Early Detection and Integrated Management of Tuberculosis in Europe

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Early diagnosis of tuberculosis

D6.2. Protocol for data transfer and analysis

WP 6 – Multi country latent and active TB in migrants databases

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History of the changes

Version	Date	Released by	Comments
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Definitions and acronyms

CXR	Chest x-ray
ECDC	European Centre for Disease Prevention and Control
E-DETECT	Early Detection and Integrated Management of Tuberculosis in Europe
FoHM	Folkhälsomyndigheten (national public health agency), Sweden
ICD	International Classification of Diseases
IGRA	Interferon-gamma release assay
KI	Karolinska Institutet, Sweden
KNCV	KNCV Tuberculosis Foundation, the Netherlands
LTBI	Latent tuberculosis infection
OSR	Ospedale San Raffaele, Italy
PHE	Public Health England, Department of Health, UK
TB	Tuberculosis
TST	Tuberculin skin test
UCL	University College London, UK
UNIB	Universita Degli Studi di Brescia, Italy
WHO	World Health Organization
WP	Work package

1. Introduction

1.1. General context

Despite international guidelines from ECDC and WHO on screening for tuberculosis (TB), there is no concrete guidance on which migrant sub-groups should be targeted, when and where they should be screened, or on the best approach for implementation of screening programmes to ensure optimal completion of the cascade of care from screening to completion of treatment.[1]

The present lack of consolidated data on the process and outcomes of screening hampers the development of such guidance.[2,3] All EU countries have a national TB registry that includes information on persons detected and notified with active TB. However, few countries systematically collect and report data on active TB or latent TB infection (LTBI) screening. Moreover, comprehensive databases for persons diagnosed and treated for LTBI are rare. While migrant TB screening data is available from selected sites or from research projects and other special initiatives, these data have not previously been collated and analyzed across countries.[4]

1.2. Deliverable objectives

E-DETECT Work Package 6 (WP6) aims to establish a multi-country database on screening for latent and active TB in migrants, corresponding to E-DETECT Objective 3.2: "To collate and evaluate multi-country data on TB in immigrants to low incidence countries."

The first step was for WP6 partners to develop and agree on a protocol for data transfer, analysis, and dissemination. This document contains the agreed protocol.

2. Protocol development steps

2.1. Creation of a steering group

A WP6 steering group was established at the start of the project with representation from each WP6 partner. A series of conference calls have been organized and a face-to-face meeting was held in October 2016. Members of the WP6 steering group are:

KI:	Knut Lönnroth and Maria-Pia Hergens (alternate: Joanna Nederby-Öhd)
FoHM:	Jerker Jonsson
PHE:	Dominik Zenner (alternate:)
UCL:	Rob Aldridge (alternate: Charlotte Jackson)
KNCV:	Connie Erkens (alternate: Gerard de Vries)
UNIB:	Georgia Sulis (alternate: Alberto Matteelli)
OSR:	Emanuele Borroni

2.2. Inventory of existing TB screening data sources

An online survey was conducted in the four countries participating in the E-DETECT project (Italy, the Netherlands, Sweden, and UK) and in four countries (Belgium, Finland, Germany and Norway) showing interest to share migrant screening data with the E-DETECT TB Project. Questions focused on screening policy, available data sources and possibilities to extract and report both numerator and denominator screening data.

The survey confirmed that few countries have national health information systems in place from which TB and LTBI screening data (such as age, gender, and country of origin), the results of screening (abnormal chest radiographs, LTBI test results) and the final diagnosis (TB or LTBI) are captured and can be analysed to evaluate the yield of screening systematically.[2] TB screening policies in the eight countries are summarized in Annex 1.

Among the countries that systematically screen subsets of migrant populations for LTBI, only England has presently a comprehensive monitoring and evaluation system to collect national key indicators (Box 1).

Box 1. Definitions of key indicators for latent tuberculosis infection screening of migrants in England.

Key indicator	**Definition**
LTBI testing and treatment programme coverage	***The number of localities that have a systematic migrant LTBI testing and treatment initiative in place*** The number of localities, which have an LTBI testing and treatment scheme according to service specifications.
LTBI testing acceptance	***Proportion of eligible migrants covered by LTBI testing programmes who accept LTBI testing*** Numerator: the number of eligible migrants, who accept to be tested for LTBI. Denominator: the total number of eligible migrants identified and offered testing.
IGRA test performance and LTBI positivity	***The proportion of positive, negative and indeterminate tests*** Numerator: (a) the number of positive IGRA tests, (b) the number of negative tests and (c) the number of indeterminate tests. Denominator: the total number of tests performed and received by the laboratory.
LTBI treatment uptake	***The proportion of migrants who take up treatment amongst those who have been offered it.*** Numerator: The number of migrants who consent to take treatment and take at least one dose. Denominator: The number of migrants who are eligible for treatment and had an offer of treatment by the appropriate healthcare professional.
LTBI treatment completion	***Proportion of migrants who complete LTBI treatment amongst those who start treatment*** Numerator: the number of migrants who completed LTBI treatment as defined by the treating nurse by routine patient enquiry, pill count and additional measures (such as isoniazid urine test) if required and appropriate. Successful completion is routinely defined as having taken 90% of the prescribed chemoprophylaxis doses Denominator: the number of IGRA positive patients who accept and start LTBI treatment (i.e. individuals have consented to treatment and have taken at least one dose).
Adverse events from LTBI treatment	***The proportion of migrants who experience significant drug events amongst those who initiated treatment.*** The number of patients with significant adverse events (a) overall and (b) significant hepatotoxicity. Denominator: the number of patients who initiated treatment. Proportions should be calculated separately for overall toxicity and hepatotoxicity.

