Early Detection and Integrated Management of Tuberculosis in Europe

PJ-03-2015
Early diagnosis of tuberculosis

D5.4
Asylum seekers screening completed and available for analysis

WP 5 – Migrant TB detection, prevention and treatment

Due date of deliverable	Month 36 – 2 June 2019
Actual submission date	14/ July/ 2019
Start date of project	3 May 2016
Duration	36 months
Lead beneficiary	UNIBS
Last editor	Alberto Matteelli
Contributors	OSR, INMI
Dissemination level	*PP*

This project E-DETECT TB has received funding from the European Union's Health Programme (2014-2020) under grant agreement N°709624.

History of the changes

Version	Date	Released by	Comments
1.0	14-07-19	Alberto Matteelli	

Table of contents

Note: Make sure to update and format the Table of contents, and to do so with each version change

TABLE OF CONTENTS **2**

KEY WORD LIST **3**

DEFINITIONS AND ACRONYMS **3**

1. INTRODUCTION **3**

1.1. GENERAL CONTEXT 3

2. METHODOLOGICAL APPROACH **4**

3. SUMMARY OF ACTIVITIES AND RESEARCH FINDINGS **5**

3.1. RETROSPECTIVE COHORT ANALYSIS 5

3.2. PROSPECTIVE CO-HORT ANALYSIS 6

3.3. ELECTRONIC DATA COLLECTION SYSTEM 7

4. CONCLUSIONS AND FUTURE STEPS **7**

5. PUBLICATIONS RESULTING FROM THE WORK DESCRIBED **8**

Key word list

Asylum seekers
Latent tuberculosis infection
Screening
Preventive therapy

Definitions and acronyms

Acronyms	Definitions
TB	Tuberculosis
LTBI	Latent tuberculosis infection
TST	Tuberculin skin test
IGRA	Interferon gamma release assays
MHC	Migrant health clinic
TBU	Tuberculosis unit
TH	Tertiary hospital

1. Introduction

- *Give a synthetic introduction to the matter dealt with in the deliverable (quote the number and title of the deliverable)*
- *Situate the deliverable with respect to the general objectives of the Project and the tasks associated to the deliverable*
- *State and make clear the specific objectives of the deliverable*

1.1. General context

There is no national Italian policy for the screening of tuberculosis (TB) and latent tuberculosis infection (LTBI) in immigrants and asylum seekers entering Italy. The responsibility for planning and implementation of such activities is devolved to the regions (21 in Italy) with significant diversity between regions.
According to the Italian health regulations, asylum seekers have access to free healthcare, including TB care, immediately after landing on the Italian coasts, in ports and in first reception centres. According to the regional health system regulations in Lombardy, all asylum seekers should undergo voluntary and free of charge screening for TB and LTBI upon relocation in hosting centres.

In our intervention area (the province of Brescia), TB and LTBI screening are performed in a network of health facilities. The first evaluation is carried out at a single first level structure (Migrant Health Clinic - MHC) immediately after immigrants' arrival. Individuals with a positive screening test are referred to a single second-level structure (TB clinic - TBU) for further investigations and to receive treatment and follow-up for LTBI. Individuals with presumptive TB are eventually referred to the only third health care level (tertiary hospital TH) for final confirmation and treatment as necessary. All the healthcare structures belong to the same administration, but they have separate management, as well as independent data recording systems. Social staff at accommodation centres ensure referral of individuals from one level to the other, as necessary. Strategies for overcoming language barriers during consultations include the presence of a cultural mediator, as well as the selection of English or French-speaking healthcare workers.

As initial step of our activity we made a retrospective analysis of TB and LTBI screening practices in Brescia, during a 2-year period (2015-2016).
Eventually, based on the results of the above analysis, and as part of the E-DETECT project activities, we conducted a research project aimed at the improvement of the local health structure for TB and LTBI screening in asylum seekers and measured the effect of such changes on the screening program indicators.

