



Early Detection and Integrated Management of Tuberculosis in Europe

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Early diagnosis of tuberculosis

D7.4

Prioritisation Document on TB action plans and toolkit production

WP 7 – Strengthening national TB programmes

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1. Introduction

National strategic planning is a core component of a national TB programme and provides the over-arching framework for the operationalisation of key activities and functions to tackle TB control and prevention priorities.

This TB Strategy Toolkit aims to assist national TB plan development or refinement by providing up-to-date guidance on core components of a TB Action Plan or Strategy by bringing together the latest EU/EEA-focused evidence and expert opinion.

2. Methodological approach

To inform the development of the TB Strategy Toolkit, between May 2017 and September 2018, an evidence portfolio was compiled, which summarised published evidence within the context of EU and EEA settings, and constitutes:

- A pan-European survey on national TB control plans and strategies, including prioritisation of action areas and barriers to the implementation of interventions for TB control and prevention (D7.1)
- Findings from a systematic review on the evidence base for interventions to control and prevent TB (D7.2)
- Findings from a systematic review and evidence synthesis of barriers and facilitators to implementation of policies, strategies and guidelines for TB control and prevention

To deliver D7.3 Public Health England, leaders for Work Package 7 (WP7) for the E-DETECT TB research project hosted an Expert Stakeholder meeting on Wednesday 24th October 2018 as part of an expert consultation exercise to populate core components underpinning national TB Action Plan or TB Strategy for prevention and control. The event brought together representatives from TB programmes and services from across EU and EEA member states, academics, civil society organisations, World Health Organisation (WHO) Europe, European Centre for Disease Control (ECDC) and the European Commission / CHAFEA.

The event was divided into a series of presentations on up-to-date evidence on core components (identified through the pan-European survey (D7.1) for national TB strategies and utilised a modified Delphi method to attain expert consensus on priority intervention areas and a targeted priority-based approach to overcome barriers.

A presentation on the draft outline of the TB Strategy Toolkit (prioritisation document on TB action plans and toolkit production) (D7.4) was delivered to experts. The aims, objectives, target audience and outlines for best practice and core components of a national TB strategy and proposed plans for integrating the evidence for these core components were also presented.

The outputs from this Expert Stakeholder meeting were utilised to develop this TB Strategy Toolkit to support national TB programme representatives and national focal points to develop or refine their national TB action plans or TB strategies. Further details on the methodological approaches to attain expert consensus can be found in the on page 43 of the TB Strategy Toolkit (appended to this report).

The TB Strategy Toolkit was populated in a way to support decision-making by national TB programme representatives on which core components to prioritise and implement, based on evidence from individual studies, consensus and relative impact that can be expected from each component. For each core component the following was provided:

- A background and justification for each core component and its related interventions;
- Evidence on effectiveness of interventions in this area;
- Descriptions of current practice related to each intervention in EU and EEA Member States;

- Evidence on factors that may facilitate or impede implementation of interventions to deliver the core component;
- Expert opinion on core components, where there are barriers to implementation and major activities or proposed solutions to address these barriers

Figure 1 summarises the main steps undertaken to develop this TB Strategy Toolkit in chronological order.

Appended to this report is the TB Strategy Toolkit (prioritisation document on TB action plans and toolkit production), which serves as an evidence-based practical instrument to support national TB programme representatives and national focal points to be equipped to develop their and implement their own strategy for the own country-level contexts. This will inform resource allocation for locally-relevant solutions, stakeholder engagement and mobilisation of high-level political commitment and stewardship functions and enhanced mobilisation of resources.

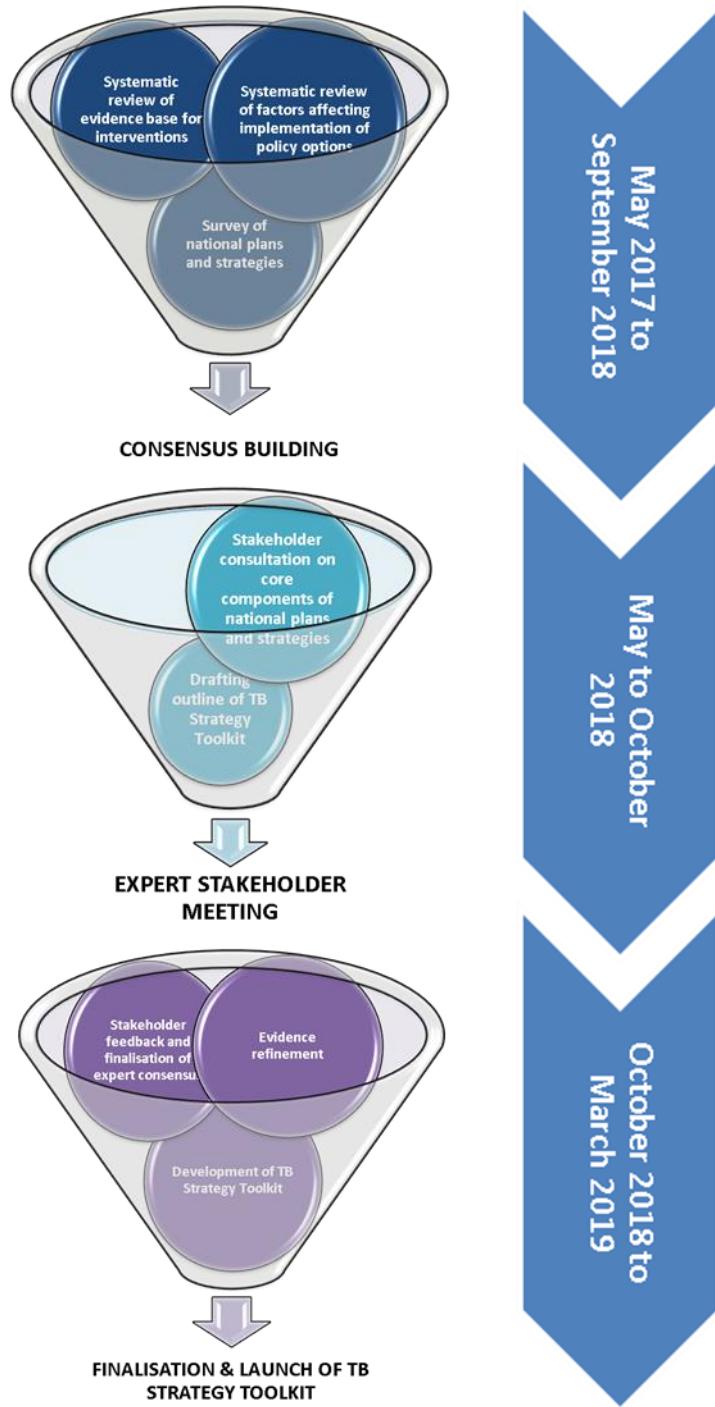


Figure 1: TB Strategy Toolkit developmental stages

3. Appendix: Prioritisation Document on TB action plans and toolkit production (TB Strategy Toolkit)



Public Health
England

TB Strategy Toolkit: supporting the development and strengthening of national TB plans in European Union and European Economic Area member states

April 2019



Karolinska
Institutet

This TB Strategy Toolkit was developed by Public Health England, in partnership with University College London, KNCV Tuberculosis Foundation and the Karolinska Institute as part of a work package to support the strengthening of national TB control programmes in European Union (EU) and European Economic Area (EEA) member states.

About Public Health England

Public Health England exists to protect and improve the nation's health and wellbeing and reduce health inequalities. We do this through world-leading science, knowledge and intelligence, advocacy, partnerships and the delivery of specialist public health services. It is an executive agency of the Department of Health and Social Care, and a distinct delivery organisation and operational autonomy. We provide government, local government, the National Health Service (NHS), Parliament, industry and the public with evidence-based professional, scientific and delivery expertise and support.

About University College London

University College London (UCL) has a global reputation for excellence in research and is committed to delivering impact and innovations that enhances the lives of people in the UK, Europe and around the world.

UCL also receives the highest share of any UK university of the UK Government's strategic investment fund, and has recently invested more than €310 million into state-of-the-art infrastructure to facilitate cutting-edge research across a broad range of disciplines

About KNCV Tuberculosis Foundation

KNCV Tuberculosis Foundation is an international non-profit organisation dedicated to the fight against tuberculosis. KNCV is an international centre for expertise for TB control that promotes effective, efficient, innovative and sustainable TB control strategies in a national and international context.

Over the past century, KNCV has built a wealth of knowledge of and expertise, initially by successfully controlling TB in the Netherlands and since the 1970s has shared knowledge and expertise with the rest of the world. KNCV is the overall lead partner in Challenge TB (CTB), the USAID-funded 5-year global programme to decrease TB mortality and morbidity in high burden countries.

About the Department of Public Health Sciences, Karolinska Institute

The Department of Public Health Sciences, Karolinska Institute conducts research, teaching and applied health work based on public health science and epidemiology. The Department hosts the Karolinska Institute Centre for TB Research and has a broad portfolio of domestic and global TB research.



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We also acknowledge national TB programme representatives' contributions to the survey of national TB plans and strategies and alongside ECDC and WHO Europe representatives as part of the Expert Stakeholder meeting,

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FOREWORD

TB remains one of the world's deadliest diseases and a major public health problem in many countries. Recent impetus, including from the WHO End TB strategy, the Sustainable Development Goals and most recently the first ever High-Level meeting on TB in the United Nations General Assembly gives hope that momentum can be gained to tackle this ancient disease. However, the complex natural history and immunology of TB, as well as structural and social determinants that drive its spread make TB control a challenging task, where only a rich portfolio of well-chosen interventions taken together can have a meaningful impact on TB incidence and outcomes. Yet, many countries do not have a national TB strategy to help deliver improved TB control.

I am therefore pleased to introduce this TB Strategy Toolkit. Developed with funding from the European Commission, and firmly grounded in the European context, it aims to provide policy makers, TB programmes and services, and many other relevant stakeholders with an overview of the available TB control tools together with their evidence and provide information on barriers and enablers to implementation. This creates a menu of choices, which we hope will help national TB programme representatives and national focal points successfully develop and implement their own strategy in their own context. We hope this Toolkit, which outlines evidence and stakeholder views for important topic areas will aid this work.

Successful TB control is hard work and achieving the targets of the WHO End TB strategy is highly ambitious, but we hope that the readers of this Toolkit will be better equipped to help in controlling this deadly infection in their country and their context.

Dr Dominik Zenner

1 Introduction and background

1.1 Aim of TB Strategy Toolkit

In keeping with the global TB strategy goals, a coordinated and coherent approach to national TB control is fundamental to delivery. Within this global context, for low incidence countries, TB elimination is the central objective.

Whilst World Health Organization (WHO) has published a generic toolkit, which aims to support countries to draft national strategic plans (WHO 2015), a more targeted and supportive approach is required to ensure that EU/EEA member states develop evidence-based national action plans or strategies. These should include ambitious, context-specific goals, which account for EU/EEA-specific TB epidemiology and some of the structural, financial and political barriers.

This TB Strategy Toolkit aims to assist national TB plan development or refinement by providing up-to-date guidance on core components of a TB Action Plan or Strategy. The Toolkit brings together the latest EU/EEA-focused evidence and expert opinion.

This TB Strategy Toolkit has been developed in collaboration with European TB stakeholders, European Centre for Disease Prevention and Control (ECDC) and WHO based on evidence, expert views and cumulative country experience in EU/EEA member state settings. It uses findings from a pan-European survey of national TB control plans and strategies, policy reviews and consensus on policy options at an expert stakeholder meeting.

1.2 Target audience

The target audiences for this TB Strategy toolkit are policy makers, institutions responsible for the planning and commissioning of health and social care measures, TB programmes and services, civil society organisations, non-governmental organisations, charities and services linked to social support systems. The toolkit is aimed at stakeholders from EU and EEA member states but will be of use to policy makers and institutions in other, comparable settings.

1.3 Prioritising tuberculosis as a public health problem in EU and EEA settings

TB incidence continues to decline across the EU and EEA and this can in part be attributed to timely diagnosis and rapid treatment of infectious TB cases, which have helped control the epidemic and have been core TB control interventions. However, despite this, projected trends suggest that an intensification of TB control efforts is needed to improve access to high quality care, which will primarily improve health outcomes for treated patients, and indirectly achieve public health impact.

Figure 1: Tuberculosis notifications EU/EEA 2007-2017 (source: ECDC/WHO 2019 Tuberculosis surveillance and monitoring)

Continuous decline between 2008 and 2017:

- Number of TB cases decreased by **34%**
- Notification rate decreased by **36%**



Twenty-six years after being declared a global health emergency, the first-ever UN High Level Meeting (UNHLM) on TB pledged to make ending this disease a priority by mobilising political commitment to accelerate global and national actions. The Lancet Commission proposed the establishment of a Tuberculosis Observatory to evaluate progress made by countries in meeting targets outlined in UNHLM declaration and help to mobilise programme and policy changes, track progress and uphold interdisciplinary and multi-sectoral responsibilities. In low incidence settings, such as the EU and EEA, targeted approaches to tackle TB in under-served and high-risk populations alongside wider system efforts to improve treatment, prevent resistance and implement new technologies are needed (Lönnroth 2015). EU member states are affected by changes in migration patterns into and within EU/EEA settings, bringing increasing social and political impact. Programmes and interventions which support integrated care and prevention and target immediate health and social needs highlights the importance of programmes which identify TB and LTBI among migrants from high incidence settings. Historical inter-country variability in policies reflects difficulties in coordinating complex interventions, cross-border issues within a delicate legal and ethical framework (D'Ambrosio, Centis et al. 2017). Collaboration with authorities to identify and coordinate innovative cross-border activities that guarantees individual human rights, which are independent of the residential status of patients will support progress towards TB elimination.

Screening for active TB and LTBI in TB contacts and selected high-risk groups is an important priority for low incidence settings and is included as a core component of WHO's End TB Strategy. Whilst programmatic management of TB is supported by WHO Guidelines (WHO 2015) and the WHO Global Task Force on LTBI (Getahun H 2016), important challenges for programmatic LTBI management have been identified in The Netherlands (de Vries G 2017). These include developing culturally-sensitive and client-centred education for migrants, securing financial resources for appropriate TB professional skills-mix for service delivery and implementation, availability of diagnostic tests and drugs,

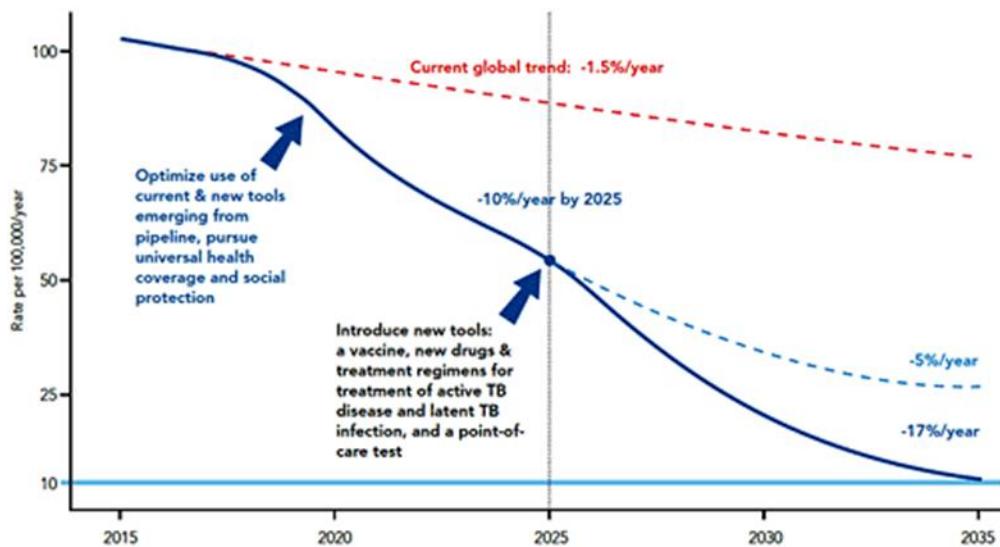
additional data collection for monitoring and evaluation to assess progress against WHO indicators for LTBI management, reducing patient costs for LTBI screening and preventative treatment and assessing cost-effectiveness and impact on TB epidemiology. An authoritative legislative framework making LTBI a notifiable condition could improve reporting coverage and provide the evidence base upon which to mitigate against these identified challenges.

