



Building a European database to gather multi-country evidence on active and latent TB screening for migrants



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ABSTRACT

Background and aim: Screening for active and latent TB among migrants in low TB incidence countries may constitute an important contribution to TB elimination. E-DETECT TB, a European multi-country collaboration, aims to address the present lack of evidence on effectiveness of migrant TB screening by collating data in an international database and perform cross-country pooled and comparative analyses of screening coverage, results and linkage to care.

Method: A database was established using migrant TB screening data from participating countries' national screening programs, national screening pilots and local research projects. All partner countries contributed to a common agreed protocol with standardized variables, pooling available numerator and denominator screening data from participating countries and sites.

Results: All collaborating members drafted and agreed upon a data sharing accord as well as a protocol that clearly defined responsibilities and data governance principles. The database has been created and data transfer is ongoing.

Conclusion: By persistence and focus the project has overcome considerable administrative, practical and legal challenges. This international collaboration provides greater power of analysis of harmonized data and thereby a unique opportunity to contribute migrant TB screening evidence. E-DETECT TB has started to invite other countries to contribute data to the database.

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Background

In 2017, 258 million people were international migrants due to conflict, inequality, financial insecurity and globalisation (Affairs, 2017). This has an impact on Tuberculosis (TB) epidemiology as some migrants move from high to low TB incidence countries (Pareek et al., 2016; Odone et al., 2015; Lönnroth et al., 2017). As TB rates are reaching pre-elimination levels in native populations in most low TB incidence countries, the proportion of foreign-born

cases increases (Pareek et al., 2016; Odone et al., 2015; Lönnroth et al., 2017; Kunst et al., 2017). Screening for active TB and latent TB infection (LTBI) in migrants in low-incidence countries are interventions that improve early detection and prevention. However, more research is needed to address the present evidence gap concerning coverage, impact and cost-effectiveness of migrant TB screening (Pareek et al., 2016; Kunst et al., 2017; Getahun et al., 2015). Screening programs without surveillance of key performance indicators could result in a substantial waste of resources (Zammarchi et al., 2015; Greenaway et al., 2018). Most national TB registries include data on notified cases of active TB, but neither screening data nor information about LTBI diagnosis or treatment are included (Kunst et al., 2017). International databases that rely on national reporting therefore have similar limitations, such as

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the TESSy database managed by the European Centre for Disease Prevention and Control (ECDC) and the World Health Organization's (WHO) global TB database of nationally aggregated TB control indicators.

E-DETECT TB is a European research consortium for the early detection and integrated management of TB in Europe. It is purposed to contribute to the ultimate elimination of TB in the EU by means of evidence-based interventions, with a special focus on generating better evidence for screening (Abubakar et al., 2018). This paper describes one of the E-DETECT TB work-packages, which aims to establish a multi-country database for assessing coverage and results of screening for active and latent TB among migrants in selected low TB incidence countries in Europe. The database will in the near future enable evaluations that can guide proper targeting of screening, appropriate screening approaches and effective mechanisms that support linkage to care and adherence.

Methods

General aim and specific objectives

E-DETECT TB has established a database which contains migrant TB screening data from national screening programs, new national screening pilots and local research projects in selected partner countries. The main aim is to collate data on migrant TB screening and perform cross-country pooled and comparative analyses to inform effective screening strategies. The specific objectives are to determine: (1) screening coverage; (2) screening yield/prevalence; and (3) treatment uptake and completion. These analyses will primarily be disaggregated by screening scheme/algorithm used, as well as age, sex and country of origin/nationality of screened individuals. For the LTBI screening cohort, reactivation rates will be estimated by

linking to TB registers, where possible. For those screened for active TB with chest X-ray (CXR), CXR findings and characteristics of clinically diagnosed TB will be assessed. The results will also be used to parameterize health economic and transmission models.

Study partners

The work is led by members of the E-DETECT TB consortium with support from national public health agencies (Home, 2018). The present collaborators are Italy (University of Brescia), the Netherlands (KNCV Tuberculosis Foundation), Sweden (Karolinska Institutet and the Public Health Agency of Sweden) and the United Kingdom (University College London and Public Health England). Additional partners and countries are invited to join the database.

