

Criteria for consideration

Four criteria and a grading system were developed based on input from the Scientific Advice Coordination Section at ECDC, and the ad hoc scientific panel members:

- **Acceptability** of the intervention by the target population (highly acceptable, likely acceptable, not acceptable, varies, don't know)
- **Feasibility** to implement the intervention (highly feasible, likely feasible, not feasible, varies, don't know)
- **Use of resources** to implement the intervention (high, medium, low, varies, don't know)
- **Anticipated cost-effectiveness** of the intervention (highly cost-effective, likely cost-effective, not cost-effective, varies, don't know).

Conclusions

This chapter outlines the key areas to be taken into consideration when designing and implementing programmes for the prevention and control of TB in vulnerable populations:

- early diagnosis
- treatment completion
- health communication, awareness and education
- programme monitoring and evaluation.

For the first three key areas we present the findings and the ECDC assessment, the fourth area covers important aspects of programme monitoring and evaluation.

Interventions to promote early diagnosis

Summary of findings

In Table 1 we summarise the systematic review results and the ad hoc scientific panel opinions, regarding interventions to promote early diagnosis of active TB, through screening, provision of incentives and contact tracing.

Table 1. Interventions to promote early diagnosis

Intervention	Outcome	Systematic review results	Ad hoc scientific panel contribution				
			Ad hoc scientific panel opinion	Grading of acceptability of the intervention by the target population	Grading of feasibility to implement the intervention	Grading of use of resources to implement the interventions	Grading of anticipated cost-effectiveness of the intervention
Screening of homeless people							
Screening for TB among homeless people by mobile chest X-ray unit (MXU)	Promote early diagnosis	A study by Bernard et al. 2012 [+] [30] provided weak evidence that screening of homeless people by MXU improved screening coverage and reduced TB transmission among homeless people using shelters, but also among non-shelter users.	Where there is suspected TB transmission among homeless populations screening by MXU seems to be an effective tool.	Likely acceptable	Likely feasible	High	Likely cost-effective
Screening of high-risk drug users (HRDU)							
Promoting screening for TB among HRDU, by active referral to TB services and involving key partners	Promote early diagnosis	A study by Ruutel et al. 2011 [+] [31] provided weak evidence that active referral of injecting drug users (IDU) to a TB clinic increased TB screening uptake among IDU for minimal extra costs. A study by Duarte et al. 2011 [-] [32] provided weak evidence that identification of active TB cases among IDU increased by using key partners to stimulate screening and promote health-seeking behaviour.	Evidence from IDU can probably be extrapolated to HRDU. Promoting screening for TB among HRDU should be performed through active referrals, and will be facilitated by involving key partners.	Likely acceptable	Likely feasible	Varies	Likely cost-effective

Intervention	Outcome	Systematic review results	Ad hoc scientific panel contribution				
			Ad hoc scientific panel opinion	Grading of acceptability of the intervention by the target population	Grading of feasibility to implement the intervention	Grading of use of resources to implement the interventions	Grading of anticipated cost-effectiveness of the intervention
Screening of prisoners							
Screening for TB among prisoners	Promote early diagnosis	A study by Yates et al. 2009 [-] [33] provided weak evidence that all prisoners should be offered TB screening by MXU regardless of whether or not the prisoners present with TB symptoms, as a substantial number of TB cases will be missed if only symptomatic prisoners will be screened. A study by Jones and Schaffner, 2001 [+] [34] provided weak evidence that screening for active TB among prisoners was most cost-effective if it was done by chest X-ray (CXR) (\$9 600 per positive case) compared to tuberculin skin test (\$32 100) or a symptom-based questionnaire (\$54 100).	Screening should be performed if prison (sub)-populations are considered to be a risk group by existing criteria. CXR is cost effective and MXU can be used.	Highly acceptable	Highly feasible	Medium	Likely cost-effective
Screening of mixed groups							
Screening with MXU	Promote early diagnosis	Three studies by Watson et al. 2007 [++] [35]; Jit et al. 2011 [+] [36]; and Story et al. 2012 [+] [37] provided moderate evidence on the effectiveness of TB screening by MXU. Watson et al. showed that TB screening by MXU reduced diagnostic delay and cases were less likely to be symptomatic. Jit et al. showed that MXU screening is effective, as 35% of the TB cases identified by MXU screening were asymptomatic and would not have presented for TB diagnostics. Story et al. showed that people detected by MXU screening were less infective and therefore TB transmission could be reduced.	MXU might be useful in detecting TB in hard-to-reach mixed groups to identify patients sooner, reduce transmission and can be cost effective (context specific as initial investment is needed for MXU).	Highly acceptable	Likely feasible	High	Likely cost-effective
Involving community health workers and key partners in promotion of TB screening	Promote early diagnosis	Two studies by Duarte et al. 2011 [-] [32]; and Goetsch et al. 2012 [-] [38] provided weak evidence on the effectiveness of involving community health workers and key partners (street teams, outpatient TB clinic, drug users support centres, shelters, local public health department and the local hospital) in promotion of TB screening.	Involving community health workers and key partners in promotion of screening may lead to an increased uptake of TB screening.	Highly acceptable	Likely feasible	Varies	Likely cost-effective
Involving peer networks to improve TB screening	Promote early diagnosis	Three studies by Ricks, 2008 [++] [39]; Pilote et al. 1996 [++] [40]; and Aldridge et al. 2015 [+] [41] provided conflicting evidence on using peers to improve TB screening uptake. Ricks and Pilote et al. showed that the screening uptake improved among drug users and homeless people when peers were used as case-managers. Aldridge et al. showed that the uptake of MXU screening did not improve after involving peers to encourage and educate homeless people, compared to shelter personnel.	Studies demonstrate the possible value of involving peers to encourage screening uptake.	Likely acceptable	Likely feasible	Varies	Likely cost-effective

Intervention	Outcome	Systematic review results	Ad hoc scientific panel contribution				
			Ad hoc scientific panel opinion	Grading of acceptability of the intervention by the target population	Grading of feasibility to implement the intervention	Grading of use of resources to implement the interventions	Grading of anticipated cost-effectiveness of the intervention
Monetary incentives in HRDU							
Providing monetary incentives to HRDU	Promote uptake of screening	One study by Perlman et al. 2003 [++] [42] provided moderate evidence that the use of small monetary incentives improved TB screening uptake in drug users.	Evidence from IDU can probably be extrapolated to HRDU. Providing monetary incentives improves TB screening uptake among HRDU.	Likely acceptable	Likely feasible	Varies	Likely cost-effective
Monetary incentives in homeless people							
Providing monetary incentives to homeless people	Promote uptake of screening	Two studies by Citron et al. 1995 [+] [43]; and Pilote et al. 1996 [++] [40] provided moderate evidence that the screening uptake improved among homeless people when a monetary incentive was given.	Providing monetary incentives improves TB screening uptake and completion among homeless people.	Highly acceptable	Likely feasible	Varies	Likely cost-effective
Contact tracing of vulnerable migrants							
Using community health workers from the same migrant community to coordinate TB contact tracing among migrants	Improve contact tracing	A study by Ospina et al. 2012 [+] [44] provided moderate evidence that contact tracing among migrants improved significantly by using community health workers from the same migrant community to coordinate contact tracing.	Using community health workers from the same migrant community for contact tracing is an effective approach.	Highly acceptable	Likely feasible	Varies	Likely cost-effective
Contact tracing of HRDU							
Involvement of peers in contact tracing of HRDU	Improve contact tracing	A study by Ricks, 2008 [++] [39] provided moderate evidence that the identification of contacts of drug users with active TB improved by using former drug users compared to healthcare workers.	Involving peers can improve contact tracing in HRDU, as part of a package for contact tracing and enhanced case management.	Highly acceptable	Likely feasible	Varies	Likely cost-effective

ECDC assessment

Screening

Early diagnosis is a cornerstone of TB control. In the process of developing national guidelines, a country would benefit from assessing which vulnerable groups are likely to require targeted screening interventions to prevent severe disease, death and onward transmission. There are many options for screening, but the decision whether and how screening should be implemented needs to be based on the epidemiology, priorities and resources in each country.