Pillar 3 of The End TB Strategy (WHO 2015) underpins the need for introducing and implementing new tools for TB control and to reach target levels, the key actions of which include:

- Discovery, development and rapid uptake of new tools, interventions and strategies
- Research to optimise implementation and impact and promote innovations

Figure 2 shows the projected acceleration of decline of global TB incidence rates to target levels if optimisation of current tools and progress towards universal health coverage and social protection and additional impact of new tools by 2025

Figure 2: Projected acceleration of decline of global TB incidence rates to target levels (source WHO End TB Strategy (WHO 2015))



As reported in the recent Lancet Commission (Goosby E 2018) tuberculosis research and development is chronically under-funded, and there is a pressing need for novel and patient-friendly treatment strategies and transformative vaccines and diagnostic tools to accelerate TB decline. There have been noteworthy significant shifts in information and communication technology and digital solutions, such as video-observed therapy (VOT) approaches (Story A 2019), which have rapidly gained momentum internationally, leading to conditional recommendations for their use (WHO 2017).

Scaling up proven interventions and increasing investments that span diagnostic, therapeutic, prevention research and development and population, policy, operational and implementation research to intensify efforts to support national programme decision makers to employ transformative research will yield important returns.

Setting and re-evaluating priorities for basic science and operational research, which target wider structural determinants of TB risk and transmission and socio-behavioural aspects of health service engagement, will support programmatic success. Such approaches require drawing upon interdisciplinary partnerships with academia, industry,

advocacy and regional and national public health institutions. Engagement with political decision makers will ensure coordinated research is aligned with global and national goals.

In our pan-European survey of national plans and strategies completed by national TB programme managers and national focal points, it was reported that one fifth of EU and EEA countries had strategies for the application of new TB control and prevention tools. These tools included: rapid diagnostic tests, 86%; treatment observation, 71%; infection control, 57%; drug susceptibility testing, 57%; surveillance, 50%; microbiology, 50%; contact tracing, 36%; outbreak investigation, 29%.

1.4 Why this TB Strategy Toolkit was developed

A robustly designed and well-implemented national TB strategy is essential (ECDC. 2008) to successful TB control as it galvanises best practice and expertise in clinical care, social support and public health to strengthen TB control efforts to reduce TB incidence, health inequalities and may ultimately lead to the elimination of TB in Europe.

Robust trans-national evidence-based interventional projects are needed to support national TB strategy development. To support this, the European Commission-funded E-DETECT TB (Early Detection and Integrated Management of Tuberculosis in Europe) was formed. It unites leading TB experts spanning national public health agencies with major academic institutions and industry to utilise evidence-based transnational approaches to reach high risk under-served populations across EU and EEA settings (Abubakar I 2018).

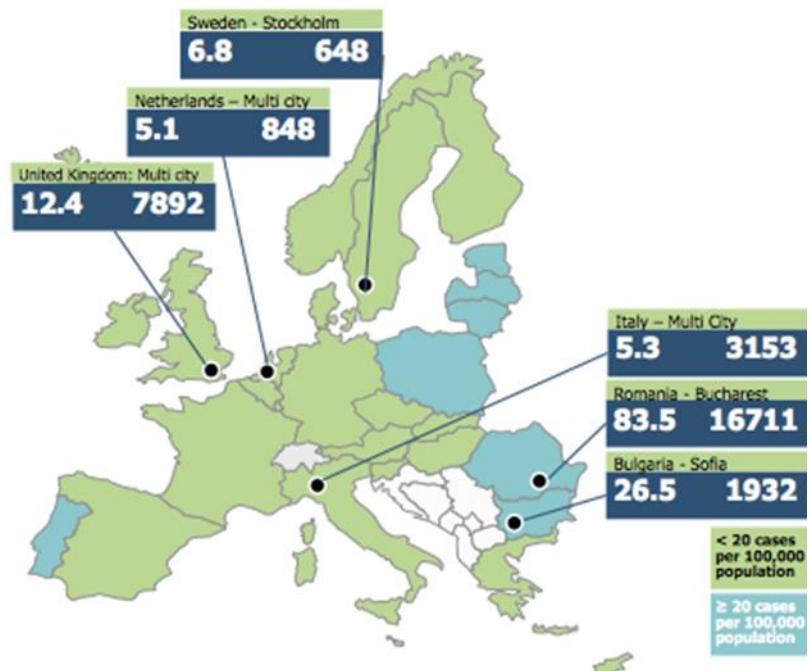
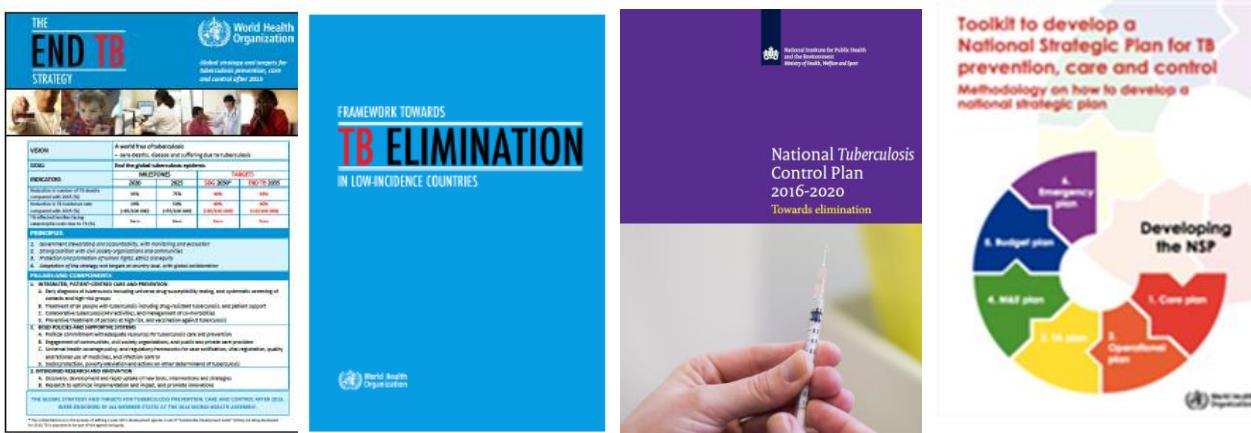


Figure 3: Map of Europe showing E-DETECT TB consortium partner countries and burden of tuberculosis by rate per 100,000 and the number of cases in 2013 (Abubakar I 2018)

This TB Strategy Toolkit aims to serve as a practical instrument for developing country-specific TB Strategies or TB Action Plans to facilitate TB strategy implementation drawing on principles from previous work, including the WHO toolkit (WHO 2015) (RIVM/KNCV 2016).



This TB Strategy Toolkit focuses on helping to prioritise key areas of TB control, such as reaching out to under-served groups, targeted screening for active TB and latent TB infection in high risk groups, implementing electronic TB case registries and tackling MDR-TB care and control in Eastern Europe. **This TB Strategy Toolkit should:**

- provide a point-of-reference for EU and EEA-specific priority areas of intervention for TB control and prevention to facilitate implementation
- support national level planning and resource allocation based on peer-reviewed evidence and primary data
- provide support for mobilising high-level political commitment and for engaging with stakeholder groups

As part of their national TB strategy, each member state will need a consolidated approach to stimulate actors and key implementers who are pivotal to implement locally-relevant solutions in areas where there is high unmet need and where greatest reductions in incidence can be achieved. The development of national strategic plans are dependent on well-budgeted plans to strengthen cases for national and international financing. Involving all stakeholders with budgetary responsibilities for TB prevention and care, including social protection, national surveillance, and research will support the mobilisation of resources, upon which to implement the goals and vision of a national strategic plan (WHO 2015, WHO 2015). WHO provides financial tools for funding gaps for intervention areas (WHO 2015) and for other special assessments of costs and benefits of launching new elements under the End TB Strategy to support NTPs. This TB strategy toolkit contains an evidence portfolio, which summarises published evidence within the context of EU and EEA settings, and constitutes:

1. An up-to-date national picture of national TB control plans and strategies, including prioritisation of action areas and barriers to the implementation of interventions for TB control and prevention (survey/situational analysis);
2. Findings from a systematic review of the evidence base for interventions to control and prevent TB;
3. Findings from a systematic review and evidence synthesis of barriers and facilitators to implementation of policies, strategies and guidelines for TB control and prevention;
4. A summary of proceedings of an Expert Stakeholder meeting, convened on 24th October 2018 in Leiden, The Netherlands with national TB programme representatives, ECDC, WHO and civil society representatives (Appendix). Experts discussed four priority intervention areas identified through consensus as difficult to implement and proposed activities or solutions to mitigate barriers in these areas in the 'core components of a national TB strategy' on page 43.

2 Key elements for TB care and treatment

Effective TB control depends on timely detection of infectious TB and prompt completion of TB treatment. Societal, socioeconomic and wider healthcare improvements and investments in a robust evidence base and research efforts are needed to strengthen cascades to contribute to reductions on TB incidence.

The provision of high-quality, prompt and evidence-based clinical care, to reduce morbidity and mortality must remain at the core of a national TB Action Plan or TB Strategy. Universal access to quality-assured diagnostic testing and treatment services coupled with compliance with standards and guidelines is vital to tackle TB across EU and EEA settings. There are groups in society which may be at higher risk of exposure and/or may face challenges in accessing and engaging with services. Among these groups the risks of poor clinical and treatment outcomes are greater. For these reasons, efforts to effectively engage health workers, social care and outreach services and care providers in the detection, diagnosis, referral and care of suspected TB cases and patients is important. Poor treatment adherence is a key reason for poor clinical and public health outcomes and significantly contributes to drug resistance, increased duration of infectivity and onward transmission of infection. This emphasises the importance of treatment completion, evaluating and reporting treatment outcomes. Supportive care delivery services that help to remove stigmatisation by tackling cultural, social and language differences and provide treatment and care irrespective of legal and residential status and should be in place. The availability of outreach services that support treatment adherence and support patients in navigating social care, accommodation and psychological services over the course of treatment should be available.

2.1 Know your epidemic through ongoing surveillance and monitoring transmission

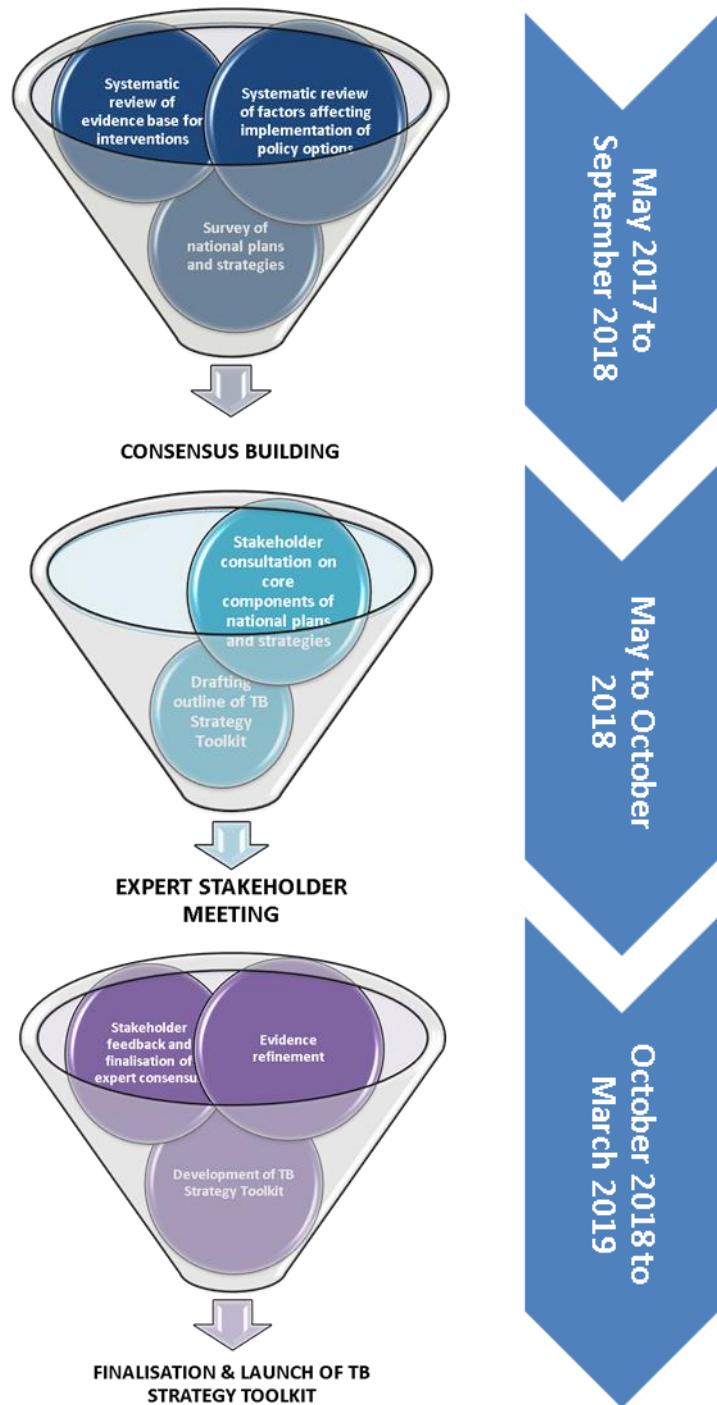
Decisions on proven and evidence-based interventions should be implemented through data-driven approaches, specifically through comprehensive health system assessment and through national and sub-national epidemiological data analysis using TB registries for surveillance and scientific research purposes. An example of the use of 'know your epidemic' is included in the Dutch National TB Control Plan 2016-2020 (RIVM/KNCV 2016) . Such assessments identify and prioritise populations at risk and the distribution of TB according to geographical boundaries (urban and rural) and by populations (under-served, including migrants).

Utilising routine surveillance activities to understand the cascade of care and where socioeconomic or sociocultural barriers to access care and treatment may arise can determine prioritisation and targeting of interventions, shown through evidence to be effective in TB control, thus support the mobilisation of investment and resources.

3 Development process of TB Strategy Toolkit for the European Union and European Economic Area member states

The main steps undertaken to develop the TB Strategy Toolkit are outlined below in chronological order

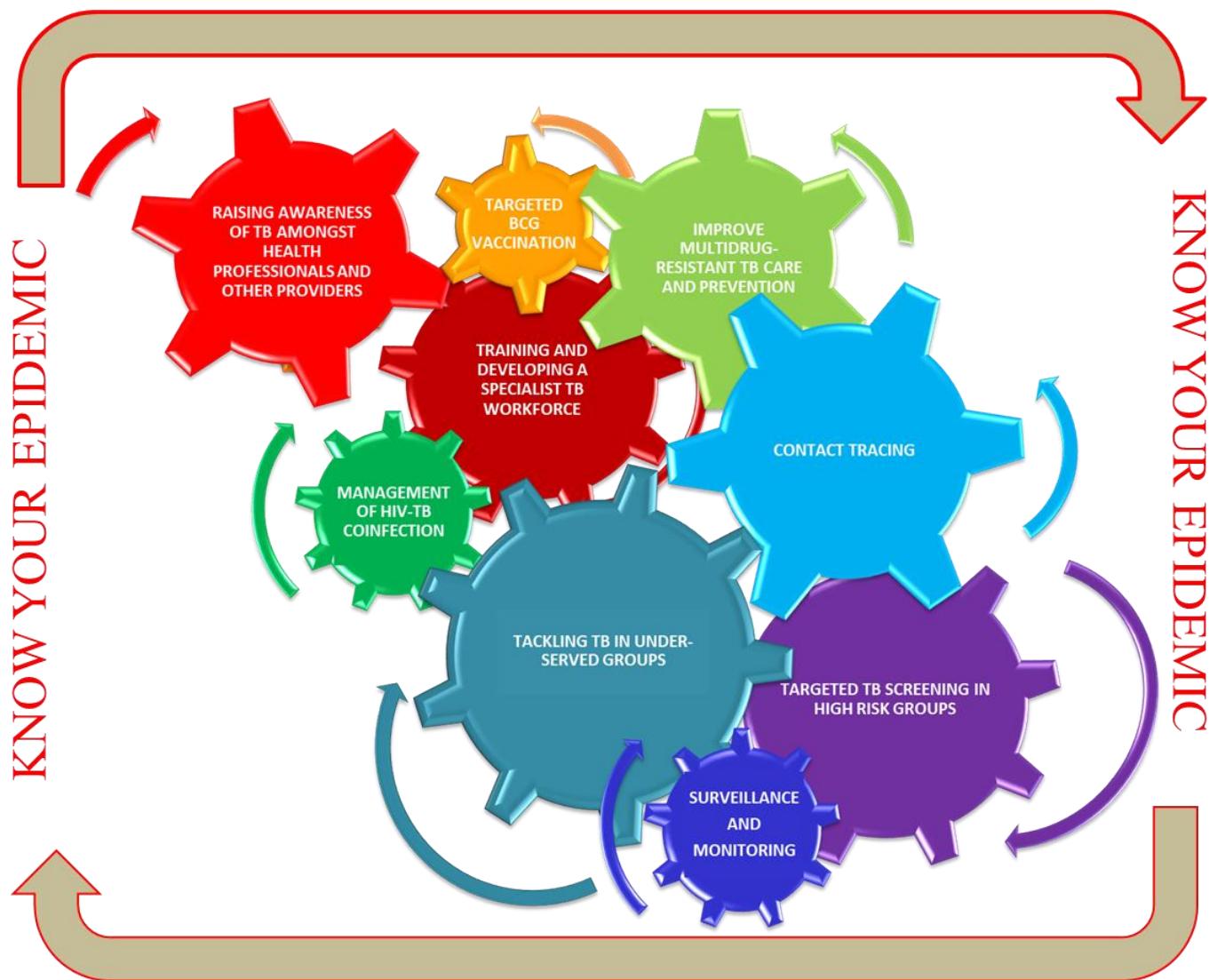
Figure 4: TB Strategy Toolkit development stages



4 Core components of a national TB strategy

To deliver a strategy and make significant advances in TB control, core components of a national TB plan or TB strategy were identified through findings from a pan-European survey. Each of the core components in Figure 5 can be broken down further into sub-components to inform clinical and support services and local and national providers and commissioning groups.