Study design

A multi-country cohort study of migrants eligible for LTBI/TB screening according to the given country's existing national policy and local screening protocols (Table 1) was conceived (Lönnroth et al., 2017). Based on careful mapping of available data on LTBI/TB screening, all partners have developed and agreed on a common protocol for data sharing, analysis and dissemination (Kunst et al., 2017). This includes a variable list with standardized variable names and codes to be used across sites. Each country created a standardized database that captures the cascade of screening and linkage to care from which a dataset will be extracted and merged with the joint multi-country database containing a cohort of individual level data. The joint database includes one module for basic demographic information, as well as five modules representing the screening and linkage-to-care cascade and reactivation (Figures 1 and 2).

Table 1
National screening policies or local project approaches at the collaborating sites of the project assessing the coverage for active and latent tuberculosis among immigrants in low incidence countries (Kunst et al., 2017).

Country	Screening strategy	Population screened	Age years	Screening for active TB		Screening for LTBI	
				WHO-estimated TB incidence in the country of origin/100 000	Screening method Compulsory (●)/Voluntary (□)	WHO-estimated TB incidence in the country of origin/100 000	Screening method Compulsory (●)/Voluntary (□)
Italy	Post-arrival, secondary reception center/health center	Asylum seekers	All	NA	Interview + CXR (●) CXR for those with positive TST or IGRA (●)	NA	Sequential TST and IGRA ^a (□) TST or IGRA ^b (□)
The Netherlands	Post-arrival, Public Health Services	Other migrants	<18	>50	CXR for those with positive TST or IGRA and no TB symptoms (●) CXR (●)	>50	TST/IGRA or IGRA ^c (□) None
			≥18	>50		NA	
Sweden	Post-arrival, central reception center	Asylum seekers	<18	>50	CXR (●) CXR (●)	>50	TST/IGRA or IGRA ^{c,d} (□) None
			≥18	>50		NA	
The United Kingdom	Post-arrival, primary care center	Asylum seekers	All	>100	CXR for those with symptoms or positive TST or IGRA (●) Interview (□)	>100 ^e	TST or IGRA (□)
	Active TB: Pre-entry, port of arrival, reception center LTBI: Post-arrival, primary care	Long stay migrants (>6 months)	<11 ^f	>40	CXR (□) CXR (●) CXR (●)	>40	TST or IGRA (□) TST or IGRA (□) IGRA (□) None
			11–15 ^f	>40		>40	
			15–16	>40		>150	
			16–35	>40		NA	
			>35				

^a From August 2017.

^b 2015–July 2017.

^c Until 2016: LTBI screening only for non-BCG vaccinated individuals <25 years.

^d From December 2016.

^e Including Eritrea, due to high-incidence in this group in Sweden.

^f Recommended, not programmatic screening.