Targeted screening programmes can be of benefit to effectively identify infected individuals and those who have developed active TB disease. As mentioned in the Introduction, this guidance focuses on active TB disease and not on latent TB infection and thus this section covers screening for active TB only. The guiding principle for screening, irrespective of whether it is screening for infection or disease, is that screening interventions should only be implemented when there is an effective system in place to ensure the management and provision of treatment for all identified cases.

Targeted screening initiatives and choice of intervention should be informed by robust epidemiological data such as data on TB incidence and diagnostic delay, and practical information on how the proposed target population can be reached and engaged. If surveillance data are not readily available, ad hoc studies could be reviewed or undertaken, supported by expert opinion, as well as input from representatives of the proposed target populations. Once the specific populations have been defined, the choice of tools to include in screening algorithms can be reviewed and defined [45].

Evidence that can be used to inform the logistics of screening programmes for specific populations is very limited. Models of mobile screening programmes have been shown to be effective in improving coverage in several vulnerable populations (moderate to weak evidence); the optimal approach needs to be tailored to the local epidemiology, specific needs and circumstances of the target population and the resources available within local programmes. Other means of increasing screening uptake comprise of providing active referrals and including key partners and community workers (weak evidence). Involving peers was also shown to improve screening uptake in some cases (conflicting evidence).

Targeted screening initiatives commonly create an 'opportunity of encounter' with vulnerable populations who are at high risk of co-infection with other important public health infections. Integrating screening activities with other targeted public health programmes, such as HIV, hepatitis B, or C, vaccine preventable disease etc. would maximise the impact on the health of the individuals reached, and be likely to improve the overall cost-effectiveness of the programme.

Incentives and enablers

Incentives and enablers (see glossary for definitions) are an important element of interventions aimed at increasing uptake of TB screening/testing. The intention of an incentive or enabler can, for example, be to motivate or help the clients to show up for testing, or to return to receive test results.

Incentives and enablers can be of a different nature, ranging from direct monetary incentives, to providing tickets for local transportation, food vouchers, mobile phones, phone top-ups, food and hygiene packages, clothes and temporary accommodation. Monetary incentives were the most prominent form of incentive and enabler that were found and reviewed in the literature. Moderate evidence for the effectiveness of monetary incentives for improving screening uptake in homeless and HRDU populations was found.

Funding for incentives and enablers may either come from the health and social service budget or through support from public-private partnerships, as charitable contributions or donations.

The specific needs of the individual are to be taken into account when implementing incentives or enablers as part of a strategy to promote uptake and completion of screening/testing. Monetary incentives might be considered most appropriate for certain vulnerable TB patients, while they may be counterproductive or lead to undesired effects for other individuals.

Contact tracing

Identifying and testing close contacts to diagnose new TB cases is a general principle and pillar of TB prevention and control. However, it brings with it some unique challenges, especially when there is a lack of trust between the staff performing the contact tracing and individuals of a certain vulnerable group. The principle challenges to effective contact investigations around cases arising from vulnerable populations are that new cases are often either unaware of who they might have infected, are reluctant to disclose contacts, or TB professionals are unable to locate contacts and motivate them to attend diagnostic tests. Failure of contact investigations as a means to limit onward transmission is the main reason to implement targeted screening initiatives for vulnerable populations. Nevertheless, challenges to identify and test contacts can often be overcome by involving partners that are already working with the specific population and know the individuals concerned. Moderate evidence demonstrates that involving community workers or peers from the affected community or populations can increase the success of reaching all potential contacts in certain migrant and HRDU populations.

Enhanced case management to improve follow up attendance and treatment completion

Summary of findings

In Table 2 we summarise the systematic review results and the ad hoc scientific panel opinions, regarding enhanced case management interventions to improve follow up attendance and treatment completion.

Table 2. Interventions for enhanced case management

Intervention	Outcome	Systematic review results	Ad hoc scientific panel contribution				
			Ad hoc scientific panel opinion	Grading of acceptability of the intervention by the target population	Grading of feasibility to implement the intervention	Grading of use of resources to implement the interventions	Grading of anticipated cost-effectiveness of the intervention
Outreach work and involvement of community workers							
Involvement of community workers in case management of homeless populations	Improve treatment completion	A study by Goetsch et al. 2012 [-] [38] provided weak evidence that enhanced case management leads to high successful treatment outcome rates in homeless people. The involvement of an experienced community worker providing education, communication management and treatment monitoring, combined with a streamlined screening service, led to 76% treatment completion.	Involving community workers (medical or non-medical staff) in providing education, communication management and treatment monitoring can improve treatment completion among homeless population.	Highly acceptable	Likely feasible	Medium	Likely cost-effective
Engage non-clinical professionals in outreach work	Improve treatment completion	Three studies by Craig et al. 2008 [-] [48]; Brent Refugee Forum, 2007 [++][49]; and Belling et al. 2008 [++][50] provided moderate evidence that the complex social and clinical interactions surrounding a patient with TB can be a challenge to participation and adherence, and that outreach TB link workers or social care workers can facilitate coordination of services.	Engaging non-clinical professionals such as social care workers can facilitate the coordination of services of a patient leading to improved treatment outcome.	Highly acceptable	Likely feasible	Medium	Likely cost-effective
Treatment provided using outreach teams	Improve treatment completion	A study by Jit et al. 2011 [+] [36] provided weak evidence that a mobile TB service is an effective intervention to identify and treat hard-to-reach individuals. The intervention was also found to be cost-effective, the incremental cost ratio for the service was £6 400 per Quality of Life Year (QALY) gained.	Outreach teams can improve TB treatment of vulnerable groups. Depending on context and setting it can be cost-effective.	Highly acceptable	Highly feasible	Varies	Likely cost-effective
Enhanced case management of drug users with TB	Improve treatment completion	Two studies by Goetsch et al. 2012 [-] [38]; and Ricks, 2008 [++][39] provided moderate evidence that enhanced case management leads to improved treatment outcome in drug users. A study by Duarte et al. 2011 [-] [32] provided weak evidence that a combination of enhanced case management and improved service models can improve treatment outcome of drug users.	Enhanced case management, including the use of peers and improved service models can improve treatment outcome of drug users.	Likely acceptable	Likely feasible	Medium	Likely cost effective

Intervention	Outcome	Systematic review results	Ad hoc scientific panel contribution				
			Ad hoc scientific panel opinion	Grading of acceptability of the intervention by the target population	Grading of feasibility to implement the intervention	Grading of use of resources to implement the interventions	Grading of anticipated cost-effectiveness of the intervention
Communication and collaboration between services and patients							
Communication and intensive contacts between TB health providers and patients	Improve treatment completion	Four studies by Ricks, 2008 [++]; Duarte et al. 2011 [-] [32]; Goetsch et al. 2012 [-] [38]; and Jit et al. 2011 [+] [36] provided weak evidence that intensive contact between healthcare workers and patients is effective. Ricks found a statistically greater probability of completing treatment if enhanced case management was provided by peer workers.	Development of relationships and collaboration between care institutions, communities, peers and patients can lead to improved treatment outcome.	Highly acceptable	Likely feasible	Varies	Likely cost-effective
Facilitating contact between migrants and healthcare services	Improve follow up attendance rate	Two studies by Bell et al. 2013 [+] [46]; and Harstad et al. 2014 [-] [47] provided weak evidence that facilitating contact between migrants and healthcare services improves follow-up attendance rates. Bell et al. report increased attendance rates and a reduced time between arrival in the country and a follow-up appointment, by providing an appointment date or a direct phone number of the appropriate instances. Harstad et al. showed that contacting the patient directly led to increased attendance rates and a shorter time until presentation at the hospital.	Facilitating contact between migrants and healthcare services seems to improve attendance rates for TB follow up evaluation.	Highly acceptable	Likely feasible	Medium	Likely cost-effective
Facilitating cooperation between healthcare services	Improve follow up attendance rate	A study by Harstad et al. 2014 [-] [47] provided weak evidence that improving cooperation of healthcare services leads to improved follow-up attendance rates. Through collaboration, public healthcare services and the hospital identified weaknesses in the existing screening system, came up with solutions and carried these out. This collaboration led to the proposed interventions, which led to improved follow-up rates.	Improving cooperation between healthcare services can improve attendance to follow up visits during TB treatment among migrants.	Highly acceptable	Highly feasible	Varies	Likely cost-effective
Incentives and enablers							
Adding incentives or enablers to DOT for drug users	Improve treatment completion	A study by Bock et al. 2001 [+] [51] provided moderate evidence that in a population in which more than 50% were drug users, adding incentives to DOT improved treatment completion rates compared to DOT alone (OR = 5.73, 95% CI 2.25–14.84).	Material incentives and enablers should be considered for marginal populations such as drug users, recently released prisoners, and homeless people in combination with Enhanced Case Management to promote clinic attendance and treatment adherence.	Highly acceptable	Likely feasible	Medium	Likely cost-effective