Figure 5: Core components of national TB strategy [size of cogs are unrelated to scale of problem]



Effectiveness, current practice and factors affecting implementation

Decisions on which of the core components to prioritise and implement for each country's national TB programme will be reached at a national level and should be led by national TB programmes representatives. Choices of interventions

will need to be pragmatic, supported by evidence from individual studies and based on local and national epidemiology, experience and expert opinion.

To support this process, below outlines the evidence, consensus and relative impact that can be expected from each component. For each core component the following is provided:

- A background and justification
- Evidence on effectiveness of interventions in this area
- Descriptions of current practice related to each intervention in EU and EEA member states
- Evidence on factors that may facilitate or impede implementation of interventions to deliver the core component.
- Expert opinion on core components, where there are barriers to implementation and any major activities or proposed solutions to address these barriers

Activities to assist implementation of core components and their respective interventions are summarised in Table 2 on page 40

The key provided below relates to findings from the evidence portfolio. Further findings from the evidence portfolio can be found in the Appendix:

Evidence from a systematic review of systematic reviews on the effectiveness of interventions for TB control and prevention

The aim of the review was to identify systematic reviews of interventions for TB control and case prevention relevant to settings of low TB incidence, to assess the quality of the reviews in relation to direct and indirect effects of the interventions on TB incidence, and to summarize the overall strength of evidence for each reviewed intervention

Evidence from a survey of national TB programmes in EU/EEA countries

The aim of the survey was to obtain an up-to-date picture of national TB control plans and strategies, including prioritisation of action areas and barriers to the implementation of interventions for TB control and prevention

Evidence from a systematic review of barriers and facilitators of implementation of interventions, guidelines and strategies for TB control and prevention

The aim was to investigate the barriers and enablers that are experienced within EU/EEA countries as TB control strategies are implemented. This review focuses on the skills, attitudes and motivations of providers of care their relationship with health system constraints and social and political factors.

Expert opinion from EU/EEA national TB programme representatives during Expert Stakeholder meeting covering 3 areas, which were considered difficult to implement:

- reaching under-served groups;
- raising awareness of TB in the community and primary care;
- TB screening in high risk groups

Experts were invited to participate in a modified Delphi process over three rounds to consider core components of national TB action plan or TB strategy for TB control and prevention. Each area is looked at in more detail on in sections 4.3, 4.3.1 and 4.4. The methods for securing consensus on prioritisation of core component can be found on page 40.

4.1 Surveillance and monitoring

The ability to track effectiveness of TB control and service performance is dependent on effective information systems for monitoring and evaluation of routine reporting. National surveillance is an important element for monitoring TB epidemiology, the evolution of trends in incidence and drug resistance, identifying outbreaks and for monitoring the effectiveness of interventions aimed to control and, ultimately eliminate TB. The inclusion of data held by laboratories is crucial for data completeness and case ascertainment.

TB surveillance systems are also important tools that support molecular cluster investigations, surveillance of drug resistance and treatment outcome monitoring. These activities help healthcare professionals, public health practitioners, service providers and commissioning groups to guide decision making and prioritisation, for example amongst high risk groups for disease and transmission.

Surveillance and monitoring is the cornerstone of TB control and decision-making to extend activities using national TB surveillance and vital registration should consider the following pieces of evidence on effectiveness of interventions:

- In a systematic review by Curtis on the impact of x-ray screening programmes for active TB in homeless populations. Findings showed active x-ray surveillance programmes in homeless communities appear to be cost-effective in reducing TB prevalence in within the homeless population, mainly in related strains and may have some benefits over passive case findings. This paper highlighted a need for further research to assess the impact of these programmes and outlines the benefits and limitations of existing programmes and included recommendations to improve maximum coverage, uptake and cost-benefit (Curtis 2016)
- Across EU and EEA settings there is a variation in policies for TB and LTBI screening in migrants and where national policies do exist they may not be locally implemented if TB control implementation is the responsibility of local health authorities. There is a need for the development and provision of guidance and knowledge exchange between European countries to ensure that policies and implementation process are harmonised to facilitate screening and linkage to care.

The production of robust scientific evidence on the effectiveness of LTBI screening and management in EU/EEA settings can be achieved through the creation and development of sufficiently large multi-centre and multi-country surveillance systems.

Evidence on current surveillance and monitoring practice in EU/EEA settings

- All EU and EEA countries had a national TB case registry, with three quarters of national programme representatives reporting that they had a strategy for monitoring and evaluation of TB control and prevention. Half of these countries reported that their strategies for monitoring and evaluation were documented in their national TB control plans or strategies. In relation to staffing provision, a median of two (range 0.5 to 8.5) full-time staff were assigned to TB surveillance in national offices.

Surveillance and monitoring is a vital component of any TB Action Plan or TB Strategy. Efforts to maintain and enhance the quality of surveillance systems to support continuous monitoring of TB control activities are key to the elimination agenda. Barriers to good surveillance are outlined below and need consideration:

- In a study on TB, MDR- and XDR-TB management by Migliori and colleagues, it was reported that microbiological evaluation was missing or unsatisfactory in 15 (7.5%) of 200 clinical files reviewed. In addition, there was a lack of information available in the treating clinical reference centres on the treatment outcome of discharged patients (Migliori, Sotgiu et al. 2012).
- In a survey on surveillance systems and policy in 11 EU and European Free Trade Association (EFTA) countries with existing TB/LTBI screening programmes, few countries had health information systems in place from which TB and LTBI screening data (such as age, sex and country of origin), screening results and final diagnosis can be captured and analysed from which to systematically evaluate yield of screening (Kunst 2017).
- Turusbekova and colleagues noted that the system for reporting TB among healthcare workers in Romania was under-developed as TB was not reported as a nosocomial infection or occupational disease (Turusbekova, Popa et al. 2016).
- Care providers reported on limited electronic access to some treatment-related information. This included test results that only arrive on paper, web-based drug information systems with restricted access, medical records from transferred patients, and protocols and treatment plans, which were only available in print (Wannheden, Westling et al. 2013).
- In a study on management of paediatric MDR-TB, a prospective data collection tool to collate information was absent. As such there was an inability to capture exposure, infection or disease and hampered the establishment of an evidence base for management guidelines (Williams, Ramroop et al. 2013).

4.2 Contact tracing

Contact tracing is a well-established pillar of TB control and prevention and includes identification, testing and treatment of active and latent TB cases in close contacts of index cases, aiming to improve early diagnosis, preventing further ongoing transmission and LTBI reactivation. This is particularly important amongst immunocompromised groups, for example in people co-infected with HIV and in children who may be more at risk of severe disease. Further guidance on conducting contact tracing is provided by Erkens and colleagues (Erkens CG 2010).

There can be a number of challenges in identifying contacts, particularly amongst under-served, including homeless persons, those with drug and alcohol abuse, prisoners or some groups of vulnerable migrants. Barriers can arise from chaotic lifestyles, distrust or scepticism between these groups and case managers performing contact tracing. Effective contact tracing can also be hampered by TB-related stigma and the reluctance or hesitancy to disclose contact information details, or TB case managers are unable to locate contacts and motivate them to undertake diagnostic tests.

Working with other health, social care and community partners can maximise the opportunities of reaching potential contacts.

Despite the paucity of evidence on cost-effectiveness of contact tracing strategies, appropriate resources should be allocated establishing the infectiousness of the source case, likelihood of *M.tuberculosis* infection among contacts and risk of development of TB disease, prioritisation of identified contacts and appropriate timing and use of TST and IGRA

testing to diagnose infection and rule out TB amongst identified contacts. Evaluation and monitoring of contact investigations will inform a better understanding on effective and cost-effective use of resources.

Contact tracing is an important priority for TB control and decision-making to support its inclusion in national TB plans and strategies should consider the following pieces of evidence on effectiveness of interventions:

- A systematic review and meta-analysis by Fox et al; 2013 found the prevalence of active TB among close contacts was 3.1% (95% CI 2.2 – 4.4%), for microbiologically-proven TB it was 1.2% (95% CI 0.9-1.8%), and for LTBI it was 52% (95% CI 47.1-55.8%). The prevalence of TB amongst household contacts was 3.1% (95% CI 2.1 – 4.5%) and amongst contacts of multidrug-resistant or extensively drug-resistant TB it was 3.4% (95% CI 0.8 – 12.6%). Specifically for high-income settings, this review showed that the prevalence of active TB among contacts was 1.4% (95% CI 1.1 – 1.8%) and the prevalence of LTBI was 28.1% (95% CI 24.2 – 32.4%). Children aged less than 5 years old and people living with HIV were at high risk of developing TB (Fox, Barry et al. 2013, Zenner, Southern et al. 2013)
- A narrative review on active case finding and screening in high-risk groups in low-incidence settings found successful activities demonstrating impact on transmission and early case detection, including effective and cost-effective active case-finding activities among groups with social risk factors with evidence of interruption of transmission (Zenner, Southern et al. 2013, Shah, Yuen et al. 2014)
- In a systematic review and meta-analysis of contact investigation of among household members of drug-resistant source cases a pooled yield of 7.8% (95% CI: 5.6-10%) for active TB and 47% (95% CI: 30-61%) for latent TB, despite highly significant statistical heterogeneity ($p<0.0001$). These findings suggest that household contact investigation in drug-resistant TB cases is an effective intervention for detection of drug-resistant TB and to prevent ongoing transmission (Fair, Miller et al. 2012, Shah, Yuen et al. 2014, Loutet, Burman et al. 2018)
- Fair and colleagues similarly demonstrated that household contact investigation improved early case detection and provided additional information of transmission from HIV-infected index cases and patients with MDR-TB. The yield for bacteriologically confirmed and clinically diagnosed TB was 4.5% of contacts investigated, in those with bacteriological confirmation the yield was 2.2%, LTBI was detected in 51% of contacts investigated. The yield was 9.4% amongst contacts investigated for HIV-positive index cases and 3.4% in contacts for MDR-TB index cases (Fair, Miller et al. 2012)

Evidence on current contact tracing practices in EU/EEA settings

- The majority of countries, 84% had a strategy to implement and ensure comprehensive contact tracing, of which half were documented in a national TB control plan or TB strategy. Recommended approaches to contact tracing include household, 96%; workplace 92%; healthcare facility, 92% and in the community 81%

Contact tracing is a vital component of any TB Action Plan or TB Strategy. Barriers to contact tracing are outlined below in the following pieces of evidence and need consideration:

- Abubakar and colleagues conducted an audit on the clinical management of TB in the UK and found ambiguity in the definition of and distinction between close and casual contacts when investigating complex networks and outbreaks (Abubakar, Chalkley et al. 2006).
- A study by Mulder and colleagues reported differences in the implementation of contact investigations and that index cases were at times unable to recall or unwilling to share contact information with case managers (Mulder, Harting et al. 2012)

4.3 Tackling TB in under-served groups

TB disproportionately affects under-served groups whose social circumstances, language, culture or lifestyle (or those of their parents or carers) make it difficult to recognise the clinical onset of TB, access diagnostic and treatment services, self-administer treatment or attend regular appointments for clinical follow-up. Problems accessing and engaging with services increases the risk of poor clinical and treatment outcomes. Falzon and colleagues highlight the need for an authoritative policy and legal framework, which adapts international standards for TB care into local policies as an important step for upholding the rights of individuals for TB treatment regardless of origin (Falzon D 2012). As such, basic TB care should be provided free of charge and kept external to any scheme which requires patients to bear costs irrespective of their legal status. The Working Group on Trans-border Migration and TB of the International Union Against Tuberculosis and Lung Disease (The UNION) cited examples from Norway and The Netherlands where regulations had been introduced to ensure that TB patients, who may be undocumented migrants do not have their treatment disrupted by deportation. Equitable access to full care and treatment should not be constrained by provenance and legal status of patients.

For these reasons, efforts to effectively engage health workers, social care and outreach services and care providers in the detection, diagnosis, referral and care of presumptive TB patients is vital. Securing appropriate cross-border care coordination and actions to support undocumented migrants who may face deportation is also important for TB control.

Under-served groups are often defined as having multiple intersecting and complex needs and experience health inequalities. Their health and social care needs often involve a combination of physical ill health and mental health problems, early life poverty and adverse childhood experiences.

The scope of under-served groups includes:

- Some migrant groups (including those with unclear legal status, asylum seekers, undocumented migrants and those in immigration detention centres);
- Individuals with current or a history of homelessness
- Individuals with current or a history of drug misuse
- Individuals with current or a history of imprisonment or contact with the criminal justice system
- Individuals with current or a history of mental health needs

Tackling TB in under-served groups is an important priority for TB control and decision-making to support its inclusion in national TB plans and strategies should consider the following pieces of evidence on effectiveness of interventions:

- A wide range of interventions for the diagnosis and treatment of TB in under-served groups, which updated and extended two earlier reviews by the UKs National Institute of Health and Clinical Excellence. This review found screening via mobile chest radiography improved screening coverage and case identification, reduced diagnostic delay and was shown to be a cost-effective intervention for homeless people, prisoners and drug users (Heuvelings, de Vries et al. 2017).

Evidence on current practice on reaching under-served groups in EU/EEA settings

- For 80% of national TB programme representatives reaching under-served groups was most frequently rated as the highest priority of 18 pre-specified priority action areas. Findings show 47% of national TB programme representatives identified undocumented migrants as having the highest unmet need for TB detection and 43% for the highest unmet need for TB treatment
- Findings also indicated that other under-served groups had high unmet need for TB detection: documented migrants (47%); refugees (50%); asylum seekers (50%); current prisoners (60%); former prisoners (48%); minority ethnic groups (50%)
- In addition, respondents from national TB programmes indicated that many of these under-served groups had high unmet need for TB treatment: documented migrants (57%); refugees (57%); asylum seekers (47%); homeless people (39%); people with alcohol problems (52%); people with drug problems (61%); people with mental health problems (58%); current prisoners (67%); former prisoners (71%); minority ethnic groups (61%)

Tackling TB in under-served groups is a vital component of any TB Action Plan or TB Strategy. Barriers to tackle TB in under-served groups are outlined below in the following pieces of evidence and need consideration:

- Belling and colleagues reported a variation in primary care referral hindered access to care amongst under-served groups in the UK. This paper discussed issues around access to TB hospital care and how it was restricted through GP referral only, which had the potential to leave under-served groups without easy access to appropriate care (Belling, McLaren et al. 2012)
- Findings from our survey with national TB programme representatives showed 74% of respondents indicated that a lack of knowledge about TB amongst under-served groups impeded TB control. Seventy per cent indicated low motivation to seek treatment
- A variation on views of perceived susceptibility to and severity of TB included several misconceptions, stigma and difficulties in healthcare access were identified by barriers to diagnosis and treatment uptake in migrants (de Vries SG 2017)

A facilitator to tackling TB in under-served groups was also identified in a systematic review by de Vries and colleagues:

- Support from nurses, family and friends facilitated treatment adherence (de Vries SG 2017)

EU/EEA expert opinion on tackling TB in under-served groups identified the following barriers to implementation amongst recipients of care:

- Distrust in healthcare system
- Stigmatisation
- Negative societal attitudes
- Cultural and language barriers (for example amongst undocumented migrants)
- Poor access and engagement with health services
- Lack of dedicated legal services
- Limited outreach activities
- Poor treatment adherence attributable to chaotic lifestyles

EU/EEA expert opinion on tackling TB in under-served groups identified the following barriers to implementation amongst healthcare professionals:

- Lack of dedicated time and human resources
- Reluctance to treat due to discriminatory attitudes to under-served groups

EU/EEA experts proposed the following activities and solutions to mitigate barriers to implementation in relation to tackling TB in under-served groups:

- Development or refinement of a dedicated community-based service, which is tailored to engender trust and build access, provide full health screening and seeks support treatment follow-up. Extensions of this service may also include mobile clinics, which can bring services to under-served groups in urban areas.
- Development of a network of stakeholders including intermediaries and statutory and voluntary health and social care services, such as NGOs, shelters and legal services

4.3.1 TB control in prisons

Prisons or congregate settings are at high risk for TB transmission due to overcrowding, poor ventilation, poor nutrition and sometimes barriers to healthcare access and insufficient infection control mechanisms. Those who are imprisoned or who come into contact with the criminal justice system tend to come from socio-economically challenged backgrounds where TB infection rates are higher and where TB transmits more frequently. Individuals with a history of homelessness and/or drug misuse are also over-represented in prison settings.