Belgium and the Netherlands compile annual reports on the results of screening among asylum seekers. The Netherlands is currently evaluating the yield and effectiveness of migrant screening for active TB, including asylum seekers, from 2011-2015, which includes 214 000 migrants. In Germany, several federal states currently undertake evaluations of the screening of asylum seekers. In Finland, surveys at reception centres have been used to evaluate screening. Other countries, including the E-DETECT TB project countries, are currently developing systems and tools to monitor and evaluate LTBI screening.

Surveillance of LTBI screening is particularly challenging since notification of this condition (which is non-symptomatic and non-infectious) is rarely compulsory. Special efforts are therefore required to gather such data for the E-DETECT TB project. Opportunities for collection of LTBI screening data in the WP6 partner countries are summarized in table 2.

Table 2. Mapping of available data on latent TB screening in the current E-DETECT TB WP6 countries

	Numerator (number diagnosed with LTBI)				**Denominator (number screened)**			**Numerator and denominator available from at least one national or sub-national source**
	National reporting / notification	ICD registry	Electronic medical record extraction	Laboratory records	Reporting number screened	Electronic medical record extraction	Laboratory records	
England	Compulsory	No	No	No	Compulsory	No	No	Yes
Italy	No	No	No	Project data	Project data	No	Project data	Yes
Netherlands	Voluntary	No	Possible sub-national	Project data	Project data	Possible sub-national	Project data	Yes
Sweden	Voluntary	Yes	Possible sub-national	Possible sub-national	No	Possible sub-national	Possible sub-national	Yes

2.3. Preparation of data collation on national level and development of agreed protocol for data sharing, analysis and dissemination

Within each WP6 partner country there has been a detailed mapping of data sources, data availability and mechanisms for data collation. Based on the mapping, in-depth discussions have been held in the WP6 steering group and within each country to identify appropriate modalities for data sharing and structure of the database.

As mentioned, UK has an existing systems for data collection and collation on national level (For LTBI screening, in England only). The Netherlands collects routine data on screening for active TB, while data on screening for LTBI is being collected within an ongoing research project, which is piloting routine screening. For UK and Netherland, no further development of data collection and collation processes were required.

For Sweden, starting in in Stockholm County, a system for TB screening data extraction from electronic medical records has been developed under the E-DETECT TB project. An inventory of similar systems has been done in all other large counties in Sweden, with a view to gradual expand to national coverage of this model. A national network of representatives from large counties has been set up. The experiences so far show that it is technically possible to extract relevant TB screening data, including data for disaggregation by age, sex and country of origin. However, legal processes to access data owned by the local (county-level) health authorities have been cumbersome and time consuming. Although ethical clearance for data extraction and creation of a database was obtained early, stakeholders on several levels (primary health care delivery, infectious disease control unit and E-health unit) have had to consult with each respective legal department and set up agreements for data sharing.

Italy has created a TB screening data recording and reporting system in selected areas, as part of the activities in E-DETECT TB WP5. The data recording and reporting model in Italy has been informed by the WP6 discussions and is now fully harmonized with the protocol outlined below.

Retroactive data will be available from The Netherlands, UK, Italy (subnational) and Sweden (subnational) at least from January 2016, and then prospectively for the entire project period for all four countries.

3. Protocol for data transfer, analysis and dissemination

3.1. General aims and specific research objectives

The main aim is to collate, pool, analyse and evaluate multi-country data on TB screening in immigrants to low incidence countries to inform effective strategies for early diagnosis of active and latent TB (E-DETECT Objective 3.2; WP 6).

The WP6 partners agrees to create a multi-country database, which will include cross-sectional and longitudinal data on migrants screened for TB and/or LTBI. In this process, the recording and reporting practices for LTBI screening and management will be standardized within and across countries.

Within the timeframe of this project (2016-2019), the analysis of this database will be restricted to the yield of screening and linkage to care in different subgroups. Where historical data exists, reactivation rates will be examined.