Intervention	Outcome	Systematic review results	Ad hoc scientific panel contribution				
			Ad hoc scientific panel opinion	Grading of acceptability of the intervention by the target population	Grading of feasibility to implement the intervention	Grading of use of resources to implement the intervention	Grading of anticipated cost-effectiveness of the intervention
Use of mobile phones and computers							
Use of Video Directly Observed Treatment (VOT)	Improve treatment completion	In a study by Garfein et al. 2015 [4] [52]** provided weak evidence that VOT was feasible and acceptable, with high adherence in both high- and low-resource settings.	VOT can be of benefit as an alternative option for performing DOT.	Likely acceptable	Likely feasible	Medium	Likely cost-effective
Use of reminder systems to improve patient attendance at TB clinics	Improve treatment completion	A systematic review by Liu Q et al. 2014 [53]** provided weak evidence that more people completed TB treatment with pre-appointment reminder phone-calls and Moderate evidence that more people completed TB treatment with a policy of default reminders.	Use of reminder systems may be of benefit to improve treatment adherence and outcome.	Highly acceptable	Likely feasible	Low	Likely cost-effective

** Garfein 2015 and Liu 2014 were not identified through the systematic reviews, but they were added in the Delphi process.

ECDC assessment

TB case management is most effective if it includes a combination of strategies tailored to the specific needs of an individual. As the standard model of care is often not sufficient to achieve high treatment completion rates among vulnerable groups, enhanced case management models can be considered.

Enhanced case management is best provided through improved service models that aim to reach out and engage the target group more effectively. Using a mix of settings and approaches for outreach, adapted to local characteristics, provides an effective way of serving vulnerable populations. Mobile solutions with, for example, outreach teams for patient support and treatment can be advantageous in certain settings to reach individuals (weak and moderate evidence). Engaging community workers and other non-clinical professionals was found to be effective for improving treatment completion (weak and moderate evidence). Peers from the affected populations can also provide invaluable support to enhanced case management (moderate evidence). One example of an intervention that uses health assistants is described in Appendix 3.

Further improving follow-up attendance rates and treatment completion can be accomplished by strengthening communication and contact between the patients and service providers (weak evidence). Improving cooperation between the health services themselves also improved follow up attendance (weak evidence). Furthermore, TB services benefited from working in close partnership with existing services for the affected populations including homeless services, drug and alcohol services and a wide variety of community workers, street outreach teams, social care professionals and third sector partners as shown in a project in Paris (Appendix 3). Vulnerable TB patients commonly have concurrent physical and mental healthcare needs in addition to their precarious social circumstances. Integration of services across specialities reduces the barriers caused by multiple appointments and effectively addresses the complexity of care that can arise from drug to drug interactions with TB treatment, such as with HIV drugs and methadone. Case management for vulnerable patients would benefit from coordination of care across multiple providers and ensuring that potential barriers to TB treatment continuity are addressed and overcome. Integrating testing and treatment programmes for HIV/hepatitis B/hepatitis C, and harm minimisation services and homeless health services is mutually effective to both patients and providers.

Incentives and enablers may be added to enhanced case management efforts in order to encourage and facilitate compliance with treatment. Adding incentives to DOT in HRDU improved treatment completion rates (moderate evidence). In a previous systematic review on incentives and enablers, both monetary incentives and material incentives were found to have positive short-term effects on clinical attendance in vulnerable populations, although it was not clear if they can improve long-term adherence to TB treatment [3]. Although not identified in the systematic reviews, the ad hoc scientific panel felt that one important enabler for the homeless and released prisoners is to insure access to accommodation that is suitable for sustaining treatment and recovery. In addition to increasing treatment completion, providing housing as early as possible after diagnosis would also mitigate the risk of onward transmission.

Use of mobile phones and computers can be another useful tool to enable regular contact with patients and improve treatment adherence and outcome. Weak and moderate evidence showed that these devices can be effective in improving treatment completion when they are used for video directly observed treatment (VOT), and reminder systems. An example of an intervention using VOD is described in Appendix 3.

Directly Observed Treatment is the standard of care for all patients who require enhanced case management. Evaluating complex interventions such as DOT is methodologically challenging and the randomised controlled trial evidence about the effectiveness of DOT is inconsistent. The panel members were unanimous about the important role of DOT in improving treatment success, as part of a comprehensive and enhanced case management approach. DOT is most effective when tailored to the specific needs of the patient and when it is as flexible and accessible as practically possible. It can be delivered effectively outside healthcare settings and is preferably administered at the most convenient place for the patient.

The panel's opinion was that, wherever possible, TB patients in institutional/residential settings would benefit from receiving DOT as a standard of care and that this can involve case managers training and delegating responsibility to observe patients taking their medication to other competent professionals. It was also noted that the specific challenges to TB treatment continuity following arrest and detention, transfer within the prison estate, release back into the community, and ensuring care coordination between justice and health professionals, need attention, as was previously stated in guidelines for TB control in prisons [54].

Health communication, awareness raising and education

Summary of findings

The systematic reviews collected evidence from qualitative studies on barriers and facilitators for TB diagnosis and treatment. We summarise the evidence that was found to be of relevance by the panel below. Addressing these barriers and facilitators through health communication, awareness raising and education could have a potential impact on improving access to diagnosis and treatment completion, although this impact was not assessed.

Barriers

Barriers to diagnosis included lack of knowledge and awareness about TB (weak evidence), and fear of death (strong evidence). Inadequate compliance to treatment could be due to the long treatment courses or the associated side effects (strong evidence). Symptom resolution was found to reduce the patient's willingness to continue treatment (moderate evidence). Stress and depression have also been shown to complicate diagnosis as well as treatment (moderate evidence).

Challenges with accessing healthcare were mentioned as a barrier. A first barrier that was identified was the lack of information about the availability of a service (strong evidence). Also, various hard-to-reach groups experienced complications with accessing care because of drug use or lack of a general practitioner (weak evidence). Other challenges preventing or delaying access to care included difficulties with transport, clinic opening hours (weak evidence), and in some cases the cost of TB services (weak evidence). Language barriers were also mentioned as potentially hampering or complicating access to care in vulnerable migrant populations (strong evidence).

A lack of confidence in the healthcare system will hamper healthcare seeking behaviour and adherence to treatment. There is evidence that members of vulnerable groups view the standard of care as low (inconsistent evidence). Also a concern about the quality of the diagnosis, especially about misdiagnosis and delayed diagnosis, was identified (strong evidence). Discontinuity regarding which health worker is visiting patients at home hindered a good patient-healthcare worker relationship (weak evidence). Another factor considered important was privacy and confidentiality, a (perceived) lack of confidentiality affected patient compliance (moderate evidence).

A TB diagnosis often leads to stigmatisation which results in discrimination and social isolation (strong evidence). The use of masks was perceived to identify a patient as a TB patient and resulted in social isolation (weak evidence). If TB and HIV hospitals were located in the same area patients felt that this would suggest that they were also HIV infected, aggravating TB stigma (weak evidence). In general, the link between TB and HIV increased concerns about stigmatisation (strong evidence). Stigma might also be aggravated by a negative presentation of population groups in the media (weak evidence). Next to external stigma, there was also evidence for internalised stigma. Feelings of guilt and shame often led to reluctance to seek testing or to non-disclosure of TB disease which was a barrier to both diagnosis and adequate TB care (moderate evidence).

Facilitators

Compliance to lengthy TB treatment could be promoted by support from family and friends (inconsistent evidence) or healthcare workers (moderate evidence). In addition, hospitalisation and a strict DOT policy could be facilitators for compliance if the approach was patient-centred and culturally sensitive. However, in some cases patients saw hospitalisation as a threat and DOT as paternalistic (conflicting evidence). Cultural-sensitivity and appropriate care increased access and adherence to treatment (moderate evidence).