National strategic plans should include appropriate infection control policies that recommend triage (promptly identify inmates with TB symptoms) and respiratory separation or isolation to be implemented. Triage and separation are necessary infection control measures to minimise TB transmission to other inmates, who may be immunocompromised. Prompt initiation of effective TB treatment to reduce transmission to other inmates and other personnel in prison or congregate settings in accordance with clinical guidance is fundamental.

WHO guidelines on tuberculosis infection prevention and control for settings where transmission of *M. tuberculosis* is likely to occur have recently been published (WHO 2019).

TB control in prisons is an important priority for TB control and decision-making to support its inclusion in national TB plans and strategies should consider the following pieces of evidence on effectiveness of interventions:

- Prisoners are at increased risk of LTBI and increased risk of progression to active TB (WHO 2015):
 - The pooled estimates of risk ratios (range) for LTBI in prisoners compared to the general population was 2.33 (2.40 – 3.57) and 2.77 (2.58 – 2.92) compared to the general population as measured by TST in low and intermediate TB burden settings, respectively.
 - The relative risk (95% CI) of active TB for LTBI-positive prisoners compared to the general population (LTBI status general population unknown) was 15.3 (7.6 – 30.5).

Evidence on current practice to control TB in prisons in EU/EEA settings

A strategy for TB control in prisons was in place in 77.4% of countries, of which nine were documented in the national TB control plan/strategy, yet only half rated TB control in prisons as a priority area

TB control in prisons or correctional facilities is a vital component of any TB Action Plan or TB Strategy. Barriers to TB control in prisons or correctional facilities are outlined below in the following pieces of evidence and need consideration:

- A lack of specialist staff: In a prospective study by Cochet and colleagues, of 22,450 inmate entries between 1st July 2005 and 30th July 2006, screening rates varied considerable between 58% and 99%. A lack of human resources in detention centres were attributed to low screening rates and long delays (Cochet and Isnard 2008).
- Funding: 71% of national TB programme representatives did not consider funding of medical facilities in prisons as a factor that impeded TB control and prevention. Comparatively 19% found inadequate funding of medical facilities in prisons served as a barrier to TB control and prevention in their settings, whereas 10% were uncertain.

- In a review by Vinkeles and colleagues reported a limited accuracy of diagnostic algorithms and inadequate laboratory facilities inhibited TB control programmes in prisons (Vinkeles Melchers, van Elsland et al. 2013).

4.4 Targeted TB screening in clinical risk groups

In line with the WHO End TB Strategy, targeted screening in selected risk groups, people living with HIV, adult and child contacts of pulmonary TB cases, patients starting anti-tumour necrosis factor (TNF) treatment, patients receiving dialysis, patients preparing for organ and haematologic transplantation and patients with. Targeted screening in these risk groups is an important intervention for any TB Action Plan or TB Strategy for low-incidence settings. It supports early detection of TB and ensures treatment is promptly started thus minimising the risk of poorer disease outcomes and adverse social and economic consequences. Its implementation should be based on an assessment of the local TB epidemiology and capacity of the health care system.

It is estimated that 1.7 billion have LTBI, which represents a large human reservoir. The WHO action framework for low-incidence countries has emphasised that tackling LTBI in low-incidence settings is a priority (WHO 2014), indicating that one of the eight priority areas for low incidence countries striving for TB elimination is to ‘undertake screening for active TB and latent TB infection in TB contacts and selected high-risk groups, and provide appropriate treatment’

A comprehensive programmatic approach to LTBI screening should include the availability and accessibility to diagnostic tests, the intention to provide LTBI treatment and promote the uptake and completion of LTBI screening procedures. Both TST or IGRA or a combination of both tests can be used to diagnose LTBI. In addition, interventions which provide information and education to increase awareness and knowledge of LTBI should also be considered.

Targeted TB screening in clinical risk groups is an important priority for TB control in EU/EEA settings. Efforts to develop or refine interventions in this area should consider the following pieces of evidence:

- We found weak evidence for population-based programmes of LTBI screening (Dobler, Fox et al. 2018) (Loutet, Burman et al. 2018) (Zenner, Hafezi et al. 2017). WHO have issued conditional recommendations for targeted systematic screening of migrants from high-incidence countries and underscores the importance of more studies evaluating their effectiveness (Kunst 2017).
- We found evidence on screening for active TB in migrants, including two on pre-entry screening and follow-up (Kahwati, Feltner et al. 2016) (Moro, Resi et al. 2005, Metcalf, Davies et al. 2007, Aldridge, Yates et al. 2014) (van de Berg, Erkens et al. 2017), one on point-of-entry screening (Jeon, Harries et al. 2010, Gerrish, Naisby et al. 2013) and four on post-entry screening of migrants from high-incidence countries (based mainly on case yield and risk of TB post-entry). However, none of these reviews have compared the effectiveness of different approaches or provided conclusive evidence of cost-effectiveness, and all of the reviews have emphasised the need for comparative studies and improved longitudinal data collection (Kunst 2017).
- A wide range of interventions for the diagnosis and treatment of TB in under-served groups, which updated and extended two earlier reviews by the National Institute of Health and Clinical Excellence. This review found screening via mobile chest radiography improved screening coverage and case identification, reduced diagnostic delay and was shown to be a cost-effective intervention for homeless people, prisoners and drug users (Heuvelings, de Vries et al. 2017).
- Heuvelings and colleagues also included two studies, which reported that the addition of sputum culture to the US pre-migration TB screening algorithm decreased the number of active cases diagnosed within 6-12 months of arrival (Heuvelings, de Vries et al. 2017) .

Evidence on current practice on TB screening in clinical risk groups in EU/EEA settings

- Seventy-seven percent of national TB programmes conduct targeted screening of active TB among asylum seekers and 74% among prisoners. Point-of-entry and post-entry screening for active TB among documented migrants was conducted by 32% and 42% of countries, respectively.
- Two member states conducted screening for active TB in social care institutions and for people entering shared community accommodation. Further details can be found in Table S2 in the published survey findings of national TB plans and strategies (Appendix).

TB screening in clinical risk groups is a vital component of any TB Action Plan or TB Strategy. Barriers to TB screening in high risk groups are outlined below in the following pieces of evidence and need consideration:

- Atchison and colleagues' study on GPs' perspectives on LTBI treatment in primary care, 82% indicated there was insufficient experience of all aspects of LTBI screening and treatment amongst GPs, with 79% suggesting that specific training and tools would be an important enabler (Atchison, Zenner et al. 2015) (Kunst 2017)
- Suggestions to meet training needs included interactive workshops or structured online learning tools. A handbook, case-based discussions and short placement within hospital-based TB specialist team were also suggested (Atchison, Zenner et al. 2015) (Kunst 2017)

4.5 Management of HIV-TB coinfection

It is well-established that the interaction between TB and HIV exacerbates both conditions in co-infected individuals. According to latest WHO TB report published in 2018, the number of TB deaths amongst HIV-positive individuals has fallen by 44% since 2000 and by 20% since 2015 (WHO 2018). The proportion of TB patients being tested for HIV in the WHO European Region has increased from 3% in 2008 to 13% in 2017. Yet the management of HIV-TB coinfection remains challenging to the development of adverse side effects of each treatment, drug interactions and pill burden thus leads to poor treatment adherence and the development of drug resistance.

The End TB Strategy advocates the need for increased access to high-quality and sustainable integrated and decentralised TB and HIV services and an assessment for barriers and enablers for collaborative HIV-TB activities (WHO 2015). Integrated HIV-TB service delivery has been shown to increase ART uptake and timeliness of ART initiation and reduce mortality from HIV-associated TB by up to 40%.

Management of HIV-TB coinfection is an important priority for TB control and decision-making to support its inclusion in national TB plans and strategies should consider the following pieces of evidence on effectiveness of interventions:

- Akolo and colleagues reported on the effectiveness of TB preventative therapy in HIV-infected adults in reducing the risk of active TB and death when compared to placebo. Based on evidence from twelve randomised-controlled trials, any TB drug compared to placebo was associated with a lower incidence of active TB (RR 0.68; 95% CI: 0.54 to 0.85) and was particularly marked those with a positive tuberculin skin test (RR 0.38; 95% CI: 0.25 to 0.57) (Akolo, Adetifa et al. 2010).
- Gray and colleagues reported a marked reduction in TB incidence when aiming to determine the impact of TB preventative therapy on TB-related incidence and death in HIV-infected children, yet was based on findings from a single randomised-controlled trial (Gray, Zar et al. 2009).
- Conversely in a review of anti-retroviral treatment for prevention of TB in adults based on eleven studies found that antiretroviral treatment was strongly associated with a reduction in TB incidence (Suthar, Lawn et al. 2012).

Evidence on current practice of management of HIV-TB co-infection in EU and EEA settings

- Sixty-one percent of EU and EEA countries reported using an integrated approach to TB and HIV control and 58% documented this in their national TB control plan or strategy. Routine testing for HIV in TB patients was conducted in 77% (24/31) of EU and EEA countries and 74% reported screening people living with HIV for TB. Sixty-one percent (19/31) of countries reported to screening for both. The majority of countries, 81% monitored HIV-TB coinfection at a national level in their respective countries.

Management of HIV-TB coinfection is a vital component of any TB Action Plan or TB Strategy. Barriers to management of HIV-TB coinfection are outlined below in the following pieces of evidence and need consideration:

- Migliori and colleagues reported on suboptimal management of HIV-TB co-infected cases, in which 35% (8/23) were inadequately prescribed treatment, which had contravened existing recommendations (Migliori, Sotgiu et al. 2012).
- There is evidence to demonstrate that there is reluctance of HIV specialist in low-incidence countries to screen for LTBI (Evenblij K 2016, White HA 2017)

4.6 Improve multidrug-resistant TB care and prevention

Multidrug and rifampicin-resistant TB occurs either through inadequate treatment of TB or through transmission of already resistant *M. tuberculosis* strains. Compared to drug-susceptible TB, the duration of treatment for drug-resistant TB is considerably longer and has a significantly higher risk of adverse reactions and poorer treatment outcomes, particularly mortality.

The importance of robust action to galvanise efforts across Europe has been set out in WHO European Region's "Roadmap to prevent and combat drug-resistant tuberculosis." As an outline of a consolidated action plan to achieve a reduction in the burden of drug-resistant TB, the seven areas of intervention are:

- Prevent the development of cases of M/XDR-TB
- Scale-up access to testing for resistance to first- and second-line anti-TB drugs and to HIV testing and counselling among TB patients
- Scale up access to effective treatment for all forms of drug-resistant TB
- Scale up TB infection control
- Strengthen surveillance, including recording and reporting of drug-resistant TB and monitor treatment outcomes
- Expand countries' capacity to scale up management of drug-resistant TB, including advocacy, partnership and policy guidance
- Address the needs of special populations

The treatment challenges associated with MDR/RR-resistant TB threaten to hamper progress towards the End TB Strategy.

This is a rapidly evolving area due to ongoing trials. At the time of writing this TB Strategy Toolkit document. It is recommended TB control programmes refer to the latest WHO consolidated guidelines on drug-resistant TB treatment (WHO 2019).

Efforts to improve MDR-TB care and prevention is an important priority for TB control and decision-making to support its inclusion in national TB plans and strategies should consider the following pieces of evidence on effectiveness of interventions:

- Bastos and colleagues found overall treatment success rates of 26% and 60% for XDR- and MDR-TB patients, respectively (Bastos, Lan et al. 2017, Loutet, Burman et al. 2018).
- Chang and colleagues made specific recommendations for drug regimens (Chang, Yew et al. 2013), specifically for treatment of XDR-TB or fluoroquinolone-resistant MDR-TB using linezolid and six- and four-drug combinations during intensive and continuation phases of XDR-TB treatment (Falzon, Gandhi et al. 2013).
- Two reviews by Fraser and colleagues (Fraser, Paul et al. 2006) and van der Werf and colleagues (van der Werf, Langendam et al. 2012) found no evidence of effectiveness for preventative (LTBI) treatment for contacts of MDR-TB cases.

All of the above evidence stated the need for more RCTs of MDR-TB and XDR-TB treatments were urgently needed.

Effort to improve MDR-TB care and prevention is vital to any TB Action Plan or TB Strategy. Barriers to reducing MDR-TB are outlined below in the following pieces of evidence and need consideration:

Decisions to implement interventions to reduce MDR-TB should consider these identified challenges:

- **Clinical mismanagement:** Migliori and colleagues reported investigations of a previous TB diagnosis were performed for 93% (186/200) of cases and an investigation of previous treatment for 99% (198/200) and previous drug susceptibility testing for 94% (188/200) of cases. In addition, microbiological evaluation was missing or deemed unsatisfactory in 7.5% (15/200) of records reviewed. This paper also reported that fewer than four active TB drugs were prescribed for 10% of cases and an incorrect drug choice in 6.5% of cases. For 56% (109/196) of cases, a definitive treatment outcome was recorded. There was insufficient information available from clinical reference centres on the final outcome of 32% (63/196) of cases, which were commonly defined as “transferred out.” (Migliori, Sotgiu et al. 2012).
- **Development of severe adverse events:** In a paper by de Vries and colleagues clinicians were unable to treat patients with second-line TB drugs in accordance to clinical guidelines due to the development of severe adverse events and tended to make adjustments to treatment regimens based on professional insights and peer-reviewed publications (de Vries, Tsolova et al. 2017).
- **Supporting treatment adherence in migrants:** Difficulties in supporting treatment adherence in migrants with MDR-TB and follow-up in another country were also reported in de Vries et al. For example, foreign-born students or workers from EU or non-EU countries diagnosed with MDR-TB returned to their country of origin during lengthy treatments. Supporting the continuation of treatment in foreign-born patients with MDR-TB was found to pose difficulties in Austria, Spain and in the UK because they migrated or were forced to leave the country where treatment was initiated (de Vries, Tsolova et al. 2017).

Evidence also identified how well-established referral routes across healthcare sectors to improve MDR-TB care and prevention in prisons and how involving NGOs in the community were found to enable care coordination and delivery:

- de Vries and colleagues reported that in the prison sector, TB screening and referral arrangements for MDR-TB patients were in place in Austria, Spain and in the UK. Bulgaria was reported to have a dedicated TB and MDR-TB prison clinic, with communication lines in place with the MDR-TB hospital and pharmacy and the ministry of health authorities (de Vries, Tsolova et al. 2017).
- Several non-governmental organisations had developed community-based initiatives to raise community awareness, case-finding and treatment support, particularly among under-served individuals. NGOs in Spain contracted by the government were also involved in providing support for care, such as housing for MDR-TB patients, support in finding work, providing DOT services and incentives and support for migrants (de Vries, Tsolova et al. 2017).

4.7 Raising awareness of TB and training and developing a specialist TB workforce, wider healthcare professionals and other providers

Improving access to TB care and treatment is an important tenet of the End TB Strategy.

Tailored training resources, which include TB as part of medical education curricula, which highlight the epidemiology of TB, its typical and atypical symptoms and clinical manifestations will help to improve early diagnosis and treatment. These should be accessible for health professionals at different tiers of the healthcare system including general practitioners (GPs) in primary care, skilled nurses, doctors, healthcare workers, community leaders, trained lay workers from community outreach services. Collaborative links between these health professional groups could support education and training and strengthen referral routes. Publications in country-level medical journals and refresher training for specialists who manage TB will also serve to improve awareness among professionals and address knowledge gaps.

An effective TB workforce will include a range of specialists from primary and secondary care from various disciplines who have a responsibility for the management and delivery of a range of services for case detection and management of TB. The maintenance of a critical mass of healthcare professionals across healthcare tiers is dependent on investment in high-quality graduate and post-graduate education for staff directly and indirectly involved in TB control and elimination. Approaches would benefit from close collaboration with universities, training institutes, professional medical and nursing and membership bodies and other relevant multi-sector agencies, such as non-governmental bodies that are aware of national policy frameworks.