2. Methodological approach

This work was conducted in Brescia, Northern Italy, an urban setting with a population of about 200,000 inhabitants with 12.9% of foreign-born residents.

Retrospective cohort analysis
Our retrospective cohort analysis was conducted in 11 structures belonging to the Italian Protection System for Asylum seekers and 34 additional hotels and apartments (extraordinary reception centre, specifically recruited by the Prefecture.
All asylum seekers deployed in the study area from 1st January 2015 to 31st December 2016 were included in the analysis. Our population was largely African, due to the fact that migrants arrived through the central Mediterranean route, while other European countries have faced the flow of migrants arriving through the Balkan route, strongly related to the Syrian crisis.

All asylum seekers were first investigated at MHC for active TB through a standardized verbal questionnaire to look for the presence of any one of the following symptoms and signs: fever of one-week duration, cough lasting two-weeks, night sweats, weight loss and haemoptysis. Screen-positive individuals were referred to TBU for chest X-ray examination. Those with abnormal chest X-ray were referred to TH for microbiological investigations, including Xpert MTB-RIF, culture, microscopic examination, and any additional investigation as appropriate for the individual case. Cases of TB were managed as inpatients or outpatients, as appropriate, until treatment completion.
Screen-negative individuals continued the medical evaluation at MHC with LTBI screening based on the administration of the tuberculin skin test (TST). Individuals with positive TST were referred to TBU

for a chest X-ray and clinical evaluation. Those with no radiological abnormalities or clinical signs were considered eligible for preventive therapy that was mainly based on 6 months of daily isoniazid.

A database was constructed by manually merging individual databases available at MHC, TBU, and TH, based on the list provided by the Prefecture.
TB cases were identified by matching the list of individuals in our cohort, with the register of notified TB cases. Data censoring was performed on May 30th, 2017.
TB prevalence was calculated as the rate between the number of notified TB cases occurring within 6 months from arrival and the number of all asylum seekers/100,000. TB incidence was calculated as the rate between the number of notified TB cases occurring after 6 months from arrival and the number of all asylum seekers/100,000 person-years. The time of follow-up used for the calculation of TB incidence was measured as the difference between six months after the time of arrival in Brescia and the time of the event (TB) or censoring.

Prospective cohort analysis

The prospective study was conducted between 2017 and 2018 to measure TB incidence and prevalence, LTBI rate, screening uptake, and LTBI treatment completion LTBI under modified health structure organization.
The intervention consisted in the use of a "client-centred approach", the decentralized and fragmented health care delivery system for asylum seekers screening was replaced (by a centralized one (one single site for all steps of the screening programme).
In this intervention, LTBI screening was performed > 6 months after arrival, based on tuberculin skin test (TST), read after 72 hours. On the initial day a chest X-ray was performed as necessary. At 72 hours the TST was read, and IGRA performed in case of positive result. Those with a positive IGRA and negative chest X-ray are considered and eventually offered preventive therapy (HR 3Mo, shorter treatment).
Outcomes were compared with those of the decentralized approach as measured in the retrospective analysis (see above).

3. Summary of activities and research findings

3.1. Retrospective cohort analysis

Of the 2,567 screened asylum seekers, 63 (2.4 %) reported possible symptoms/signs of TB at the verbal questionnaire. Among them, 27 (43.6%) completed diagnostic investigations with a documented chest x-ray. The radiological coverage for screen-positive cases was clearly inadequate.

Overall, 18 new TB cases were notified in our cohort. All of them originated from African countries. Eleven cases were confirmed by culture and 9 isolates were susceptible to rifampicin and isoniazid. All were offered and started standard TB therapy. Based on the timing of onset, 14 were classified as prevalent TB cases, with a TB prevalence rate of 545 / 100,000 persons (95%CI: 298 - 913).