ECDC assessment

Tuberculosis remains a highly stigmatised and sensitive issue for many vulnerable populations. Effectively communicating health messages and raising awareness needs to be done in a culturally sensitive and appropriate way that respects patient rights, tackles discrimination and reinforces the public health implications of delayed diagnosis and poor adherence to treatment.

The aim of health education and communication is to ensure that symptomatic or exposed individuals can recognise the onset of TB, know how to access diagnostic services and take up opportunities for screening, and are well informed about treatment and the importance of adherence to treatment. Increasing awareness and addressing misconceptions about TB in both the general and vulnerable populations, as well as in allied professionals, is a central function of TB services that requires tailored and targeted communication delivered in a non-judgemental and culturally appropriate way. Establishing, sustaining and resourcing health communication and education activities as a central component of service provision to prevent diagnostic delays, loss to follow up and reduce health inequalities, can improve TB control.

Topics to address when developing health communication, awareness and education programs include potential barriers and facilitators to diagnosis and treatment. A number of barriers can hamper access to diagnostic services of individuals belonging to vulnerable populations, while others can make it difficult to start or adhere to treatment. These barriers can relate to personal perceptions, stigma or lack of access to healthcare. Facilitators can enhance access to diagnostic services and compliance to treatment.

Health communication, awareness and education can be supported by high-quality evidence-based TB information in relevant languages (example in Appendix 3), and different formats, such as for vision- or hearing-impaired people. Ideally, the core information resources would also be tailored to the needs of specific vulnerable populations including homeless people, high-risk drug users, people in prison or in enforced segregation, vulnerable migrant populations and other vulnerable groups identified locally. Representatives from the TB-affected populations, including former patients, can be closely involved in developing and disseminating communication and education resources. For many vulnerable populations, written materials are of secondary importance to verbal messages due to poor literacy. Local services could work to recruit, support and train local peer educators and health advocates from the affected communities to work as TB champions.

The ad hoc scientific panel considers that suitable topics for a programme for health communication, awareness and education on TB among vulnerable populations include:

- Basic facts about TB including how it is spread, symptoms, diagnosis and treatment. These should be tailored to the local language and cultural needs including the needs of children.
- Information on how to access healthcare and counselling services.
- Resources to promote a high index of clinical suspicion among frontline professionals working with vulnerable populations including information on local referral pathways for symptomatic individuals. Web-based learning and training modules for health and social care professionals can be a highly effective and efficient way of training the workforce and ensuring that resources are up to date and evidence-based.
- Information for newly diagnosed cases on importance and methods for enabling treatment adherence, DOT, potential side effects, contact investigations, access to incentives and enablers and support groups.
- Information for vulnerable people co-infected with blood-borne viruses such as HIV and hepatitis C.
- Information for contacts of TB cases including resources for children.
- Targeted information to promote uptake of screening in vulnerable populations.

Communication, awareness and education resources can be made available in a variety of formats and increasingly, digital media are replacing more traditional paper-based resources. Digital media can include online video content, smart phone apps and web based learning modules. The effectiveness of digital media resources will depend on access to technologies and this can only be assessed and determined locally. Since access to smart phones and online tools may be difficult for many vulnerable individuals, written and verbal format resources may need to be made available taking into consideration levels of literacy.

Programme monitoring and evaluation

ECDC assessment

Monitoring and evaluation is important in all stages of the planning, design, implementation, improvement and expansion of interventions. The planning and design of interventions to achieve TB prevention and control in vulnerable populations requires base-line knowledge about the characteristics of the TB epidemic in the area or country, including information on the main risk factors, vulnerable groups and differences between cities and rural areas. Analysis of routine surveillance data, complemented by cohort reviews, and ad hoc studies can provide this information. Information from these sources will also help to monitor and evaluate the impact of specific interventions and the overall effectiveness of the TB programme.

Monitoring and evaluation of interventions is necessary to inform national decisions about whether to discontinue, modify or expand them. It would be ideal if these decisions were founded on a strong evidence base extracted from high-quality research studies that have strong study designs (such as randomised control trials). However, as is clear from the systematic reviews described here, such evidence is not always available and it may not be feasible to undertake trials or other experimental studies to generate the evidence that is missing. Alternatively, effectiveness of an intervention could be assessed through comparison of the population receiving the intervention with a similar population that did not receive the intervention. When a control group is not available, outcomes could be compared with existing data collected from the population receiving the intervention before the intervention was implemented.

Some of the interventions identified through the systematic reviews were implemented in a specific vulnerable group, while others were used in mixed populations. Where some interventions in one vulnerable group would be likely to have a similar effect in other vulnerable populations, others may only be applicable to specific groups. Therefore it is important to assess whether an intervention could be applied to other vulnerable groups, or analyse the outcomes of an intervention in a mixed population by specific sub-populations or vulnerable groups. In complex interventions, where several intervention activities or elements are combined, it is important to assess the effectiveness of each component of the intervention.

To allow for comparison of intervention outcomes in different populations, it is important to make sure that the outcome indicators are the same across the different populations. A challenge in the data collection and analyses of TB in vulnerable groups is often that different definitions are being used. The use of standardised definitions to describe the population, as well as the intervention elements, would facilitate consistent and harmonised data analysis.

To complement the data collection, cost-effectiveness studies should ideally be conducted in different contexts and settings. Mathematical modelling can also be applied in order to assess cost-effectiveness in diverse settings where the costs and contexts differ. From the literature, there are examples where molecular epidemiological tools have been used to identify and characterise epidemiological changes, and it could be assessed whether these tools are of benefit in specific local settings.

Possible implications for public health practice and research

The ad hoc scientific panel reflected on the possible implications for public health, specifically on: acceptability of the intervention by the target population; the feasibility to implement the intervention; the use of resources to implement the interventions; and the anticipated cost-effectiveness of the intervention (Table 1 and 2). The implications of implementing interventions to prevent and control TB in vulnerable populations are context-specific and depend upon others in the healthcare system, available resources, and type of vulnerable population. In Appendix 3 we provide illustrative examples of interventions that are currently implemented in the EU.

In order to fill the knowledge gaps that exist when it comes to interventions aiming to improve TB prevention and control in vulnerable populations, future research is needed to provide strong evidence of the feasibility, effectiveness and impact of interventions.

As a first step, identifying the characteristics of different vulnerable populations in the different areas and countries and their TB epidemiology and challenges with accessing diagnosis and treatment is essential in order to determine which populations should be targeted, and what kind of interventions are needed. This epidemiological research would benefit from standardised case definitions for vulnerable populations.

Interventions that aim at improving TB diagnosis and treatment of vulnerable populations are preferably assessed for effectiveness and costs using an established study design such as before-after study or (step-wedged) cluster randomised controlled trial. Intervention studies on improving diagnosis could focus on making diagnosis more accessible and acceptable. Intervention studies for improving treatment outcomes could focus on different kinds of DOT and patient support, including the assessment of innovative approaches using media and technology. In addition, interventions targeting vulnerable populations that have shown (cost)-effectiveness for other diseases may be tested for their effectiveness in improving TB prevention and control. Since vulnerable groups differ in their behaviour, preferences etc. interventions that have shown (cost)-effectiveness in one specific vulnerable group may not work for others. Therefore, interventions may need to be adapted and re-assessed for use in different vulnerable groups.

Collection of evidence on acceptability, feasibility, effectiveness and cost effectiveness can be considered when evaluating interventions in vulnerable populations. Acceptability, feasibility and effectiveness of an intervention may vary in different settings and between different target groups and thus effect the usefulness of an intervention. Cost-effectiveness evaluations in particular may provide different results in different settings, since resources and costs are extremely context-specific. Mathematical modelling can be a useful tool to assess the cost-effectiveness of interventions. Modelling can be especially helpful in understanding the contribution of each element to the intervention's success.

This guidance will be reviewed five years after publication to determine whether all or part of it should be updated depending on new available evidence or developments in EU/EEA Member States.