A review of evidence to assess the effectiveness of interventions for raising awareness of TB and training and developing a specialist TB workforce was conducted but did not yield any findings in this area

Evidence on current practice of raising awareness of TB amongst healthcare professionals and other providers in EU/EEA settings

- Sixty-eight percent of EU and EEA countries had programmes for raising awareness of TB in community and primary care levels, of which 2% were documented in their national TB control plans or TB strategies.
- Representatives for national programmes reported links with a range of community or primary care groups, which included: primary care doctors or general practitioners, 95%; primary care health workers, 76%; social workers 67%; and the general public 57%. Other groups involved in raising awareness of TB included services for people living with HIV, prisons, schools and NGOs with under-served groups.

Evidence on current practice for training and developing a specialist TB workforce in EU/EEA settings

Fourteen countries had a strategy for training and development of a specialist TB workforce. The perceived need for training and development of the TB workforce was greatest amongst the following specialties: community health workers, 59%; specialist nurses, 52% specialist doctors, 37%; microbiologists, 33%; epidemiologists, 33%; surveillance scientists, 19%.

- Other needs for training and development highlighted by representatives from five countries included: general practitioners (three countries); radiologists, pulmonologists and chest x-ray specialists (1 country) and immigration and prison services (1 country).
- Representatives from five countries stated that low TB incidence led to low knowledge and experience of TB because healthcare professionals encountered few TB cases. Representatives from two countries indicated there was a need for knowledge updates among healthcare workers and general practitioners.

Barriers to raising awareness of TB amongst healthcare professionals and other providers are outlined below:

- There was a low index of suspicion of TB amongst GPs and a lack of TB awareness amongst patients and primary care staff was perceived to negatively impact on early diagnosis and disease transmission control (Belling, McLaren et al. 2012).
- An over-reliance on social risk factors as part of diagnosis making sometimes meant that GPs might have delayed diagnosis in cases where poor living conditions were not an issue. Atypical presentations and low clinical suspicion of TB also imposed challenges to TB identification and misdiagnosis. GPs felt more confident diagnosing TB when faced with a classical presentation (Metcalf, Davies et al. 2007).
- Despite the provision of correct information by TB specialist practitioners, many patients expressed deeply rooted inaccurate, socio-cultural beliefs about TB (Gerrish, Naisby et al. 2013).
- There was uncertainty about appropriate clinical practice in the treatment of specific subgroups of patients, such as the elderly or immigrants. TB is often not considered in the differential diagnosis for elderly patients (Moro, Resi et al. 2005, Atchison, Zenner et al. 2015, Morton 2015).
- In emergency departments an awareness of the groups that are vulnerable was not always evident and some feared it could be seen as a form of prejudice if they singled out immigrant patients or those with social problems. The fast-paced environment of emergency departments was found to impose significant challenges on TB identification (Cochet and Isnard 2008, Belling, McLaren et al. 2012, Morton 2015, Blok, van den et al. 2016).
- A lack of awareness of particular needs of adolescents with TB leading to poor adherence in the European region. A lack of knowledge of the safety and effectiveness of second- and third-line drugs in adolescents with drug-resistant-TB was also reported (Gerrish, Naisby et al. 2013, Wannheden, Westling et al. 2013, Blok, van den et al. 2016).
- Physicians and nurses working with HIV felt that they had insufficient knowledge and experience of anti-tuberculosis treatment, in particular regarding the choice of treatment strategy and monitoring routines (Belling, McLaren et al. 2012, Wannheden, Westling et al. 2013, Dara, Solovic et al. 2016, Turusbekova, Popa et al. 2016).

Facilitators to raising TB awareness amongst healthcare professionals and other providers included:

- Educational outreach interventions were found to improve active and latent TB identification (Bothamley Graham, Kruijschaar Michelle et al. 2011, Belling, McLaren et al. 2012).

Training and development of a specialist TB workforce is a vital component of any TB Action Plan or TB Strategy. Barriers to training and development of a specialist TB workforce are outlined below and need consideration:

- A lack of nurses and/or TB case managers, specialist TB physicians, laboratory expertise and interpreters (Abubakar, Chalkley et al. 2006) (Atchison, Zenner et al. 2015) (Belling, McLaren et al. 2012) (Cochet and Isnard 2008) (Dara, Solovic et al. 2016) (Gerrish, Naisby et al. 2013) (Turusbekova, Popa et al. 2016).

These barriers were shown to have an impact on continuity of care, active case-finding in prisons, triage in emergency care departments, outreach services and treatment administration support through DOT (Bothamley Graham, Kruijschaar Michelle et al. 2011) (Mehay, Raj et al. 2017) (Metcalf, Davies et al. 2007) (Turusbekova, Ljungqvist et al. 2016, Mehay, Raj et al. 2017) (Metcalf, Davies et al. 2007, Wannheden, Hvitfeldt-Forsberg et al. 2017)

EU/EEA expert opinion on raising awareness of TB in the community and primary care identified the following barriers to implementation:

At community level:

- Stigma in some communities; some groups do not want to engage with the issue of TB
- Lack of awareness of TB in high risk groups, for example in migrants from high to low burden settings, and in those who have undergone a pre-entry x-ray for pulmonary TB as a visa condition
- Many migrants to EU/EEA settings, for example in the UK do not register with primary care in the first two years of arrival (when risk of reactivation is heightened). By virtue of being external to the healthcare system, these migrants may only present to hospitals when symptoms have advanced
- Community-based organisations working with affected communities are themselves not aware of TB issues and have minimal resource to dedicate to the issue

At primary care level:

- Primary care organisations are under pressure, TB cases rarely present to primary care practitioners. As a result, they may feel as though TB awareness sessions are not worth their time due to small caseloads.
- TB is a rare (particularly in low-incidence settings) and treatable infectious disease. As a result, other issues may compete for the attention of primary care and community care workers.
- TB is not an immediate emergency (as compared to Ebola) and so interest in the topic area is low

EU/EEA expert opinion included the following activities or solutions, which could mitigate barriers to implementation on raising awareness of TB in the community and primary care:

Community targeted:

- Development of a communication strategy to reach primary care and community audiences with basic / minimum information. Clarity on the type of knowledge these groups would need and why could be included.
- Introduction of TB-related topics to postgraduate training programmes of primary care specialists.
- TB-related communication through circular letters to primary care institutions, social media, public transport networks (digital screens, paper leaflets distributed in primary care organisations).
- Use of E-learning tools for medical students, nurses and public health staff
- Continuing medical education articles on peer-reviewed medical journals with wide readership.
- Specialist TB training for TB coordinators in general hospitals

Primary care targeted:

- Provide training resources for TB nurses to deliver training to GPs during 'protected learning time.' Please follow this link: [TB Specialist Nurse Resource Pack](#)
- An example of online training is provided here [Royal College of GPs](#)
- Develop [animations that can be screened](#) in primary care practices

4.8 Targeted BCG vaccination

The Bacille Calmette-Guérin (BCG) vaccine is recognised as an important element for TB control and prevention. Currently BCG is the only commercially available vaccine for TB. Historically, BCG was offered universally across Europe. Previous evidence had shown differential effectiveness ranging from no protection to between 70 to 80% protective efficacy in UK school children (Sutherland I 1987, Rodrigues LC 1991). Findings from a meta-analysis have shown it can provide about 70 to 80% protection against severe forms of TB, such as meningitis in children (Rodrigues LC 1993). More recent evidence has demonstrated protection against TB disease and LTBI (Roy A 2014).

In low incidence settings, it is recommended that BCG is made available for neonates who are born to parents who originate from high incidence countries or who may have lived in a high TB burden country for prolonged periods of time. For the few countries in the EU with a TB incidence that exceeds 40 per 100,000 cases (Romania; Lithuania), a single dose of BCG vaccine should be given to all infants as soon as possible after birth.

Targeted BCG vaccination is an important priority for TB control and decision-making to support its inclusion in national TB plans and strategies should consider the following pieces of evidence on effectiveness of interventions:

There was good evidence of the effectiveness of BCG vaccination in protecting infants from pulmonary and extra-pulmonary TB, with lasting protective effects of up to 10 years. Vaccine efficacy was found to vary by age and tuberculin sensitivity status at the time of vaccination and was greatest when comparing naïve individuals with naïve unvaccinated individuals. Evaluation of BCG vaccination programmes have demonstrated cost-effectiveness when applied as part of a strategy targeted at high-risk groups, including close contacts of active TB cases or infants from high incidence settings. (Abubakar et al; 2013, Health Technology Assessment Database 2016, Mangtani et al; 2014, Roy et al; 2014)

Evidence on current practice of BCG vaccination policy options in EU/EEA settings

- Two thirds of EU/EEA countries had a strategy to provide and promote BCG vaccination, of which approximately half were documented in national TB control plans and TB strategies.
- From a selection of priority action areas, BCG was most frequently rated as low priority amongst over half of national TB programme representatives, 57%. The proportion of BCG vaccination strategies that included universal infant, high-risk infant and high-risk adult BCG vaccination were 42%, 58% and 21%, respectively.

Improving BCG vaccination uptake is a vital component of any TB Action Plan or TB Strategy. Barriers to improving BCG vaccination uptake are outlined below and need consideration:

- In a study by Metcalf and colleagues on diagnosing TB in primary care in the UK despite the awareness of local specialist services, there was a lack of knowledge on the current status of the BCG immunisation programme (Metcalf, Davies et al. 2007)
- The knowledge of vaccination guidelines and good awareness of TB were associated with a higher rate of BCG immunisation in France. Of 142 children who were eligible for a new targeted vaccination campaign in France, 56% were not vaccinated. The primary reasons for this included the GP's inability to identify the child as belonging to the target group; 33% (47/142 children) and parental refusal; 11% (16/142 children) (Rossignol, Guthmann et al. 2011)

5 Additional components of a national TB strategy especially important for medium to high incidence settings

In EU and EEA settings the epidemiological picture is diverse. In some member states the TB incidence is steadily declining and strategies tend to be anchored on preventing new infections, sustaining technical expertise to remain abreast of case detection and appropriate care, maintaining awareness amongst healthcare professionals, policymakers and the general public and reaching and intensifying support for under-served groups who are at higher risk of infection and poor clinical and treatment outcomes, complex multi-morbidity, including MDR-TB.

In other member states with medium to high incidence settings (≥ 10 per 100,000) there may be other priorities, and in those without robust laboratory infrastructure and/or high TB resistance rate, laboratory infrastructure including for detecting drug-resistance may require further investment.

As part of the survey of national TB control plans and strategies, medium to high TB incidence countries were more likely to identify **HIV/TB** and **MDR-TB** as high priorities (evidence for these areas can be found on page 23 and page 24, respectively). Whilst the median number of factors identified as barriers to TB control and prevention were similar in low and medium to high incidence countries, findings from the evidence portfolio indicate that countries of medium to high TB incidence may wish to consider evidence for other additional components of a national TB strategy as shown in Figure 6.

Figure 6: Additional components of a national TB strategy for medium to high TB incidence settings



5.1 Ensuring continuity of drug supply

Poor programmatic management and individual care of patients with TB has contributed to the emergence of drug resistance in EU and EEA settings. Accessibility to second-line drugs is an important factor in the provision of care, treatment and controlling the spread of TB, MDR-TB and XDR-TB strains. This is reliant on engaging a range of stakeholder groups in the production of high quality and affordable second-line drugs. Key implementers need to be involved in the assessment of drug availability, patterns of use and their mobilisation. Manufacturers are needed to ensure the production of high quality and affordable second-line drugs. National governments of respective EU and EEA countries are crucial for the regulation of drugs for first and second-line treatment, procurement methods and management of drug supply chains for the adequate distribution and availability of treatment.

A review of evidence to assess the effectiveness of interventions to improve the continuity of TB drug supplies in medium to high incidence settings was conducted but did not yield any findings in this area

Evidence on current practice on the distribution of drug supplies in EU/EEA settings

- Ensuring the continuity of the TB drug supply was reported to be of high priority in 60% (6/10) countries with a medium to high TB incidence (≥ 10 per 100,000). Additionally, 38% (8/21) of countries with a low TB incidence ($< 10/100,000$) reported this to be of high priority for their settings.

Ensuring the continuity of drug supply is a vital component of any TB Action Plan or TB Strategy. Barriers to ensuring the continuity of drug supply are outlined below and need consideration:

- Concerns were expressed on the sustainability of drug supplies for MDR-TB treatment in Bulgaria once external funding from The Global Fund ceased (de Vries, Tsolova et al. 2017).
- Despite being registered with the Drug and Food Administration in the United States 2014, Rifapentine was not available in the European market to scale-up management of LTBI in the Netherlands. The Netherlands also experienced a shortage of isoniazid drug production due to the Fukushima nuclear disaster where materials for drug developments are procured (de Vries G 2017)
- Gunther and colleagues reported on the variation in the availability of drugs for MDR-TB treatment regimen. Prothionamide/ethionamide and cycloserine/terizidone are essential in the preferred treatment regimen for MDR-TB, while para-aminosalicylic acid (PAS) is essential in the alternative MDR-TB regimen. These drugs were available in 31 (86%), 32 (86%) and 26 (70%) countries, respectively. Three countries did not have any of these drugs available (Albania, Serbia, Greece), while another two countries (Bosnia and Herzegovina, Slovakia) had just one of these drugs available (Gunther, Gomez et al. 2015).
- There was also a variation in the availability of drug for XDR-TB treatment. For example, Linezolid was available in 29 (78%) countries and Clofazimine in 17 (46%). Five (14%) countries had neither of these two drugs available. (Gunther, Gomez et al. 2015).
- There were differences in the costs of drugs, differences in procurement practices or accessibility to discounted prices through international donors or organisations (Gunther, Gomez et al. 2015).

5.2 Developing external quality assurance for TB diagnostic services

TB control is dependent on the availability and efficiency of TB diagnostic capability for early and accurate identification of TB and drug resistance. Radiography is an essential and basic technology that should be available and accessible. National strategic plans should be underpinned by quality of laboratory-based diagnostic services to support clinical and public health needs across EU and EEA settings. The high prevalence of MDR-TB and the increase of XDR-TB strains in some EU and EEA member states underscores the importance of robust standards for TB diagnostic services and control policies. Important diagnostic tools including smear microscopy, bacterial culture, Xpert MTB/RIF and WGS are vital for timely identification of positive and infectious cases to support clinicians and understand directionality of transmission. This is crucial to inform the implementation of appropriate infection control and timely treatment initiation.

Prioritising the development of new and rapid diagnostic tools, from routine culture and smear microscopy to molecular techniques and maintaining safe infrastructure coupled with the provision and retention of a skilled laboratory workforce need continued support and investment.

A review of evidence to assess the effectiveness of interventions to develop external quality assurance for TB diagnostic services in medium to high incidence settings was conducted but did not yield any findings in this area.

Evidence on current use of external quality assurance policy options for TB diagnostic services in EU/EEA settings

- Taking part in external quality assurance schemes for laboratory services was indicated as a high priority for 50% of medium to high TB incidence (≥ 10 per 100,000) countries. Thirty-three percent countries with low TB incidence (10 per 100,000) reported this as a high priority for their settings as well.

Developing external quality assurance for TB diagnostic services is a vital component of any TB Action Plan or TB Strategy. Barriers to availability of quality-assured laboratory-based diagnostics are outlined below and need consideration:

- It was reported that rapid molecular tests for the diagnosis of MDR-TB were not available in some hospitals and criteria for their use were either lacking or not known according to respondents from Austria, Spain and the UK (de Vries, Tsolova et al. 2017).

6 Conclusions

National strategic planning is a core component of a national TB programme and provides the over-arching framework for the operationalisation of key activities and functions to tackle TB control and prevention priorities. This is an essential step to drive political commitment, effective government stewardship and enhanced mobilisation of resources.

In this TB Strategy Toolkit, we outline and link the relevant aspects of current practice in EU/EEA settings, intervention effectiveness and barriers to implementation for each of the core components selected as priorities in EU/EEA settings by national TB programme leads and expert opinion. We emphasise effective TB control is dependent on timely detection of TB and prompt and supportive completion of TB treatment. To reduce morbidity and mortality, the provision of high-quality, prompt and evidence-based clinical care and social support must be at the heart of any National TB Action Plan or TB Strategy.

Societal, socioeconomic and wider healthcare improvements and investments in a robust evidence base and research efforts and international TB control are needed to strengthen cascades to contribute to reductions in TB incidence.