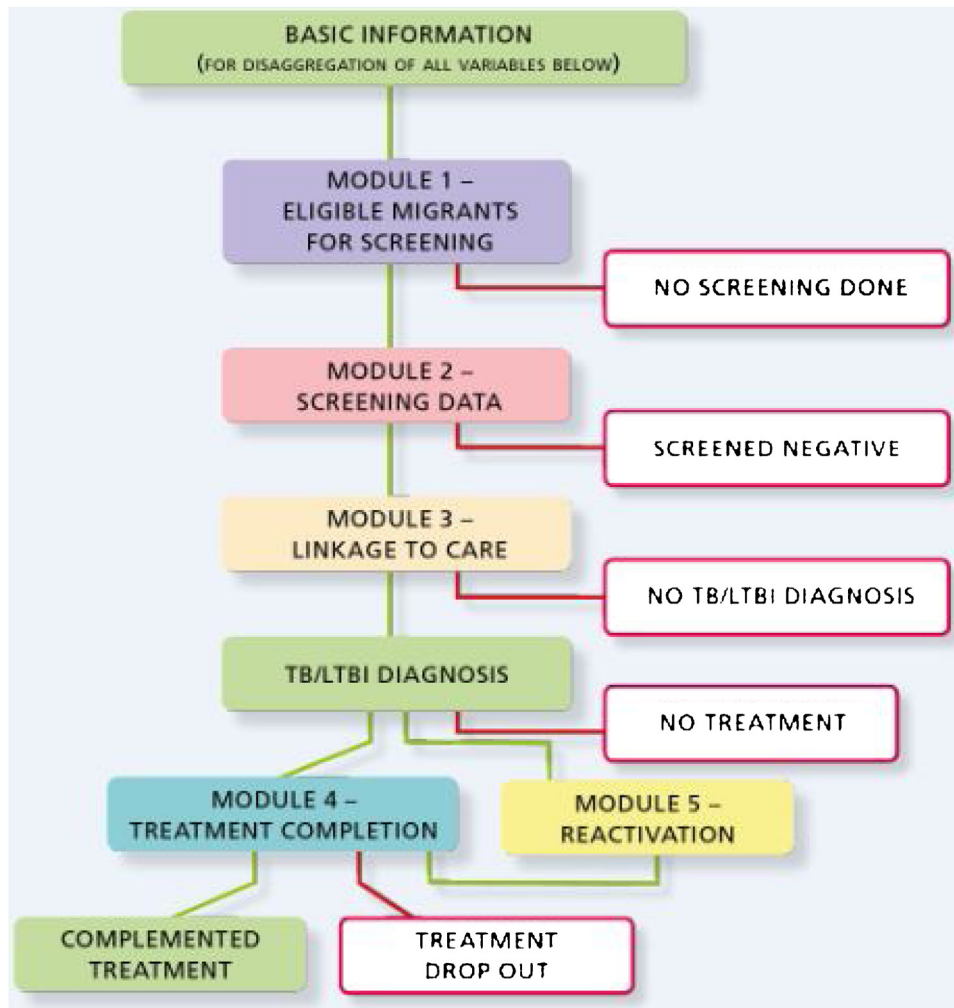


Figure 1. The screening and linkage-to-care cascade.

Participant eligibility

All those included in systematic screening and logged in the national or project databases are eligible for inclusion in the cohort. Data on screening for active TB is available from the UK (pre-migration, for visa applicants) and the Netherlands (post arrival, for selected migrants) on a national level. LTBI screening data is available from England and from selected sites in Italy, the Netherlands and Sweden.

Duration of study

The database was created in 2018. Retrospective data has been transferred from each site from the first year available and at least up to December 2017. Further prospective data will be added yearly. The initial analyses will be performed employing data from 2005 to 2018. In 2019, additional countries will be invited to contribute data. Our vision is that the database will continue to be used in perpetuity.

Data collection

Each partner collects, cleans and recodes the individual level data according to the agreed variable list, before transfer to the joint database. Variation in screening policies, data collection and recruitment make the data somewhat heterogeneous and not all partners contribute to all data modules. The variables essential to the objectives of the project are:

country of screening, screening scheme, sex, age, country of origin, screening performed and screening results. Where available, data on initiated and completed treatment will be included.

For active TB, the Netherlands collect data from national data registry on new immigrants reporting for TB screening at the Public Health Services, whereas the United Kingdom collect data from overseas clinics for pre-entry screening.

For latent TB, Italy and the Netherlands have projects wherein they collect data.

Sweden collects data on migrants invited to a health examination (which includes TB screening) both for attending and declined individuals. The data is collected by use of the invitation and monitoring tool called “Hälsoplan”, which is based on data from a registry kept by the Swedish Migration Authority and data in electronic medical records in Stockholm Region’s Health Services. TB screening results and cascade of care data is extracted centrally from electronic medical records. So far, only data from Stockholm County is included, but additional regions will be invited.

The United Kingdom has an LTBI testing and treatment data collection system wherein data is collated from GP-systems, laboratory systems and secondary care.