References

1. Volmink J, Garner P. Directly observed therapy for treating tuberculosis. *Cochrane Database Syst Rev.* 2007 (4).
2. Beith A, Eichler R, Weil D. Performance-based incentives for health: A way to improve tuberculosis detection and treatment completion?: CGD Working Paper #122. London: Center for Global Development; 2007. Available from: http://www.cgdev.org/sites/default/files/13544_file_TB_final.pdf.
3. Lutge EE, Wiysonge CS, Knight SE, Sinclair D, Volmink J. Incentives and enablers to improve adherence in tuberculosis. *Cochrane Database Syst Rev.* 2015;9.
4. Royal College of Nursing. Tuberculosis case management and cohort review: guidance for health professionals. London: Royal College of Nursing; 2012. Available from: https://www2.rcn.org.uk/_data/assets/pdf_file/0010/439129/004204.pdf.
5. Munro SA, Lewin SA, Smith HJ, Engel ME, Fretheim A, Volmink J. Patient adherence to tuberculosis treatment: a systematic review of qualitative research. *PLoS Med.* 2007 Jul 24;4(7):e238.
6. Rizzo M, Martin A, Jamal F, Lehmann A, Llewellyn A, Marrero-Guillamon I, et al. Evidence review on the effectiveness and cost-effectiveness of service models or structures to manage tuberculosis in hard-to-reach groups. Matrix evidence: National Institute for Health and Clinical Excellence (NICE), 2011.
7. Rizzo M, Martin A, Cliff-Matthews V, Jamal F, Lehmann A, Llewellyn A, et al. Evidence review on the effectiveness and cost-effectiveness of interventions aimed at managing tuberculosis in hard-to-reach groups. Matrix evidence: National Institute for Health and Clinical Excellence (NICE), 2011.
8. Rizzo M, Martin A, Cliff-Matthews V, Jamal F, Lehmann A, Llewellyn A, et al. Evidence review on the effectiveness and cost-effectiveness of interventions aimed at identifying people with tuberculosis and/or raising awareness of tuberculosis among hard-to-reach groups. Matrix evidence: NICE – National Institute for Health and Care Excellence, 2011 July 2011.
9. World Health Organization. Towards tuberculosis elimination: An action framework for low-incidence countries. Geneva: WHO; 2014. Available from: http://apps.who.int/iris/bitstream/10665/132231/1/9789241507707_eng.pdf?ua=1.
10. National institute for health and care excellence (NICE). Tuberculosis: identification and management in under-served groups. London: NICE; 2012. Available from: <https://www.nice.org.uk/guidance/ph37/resources/tuberculosis-identification-and-management-in-underserved-groups-1996302512581>.
11. European Centre for Disease Prevention and Control. Framework action plan to fight tuberculosis in the European union. Stockholm: ECDC. February 2008.
12. Migliori GB, Zellweger JP, Abubakar I, Ibraim E, Caminero JA, De Vries G, et al. European union standards for tuberculosis care. *The European respiratory journal.* 2012 Apr;39(4):807-19.
13. Lönnroth K, Migliori GB, Abubakar I, D'Ambrosio L, de Vries G, Diel R, et al. Towards tuberculosis elimination: an action framework for low-incidence countries. *The European respiratory journal.* 2015 Apr;45(4):928-52.
14. de Vries G, Aldridge RW, Cayla JA, Haas WH, Sandgren A, van Hest NA, et al. Epidemiology of tuberculosis in big cities of the European Union and European Economic Area countries. *Euro surveillance: bulletin Europeen sur les maladies transmissibles/European communicable disease bulletin.* 2014;19(9).
15. van Hest NA, Aldridge RW, de Vries G, Sandgren A, Hauer B, Hayward A, et al. Tuberculosis control in big cities and urban risk groups in the European Union: a consensus statement. *Euro surveillance : bulletin Europeen sur les maladies transmissibles/European communicable disease bulletin.* 2014;19(9).
16. European Centre for Disease Prevention and Control/WHO Regional Office for Europe. Tuberculosis surveillance and monitoring in Europe 2016. Stockholm: European Centre for Disease Prevention and Control; 2016.
17. Ploubidis GB, Palmer MJ, Blackmore C, Lim TA, Manissero D, Sandgren A, et al. Social determinants of tuberculosis in Europe: a prospective ecological study. *The European respiratory journal.* 2012 Oct;40(4):925-30.
18. Suk JE, Manissero D, Buscher G, Semenza JC. Wealth inequality and tuberculosis elimination in Europe. *Emerg Infect Dis.* 2009 Nov;15(11):1812-4.
19. Reeves A, Basu S, McKee M, Stuckler D, Sandgren A, Semenza J. Social protection and tuberculosis control in 21 European countries, 1995-2012: a cross-national statistical modelling analysis. *Lancet Infect Dis.* 2014 Nov;14(11):1105-12.
20. Ortblad KF, Salomon JA, Barnighausen T, Atun R. Stopping tuberculosis: a biosocial model for sustainable development. *Lancet (London, England).* 2015 Oct 23.

21. Lönnroth K, Jaramillo E, Williams BG, Dye C, Raviglione M. Drivers of tuberculosis epidemics: the role of risk factors and social determinants. *Social science & medicine* (1982). 2009;68(12):2240-6.
22. Semenza JC. Strategies to intervene on social determinants of infectious diseases. *Euro surveillance : bulletin Europeen sur les maladies transmissibles. European communicable disease bulletin*. 2010 Jul 8;15(27):32-9.
23. Story A, Murad S, Roberts W, Verheyen M, Hayward AC, London Tuberculosis Nurses N. Tuberculosis in London: the importance of homelessness, problem drug use and prison. *Thorax*. 2007 Aug;62(8):667-71.
24. Noyes J, Popay J. Directly observed therapy and tuberculosis: how can a systematic review of qualitative research contribute to improving services? A qualitative meta-synthesis. *J Adv Nurs*. 2007 Feb;57(3):227-43.
25. The European Federation of National Organisations working with the Homeless (FEANTSA). *ETHOS Typology on homelessness and housing exclusion* [internet]. Brussels: FEANTSA; 2011 [cited 2015 9 Dec]. Available from: <http://www.feantsa.org/spip.php?article120&lang=en>.
26. European Monitoring Centre for Drugs and Drug Addiction. *European drug report 2015: Data and statistics. Problem drug use: an overview of the methods and definitions used* [Internet]. Lisbon: EMCDDA; 2015 [cited 2015 Dec 8]. Available from: <http://www.emcdda.europa.eu/data/stats2015/methods-pdu>.
27. World Health Organization Department of Mental Health and Substance Dependence. *The alcohol use disorders identification test: Guidelines for use in primary care*. Geneva: WHO; 2001. Available from: http://apps.who.int/iris/bitstream/10665/67205/1/WHO_MSD_MSB_01.6a.pdf.
28. O'Mara A, Marrero-Guillamon I, Jamal F, Lehmann A, Cooper C, Lorenc T. Tuberculosis evidence review 1: Review of barriers and facilitators. Systematic Review. Matrix evidence: NICE – National Institute for Health and Care Excellence, 2010 October 2010.
29. Eastern Partnership. *Joint riga declaration on tuberculosis and its multi drug resistance*. Eastern partnership ministerial conference on tuberculosis and its multidrug resistance; Riga2015.
30. Bernard C, Sougakoff W, Fournier A, Larnaudie S, Antoun F, Robert J, et al. Impact of a 14-year screening programme on tuberculosis transmission among the homeless in Paris. *International Journal of Tuberculosis & Lung Disease*. 2012 May;16(5):649-55.
31. Ruutel K, Loit HM, Sepp T, Kliiman K, McNutt LA, Uuskula A. Enhanced tuberculosis case detection among substitution treatment patients: a randomized controlled trial. *BMC Res Notes*. 2011;4:192.
32. Duarte R, Santos A, Mota M, Carvalho A, Marques A, Barros H. Involving community partners in the management of tuberculosis among drug users. *Public Health*. 2011 Jan;125(1):60-2.
33. Yates S, Story A, Hayward A. Screening prisoners for Tuberculosis: What should the UK do? [Poster]. *Thorax*. 2009;64(Suppl 4):A105-.
34. Jones TF, Schaffner W. Miniature chest radiograph screening for tuberculosis in jails: a cost-effectiveness analysis. *Am J Respir Crit Care Med*. 2001 Jul 1;164(1):77-81.
35. Watson J, Abubaker I, Story A, Welfare R, White P, Garnett G, et al. *Mobile targeted digital chest radiography in the control of tuberculosis among hard to reach groups*. London: Health Protection Agency Centre for Infections; Department of Health. 2007.
36. Jit M, Stagg H, Aldridge R, White P, Abubakar I. Dedicated outreach service for hard to reach patients with tuberculosis in London: observational study and economic evaluation. *BMJ (Clinical research ed)*. 2011;343:d5376.
37. Story A, Aldridge RW, Abubakar I, Stagg HR, Lipman M, Watson JM, et al. Active case finding for pulmonary tuberculosis using mobile digital chest radiography: an observational study. *International Journal of Tuberculosis & Lung Disease*. 2012 Nov;16(11):1461-7.
38. Goetsch U, Bellinger OK, Buettel KL, Gottschalk R. Tuberculosis among drug users and homeless persons: impact of voluntary X-ray investigation on active case finding. *Infection*. 2012 Aug;40(4):389-95.
39. Ricks PM. *Tuberculosis control among substance users: The indigenous leadership outreach model vs. standard care*: University of Illinois at Chicago; 2008.
40. Pilote L, Tulskey JP, Zolopa AR, Hahn JA, Schecter GF, Moss AR. Tuberculosis prophylaxis in the homeless. A trial to improve adherence to referral. *Archives of Internal Medicine*. 1996;156(2):161-5.
41. Aldridge RW, Hayward AC, Hemming S, Possas L, Ferenando G, Garber E, et al. Effectiveness of peer educators on the uptake of mobile X-ray tuberculosis screening at homeless hostels: a cluster randomised controlled trial. *BMJ Open*. 2015;5(9).
42. Perlman DC, Friedmann P, Horn L, Nugent A, Schoeb V, Carey J, et al. Impact of monetary incentives on adherence to referral for screening chest x-rays after syringe exchange-based tuberculin skin testing. *Journal of Urban Health*. 2003;80(3):428-37.