This database will build on existing retrospective information, as well as include new standardized prospective data. The project will initially include data from the four low-incidence countries that are represented in E-DETECT; Italy, The Netherlands, Sweden and the UK (England data only). In The Netherlands, Sweden and England, LTBI screening is underway and will be expanded in the near future. In Italy, the LTBI screening is starting in selected sites (see E-DETECT TB WP 5). Other EU countries will be invited to participate once the database has been created.

Once the database has been created, the primary specific research objectives are:

Concerning screening for LTBI

1. To determine screening coverage, target groups and reasons for LTBI screening (data collected by services responsible for LTBI screening, and migration authorities)
2. To determine results of the initial LTBI screening (data collected by services responsible for LTBI screening)
3. To determine LTBI treatment uptake and completion (data collected by LTBI treatment services)
4. To estimate reactivation rates of active TB amongst LTBI screening cohort (collected through data linkage by centers responsible for surveillance of active disease, after the project period).

Concerning screening for active TB

5. To determine screening coverage, target groups and reasons for chest X-ray (CXR) screening for active TB (data collected by services responsible for TB screening and migration authorities)
6. To determine results of the initial chest X-ray screening (data collected by services responsible for TB screening)
7. To determine TB treatment uptake and completion (data collected by TB treatment services)

Basic analyses related to above objectives will be both pooled (e.g. when specific target groups are screening in a similar way in several countries) and comparative (e.g. when different screening approaches are used in different countries.

Further analytical work may include:

- Estimation of the number needed to screen to detect a case of TB/LTBI in different groups and with different screening approaches.
- Trend analyses of screening and detection (within and across countries/sub-groups), and correlations between screening trends, migration trends, and TB incidence trends.
- Use of data to parameterize mathematical models, e.g. to determine:
  - Number of LTBI needed to screen/treat to prevent one case of TB
  - Potential impact of TB/LTBI screening on TB transmission/incidence
  - Cost-effectiveness of TB/LTBI screening).

3.2. Data to be shared

The aim is to share case-based data for migrants screened for LTBI/TB. Since countries are at different levels of implementation, it is recognized that not all countries may be able to provide data relevant to all objectives. The dataset will therefore be divided into different modules representing the increased complexity of data collection.

Where only aggregated data is available, there will be an option to report that instead (see below).

The agreed screening and linkage-to-care cascade of interest is shown in figure 1 and 2.