Data management and analysis

The pooled data is stored in the Data Safe Haven (DHS) at the Institute of Health Informatics at University College London (UCL)

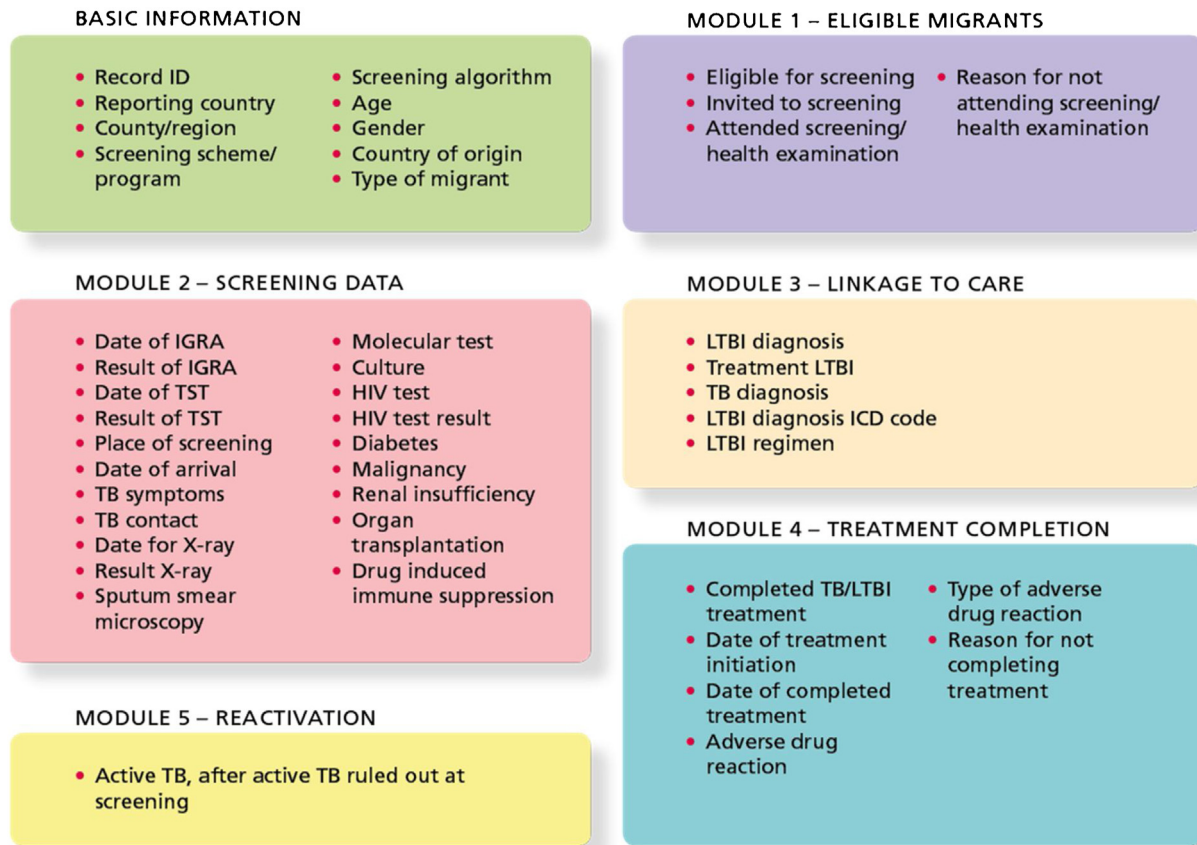


Figure 2. Data modules for the different steps in the screening and linkage-to-care cascade.

(Informatics, 2018). The DSH has been certified to the ISO27001 information security standard and is built using a walled garden approach, where the data is stored, processed and managed within the security of the system. It includes a simple and secure file transfer mechanism (Informatics, 2018). Pseudonymized data (no personal identifiers) is uploaded to the DSH by the data controller/manager for each study partner. To access the DHS an Information Governance training and certification from DSH is needed. Data are transferred, and stored following the principles of the EC Directive on personal data protection and confidentiality, the General Data Protection Regulation (GDPR) (EC/2016/679) (Union, 2018).

The joint database does not include personal identifiers, instead each individual has a serial number. Each partner keeps personal identifiers in the original country or partner database (in accordance with GDPR and local ethics clearance), with a key linking serial number to the personal identifier. This level of anonymity could enable future linkage by a trusted third-party collaborator. Data regarding reactivation will be collated and a research structure for TB reactivation is under development in each country.

The E-DETECT TB steering group is the overall data controller and will decide on all data analysis and presentation, as well as on allowing contribution and access to data for future partners.