43. Citron KM, Southern A, Dixon M. Out of the shadow Detecting and treating tuberculosis amongst single homeless people. London: Crisis 1995.
44. Ospina JE, Orcau A, Millet JP, Sanchez F, Casals M, Cayla JA. Community health workers improve contact tracing among immigrants with tuberculosis in Barcelona. *BMC Public Health*. 2012;12:158.
45. World Health Organization. Systematic screening for active tuberculosis: principles and recommendations. Geneva: WHO; 2013. Available from: http://apps.who.int/iris/bitstream/10665/84971/1/9789241548601_eng.pdf?ua=1.
46. Bell TR, Molinari NM, Blumensaadt S, Selent MU, Arbisi M, Shah N, et al. Impact of port of entry referrals on initiation of follow-up evaluations for immigrants with suspected tuberculosis: Illinois. *J Immigr Minor Health*. 2013 Aug;15(4): 673-9.
47. Harstad I, Henriksen AH, Sagvik E. Collaboration between municipal and specialist public health care in tuberculosis screening in Norway. *BMC Health Serv Res*. 2014;14:238.
48. Craig GM, Booth H, Hall J, Story A, Hayward A, Goodburn A, et al. Establishing a new service role in tuberculosis care: the tuberculosis link worker. *J Adv Nurs*. 2008 Feb;61(4):413-24.
49. Knowledge, perceptions and barriers and the social meaning of tuberculosis among asylum seekers, homeless people and refugee communities in Brent 2004–2006. London: Brent Refugee Forum, 2007.
50. Belling R, Woods L, Boudioni M, McLaren S. Pan London Tuberculosis services: An audit evaluation. Institute for Strategic Leadership and Improvement. London South Bank University: London, 2008.
51. Bock NN, Sales RM, Rogers T, DeVoe B. A spoonful of sugar: improving adherence to tuberculosis treatment using financial incentives. *The international journal of tuberculosis and lung disease : the official journal of the International Union against Tuberculosis and Lung Disease*. 2001 Jan;5(1):96-8.
52. Garfein RS, Collins K, Munoz F, Moser K, Cerecer-Callu P, Raab F, et al. Feasibility of tuberculosis treatment monitoring by video directly observed therapy: a binational pilot study. *The international journal of tuberculosis and lung disease : the official journal of the International Union against Tuberculosis and Lung Disease*. 2015 Sep;19(9):1057-64.
53. Liu Q, Abba K, Alejandria MM, Sinclair D, Balanag VM, Lansang MA. Reminder systems to improve patient adherence to tuberculosis clinic appointments for diagnosis and treatment. *Cochrane Database Syst Rev*. 2014;11.
54. Tuberculosis Coalition for Technical Assistance and International Committee of the Red Cross, Dara M, Grzemska M, Kimerling ME, H R, A Z. Guidelines for control of tuberculosis in prisons. Washington: USAID; 2009. Available from: http://pdf.usaid.gov/pdf_docs/PNADP462.pdf.

Appendix 1. Terms of Reference for ad hoc scientific panel

Background

Targeted interventions are needed for the prevention and control of tuberculosis in individuals that are hard-to-reach by the healthcare system. These are individuals who have difficulties in recognising symptoms and accessing health services, and patients with difficulties taking medication. The individuals and patients who are hardest to reach through traditional hospital-based tuberculosis services are also the most vulnerable and include homeless people, people with drug or alcohol addiction, prisoners or people with a history of imprisonment, and some vulnerable migrant populations, including Roma populations.

A number of interventions are at hand that may be of relevance for hard-to-reach and vulnerable populations. These interventions may target structural and intermediate determinants that affect the vulnerability of an individual or may be tuberculosis-specific interventions that aim to interrupt disease transmission, progression of infection to disease, or treatment of tuberculosis disease.

Scope and purpose of scientific advice

In line with the Framework Action Plan, the European Union Standards for Tuberculosis Care (ESTC), the action framework for tuberculosis elimination in low-incidence countries, and the concepts of how to address tuberculosis control in urban risk groups, ECDC plans to issue scientific advice on interventions and service models for tuberculosis prevention and control in hard-to-reach and vulnerable populations. The aim is to present the latest evidence base on the topic, provide an overview of interventions and service models, as well as provide evidence-based consensus opinions on options for how to best work with the target groups.

Methods for developing the scientific advice

ECDC is a resource of scientific advice on infectious diseases for the EU. Depending on the level of evidence provided and the methodology used, this advice is typically conveyed through a Guidance (based upon a systematic review of scientific evidence and appraised by a scientific panel of experts), a Systematic Review (report that identifies, appraises and synthesises the evidence) or an Expert Opinion (scientific view based on an informal review of evidence). Each category of scientific advice follows a strict application of respective methodologies.

The scientific advice on interventions for tuberculosis prevention and control in hard-to-reach and vulnerable populations will be in the format of a Guidance document. It will be developed through the following methods: systematic literature reviews, input from an ad hoc scientific panel, and development of the final guidance document by ECDC.

The literature reviews aim at synthesising a comprehensive portfolio of interventions that have been used to target vulnerable populations and will summarise the effect of these interventions. The reviews summarise both quantitative studies of effectiveness of interventions, and qualitative descriptions of interventions and service models, as well as evidence on barriers and enablers to implement specific interventions for the target populations.

The ad hoc scientific panel will advise ECDC on the content of the guidance, review and assess the systematic literature reviews, and based on the evidence and their own expertise formulate expert opinions.

ECDC will be responsible for writing the guidance document, incorporating the findings of the systematic reviews with the statements by the ad hoc scientific panel, and adding additional considerations and statements as found relevant by ECDC. ECDC will further work towards a draft document and will consult the ECDC Advisory Forumⁱ before a final guidance document is produced.

ⁱ The Advisory Forum advises on the quality of the scientific work undertaken by ECDC. It is composed of senior representatives of national public health institutes and agencies, nominated by the Member States.

Process to establish an ad hoc scientific panel

ECDC has the possibility to establish ad hoc scientific panels that will aid ECDC and provide independent advice on a topic during a limited time and with a specific scope. The process to set up such an ad hoc scientific panel follows a strict methodology and includes the following main steps: Identification of experts; collecting declarations of interests of experts; evaluating the eligibility and rule out conflict of interests of experts through clearance by the ECDC compliance officer; formal appointment of panel members by the ECDC Director; ECDC assigns a Chair of the panel.