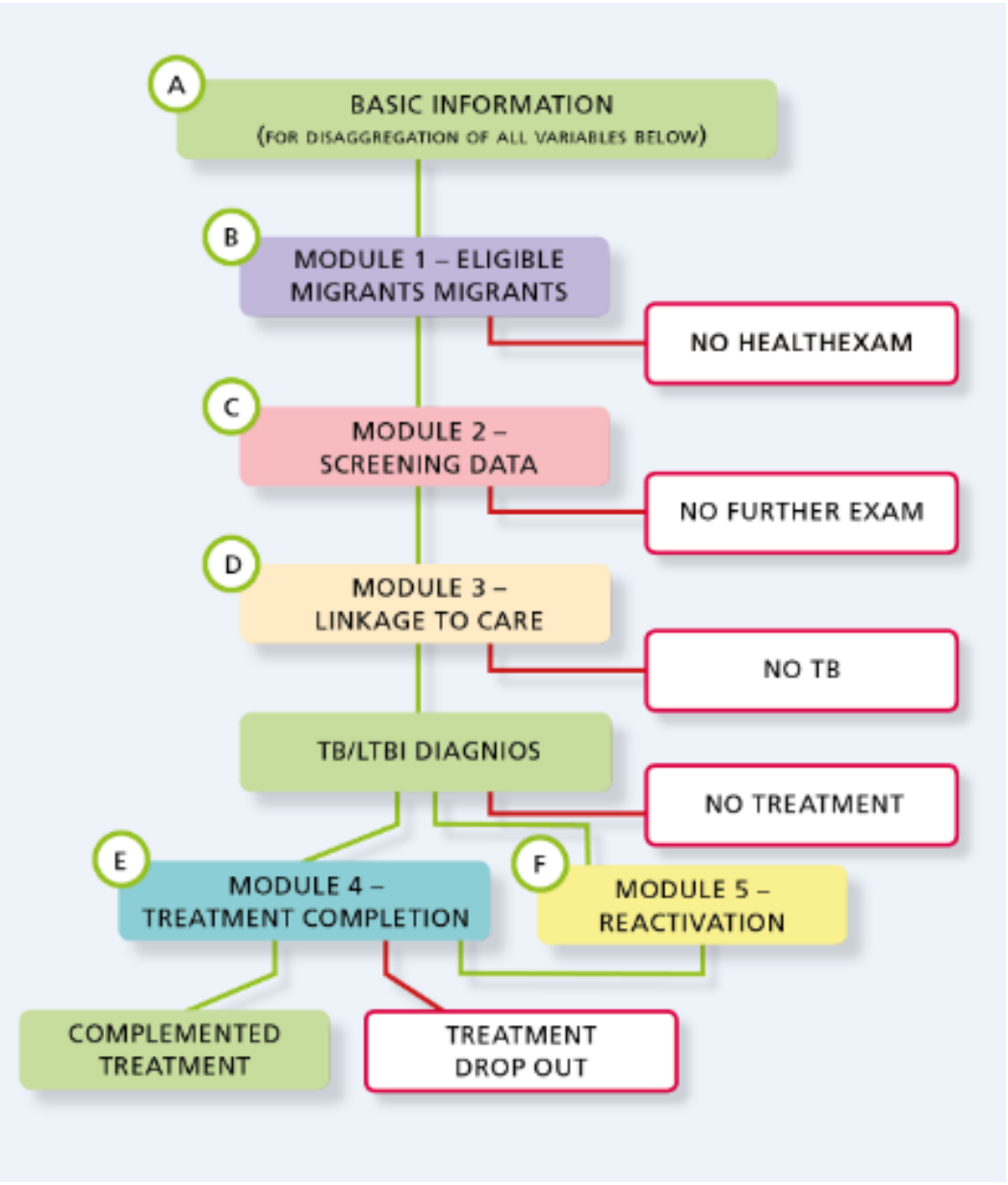

Figure 1. The screening and linkage-to-care cascade

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

Case-based data

The database will include one module for basic information (to enable disaggregated analyses) and five modules representing the screening and linkage-to-care cascade and reactivation. Each country (or region within country) may contribute to one, several or all of them depending on data availability:

- Basic information (for disaggregation of data in below modules)
- Module 1: migrants eligible for screening.
- Module 2: screening data
- Module 3: linkage to care
- Module 4: LTBI treatment completion

- Module 5: reactivation

A detailed list and description of variables is found in Annex 2.

Anonymized data

Only anonymized data should be transferred, following the EC Directive on personal data protection and confidentiality (EC/2016/679).[1] The following principles will be applied:

- No personal identifier (national ID number, social security number, or similar that can be linked to the individual) should be included.
- A record number will be created in the international database which will be linkable back to national register and personal identifier used in each country through a record number key, which should be kept in each country/institution.
- If required, as per country and EU principles for anonymized data, age-brackets will be used instead of age, in order to minimize risk of identification.
- If required, as per country and EU principles for anonymized data, categories for country of origin may be used if only a few individuals from a certain country (e.g. categorized as "Other countries in Africa south of Sahara" rather than Gambia).

Main variables and indicators

Priority will be made for variables that are required for the calculation of essential indicators corresponding to the primary research objectives. However, not all countries can report the required variables for all essential indicators and therefore some of them will be calculated only for a subset of countries.

Essential and useful indicators are listed below. They should, to the extent possible, be disaggregated by:

- Reporting country
- Type of screening scheme
- Country of origin of the screened individual
- Type of migrant
- Age
- Gender

Essential LTBI screening indicators:

- Number of persons screened for LTBI (with IGRA or TST)
- Proportion of those screened who have a positive LTBI test result
- Proportion of those with positive LTBI test result that start LTBI treatment

[1] Preamble No 26 (page 5) states that; "The principles of data protection should apply to any information concerning an identified or identifiable natural person. Personal data which have undergone pseudonymisation, which could be attributed to a natural person by the use of additional information should be considered to be information on an identifiable natural person. To determine whether a natural person is identifiable, account should be taken of all the means reasonably likely to be used, such as singling out, either by the controller or by another person to identify the natural person directly or indirectly. To ascertain whether means are reasonably likely to be used to identify the natural person, account should be taken of all objective factors, such as the costs of and the amount of time required for identification, taking into consideration the available technology at the time of the processing and technological developments. The principles of data protection should therefore not apply to anonymous information, namely information which does not relate to an identified or identifiable natural person or to personal data rendered anonymous in such a manner that the data subject is not or no longer identifiable. This Regulation does not therefore concern the processing of such anonymous information, including for statistical or research purposes."

- Proportion started on LTBI treatment that complete treatment

Useful LTBI screening indicators:

- Disaggregation of above indicators by risk factors, symptoms, contact
- Proportion of eligible migrants that are invited / screened
- Proportion with adverse drug reactions during LTBI treatment
- Reactivation rate

Essential indicators for active TB.