Ethical and legal considerations

Measures have been taken to eliminate the risk of identification of individual subjects in the pseudonymized multi-country database, including collapsing country of origin categories when there are only few screened individuals from one specific country. Each partner is responsible for legal and ethical considerations for data extraction, sharing and analysis. The sharing of data follows

the regulations of each respective participating country, and the principles of GDPR (Union, 2018). Data sharing agreements have been established between project partners and UCL, defining data management, access, and safety in line with each institution's and country's regulation.

The UCL partner was approved per the notification of Ethics Approval with Provisos Project ID/Title: 12371/001: Early detection and integrated management of tuberculosis in Europe – EDETECT TB database for Work Package 6. Stockholm Region was granted two ethical approvals and one amendment for this project from the Regional Ethical Review Board in Stockholm (2016/1974-31/5, 2018/1901-32 and 2016/1648-32). Ethics approval for Italian data collection was received from the competent Ethics Committee (Comitato Etico Provinciale di Brescia) (NP 2808 and NP 2901).

Discussion

The present lack of systematically collected and reported, consolidated data on the process and outcomes of systematic screening for active and latent TB hampers the development of policies and guidelines (Pareek et al., 2016; Odone et al., 2015). All EU countries have a national TB registry that includes notified information on individuals detected with active TB. However, LTBI is generally not notifiable, and few countries collect data on the number of persons diagnosed with LTBI, or persons receiving preventive treatment. Absolute numbers for active TB are most often available and absolute numbers of LTBI cases are sometimes available, but denominator data on number of people screened are rarely available, for both active and latent TB (D'Ambrosio et al., 2014; Erkens et al., 2016). Therefore, from existing national and international surveillance systems the number needed to screen to detect one case and contribution to case detection from screening

are mostly unknown. This international collaboration, which is standardizing and pooling available numerator and denominator screening data from several countries provides greater power of analysis of harmonized data.

Data on screening results alone are not enough to assess the public health impact of screening. It is also important to gather data on the completeness of the care cascade from screened to completed treatment and, in case of LTBI, determine rate of reactivation for non-treated and treated individuals (Pareek et al., 2016; D'Ambrosio et al., 2014; Erkens et al., 2016). The present project represents a unique opportunity to obtain such data across several countries.

The establishment of a joint international database necessitates for several technical, administrative and legal challenges to be addressed. A main technical challenge was the lack of a standardized national recording and reporting routines for TB screening. Furthermore, differences between countries with regard to data sources, data variables collected, and definitions used added complexity. In some sites, collecting data from existing data sources in diverse data formats entailed practical and time-consuming challenges. Indeed, by identifying challenges for data extraction and collation, the E-DETECT TB project has already helped improve data availability and quality for some partners. The process of analysing existing data sources and developing the protocol has stimulated discussions on how data recording and reporting can be improved and standardized. For example, the E-DETECT TB project has helped facilitate improvements in the data recording and reporting in Stockholm, where structured data recording for LTBI/TB screening of asylum seekers now includes; the screening done, screening results, country of origin, age and sex as directly extractable variables. Moreover, in the Italian sites the monitoring and evaluation systems for the migrant TB screening has become more standardized and are now fully harmonized with the E-DETECT TB protocol.

Administrative, practical and legal challenges have not been trivial. Collecting and analysing sensitive data of vulnerable groups such as migrants need thorough ethical consideration with sensitivities applied to the responsible presentation of the results. Establishing the necessary permissions, to be allowed to extract data from medical records is a time-consuming process that often includes numerous meetings with involved parties to facilitate a common understanding of the significance of the project. A rigorous data governance and management system has now been set up and agreed as a result of this process. Data ownership and uncertainties on how to share data within and across countries have been thoroughly investigated within the project. A data sharing agreement and protocol that clearly defined responsibility and safeguarding of data was drafted and agreed upon by all members. An agreement that will also be useful for eventual future collaborators.

The database has now been created, data transfer is ongoing, and E-DETECT TB has started to invite other countries to contribute

data to the database. The database will be a useful source of knowledge for EU-members states as well as other countries with a low incidence of TB and a large part of TB cases among the foreign-born population.

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Conflict of interest

No conflict of interest.

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