The identification of experts can be done in several ways: inventory of key experts that publish scientific literature in the area, request for suggestions of experts by the ECDC Advisory Forum, and through other means that involve contacting our network and partners for suggestions. It is for ECDC to decide on the composition of the panel, taking into account for example country/setting representativeness, and balance of specific expertise and experience of panel members.

Objective of the ad hoc scientific panel

Towards developing this Guidance document, an ad hoc scientific panel of experts in the field will be assembled. This scientific panel will be tasked to advise ECDC on the content of the document. The experts of the panel will review the systematic literature reviews of the evidence collected, assess the evidence and contribute with their expert knowledge in formulating expert opinions.

Expected work of the panel

Before the panel meeting: ECDC will provide panel members with the systematic literature reviews to review the content of these. A draft outline of the guidance document will also be distributed for possible advance comment if the Chair finds this valuable. If the panel and the Chair of the panel so wish, ECDC can also arrange a telephone conference before the panel meeting to initiate the discussion on providing advice and to discuss the guidance document to be developed.

At the panel meeting: ECDC will ask the panel members to attend a two-day ad hoc scientific panel meeting. The meeting will take place 7–8 September 2015 in Stockholm, Sweden. During this meeting, panel members are expected to formulate advice on the topic, based on the preparatory work of the agency, the work done before the panel meeting and their own expertise. The aim is to reach consensus on key messages and options for interventions that the panel considers relevant as a result of the assessment of the evidence-base and their own expertise. It is the responsibility of the chair of the panel to lead the discussion so the panel can formulate expert opinions and reach consensus on key messages and options.

After the panel meeting: the Chair will deliver the formulated expert opinions to ECDC, and ECDC will then incorporate these statements into the Guidance document. If ECDC so decides, the panel will be asked to review the draft Guidance document and provide additional input.

Terms and conditions of panel members

ECDC will provide the panel members with per-diem compensation as well as cover the costs of accommodation and travel related to attendance to the above panel meeting, in accordance with EU Commission rules and regulations. ECDC does not provide experts with any other fee for the work they perform during the process before and after the actual panel meeting.

ECDC will acknowledge all experts for their work in the final guidance document as having been a part of the ad hoc scientific panel. The final document will be in the public domain.

Mandate of panel members

ECDC asks for experts to provide advice based on their professional and scientific merits. Opinions expressed and advice in the ad hoc scientific panel shall be considered the personal professional advice of the expert. Experts in the ad hoc scientific panel may not represent the interests of a commercial body, a Member State or a professional body. Membership of the latter does, however, not automatically disqualify a candidate from participation. Selected experts will be asked to submit declarations of interests using an ECDC procedure before they are officially appointed by the ECDC Director to be members of the panel.

Members of the ad hoc scientific panel officially appointed by ECDC's Director

Name	Organisation	Country
Chryssoula Botsi	Hellenic CDCP	Greece
Thierry Comolet	Ministry of Health and Social Affairs	France
Monica Dan	The Romanian Association Against AIDS (ARAS)	Romania
Raquel Duarte	National Directorate of Health Portugal	Portugal
Enrico Girardi	National Institute for Infectious Diseases (INMI), L. Spallanzani IRCCS	Italy
Martin Priwitzer (Chair)	Stuttgart Local Health Authority, German Central Committee against Tuberculosis	Germany
Tore Steen	City of Oslo, Health Agency	Norway
Mihaela Stefan	Marius Nasta Institute	Romania
Alistair Story	University College London Hospitals, Find&Treat at University College Hospitals, NHS Foundation Trust	United Kingdom
Petra Svetina	University Clinic of Respiratory and Allergic Diseases Golnik	Slovenia
Rob van Hest	Municipal Public Health Service Rotterdam- Rijnmond	the Netherlands

Observers of the ad hoc scientific to join the meeting

Name	Organisation	Country
Sophie de Vries	Academic Medical Centre, University of Amsterdam	the Netherlands
Martin Grobusch	Academic Medical Centre, University of Amsterdam	the Netherlands

The Compliance Officer reviewed the submitted declarations of interest and approved the participation of the experts without any mitigation measures.

Before the actual meeting all experts confirmed that their submitted annual and specific declarations are complete and up to date. All read the agenda for the meeting and none declared any additional specific interests related to the work of the panel. All agreed that their names, affiliation and declarations of interests be published on the website of ECDC as recorded in the minutes of the expert panel's meeting.

Appendix 2. Methodology

Systematic reviews

The protocols for the four systematic reviews were registered in the online international database of prospectively registered systematic reviews in health and social care, PROSPERO.

- Review 1 - Tuberculosis among hard-to-reach groups: barriers and facilitators: CRD42015019450.
- Review 2 - Evidence review of the effectiveness and cost-effectiveness of interventions aiming at identifying people with tuberculosis and/or raising awareness of tuberculosis among hard-to-reach groups, including a qualitative description of these interventions: CRD42015017660.
- Review 3 - Evidence review of the effectiveness and cost effectiveness of interventions aiming at managing tuberculosis in hard-to-reach groups, including a qualitative description of these interventions: CRD42015019449.
- Review 4 - Evidence review of the effectiveness and cost effectiveness of service models or structures aiming to manage tuberculosis in hard-to-reach groups, including a qualitative description of these service models or structures: CRD42015017865.

Delphi process

Round 1

Collection and compiling opinions before meeting

The purpose of this round was to familiarise the ad hoc scientific panel with the evidence base and for them to provide inputs on panel opinions to be made. In addition, the aim was to collect the panel's comments on the draft guidance document, reflections on the evidence base, and opinions on the options for interventions targeting hard-to-reach and vulnerable populations.

The panel members were asked to provide comments and opinions on the following:

Content and structure of guidance documents - opinions on the content and structure and suggestions on content or sections that should be added or deleted from the document, including suggestions for annexes to be included. The expressed suggestions and opinions were summarised in a qualitative approach. When different suggestions that lead to different options for structure and scope of the documents arose, they were brought up for discussion at the meeting, as part of round 2 of the Delphi process.

Evidence and ad hoc scientific panel opinions to be made – The panel was asked to use their expert knowledge and experience to provide their opinion on the evidence collected through the systematic reviews. They were asked to indicate whether they consider the systematic review results to be relevant to include, to propose an opinion that would be linked to the respective systematic review result, and to suggest which population it was applicable to. The panel was also asked to consider combining several systematic review results into one opinion, or apply the same opinion to more than one vulnerable group.

The systematic review results included in this round were those solely based on the findings of the literature review and were ranked according to the strength of the evidence (quality of studies, coherence in findings across studies, risk of bias etc). The panel opinions were based on the systematic review results and the certainty of evidence. The panel opinions are an outcome of the work of the panel, i.e. a statement on an option for an intervention or action that could be taken into consideration when developing policies, strategies or guidelines.

The responses on relevance given by the scientific panel members were coded as 1 for Yes and 0 for No, indicating whether a specific systematic review result merits to be included in the guidance document. The average score was calculated (sum of scores, divided by number of panel members that provided a response for the specific systematic review result). The average scores were colour coded, to highlight systematic review results that scored more than 0.5 (indicating that more than half of the panel members responded 'Yes'). This document was presented to the scientific panel during the panel meeting (Round 2 of the Delphi process).

Additional opinions and proposals – The ad hoc scientific panel was asked to use their knowledge and experience and provide opinions on whether they consider there are gaps where there is no evidence identified through the systematic reviews, and to propose interventions, evidence and opinions to be included in the guidance. Any additional proposals were qualitatively summarised and brought to the panel's attention during the meeting.

Round 2

During the panel meeting the panel took the results of Round 1 and used it as a guide to steer the discussions. The outcomes of the discussion were included in the summary of findings tables and in the draft guidance document. Voting was applied in those instances where there was a difference in opinion.

After the meeting, the Chair of the panel and ECDC developed a proposal for the criteria for consideration to include for each intervention (acceptability, feasibility, use of resources, anticipated cost-effectiveness). The ad hoc scientific panel was then asked to review the suggestion for criteria and scale of grading, as well as the list of options for interventions.

Round 3

Grading of criteria for consideration

After the criteria and scale for grading were agreed upon, the ad hoc scientific panel was asked to grade each intervention according to the criteria chosen for consideration.