- Number screened with chest radiography
- Proportion of screened who have active TB (by type of TB, and confirmed vs. unconfirmed)

Useful indicators for active TB *(the first two are also essential, but are covered in general surveillance)*

- Proportion of active TB that start treatment
- Proportion started on treatment that complete treatment
- Details about CXR and bacteriological test results

Aggregated data

A separate database is needed for when only aggregated data can be reported. Ideally, aggregated numerator and denominator data should be reported separately, with at least disaggregation for age, sex and country of origin, so that percentage with a positive test, percentage starting and completing treatment, etc, can be compiled. Adjusted and unadjusted averages across countries can then be calculated. A dummy table for possible aggregated data is presented below.

Table. Indicative dummy table for reporting of aggregated data

Reporting	Origin	Age	Migrants		Screening		Positive		Treated		Completed	
			M	F	M	F	M	F	M	F	M	F
Sweden	Somalia	0-15										
		16-35										
		35-60										
		>60										
	Eritrea	0-15										
		16-35										
		35-60										
		>60										
	Etc											
	TOTAL											
England												

3.3. Data transfer, storage and access

Each country will gather data on national level and format the data in Excel as suggested in the Excel document corresponding to Annex 2.

The pooled data will be stored on the Farr Institute of Health Informatics and Research (Farr Safe Data Haven) at University College London, 222 Euston Road, London, NW1 2DA, UK (http://www.farrinstitute.org).[5]

Transfer of data should take place regularly, tentatively every 6 months or every 12 months depending on timing of data availability in each country.

Anonymized data (see above) will be transferred over secured and encrypted internet link or directly to the Farr Safe Data Haven by the data controller/manager for each WP6 partner, or another member of each respective partner appointed by the controller/manager, in accordance with each country's or institution's rules for data transfer.

Anyone uploading data to the Data Safe Haven at UCL, will be required to get a UCL honorary staff contract (to be coordinated by Prof Abubakar's team at UCL, see below) and undergo mandatory information governance training.

The Data controller at Farr will be Dr Robert Aldridge who may delegate some of his responsibilities to appropriately trained members of UCL staff.

A data controller/manager will be appointed in each country, who will be responsible for each country's dataset. Tentatively, the data controllers are the same as the members of WP6 steering group (see below).

The selected members of the WP6 steering group will be able to access the dataset at Farr Institute of Health Informatics and Research through a secured, certified internet connection.

Statistical software possible to use through remote access are specified here: https://www.ucl.ac.uk/isd/itforslms/services/handling-sens-data/tech-soln/software-on-idhs

3.4. Ethical approval and approval of data sharing within and outside the country

Legal and ethical approval for data extraction, sharing and analysis is obtained in all participating countries and institutions. Ethical approval and approval to share data will follow the regulations of each respective participating country, and follow the principles set out in the EC Directive on personal data protection and confidentiality (EC/2016/679).[2]

A data sharing agreement is established between each project partner and Farr Safe Haven at University College London, which defines data management, access, and safety in line with each institutions and country's regulation.

3.5. Data management and analysis

Data cleaning and data management will be coordinated by Dr Robert Aldridge and members of his team at UCL. Data analysis will be coordinated by KI. The WP6 steering group will have to approve all decisions regarding data cleaning and data analysis. A log of decisions taken by the steering group will be kept by KI.

The analysis should follow the aims and objectives and list of indicators listed above. Detailed protocols for specific analysis will be developed during the project period, and these need to be approved by the WP6 steering group.

Once analyses have been completed the data controller/manager for each WP6 partner (or another member of each respective partner appointed by the controller/manager) will then be required to request the export of final tables, results and figures from the Farr Safe Data Haven. This request will be authorized by Dr Robert Aldridge (or an appropriate member of his team) who will check compliance of the exported data with all data sharing agreements and information governance rules before releasing the data.

3.6. Collaborating countries

The database will initially include data from the four countries represented in WP6; England, Italy, Netherlands, and Sweden. Other EU countries will be invited to participate after the database has

[2] Special note is taken of Article 9.2 "**Processing of special categories of personal data":** 1.Processing of personal data revealing racial or ethnic origin, political opinions, religious or philosophical beliefs, or trade union membership, and the processing of genetic data, biometric data for the purpose of uniquely identifying a natural person, data concerning health or data concerning a natural person's sex life or sexual orientation shall be prohibited.
2.Paragraph 1 shall not apply if one of the following applies:
(…)
i) "processing is necessary for reasons of public interest in the area of public health, such as protecting against serious cross-border threats to health or ensuring high standards of quality and safety of health care"
j) "processing is necessary for archiving purposes in the public interest, scientific or historical research purposes or statistical purposes in accordance with Article 89(1) based on Union or Member State law which shall be proportionate to the aim pursued, respect the essence of the right to data protection and provide for suitable and specific measures to safeguard the fundamental rights and the interests of the data subject."

been piloted. Each additional country will have to sign the data pooling agreement and protocol for data transfer sharing and analysis, and will appoint one representative to the steering group.