Data-driven approaches which utilise national and sub-national epidemiological analysis of TB case registries for routine and enhanced surveillance activities should inform decisions upon which proven and evidence-based interventions should be prioritised and implemented.

Each Member State will need a consolidated and multi-sectoral approach to develop their own locally-relevant national TB strategy or TB action plan that accounts for their country's specific TB epidemiology, patient and service provider needs, resources and service structure landscapes and specific barriers. For example, in settings with high numbers of TB cases in prisons or congregate settings, national plans and strategies may wish to focus on these settings and prioritise on strengthening infection control and prompt identification and treatment initiation and support adherence to minimise TB transmission, whilst priorities in Member States with high MDR-TB incidence may include diagnostics, infection control and appropriate treatment. Conversely, low incidence countries with a high proportion of migrant populations may wish to focus on screening efforts for TB and LTBI, early detection and early, appropriate and equitable linkage to care.

Approaches will need to stimulate actors and key implementers who are pivotal to implement locally-relevant solutions in areas where there is high unmet need and where greatest reductions in incidence can be achieved.

The End TB Strategy and the first ever United Nations General Assembly High Level Meeting on TB in September 2018 have resulted in an unprecedented commitment to the elimination of TB, based on a multi-sectoral approach and country ownership. The establishment of a sound national strategic plan demonstrates a consolidated starting point to the prioritisation of TB control and elimination.

7 Summary points for core components of national strategic plans for TB prevention and control to inform EU/EEA country-level prioritisation

Core components

Surveillance and monitoring	<ul style="list-style-type: none">• Robust and timely national surveillance is a key element for monitoring TB epidemiology, to analyse trends in incidence and drug resistance and to identify outbreaks• Routine national and sub-national epidemiological analyses can help to determine the distribution of TB in the population and to identify and prioritise populations at risk in order to inform the targeting of proven and evidence-based interventions
Contact tracing	<ul style="list-style-type: none">• Contact tracing is essential and should be guided by a risk assessment, including the time and proximity of contact (such as adult and child contacts), the infectiousness of the index case, and the vulnerabilities and co-morbidities of the contacts.• Individuals detected with LTBI should be offered effective preventative treatment• European consensus on evidence-based and policy-based recommendations can provide a basis for national guidelines• National strategic plans should be tailored and responsive to the needs of under-served groups that are at increased risk of TB or TB transmission or face specific barriers to high quality-care or face difficulties in adhering to TB treatment
Tackling TB in under-served groups	<ul style="list-style-type: none">• Epidemiological assessments can help identify groups at increased risk and unpack the socio-economic contexts that frame the realities of inequitable access to services. This can support targeting of tailored and supportive interventions• Individuals with a history of homelessness, alcohol or drug misuse, imprisonment, mental health problems and some migrant groups are at increased risk of TB and have complex and intersecting needs. The design and delivery of integrated models of care and social support should be adapted to special needs of different under-served groups• Targeted screening for active and LTBI in selected risk groups is highly recommended: those living with HIV, and immunosuppressed and conditionally for migrants from high incidence settings Screening also supports early detection and treatment initiation.• Targeted screening of under-served groups using mobile chest radiography is an effective and cost-effective intervention to improve screening coverage, case identification and reduce diagnostic delay.
Targeted TB screening in clinical risk groups	<ul style="list-style-type: none">• Effective management of TB-HIV coinfection is reliant on access to high-quality and integrated TB and HIV services to support improved uptake and timeliness of antiretroviral treatment initiation and reduce mortality from HIV-associated TB.• National strategic plans should uphold key principles to improve multidrug-resistant TB care and prevention, which include:<ul style="list-style-type: none">- Prevent transmission of M/XDR-TB- Scale-up and sustain access to testing for resistance to first- and second-line anti-TB drugs and to HIV testing and counselling
Management of HIV-TB coinfection	
Improve multidrug-resistant TB care and prevention	

Raising awareness of TB and training and developing a specialist TB workforce, wider healthcare professionals and other providers

- among TB patients
- Scale up access to effective treatment, care and support for all forms of drug-resistant TB
- Scale up TB infection control
- Strengthen surveillance, including recording and reporting of drug-resistant TB and HIV-comorbidity and monitor treatment outcomes
- Address the needs of special populations
- The inclusion of TB as part of medical education curricula, publications in country-level medical journals and refresher training for specialists who manage TB can help to improve awareness among professionals and address knowledge gaps and contribute to the reduction of diagnostic delay.
- Strengthening collaborative links between different tiers of the healthcare system through education and training can also strengthen referral routes.
- An effective, skilled and supportive TB workforce is fundamental to delivery of specialist TB services in all stages of the care cascade and can be further strengthened by nurses in leadership positions.
- Continuous development of knowledge and skills can be maximised through the inclusion of TB in medical education curricula, country-level medical journals and refresher training for TB specialists. Widening collaborative networks to include community or outreach workers and social care workers can play an important role in strengthening services, and support a socially and culturally-sensitive environment

Targeted BCG vaccination

- National strategic plans for low incidence settings may consider targeted BCG vaccination for neonates born to parents from high incidence countries or who may have lived in a high TB burden country for prolonged periods of time.
- For the few countries in the EU with a high TB incidence, a single dose of BCG vaccine should be given to all infants as soon as possible after birth.

Ensuring continuity of drug supply

- Sustained access to effective, high-quality and affordable TB drugs is vital for TB control and to improve programmatic management of TB.
- National strategic plans will need to account for engagement with key implementers who will need to be involved in the assessment of drug availability, patterns of use and their mobilisation.
- National TB programme decision-makers will need to work closely with governments in their countries to ensure sustain the regulation of first- and second-line treatment, procurement methods and management of drug supplies chains for the adequate distribution and availability of treatment.

Developing external quality assurance for TB diagnostic services

- National strategic plans should be supported by efficient TB diagnostic capability for early and accurate identification of TB and drug resistance. Radiography is an essential and basic technology that should be available and accessible.
- High-quality laboratory-based diagnostic services and robust standards should inform the implementation of appropriate infection control and timely treatment initiation
- Availability and accessibility to important diagnostic tools:

microscopy, bacterial culture, Xpert MTB/RIF, smear microscopy, rapid molecular testing, or whole genome sequencing where applicable are vital for timely identification of TB cases and to understand directionality of TB transmission

Appendix 1: Expert Stakeholder meeting

On Wednesday 24th October 2018, Public Health England, leaders for Work Package 7 (WP7) for the E-DETECT TB research project hosted an Expert Stakeholder meeting to populate core components underpinning national TB Action Plan or TB Strategy for prevention and control. The event brought together representatives from TB programmes and services from across EU and EEA member states, academics, civil society organisations, World Health Organisation (WHO) Europe, European Centre for Disease Control (ECDC) and the European Commission / CHAFEA.

The event was divided into a series of presentations on up-to-date evidence on core components for national TB strategies and utilised a modified Delphi method to attain expert consensus on priority intervention areas and a targeted priority-based approach to overcome barriers.

The outputs from this meeting were utilised to develop this TB Strategy Toolkit to support national TB programme representatives and focal points to develop or refine their national TB action plans or TB strategies.

There were two breakout sessions, which focused on the following:

- a) prioritising core components of a national TB plan or TB strategy
- b) identifying key barriers to the implementation of prioritised core components and any activities or solutions that could be considered

A **modified Delphi method** was used to identify and rank policy options by priority based on their respective EU/EEA country setting.

For breakout session (a): to assist in the development and refinement of national TB plans or strategies, the options were as follows:

Intervention area number	Intervention area description
1	BCG vaccination
2	Contact tracing and outbreak investigation
3	Raising awareness of TB in the community and primary care
4	Establishing and managing local TB control boards
5	HIV-TB co-infection in high risk groups
6	Multidrug-resistant TB in high risk groups
7	TB control in prisons
8	Reaching under-served groups
9	Screening for active TB in migrant from high incidence settings
10	Targeted screening for active TB in high risk groups
11	Latent TB infection screening in high risk groups
12	Training and developing a specialist TB workforce
13	Staffing and expertise for national TB surveillance
14	Publishing and disseminating clinical guidelines
15	Ensuring continuity of TB drug supplies
16	External quality assurance for laboratory services
17	Introducing and implementing new tools for TB control
18	Implementing electronic TB case registries

Table 1: Possible intervention areas for core components of national TB action plan or TB strategy for TB control and prevention in EU/EEA settings

A Delphi method is recommended as a means of determining consensus. It is an iterative process that uses systematic progression of repeated rounds of voting and is an effective process for determining expert group consensus where opinion is important. The modified Delphi method included two rounds and a final face-to-face meeting, which allowed for expert interaction and provide any further clarification and present any arguments to justify their viewpoints. Our modified Delphi method included the following steps:

1. **Round 1:** A comprehensive list of intervention areas were included in a survey of national TB control plans and strategies. Participants included National TB programme representatives and national focal points. We received a 100% response rate, with all 31 member states participating, published here (Simon M. Collin 2018).
2. **Round 2:** Participants were asked to rank the same intervention areas by priority and provide feedback using SelectSurvey (SelectSurvey.NETv4, ClassApps LLC, Kansas City, MO, USA). The survey questions can be found in the Appendix 1.
3. **Round 3:** Consolidation of scores for intervention areas, discussion at Expert Stakeholder meeting, review by panel participants and securing consensus

Scoring: For rounds one and two each option was ranked 'low', 'medium' and 'high' priority by respondents and were assigned scores: low=0, medium=1 and high=2. We converted the total score for each area into a percentage by dividing the total by the maximum possible score (=62 if participants indicated 'high' priority). We calculated the average scores for both rounds and these are shown in Figure 2.

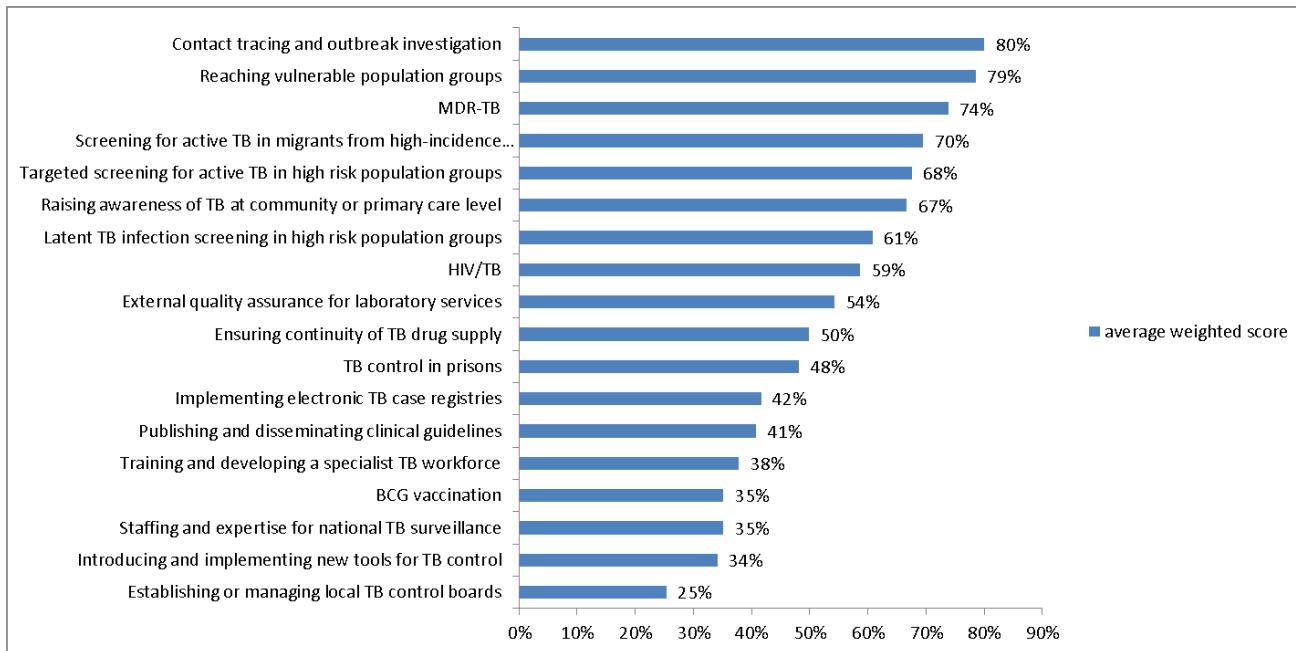


Figure 7: Interventions and their weighted scores considered as possible core components of a national TB action plan or TB strategy. Questionnaire items which asked respondents to rate priorities as high/medium/low were given an overall percentage score, which was calculated by dividing a weighted sum of individual responses (coded as low=0, medium=1, high=2) by the theoretical maximum score.

Results of the previous two modified Delphi rounds were fed back to attendees (Figure 2) and national TB programme representatives were allocated to sub-groups. Sub-groups were stratified by whether participants were from high and low TB incidence settings, high and low MDR-TB incidence settings, whether their national programme had a TB Action Plan or TB Strategy and whether their settings were in Eastern or Western Europe. Sub-group discussions were facilitated by E-DETECT TB work package 7 co-investigators.

After discussion in sub-groups, the groups re-convened and a nominated rapporteur from each sub-group summarised each their discussion on intervention areas which were as priorities. After reflection and with the opportunity to change

their minds, participants took part in a third Delphi round to seek consensus on priority areas for intervention. Participants were asked to rank each intervention area by 'relevance' i.e. based on its importance and suitability for addressing TB control and prevention in their EU/EEA setting (0 = not relevant at all and 10 = extremely relevant) and by 'ease of implementation' i.e. ease with which constraints to implement relevant intervention area(s) could be minimised or overcome (0 = very difficult to implement and 10 = very easy to implement). Figure 5 shows the ranked average scores for each intervention area. A full list of participants can be found in Appendix 3.

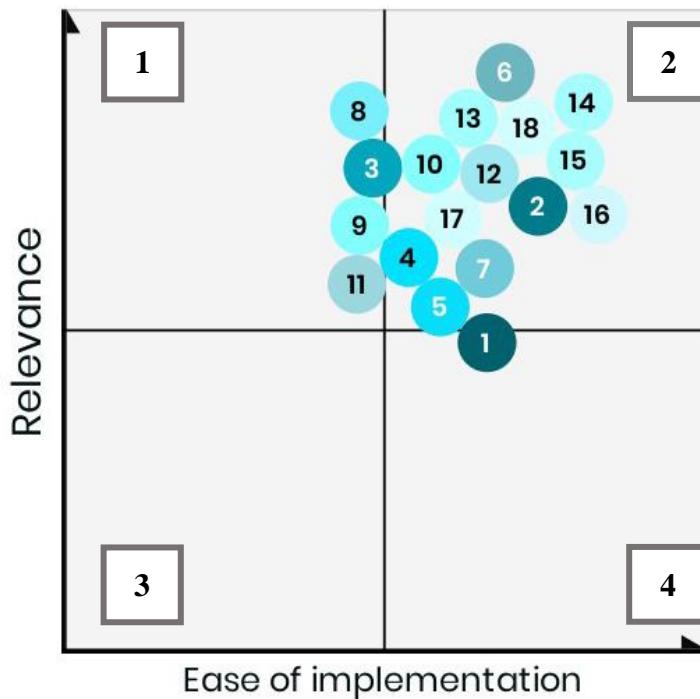


Figure 7: Priority areas for TB Action Plans or TB Strategies. The option numbers relate to those described in Table 1 and are described alongside this Figure. This plotted options which are relevant to TB control and prevention and ease of implementation on a continuous scale

Expert consensus showed against a continuous scale the majority of options were considered relevant to TB control and prevention action plans and strategies and were considered to be relatively easier to implement. Publishing and disseminating guidelines, ensuring the continuity of TB drug supplies and implementing electronic TB case registries were considered to be highly relevant and easier to implement. Comparatively, establishing and managing local TB control boards and managing HIV-TB coinfection in high risk groups were less so. Despite this, all options appear in the upper right quadrant.

The following four options were selected expert consensus as they are both relevant to TB control and prevention action plans and strategies but difficult to implement:

- 3. Raising awareness of TB in the community and primary care
- 8. Reaching under-served groups
- 9. Screening for active TB in migrant from high incidence settings

For breakout session (b) further discussion of these areas was undertaken at the Expert Stakeholder meeting. Participants were asked to discuss the barriers in these areas, any major activities or proposed solutions to address these barriers and identify the key implementers who would need to be involved in developing any proposed solutions. The key points noted in these discussions are provided in Table 2.