Acceptability	Feasibility	Use of resources	Anticipated cost-effectiveness
Highly acceptable	Highly feasible	High	Highly cost-effective
Likely acceptable	Likely feasible	Medium	Likely cost-effective
Not acceptable	Not feasible	Low	Not cost-effective
Varies	Varies	Varies	Varies
Don't know	Don't know	Don't know	Don't know

Since the grading 'varies' was hard to interpret, those who selected 'varies', were asked to provide a justification for this response.

In this round of the Delphi, 9 out of 11 members provided scores. The variation in scoring was assessed by the following method:

- Low variation: all replies were distributed within one or two neighbouring grades (e.g. highly acceptable and likely acceptable).
- Medium variation: more than 50% of the scores were within one specific grade, but there were three or more different grades given among the replies.
- High variation: the whole range of grades was given among the replies.

For each criteria a summary score was assigned based on the following principle:

- Given that the variation was low or medium, the grade that a majority (more than 50%) of the members responded was selected. If two grades reached exactly 50% each, then the "lower" level of grade was selected (e.g. 4 responded 'highly acceptable', 4 responded 'likely acceptable' and 1 responded 'don't know': then the summary score is 'likely acceptable').
- If the variation was high, but one grade was in a majority (more than 50%) of the member's responses, that grade was selected. If no single grade was in majority 'varies' was selected.

Round 4

Collection of opinions on heterogeneity in replies from Round 3

Since the panel had not reached consensus in the grade scoring for the different criteria on several interventions, another round of review for criteria with high variation in the scores was done. In this round, a summary score for each criteria and for each intervention, and the level of variation in scoring between the panel members (low, medium, high) were provided. Panel members were asked to mention if they disagreed on a summary score, provide a short justification for their disagreement and a suggested new score.

Additionally, a main problem that was encountered was with the criterion 'Use of resources'. Since there was high variation in responses to this criterion, it was often assigned as 'varies'.

At the end of this round, the sum scores and the approach of grade scoring as 'varies' when the heterogeneity in responses by the panel members were high, as outlined above, were agreed upon.

Appendix 3. Case studies and examples of service models

The case-studies described below are illustrative examples of interventions that are currently implemented in the EU. Their inclusion in this guidance does not mean that ECDC endorses these interventions or the implementing organisations. All information given in the below text was provided by the respective organisation.

Find&Treat, London, UK

Find&Treat are a specialist outreach team that work alongside health services to tackle TB in vulnerable populations such as homeless people, drug or alcohol users, vulnerable migrants and people who have been in prison.

The Find&Treat multidisciplinary team include former TB patients who work as peer advocates, TB nurse specialists, social and outreach workers, radiographers and expert technicians, and who take TB control into the community. Their service spans the TB pathway from detection, to diagnosis and onward care. Finding includes raising awareness among service users and frontline professionals, and screening high risk people using a mobile digital x-ray unit. Treating includes helping referred patients by locating those who have stopped TB treatment before completing the full course, setting up and supporting Directly Observed Treatment (DOT) in the community and providing practical assistance and advice on accommodation.

The team uses state of the art point of care diagnostics and online tools to support TB patients (see following section on the Find&Treat Video directly observed treatment project). With a patient-centered approach, they cater for the needs of the people they serve and address the underlying determinants of disease to improve health outcomes. They are working to widen their scope to also include the screening and management of latent TB, as well as other co-morbidities such as hepatitis C, B and HIV, and even provide vaccinations to protect individuals within the target population.

Find&Treat services were demonstrated to be highly cost effective and potentially cost saving. Find&Treat screen almost 10 000 high risk people and provide treatment and care for about 300 complex and vulnerable patients, per year.

Video Observed Treatment, Find&Treat, London, UK

Video Observed Treatment (VOT) is a new method of Directly Observed Treatment (DOT) using a computer or smart phone to virtually observe the taking of TB medication and to support patient-provider communication.

In the UK, DOT is offered to selected TB patients who are likely to need extra support due to social risk factors or clinically complex disease. Since DOT programs are labour-intensive, costly and logistically complicated, there has been a gap between those eligible and those who are offered DOT. Thus, there was a need to make DOT adherence as feasible and convenient as possible for both patients and providers.

VOT has the flexibility and 'empowering' capacity that enables people to have more control over where and when they take their medication. It also reduces travel time and costs for both providers and patients.

Eligible patients for VOT include patients whose social circumstances make it difficult for them to keep appointments and be available at given times. These include vulnerable populations such as refugees and asylum seekers, those affected by homelessness, substance misuse and mental health issues.

Pilot studies have demonstrated that VOT can be as or more effective in maintaining adherence than traditional long-term DOT therapy, and a randomised control study is underway to robustly compare VOT with DOT to determine the relative effectiveness and cost-effectiveness of the intervention.

Find&Treat has supervised over 100 patients on VOT since 2009, including 29 with multi-drug resistant TB and 5 with extensively drug-resistant TB. Two-thirds of the patients have successfully completed their treatment.

Mobile medical outreach team (net) working for TB treatment adherence (EMLT), Paris, France

Equipe mobile de lutte contre la tuberculose (EMLT) aims at actively supporting the homeless, migrants and other socially vulnerable populations with TB to complete their treatment.

Studies from 2000 revealed that over 50% of homeless and undocumented migrant TB patients were lost to follow-up after discharge from acute hospitals in Paris. At that time, there was no mechanism of finding people who went missing.

EMLT was designed to find people who are at risk of being lost to follow-up and to support them in whatever way needed to help ensure completion of treatment. This support includes delivering TB medication and observing the taking of the medication. The focus is on active multi-disciplinary case management with mobile units staffed by medical, nursing and social workers, who are in direct contact with people on the street, in hostels, hospitals and prisons. The teams approach to the patients is respectful and supportive, and although their main aim is to increase TB treatment adherence, they also try to help the patients with their other concerns and needs. For this, the program has also established broad network with a vast array of social, health, legal, immigration and other support agencies.

Since EMLT was started in 2000, 'lost to follow-up' rates have dropped to less than 10%. The program actively follows 250–300 patients a year, of which roughly 30–50% complete their treatment.

Roma Health Assistants – Velka Lomnica - Slovakia

In Slovakia, 25% of all TB cases belong to the Roma communities, and around 84% of all TB cases in children are Roma. Due to barriers in accessing the health system and prevention services, diagnosis and treatment of TB cases belonging to certain Roma communities has been challenging.

To improve TB control in Roma settlements, new ways to provide TB care (as part of comprehensive health education, prevention and care services) in the community were developed.

One strategy that was tested in Velka Lomnica is the involvement of Roma health assistants in TB case finding, contact tracing and treatment adherence. Roma health assistants are residents of the Roma settlement who work as health mediators and community health workers. They serve the population that lives in the segregated Roma community, with the overall goal of improving their health.

Key persons from the Roma settlement were identified to work as Roma health assistants and to facilitate health communication and education, and to support patients. With regards to TB diagnosis, the role of the Roma health assistants is to work in the community to assist in contact tracing, especially with identification and investigation of contacts, and to provide transportation to the doctor. With regards to TB treatment, Roma health assistants bring patients to their appointments, ensure they get their drugs, are in daily contact with them and directly observe the daily intake of drugs, and keep patient records. They are also trained to be able to judge the possible side-effects of treatment.

As a result of the systematic work of Roma health assistants in Slovakia, over 80% of adult Roma people with TB have been successfully treated, and all index cases for children's TB cases have been identified. In addition, the program helps insure that the high-risk Roma community is under constant TB surveillance and every outbreak of TB is immediately identified and contained.

ExplainTB - Global (based in Germany)

ExplainTB is a smartphone-based aid for patients and healthcare workers. It is free of charge and provides vital medical information about tuberculosis in 26 languages via a website (<http://www.explaintb.org/>) and smartphone app. Forty one chapters include topics on symptoms, transmission, diagnosis, treatment and TB in special situations.

It has been shown that patient education is more effective in the patient's mother tongue. The growing availability of smartphones allows point-of-care education via written media, videos and audio tunes (e.g. for children and people who are illiterate). Additionally, tailored bilingual handouts for patients can be created through the project website in any two languages on any selected topics. In the last year, the project website was visited by more than 12 000 users from 128 countries with most users from Germany (37%), Russia (18%) and USA (12%). The educational videos were downloaded more than 600 times and the app was installed on more than 900 devices.

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