3.7. Data ownership and governance

All countries and institutions contributing with data will have equal rights to and ownership of the multi-country dataset. However, access to the database will be restricted to persons designated by the WP6 steering group, which will also approve all decisions regarding data cleaning and data analysis.

This will not restrict the ownership and right to perform separate analyses of country/institutional data contributed to the database.

3.8. Publications and dissemination

Results will be published in project reports as per E-DETECT reporting requirements. In addition, results will be published in peer reviewed journals and disseminated at relevant national and international conferences.

The WP6 steering group, as well as the E-DETECT TB steering committee, have to approve final reports before publication and manuscripts prepared for publication in peer-reviewed journals before submission. Reporting of multi-country data in national reports also has to be approved by the WP6 steering group. Countries and institutions which contribute data must be acknowledged in the publications, and representatives should be included as co-authors in accordance of international authorship guidelines.

Peer review by the WP6 steering group and the E-DETECT TB steering committee will ensure that the scientific quality and the arguments discussed in the manuscript are in line with the E-DETECT TB objectives and collaborative principles.

4. Conclusions and future steps

Based on a careful mapping of available data on TB screening and opportunities to improve existing data collection and collation mechanism, the WP6 partners have developed an agreed protocol for data sharing, analysis and dissemination. The database will now be created and data transfer will start quarter 3-4 2017. As per the E-DETECT TB deliverables and milestones timeline, data analysis will start quarter 1 2018.

A main challenge has been the lack of a standardized national recording and reporting of TB screening in several countries, as well as differences between countries in data sources, data

variables collected and definitions used. While identifying challenges for data extraction and collation, the E-DETECT project has already helped improve data availability and quality. The process of analysing existing data sources and developing this protocol has stimulated discussions on how data recording and reporting can be improved and standardized. As mentioned, the monitoring and evaluation systems for the migrant TB screening project in Italy under WP5 is now fully harmonized with the WP6 protocol. Moreover, in Sweden (starting in Stockholm), the E-DETECT TB project has helped facilitate improvements in the data recording and reporting: data recording for TB screening of asylum seekers now includes directly extractible variables on screening done, screening results, country of origin, age and sex, which was previously only in free text in medical records and thus cumbersome to extract and analyse.

The E-DETECT TB project, including WP6, has already been widely disseminated (see list of publications below and E-DETECT TB Internal Report 1). One result of this is that there is growing interest among other member states to become part of the project and share data. Once the database has been created, E-DETECT TB WP6 will formally invite other countries to contribute data to the database, tentatively including Belgium, Denmark, Germany, Norway, and Finland.

We will also seek opportunities to link our database with other existing research databases on TB screening, including data on LTBI reactivation, in order to broaden the scope of pooled analyses.

5. Publications resulting from the work described

Lönnroth K, Zenner D, Abubakar I. Monitoring migrant LTBI screening - a comparative analysis of data sources for surveillance in selected European countries. Abstract presented at the 47th Union World Conference on Lung Health, 26 - 29 October, 2016, Liverpool, United Kingdom.

Lönnroth K, Mor Z, **Erkens C**, **Bruchfeld J**, Nathavitharana R, van der Werf M, Lange C. Tuberculosis in migrants in low-incidence countries: epidemiology and intervention entry points. Int J Tuberc Lung Dis 2017 (in press)

Zenner D, Hafezi H, Potter J, **Capone S, Matteelli A**. Effectiveness and cost-effectiveness of screening migrants for active tuberculosis and latent tuberculosis infection: a narrative review of the evidence. Int J Tuberc Lung Dis 2017 (accepted).

Kunst H, Burman M, Arnesen T, Fiebig L, **Hergens MP**, Kalkouni, R, Klinkenberg E, Soini H, Sotgiu G, **Zenner D, de Vries, G**. Tuberculosis and latent tuberculosis infection screening in migrants in Europe. Int J Tuberc Lung Dis 2017 (accepted).

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2. Lönnroth K, Mor Z Erkens C, Bruchfeld J, Nathavitharana R, van der Werf M, Lange C. Tuberculosis in migrants in low-incidence countries: epidemiology and intervention entry points.. Int J Tuberc Lung Dis 2017 (in press)
3. Zenner D, Hafezi H, Potter J, Capone S, Matteelli A. Effectiveness and cost-effectiveness of screening migrants for active tuberculosis and latent tuberculosis infection: a narrative review of the evidence. Int J Tuberc Lung Dis 2017 (accepted).
4. Kunst H, Burman Matthew, Arnesen T, Fiebig L, Hergens MP, Kalkouni, R, Klinkenberg E, Soini H, Sotgiu G, Zenner D, de Vries, G. Tuberculosis and latent tuberculosis infection screening in migrants in Europe. Int J Tuberc Lung Dis 2017 (accepted).
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Annex 1. Selected EU/EFTA countries TB and LTBI screening policies of migrants to their countries