Table 2: Barriers to implementation of intervention areas and proposed solutions for consideration as part of national TB action plans and TB strategies

Intervention area	Barriers to implementation	Major activities and proposed solution(s)	Key implementers: who needs to be involved
Amongst recipients of care			
Reaching under-served groups	Distrust in healthcare system Stigmatisation Negative societal attitudes Cultural and language barriers (for example amongst undocumented migrants) Poor access and engagement with health services	Development or refinement of a dedicated community-based service, which is tailored to engender trust and build access, provide full health screening and seeks support treatment follow-up. Extensions of this service may also include mobile clinics, which can bring services to under-served groups in urban areas.	<ul style="list-style-type: none"> • Outreach services (for example NGOs) • Link support workers • Specialist TB nurses • Social services • Interpreters and cultural mediation • Legal services support to access care and treatment • Pharmacy
Amongst healthcare professionals			
	Lack of dedicated time and human resources Reluctance to treat due to discriminatory attitudes to under-served groups		

Intervention area	Barriers to implementation	Major activities and proposed solution(s)	Key implementers: who needs to be involved
Raising awareness of TB amongst wider healthcare professionals and other providers	<p>Community: Stigma in some communities; some groups do not want to engage issue of TB</p> <p>Lack of awareness of TB in high risk groups, for example in migrants from high to low burden settings, individuals with LTBI (particularly if undiagnosed) and in those who have undergone a pre-entry x-ray for pulmonary TB as a visa condition.</p> <p>Many migrants to EU/EEA settings, for example the UK do not register with primary care in the first two years of arrival (when risk of reactivation is heightened). By virtue of being external to the healthcare system, these migrants may only present to hospitals when symptoms have advanced.</p> <p>Community-based organisations working with affected communities are themselves not aware of TB issues and have minimal resource to dedicate to the issue.</p> <p>Primary Care:</p>	<p>Development of a communication strategy to reach primary care and community audiences with basic / minimum information.</p> <p>Clarity on the type of knowledge these groups would need and why could be included.</p> <p>Introduction of TB-related topics to postgraduate training programmes of primary care specialists.</p> <p>TB-related communication through:</p> <ul style="list-style-type: none"> - Circular letters to primary care institutions - Social media - Public transport networks (digital screens, paper leaflets distributed in primary care organisations). <p>Use of E-learning tools for medical students, nurses and public health staff</p> <p>Continuing medical education articles on peer-reviewed medical journals with wide</p>	<ul style="list-style-type: none"> • National TB programme representatives • Ministry of Health • Public health teams/institutions related to TB or TB programmes • Universities, medical and postgraduate education institutions • Community-based organisations • Medical societies (including paediatricians, gynaecologists/obstetricians) • 'GP TB Champions' • NGOs with expertise in TB case management • Providers of healthcare for undocumented migrants and under-served groups without health insurance coverage • Immigration authorities and organisations with responsibility for supporting integration of immigrants and asylum seekers into communities • Media organisations

Intervention area	Barriers to implementation	Major activities and proposed solution(s)	Key implementers: who needs to be involved
	<p>Primary care organisations are under pressure, TB cases rarely present to primary care practitioners. As a result they may feel as though TB awareness sessions are not worth their time due to small caseloads.</p>	<p>readership.</p> <p>Specialist TB training for TB coordinators in general hospitals</p> <p>Community-targeted: Free TB symposia for public health and medical professionals</p>	
	<p>TB is a rare (particularly in low-incidence settings) and treatable infectious disease. As a result other issues compete for the attention of primary care and community care workers.</p>	<p>Exchange programmes between low- and high-incidence settings</p>	
	<p>Decreasing number of experts who have an impact on medical training curriculums</p>	<p>Nationally-driven social media campaigns can effectively reach affected communities.</p>	
	<p>TB is not an immediate emergency (as compared to Ebola) and so interest in the topic area is low</p>	<p>Integrate TB awareness raising activities with other health issues, such as sexual health, diabetes, healthy eating.</p>	
	<p>There is a lack of interest in TB, particularly if there do not become a contact and do not feel direct threat.</p>	<p>Broker relationships between health and local government stakeholders with larger community-based organisations who have potential to be commissioner to deliver focused local awareness campaigns.</p>	
		<p>Primary care targeted: Provide training resources for TB nurses to deliver training to</p>	

Intervention area	Barriers to implementation	Major activities and proposed solution(s)	Key implementers: who needs to be involved
		<p>GPs during 'protected learning time.' Please follow this link: TB Specialist Nurse Resource Pack</p> <p>Any example of online training is provided here Royal College of GPs</p> <p>Develop animations that can be screened in primary care practices</p>	

Appendix 2: Evidence portfolio



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Appendix 2.1 EVIDENCE BRIEF

Survey of up-to-date national picture of national TB control plans and strategies

WORK PACKAGE 7

AIM: to provide national TB programme leaders and experts across the EU/EEA with an up-to-date picture of current strategies, including priority action areas within national TB strategies (whether current or under development) and barriers to the implementation of national TB strategies for TB control and prevention.

METHODS: The study used an online questionnaire to collect data from national TB programme leads or representatives from 31 EU/EEA member states.

RESULTS: The response rate was 100% (31 countries). 55% of countries reported having a national TB strategy, all of which were in implementation; five were preparing a strategy. 74% have a defined organisational TB control structure with central coordination, and 19% have a costed programme budget; few organisational structures included patient/civil society representation. The most frequently mentioned priority TB control actions were: reaching vulnerable population groups (80%); screening for active TB in high-risk

groups (63%); implementing electronic registries (60%); contact tracing and outbreak investigation (60%); and tackling MDR-TB (60%). Undocumented migrants were the most commonly (46%) identified priority population. Perceived obstacles to implementation included barriers related to care recipients (lack of TB knowledge, treatment seeking/adherence), care providers (including need for specialist training of nurses and doctors) and health system constraints (funding, communication between health and social care systems).

DISCUSSION: This survey has provided an up-to-date picture of the availability, implementation and content of national TB control plans in EU/EEA countries, and insights into priority action areas, population groups, and barriers to programme implementation. It shows that just over half of EU/EEA countries have a national TB strategy, of which all have been or are being implemented. Although the majority of countries have a defined organisational structure, and half have central coordination, a minority have a costed

programme budget, suggesting sub-optimal capacity to coordinate activities at the national level. Of note is that few national TB control boards included patient or civil society representatives.

A majority of respondents mentioned vulnerable population groups, screening for active TB in high-risk groups, implementing electronic case registries, and MDR-TB as priority actions. These were selected by respondents from a list of 18 action areas, which we specified under the tacit assumption that they are not 'more important' than ensuring the fundamentals of TB diagnosis and treatment within a universal healthcare system, or guaranteeing social protections and minimum socioeconomic conditions to prevent TB on a societal level. Rather, they represent specific areas for new or scaled-up interventions as part of an overall strengthening of efforts to control and prevent TB. As might be expected, a higher proportion (62%) of low TB incidence countries identified undocumented migrants as having high unmet need for TB detection and treatment than did

low-medium TB incidence countries (21%), reflecting the disproportionately high number of TB cases occurring in migrant groups in low TB incidence countries.

One third of respondents indicated a lack of government recognition of TB control as a public health priority, but the most commonly cited barriers related to recipients of care, care providers (mainly specialist training) and health system constraints. The perception that TB control can be impeded by factors related to recipients of care, namely lack of TB knowledge, seeking care and adherence, must be interpreted as a challenge to providers to address issues of awareness and stigma and to develop and deploy evidence-based interventions. The importance of good communication and coordination within the health care system and between health and social care systems has been demonstrated in reports of cases and outbreaks in EU/EEA countries.

[Survey findings in the context of other studies](#)

A 2013 survey of 38 European national TB programme representatives found that, of 26 countries also included in our survey, 15/26 had a national TB control plan. In our study this proportion was unchanged, but three additional countries now indicated that they had a plan (for 2007-2016, 2013-2018 and 2015-2020) and three countries that previously had a plan responded as follows: one had a formalised TB programme during 2007-2009 which was finished to limit the number of vertical plans and committees in public health, although the framework was still in place and a new programme was

planned for 2017-2020; one has a federal structure with legally-established local, regional and national responsibilities and a coherent approach to TB control and prevention which was considered to replace the need for a national programme; and one has a plan scheduled for 2019-2021. The availability of a (costed) national TB control plan which has been formally adopted by the national government is one of the core indicators for the Framework Action Plan to Fight TB in the EU. Our survey results indicate that two thirds (20/31) of EU/EEA countries will have implemented a national TB control plan before 2020.

The single most important priority for stakeholders was TB control amongst vulnerable, particularly migrant populations. This perception of need may in part be attributed to recent experience of large refugee movements across continental Europe. Barriers to accessing services and the large numbers of people affected would make it likely that there is a significant unmet need in these population groups, but robust evidence for the effectiveness of targeted TB interventions is surprisingly scarce and urgently needed. Other under-served populations have been frequently mentioned as priority groups, and TB control among these groups remains a challenge. A key part of our survey was to identify perceived barriers to strategy implementation. Here, an important observation was that clinical, particularly tertiary services were felt to be prioritised compared to public health and prevention opportunities in some settings. Whilst it is uncertain to what extent this represents respondents' personal views, a perceived under-prioritisation of

public health services is cause for concern.

[Implications and recommendations for TB policy and practice in EU/EEA countries](#)

Progress in the availability of national TB strategic plans has been slow, with half of EU/EEA countries not having a plan in place at the time of this survey despite publication of the WHO End TB Strategy in 2015. Whether recent international meetings such as the Global Ministerial Conference on Ending TB in the Sustainable Development Era (Moscow, November 2017) and the UN High-Level Meeting on TB (New York, September 2018) will increase government commitment to, and prioritisation of, TB control and elimination across the EU/EEA remains to be seen. Clearly, having a plan is only the first step - implementation requires centralised coordination, sufficient funding and evidence-based interventions.

The EU/EEA has favourable indices for determinants of trends in TB incidence such as economic growth, human development and public resources, and annual rates of decline for the region (4.3% during the period 2007-2016) are faster than all other regions. However, this downward trend is still unlikely to meet the WHO target of TB elimination by 2050 in European low-incidence countries. A key issue with regard to recommendations for policy and practice in the EU/EEA is the considerable social, economic and epidemiological heterogeneity between and within countries. As our survey has shown, EU/EEA countries which carry a high burden of TB in their native population, e.g. Romania accounted for almost one quarter of reported cases in 2016, are understandably

much less concerned about cases in foreign-born population groups than countries where these represent the vast majority of reported cases, e.g. 90% in Sweden and 96% in Malta. However, commonalities (and common borders) exist which provide potential for EU/EEA-wide and local interventions. Several such areas were highlighted in the most recent ECDC/WHO TB monitoring and surveillance report for Europe, and it is instructive to match these with responses to our survey and with evidence for effective interventions. Identifying and treating TB cases of foreign origin, and ensuring good access to healthcare for migrants and other vulnerable population groups, is clearly a priority in countries where these are foci for the majority of cases. Limited evidence for the effectiveness of interventions in vulnerable populations and for active and latent TB screening in migrants should give impetus to rigorously-conducted large-scale evaluations of different approaches to addressing this issue, given that any successful approach is likely to be generalizable across low TB incidence EU/EEA countries, and many migrants cross internal EU/EEA borders in journeys from their ports of arrival.

Prisons are a focus of higher TB and MDR-TB incidence in most countries and, although three quarters of countries in our survey have a strategy for TB control in prisons, only half rated this as a priority area. Data on TB in prisons in EU/EEA countries is scarce, with only 18 countries providing monitoring data in the years to 2016. We echo the ECDC/WHO recommendation that all EU/EEA

countries collect information to support accurate monitoring of TB in prisons at EU/EEA level, and again, we would advocate for evaluations to provide an evidence base for interventions that are likely to be effective regardless of country.

Our survey highlighted a perceived need for investment in human resources/expertise. This indicates a need in higher TB incidence EU/EEA countries to expand specialist training for clinical staff, whilst low TB incidence countries can contribute collaboratively through guideline development, providing technical assistance, exchanging technology, and strengthening research capacity. Indeed, cross-border collaboration between high and low TB incidence countries is one of 8 priority action areas within the WHO/European Respiratory Society framework towards TB elimination. This will also address the issue in low TB incidence EU/EEA countries of clinicians having insufficient first-hand experience to manage TB cases, with TB being so rare in some countries that there is a danger of losing local knowledge and expertise.

‘Inadequate systems for TB control programme monitoring and evaluation’ was identified as a factor impeding TB control by only one quarter of survey respondents, and three quarters of countries had a strategy for monitoring and evaluation, yet the ECDC/WHO report indicated that only 14 of 26 WHO targets could be effectively monitored based on data from EU/EEA countries, with reporting of LTBI, HIV status and treatment outcomes as areas requiring most improvement. Monitoring EU/EEA-

wide treatment outcomes is important given an apparent decline in success rates (from an average of 77% during 2011–2013 to 74% in 2014–2015), substantial between-country variation and success rates for both MDR and XDR TB that are far below WHO targets. Benchmarking and identifying differences is essential if countries are to disseminate and share best clinical practice. At an epidemiological level, a common strategy enables monitoring of emerging threats, such as the increasing proportion of XDR TB among MDR TB cases (from 14% in 2012 to 21% in 2016).

We note that routine collection of complete data from all countries for the wide range of indicators included in ECDC/WHO report, which could be gradually expanded to collect data on, for example, palliative care for XDR-TB and comorbidities such as diabetes and mental health, largely obviates the need for future one-off surveys. In the meantime, we trust that our survey findings will serve to inform the development of an evidence-based toolkit which EU/EEA and other countries can use to design national TB strategies, thereby supporting these countries to work collaboratively towards TB elimination.

The full research article is published in the European Respiratory Review journal and can be accessed by following this link: <https://erj.ersjournals.com/content/early/2018/10/04/13993003.01449-2018>

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Appendix 2.2 EVIDENCE BRIEF

Effectiveness of interventions for TB control and prevention in countries of low and medium TB incidence: a systematic review of reviews

WORK PACKAGE 7

AIM: To provide an evidence base to inform the development and implementation of national TB plans.

METHODS: We conducted a systematic review of systematic reviews of interventions for TB control and prevention relevant to low TB incidence settings (<10 cases/100,000 population). Our analysis was stratified according to 'direct' or 'indirect' effects on TB incidence. Review quality was assessed using AMSTAR 2 criteria. We summarised the strength of review-level evidence for interventions as 'sufficient', 'tentative', 'insufficient' or 'no' using a framework based on the consistency of evidence within and between reviews.

RESULTS: We found sufficient review-level evidence for direct effects on TB incidence/case prevention of vaccination and treatment of latent TB infection. We also found sufficient evidence of beneficial indirect effects attributable to drug susceptibility testing and adverse indirect effects (measured as sub-optimal treatment outcomes) in relation to

use of standardised first-line drug regimens for isoniazid-resistant TB and intermittent dosing regimens. We found insufficient review-level evidence for direct or indirect effects of interventions in other areas, including screening, adherence, MDR-TB, and healthcare-associated infection.

DISCUSSION: Our review focused on interventions for which reduction in TB incidence and prevention of TB cases was a directly measurable outcome, or could be inferred indirectly from another reported outcome, based on evidence from systematic reviews. Clearly, we recognize the basic obligation to provide TB patients with high-quality evidence-based clinical care that reduces suffering and mortality, and to make this standard of care accessible to everyone. From this point of departure, our review identified two interventions supported by sufficient review-level evidence of direct effects in reducing TB incidence and preventing TB cases, namely BCG vaccination and treatment of LTBI to prevent progression to active TB. The insufficient review-level evidence of direct effects in other

intervention areas is a consequence of two related factors: 1) the lack of good quality primary studies; 2) the lack of good quality systematic reviews. The first of these may be because policymakers perceive no added value in testing interventions which, by simple logic, should have a beneficial impact (or where effectiveness, e.g. of drug regimens for uncomplicated TB, is not disputed). Such testing may be unethical or would require randomised controlled trials of complex interventions at large enough scale and of sufficient duration to detect an effect on TB incidence. The second factor follows from the first or, where experimental evidence is available, reflects the difficulty of synthesizing evidence with substantial heterogeneity in settings, interventions and outcomes. In the absence of a comprehensive, consistent and robust review-level evidence-base, the choice of interventions for TB control plans and programmes will continue to be pragmatic, at best supported by evidence from individual studies, but otherwise based on local TB epidemiology, expert opinion and

accumulated national and international experience. One of the main challenges to building an evidence base in TB control and prevention at national level is the interconnectedness of interventions along the 'cascade of care' from detection of TB through to successful completion of treatment [181]. This implies that interventions need to be evaluated in a joined-up rather than standalone manner. Also, the biggest impact on TB incidence over time has come from societal, socioeconomic and wider healthcare improvements, which are beyond the remit of a TB control plan. These changing factors, together with non-static populations, preclude before-and-after studies as an unbiased method for evaluating TB-specific interventions [205]. Without substantial investment to strengthen the evidence base, the pragmatic alternative is to accept that 'good' interventions may not be supported by 'hard' evidence, and to trust that implementing a range of common-sense interventions, alongside population-level improvements in social determinants and risk factors and continual improvements in the effectiveness and quality of clinical care, will eventually lead to elimination of TB. A persuasive counter-argument can be made that interventions deemed to be 'good' even by the application of logic may not be as effective as thought, or could be made more effective, hence that more investment in research is essential. This research may require methodological innovation, such as using a factorial trial design to add interventions, e.g. screening, reminder systems, to an optimised programme of diagnosis and treatment, and

measuring transmission (using molecular methods) as an outcome.