			Screening for pulmonary tuberculosis		Screening for latent TB infection (LTBI)	
Country	**Migrant group**	**Age (in years)**	**WHO estimated TB incidence in country of origin (per 100 000)**	**Main screening method**	**WHO estimated TB incidence in country of origin (per 100 000)**	**LTBI screening test**
Belgium	Asylum seekers	<5 or pregnant	All	CXR for those with LTBI	All	TST
		≥5 (excl. pregnant)	All	CXR[1]	N/A	None
	Other migrants		N/A	None	N/A	None
Finland	Asylum seekers	All	>50 or from conflict areas <50 (Syria, Iraq)	CXR	N/A[2]	None
	Other migrants	All	>50	CXR	N/A	None
Germany	Asylum- seekers in community/ reception centres	<15 or pregnant	All	Initial TST/IGRA followed by further active TB diagnostics for those positive	N/A	None[3]
		≥15 (excl. pregnant)	All	CXR	N/A	None
	Other migrants	N/A	N/A	None	N/A	None
Greece	Asylum seekers/ undocumented migrants in reception centres	All	All	Interview[4]	N/A	None
	Asylum seekers entering hosting structures	All	All	CXR[4]	All	TST
	Other migrants	All	All	CXR [4]	All	TST
Italy	Asylum seekers and other migrants	N/A	N/A	[5]	N/A	None
Netherlands	Asylum seekers	<18	>50	CXR	>50 (not yet implemented)[2]	Not yet decided
		≥18	>50	CXR[1]	N/A	None

	Other migrants	<18	>50	CXR for those with LTBI	>50	TSTor IGRA
		≥18	>50	CXR[1]	N/A	None
Norway	Asylum seekers	<15	All	CXR for those with LTBI	All	IGRA
		15-34	All	CXR	>200[6]	IGRA
		≥35	All	CXR	N/A[6]	None
	Other migrants	<15	>40	CXR for those with LTBI	>40[6]	IGRA
		15-34	>40	CXR	>200[6]	IGRA
		≥35	>40	CXR	N/A[6]	None
Spain	Asylum seekers and other migrants	All	High incidence countries[7]	CXR for those with LTBI	High incidence countries[7]	TSTor IGRA
Sweden	Asylum seekers	All	>100	CXR for those with LTBI	>100[8]	TST or IGRA
	Other migrants	N/A	N/A	None	N/A	None
Switzerland	Asylum seekers	All	All	Interview	N/A	None
	Other migrants	N/A	N/A	None	N/A	None
United Kingdom	Long stay migrants[9]	<11	>40	Interview (pre-entry)	>40	TST or IGRA
		11-15	>40	CXR (pre-entry)		
		16-35	>40	CXR (pre-entry)	>150	IGRA
		>35	>40	CXR (pre-entry)	N/A	None

Abbreviations: CXR = chest x-ray; IGRA = Interferon Gamma Release Assay; LTBI = Latent tuberculosis infection; N/A = not applicable; TB = tuberculosis; TST = Tuberculin Skin Test; WHO = World Health Organization

Note: A positive TST test is often followed by an IGRA test in several countries.

[1]Belgium and the Netherlands offer half-yearly follow-up CXR screening for 1 and 2 years respectively to migrants from high-incidence countries

[2]In Finland and the Netherlands, LTBI testing is currently only offered to children <7 years and <12 years respectively, if a BCG scar is absent and the TST is negative

[3]In Germany there is officially no LTBI screening, TST and IGRA is used for active TB screening

[4]In Greece, all undocumented migrants/ asylum seekers at reception centres are screened for active TB. Refugees and asylum seekers entering hostels and documented migrants entering on visas longer than six months are screened for active TB/ LTBI

[5]Although no national policy, triaging on symptom followed by CXR or sputum examination is done in several centres in the country

[6]Plus Eritrea and Afghanistan. In addition, LTBI testing is recommended in Norway to all migrants with medical risk factors for progressing to TB-disease.

[7]Arrived to the country < 5 years ago. In Catalonia high incident country is defined more than three times the local TB incidence

[8]LTBI testing in asylum seekers ≥35 years in Sweden is to identify those eligible for CXR screening, not for preventive treatment.