Our findings in context

Vaccination

We reported sufficient evidence of protection against TB by BCG vaccination from four reviews. These indicate that an important role remains for vaccination targeted at high risk groups who are most likely to benefit because of higher risk of exposure, with recent research suggesting >15 years' duration of protection by BCG [206, 207]. Although RCT evidence for the use of BCG in high risk groups is unlikely to be forthcoming for ethical reasons, TB control programmes should probably adopt this approach whilst the search for a new and more effective TB vaccine continues [208].

Diagnosis and treatment

Perhaps unsurprisingly, these two areas accounted for the highest number of high-quality core reviews (21/45 core reviews in total, 8 in diagnostics, 13 in treatment). This reflects the relative ease with which comparative clinical studies of diagnostic methods and treatment regimens can be designed, conducted and systematically reviewed, compared with evaluations of complex interventions. Clinical studies tend to capture outcomes such as treatment success and diagnostic accuracy hence, the majority were categorized as having indirect effects on TB incidence that were not quantified as an outcome of the included systematic review. Translating outcomes such as treatment efficacy into effects on TB incidence is an area where modelling can be of some use [209]. That we did find review-level evidence for direct effects on TB

incidence of LTBI treatment and indirect effects of drug susceptibility testing and sub-optimal treatment highlights the importance of continuing to build a high-quality evidence base to support best practice in clinical care, and of continuing to develop more accurate diagnostic tests and more efficacious and safer drugs.

Screening and LTBI

We found that evidence for the efficacy of LTBI treatment in contacts and persons with certain co-morbidities is robust, whilst evidence for LTBI screening, especially population-based programmes, is much weaker. This lack of evidence is particularly important in view of south-north migration [210-213]. The recent push towards TB elimination in low-incidence countries in keeping with the ambitious End TB Strategy has increased interest in systematic LTBI screening and treatment, because most TB disease in these countries is a result of LTBI reactivation. It is worth noting that WHO issued strong recommendations for LTBI treatment of persons with certain co-morbidities, such as underlying immunosuppressive diseases or medications, whilst only issuing conditional recommendations for wider screening of migrants from high incidence countries [214]. The trade-off and tension between provision of LTBI treatment to only a few high-risk patients who have high likelihood of individual benefit from treatment, but with little or no effect on country-level incidence, versus provision of screening to a larger group at lower risk (such as migrants) with lower expected individual benefit but higher likelihood of reducing population-level incidence, remains unresolved. Ultimately, national TB strategic

planning must base decisions about screening programmes on context, cost considerations and local TB epidemiology, including the rate of MDR TB, for which LTBI treatment is still in its infancy.

Adherence

Many variants on interventions to improve treatment adherence have been evaluated, particularly in higher TB burden settings. Recent WHO guidelines [215] recommend that treatment should be based on an assessment of individual patients' needs, providers' resources and conditions for implementation. The paucity of review-level evidence for direct effects on reducing the incidence of active TB in low-incidence countries suggests the need for evaluation studies that can account for the complex and intersecting determinants of poor adherence, which can vary both within an individual and over the course of treatment. Under the auspices of the End TB Strategy there is a need to intensify efforts to design and test public health interventions that explicitly target modifiable social and behavioural determinants of adherence, thereby supporting high risk groups in accessing and engaging with patient-centred care.

Strengths and limitations

The main strength of our study is the consistent methodology applied to all reviewed systematic reviews, covering a wide range of interventions. We applied rigorous quality assessment criteria, the results of which are consistent with an earlier assessment of the quality of systematic reviews on TB [216]. The main limitation of a 'review of reviews' approach is that evidence from primary studies will not be

assessed if those studies have not been systematically reviewed. Where studies have been reviewed, some 'detail' may be lost because we are synthesising evidence which has already been synthesised. We did report some pertinent details from individual studies included in systematic reviews, where these primary studies provided the only evidence for a particular intervention, but un-replicated single-study evidence must be interpreted with caution. It has also been argued that systematic reviews may fail to capture effects of complex interventions, such as DOT, particularly where simplified outcome measures are used [217]. This is an area where qualitative systematic reviews could potentially contribute to evidence of effectiveness. Where we found sufficient evidence for effects of interventions on TB incidence, we did not attempt to quantify the magnitude of these effects. For example, BCG vaccination of infants in high risk groups will have little impact on overall TB incidence and case numbers in low-incidence countries because children represent a small proportion of TB cases. As a public health intervention in low-incidence countries, BCG will be more effective in preventing life-threatening paediatric TB cases, e.g. meningitis, than in reducing overall TB incidence.

Implications of our findings for TB control plans and strategies

The objective of our review was to synthesise an evidence base for the effectiveness of interventions for TB control and prevention in low-incidence settings. Our aim was to use this evidence to inform the development of a TB Strategy

Toolkit for EU/EEA countries, which will include guidance on the prioritisation of interventions within national TB control plans. The toolkit will be developed through a consensus approach, incorporating other types of evidence including a survey of current practices and priorities in EU/EEA countries [6], qualitative reviews of barriers and enablers to TB control [218, 219], current international standards, and WHO and ECDC guidelines [220]. This consensus process will address questions such as how to link national TB plans, which need to focus on strategic choices around interventions to reduce the overall burden of TB in the population, with continually evolving guidelines and evidence around best practice in TB patient care. Our review of reviews has shown the need for more evidence to support expert opinion and to support local experience when making policy decisions in TB control and prevention.

The full research article has been accepted for publication in the European Respiratory Review journal on 15th February 2019

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AIM: This systematic review aimed to identify the factors, which facilitate or impede the implementation of policies, strategies and guidelines for TB control or prevention in EU and EEA settings. By integrating published survey findings from Collin *et al*; 2018, with a review of the skills, attitudes and motivations of providers of care, health system constraints and social and political factors will provide a more granular understanding of how they impede TB control. This review aims to strengthen the evidence base on which to develop a TB Strategy toolkit for EU and EEA settings and support the strengthening of national TB programmes.

METHODS: A barrier was defined as any factor, which impeded or prevented the implementation of TB control or prevention policy, strategy, guideline or intervention whether at local, regional or national (international) level. Conversely, a facilitator was defined as any factor which assisted or accelerated the implementation of a TB control or prevention policy, strategy, guideline or intervention.

The following databases were searched between periods January 1997 to May 2017: Medline, EMBASE, CINAHL, Scopus, Global Health, Trip, The Cochrane Library, social Policy and Practice, The Health Management Information Consortium (HMIC).

To structure data synthesis, we used the SURE checklist (The SURE Collaboration) and its descriptions of barriers to code papers in EPPI-Reviewer according to the pre-specified checklist's barriers and facilitators. These were grouped under four sub-headings: providers of care (3 factors); other stakeholders (3 factors); health system constraints (17 factors); and social and political constraints (8 factors).

Further details on the search strategy, study selection, data extraction will be provided at a later date in a full manuscript for publication in due course

RESULTS: We identified 2,442 references, including 434 from MEDLINE, 734 from EMBASE, 92 from CINAHL, 628 from Scopus, 335 from Global Health, and 179 from

Appendix 2.3 EVIDENCE BRIEF

Barriers and facilitators to TB control and prevention in EU/EEA settings: a systematic review and evidence synthesis

WORK PACKAGE 7

Trip. Of these, 973 were removed by de-duplication and 1,469 to be screened by title and abstract. Screening by title and abstract eliminated 1,000 references, leaving 469 references for full text review. Forty-seven primary studies are included in this review. Findings highlight prominent barriers to TB control and prevention policy options including the variability of knowledge and adherence to clinical guidelines; human resource constraints and the need for specialist TB training, as well as the need for robust cross-border TB surveillance systems.

Adherence to guidance

Proper implementation of the current guidelines is an essential element of implementing TB care and therefore important for control strategies.

We found evidence of variation to in adherence to TB clinical guidelines across a spectrum of topics including: poor adherence to guidelines on contact investigations, insufficient implementation of active case-finding in English prisons, intra and inter-country difficulties in diagnosis and

management of TB in specified sub-groups (namely the elderly, foreign-born and immunocompromised patients) and difficulties following guidelines in circumstances with high numbers of refugee arrivals. There was also evidence on the lack of access to facilities needed to implement appropriate infection control such as access to negative pressure rooms, respiratory isolation rooms and environmental infection control measures.

Human resource issues amongst providers of care

We found inadequate availability of healthcare workers, specifically specialist TB physicians, TB case managers (nurses), interpreters in primary care and laboratory expertise. Evidence also indicated that limited staffing capacity had an impact on the continuity of care, active-case finding in prisons, triage in emergency care departments, outreach services and treatment administration support through directly-observed treatment.

Human resources were often negatively impacting on appropriate referral of patients. Papers also described a lack of continuity of care between physicians and nurses that impacted on the ability to deliver TB control interventions. A lack of timely support from specialist TB services was concern amongst GPs in primary care for the coordination a primary care-based LTBI service for migrant communities in the UK. Low specialist staffing levels were also reported to impose barriers to TB screening rate in detention centres in Paris. Nurses were reportedly asked to minimise their specialty roles for general respiratory work in acute settings. Reduced staff continuity and shortages were also evident for HIV-TB co-infected

patients, thus hampering the ability to plan and coordinate care to seek physician support for urgent circumstances.

Surveillance and monitoring

The ability to track performance of TB services is dependent on effective information systems for monitoring and evaluation of routine reporting. Concerns about the lack of interoperability between data capture systems, causing double documentation burden and the risk of missing important information were reported. This was of concern when tracking patient follow-up during migration and for recording the final outcome of discharged patients. There was also evidence of under-reporting of under-served groups in national surveillance systems, specifically mobile, homeless and migrant groups. The need for the adoption of regional MDR surveillance and performance indicators was also described. We also found evidence that the absence of a prospective data collection tool for paediatric MDR-TB caused difficulties for the development of paediatric guidelines for MDR-TB management.

Facilitators

Facilitators were most often relevant to positively documented motivations of healthcare workers to change or adopt new behaviours or related to good internal communication between different levels of the healthcare system facilitating the delivery of TB interventions. Papers described the positive effects that an adequate supply and distribution of human resources had on TB intervention delivery, particularly in relation to perceived benefits of link support

workers, social care workers, outreach staff and NGO staff).

DISCUSSION:

This systematic review describes a large number of barriers and some facilitators from peer-reviewed journal articles that affect TB control in EU/EEA settings. Our analyses of the most commonly reported factors and relationships between them constitute real-world obstacles, which impede the implementation of strategies for TB control and prevention across EU/EEA settings. The strength of this evidence derives from it being based on data extracted from 47 studies in 13 EU/EEA countries from 2000 to 2017.

We found that barriers to implementing TB control strategies most often described TB practices deviating from relevant norms and standards. These types of barriers were linked to others, such as non-adherence attributed to a poor knowledge or acceptance of TB guidelines (particularly surrounding LTBI diagnostics and treatment) or lack of facilities or resources required to implement guidelines. The acceptance of guidelines by healthcare workers is a crucial aspect to their implementation as part of a TB control strategy. Our paper has indicated that there are areas of TB control where guidelines are perceived as insufficient by providers of care, including contact tracing, diagnosing and treating specific patient sub-groups such as the elderly, foreign born and immunocompromised, and , LTBI diagnostics and treatment. Questioning the validity of guidelines paves the way for disengagement from guidelines and leads to care delivery based on

experience, which can be detrimental to a uniform approach. Based on our analysis of association between types of barriers, improving the care providers' interaction with TB guidelines could have a positive impact on a wide range of other specific barriers. This indicates the need for information and educational strategies that provide support and technical assistance for the implementation of guidelines. Improving the factors surrounding providers of care in implementing guidelines as part of a strategy needs to be supported by a focus on the dissemination of guidelines and educational aspects. It is well-established that an early TB diagnosis is crucial to patient outcomes and minimises the risk of TB transmission to susceptible contacts. Adequate staffing levels are needed to ensure early diagnosis and prompt TB treatment and engagement with additional activities, such as awareness-raising, extended contact tracing or screening. Our findings show that a lack of human resources was an important barrier to implementing TB control strategies. The lack of a TB specialist workforce was reported to have adverse effects on screening, time-to-diagnostic and overall treatment pathways. Insufficient provision of specialist services and coordination of care has been documented in several low TB incidence EU/EEA countries, indicating a need to equip the TB workforce with knowledge, skills and infrastructure commensurate with management of TB cases with complex clinical and social interactions. The role of nurses in TB care and service delivery is crucial to the TB control agenda, specifically in circumstances where there is a limited consultant capacity or input. Positioning TB

specialty nurses in leadership and management positions strengthens care coordination by empowering nurses to oversee all aspects of patient care: diagnosis, contact screening, clinical patient reviews and supporting treatment adherence through engendering trust and building rapport. These results are in line with previously reported survey findings by Collin and colleagues which found that 57% of national TB programme representatives indicated that there was a need for specialist TB nurses in patient care. We found good evidence that the representation from link support workers, social care workers and outreach staff played a vital role in strengthening services. We found evidence of insufficient surveillance and monitoring systems, where a lack of interoperability between databases, including follow-up and recording of treatment completion and outcomes particularly in underserved populations, such as migratory groups. Robust surveillance systems that can adapt to the variation in TB epidemiology across the EU/EEA are vital to the development of cross-sectoral guidance and to support integrated case management. Our findings highlight key systemic barriers to the implementation of policy options for TB control. This evidence will provide context for and inform the development of a TB Strategy Toolkit for TB programme leaders in EU/EEA countries. Ideally, TB strategies would include measures to remove barriers, but where this is beyond the remit of a TB programme, the strategy can be designed to mitigate for known barriers. Efforts to support national TB programmes with a robust trans-national evidence base on key

barriers to TB control will help locally-based decision makers to coordinate activities that are responsive to these barriers. Prioritisation of interventions and resource allocation will need to consider these factors with expert opinion to support implementation as part of National TB Plans or TB Strategies and strengthen their alignment with the key pillars of The End TB Strategy.

[The full research article for this evidence brief is being prepared for submission to a journal](#)

Appendix 3: Expert meeting attendees

1. Name
2. Representation
3. Ana Maria Duca
4. NTP representative for Romania
5. Maryse Wanlin
6. NTP representative Belgium
7. Sarah Anderson
8. NTP representative for United Kingdom & E-DETECT TB Work Package 7 co-investigator
9. Nita Perumal
10. NTP representative for Germany
11. Thierry M. Comolet
12. NTP representative for France
13. Kevin Kelleher
14. NTP representative for Ireland
15. Peter Henrik Andersen
16. NTP representative for Denmark
17. Trude Margrete Arnesen
18. NTP representative for Norway
19. Gerard de Vries
20. NTP representative for Netherlands & E-DETECT TB Work Package 7 co-investigator
21. Cindy Schenk
22. NTP representative for Netherlands
23. Ivan Solovic
24. NTP representative for Slovakia
25. Stamatoula Tsikrika
26. NTP representative for Greece
27. Jurgita Pakalniškienė
28. NTP representative for Lithuania
29. Ibrahim Abubakar
30. E-DETECT TB Lead Coordinator
31. Dominik Zenner
32. E-DETECT TB Work Package 7 Lead
33. Knut Lönnroth
34. E-DETECT TB Work Package 7 co-investigator
35. Fatima Wurie
36. E-DETECT TB Senior Scientist
37. Simon Collin
38. E-DETECT TB Senior Scientist
39. Mike Mandelbaum
40. TB Alert
41. Paul Sommerfeld
42. TB Alert & TB Europe Coalition
43. Cinthia Menel-Lemos
44. CHAFEA
45. Martin Van Den Boom
46. World Health Organisation European Region
47. Marieke van der Werf
48. European Centre for Disease Control
49. Lisa Kawatsu
50. Japan Anti-TB Association (observer)
51. Akihiro Ohkado
52. Japan Anti-TB Association (observer)

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