[9] NICE recommendations, not programmatic screening

Annex 2. Variable list for the E-DETECT TB WP6 multi-country pooled database

	Variable	Description	Answer categories
Basic information (for disaggregation of all variabled below)	Record ID	Unique identifier for each record within international database linkable to the national surveillance system through key kept in each country	######
	Reporting country	The country reporting the record.	Country name
	Region/province/county/district	The geographical region within country that reported	Region name
	Screening scheme/programme	Categorized schemes when several exist in a country, e.g. pre-migration (England) or E-DETECT project (Italy)	##, Coded, with explanation
	Screening algorithm	Categorized algorithm when several exist in a country	##, Coded, with explanation
	Age at arrival in country	Age corresponds to the age of the person att arrival to recieving country	##
	Agegroup, at arrival in country	Age corresponds to the age of the person att arrival to recieving country	age groups: 0-4, 5-14, 15-24, 25-34, 35-44, 45-54, 55+
	Age at screening		##
	Agegroup, at screening		age groups: 0-4, 5-14, 15-24, 25-34, 35-44, 45-54, 55+
	Gender	Common variable. Transsexual coded as O - Other	male, female, other, unknown
	Country of origin	Identifies the country where the patient was born. Countries are defined by their current borders. For patients born in countries which do not exist any more, please use the code of the closest current country.	Country name, or ##, Coded
	Type of migrant		Category name, or ##, Coded
Module 1 - eligible migrants	Eligible for screening	Belongs to the target group for screening	yes / no
	Invited to screening		yes / no
	Attended screening / health examination	Attending, with or without doing LTBI test	yes / no
	Reason for not attending		Category name, or ##, Coded

Module 2-screening data	IGRA done		Not done/ done but no result / done with result / unknown
	Date of IGRA	The most complete date should be provided. Exact date is preferred. If not available it should be coded as Unk.	YY/MM/DD
	Result IGRA, pos/neg	Using the cut off defined by the manufacturer	positive / negative
	Result IGRA, value		##
	TST done		Not done/ done but no result / done with result / unknown
	Date of TST	The most complete date should be provided. Exact date is preferred. If not available it should be coded as Unk.	YY/MM/DD
	TST result, pos/neg	As per cut-off for country/risk group	positive / negative
	Result TST, value		##
	Place of screening	Ambuloatory, primary care or specialist care	Category name, or ##, Coded
	Date of arrival	The most complete date should be provided. Exact date is preferred. If not available it should be coded as Unk.	YY/MM/DD
	TB symptom	Yes= any of the following: cough, fever, night sweats, weight loss, (or as deined in country)	yes / no
	TB-contact	Close (family?) contact with person with TB	yes / no

	Chest X-ray done		Not done/ done but no result / done with result / unknown
	Date for chest X-ray	The most complete date should be provided. Exact date is preferred. If not available it should be coded as Unk.	YY/MM/DD
	Result of chest X-ray		normal, suspect TB, other abnormalities
	Sputum smear microscopy		pos / neg / not done / unknown
	Molecular test		pos / neg / not done / unknown
	Culture		pos / neg / not done / unknown
	Hiv testing		Tested / not tested / unknown
	HIV test result	HIV status; previous positive test.	Positive / negative / unknown
	Diabates	Type 1,2, other	Diagnosis reported / not reported / unknown
	Chronic lung disease		Diagnosis reported / not reported / unknown
	Kidney disease	including dialysis, transplant and CKD	Diagnosis reported / not reported / unknown
	Immunosuppression	including on immunosuppressive therapy	Diagnosis reported / not reported / unknown
	Liver disease		Diagnosis reported / not reported / unknown
	Smoking	Current, former, never	Current, former, never

Module 3 - linkage to care	LTBI-diagnosis	Regardless of treatmentindication, active TB ruled out	yes / no / unknown
	Date for LTBI diagnosis	The most complete date should be provided. Exact date is preferred. If not available it should be coded as Unk.	YY/MM/DD
	Treatment LTBI	Treatment prescribed/initiated	yes / no / unknown
	LTBI regimen		6h, 9h, 3RH, 4R, 2RHZ(E)
	TB-diagnosis	Case classification according to EU TB case definition	##, coding of case classification according to EU TB case definition
	Date for TB diagnosis	The most complete date should be provided. Exact date is preferred. If not available it should be coded as Unk.	YY/MM/DD
	TB treatment		##, coding of regimens

Module 4 - LTBI treatment completion	Completed LTBI treament		yes / no / unknown
	Date of treatment initiation	The most complete date should be provided. Exact date is preferred. If not available it should be coded as Unk.	YY/MM/DD
	Date of completed treatment	The most complete date should be provided. Exact date is preferred. If not available it should be coded as Unk.	YY/MM/DD
	Adverse drug reaction	Symptoms and signs related to drug reaction, resulting in treatment interruption or change of therapy	yes / no / unknown
	Type of adverse drug reaction		Hepatic disfunction Neurological dysfunction Psychological dysfunction Visual impairment Allergy Joint pains Other
	Reason for not completing treatment		adverse events, decision of patient to stop, active TB, unknown
Module 5 - reactivation	Active TB, after active TB ruled out at screening	Active TB recorded in national TB registry	yes / no / unknown
	Date of active TB, after active TB ruled out at screening	Date of active TB recorded in national TB registry	YY/MM/DD