TB screening was performed by symptoms investigation s recommended by national and international bodies. The yield of this approach was as low 155 / 100,000, and it captured only 28.6% of prevalent TB cases. The screening tool demonstrated to be inaccurate as symptoms were absent in the majority of notified prevalent TB cases at first evaluation. Screening yield was inferior to the pooled yield of 304 (95% CI: 224–396) per 100,000 reported in a recent meta-analysis by Bozorgmehr et al. where, however, chest X-ray was also used as initial screening tool.
TB prevalence in our cohort was higher than the weighted average incidence in countries of origin. Several factors related to migration travels (i.e. precarious living conditions in crowed camps, living in prisons in transition countries, increased risk of acquiring HIV or comorbidities) might account for this observation.
The time between screening and TB diagnosis in the 14 prevalent cases was 47 days. Treatment initiation was significantly delayed, potentially leading to increased transmission in the community and secondary cases.
The cohort for TB incidence calculation consists of 2,433 individuals with no prevalent TB and a follow-up time of at least 6 months. The total follow-up time was 1,818.6 years beyond the first 6 months, the mean follow-up time was 273 days (range 1 – 841 days), and TB incidence was 220 / 100,000 individuals / person-years (95%CI: 60 - 563). Three out of four incident TB cases were TST negative upon arrival, which points to a recent infection transmission either in countries of transit or in Italy.

The LTBI screening uptake was completed by about three-quarters of the eligible persons. However, one-half of the individuals with a positive TST was not further investigated, and only 10.8% of them eventually completed treatment.
Easier access to radiological examination to exclude active TB by improved integration of services could significantly reduce losses. Further significant losses occurred in treatment uptake with many potentially eligible individuals not starting treatment due to a clinical decision. Such provider-related barrier could benefit from strengthened training and supervision.

These data show a very high rate of loss to follow-up among screen-positive individuals. LTBI screening and treatment uptake losses were mainly attributed to the defragmentation of healthcare services coupled with the absence of a recording and reporting system.

3.2. Prospective co-hort analysis

To overcome the problems identified in the pre-intervention analysis (defragmentation of healthcare services coupled with the absence of a recording and reporting system) we modified the screening procedures and established an independent recording and reporting system.

Preliminary results were obtained comparing 145 asylum seekers enrolled in the intervention (centralized approach) with 1,211 controls. The groups were comparable, except for the place or origin, with more persons from Africa in the intervention group (93% vs, 74%).

The centralized approach allowed for a 100% increase in the screening pick-up (from 49% to 98%).
Treatment initiation rate was very high in the intervention arm: of 43 eligible asylum seekers 42 initiated treatment. Treatment initiation rate increased by 100% from 48% to 97.7%

3.3. Electronic data collection system

A mobile-Health device, the E-DETECT TB App (to be used on mobile phones) was designed and finalized to help data recording and reporting. A touch screen icon-based application for Android smartphones was designed and developed following the WHO guidelines for active TB and LTBI screening. The app is now available in English, and it is structured in five modules:

1. A questionnaire including:
   - -patient identification and informed consent
   - Socio-demographic data, personal information, migration information
   - Past medical history (relevant for the screening pupose)
   - Risk factors such as smoking, alcohol, intravenous drug use, diabetes and HIV
   - TB symptoms (cough, fever, haemoptysis, night sweats, weight loss)
2. Microscopy section
3. Other investigations for TB diagnosis
4. LTBI section
5. Treatment and follow-up

Data are stored in the smart-phone and immediately transferred to the cloud, hosted at San Raffaele Hospital, Milano. Data stored in the cloud can be directly exported for analysis. The application allows an easy on-spot data recording, the data monitoring and the direct exportation of all the data collected in a Excel database for epidemiologic and scientific analysis. Data recorded with the phone App are organized in patient's personal schedule.
UNIBS contributed by developing the LTBI section of the software.
The software was piloted in the intervention trial in Brescia and proved to be a suitable tool for monitoring of the activities.

4. Conclusions and future steps

Please summarise in a concise and very clear way the status of the work in relation with the overall goals of the project

Work-package 5 aimed at elucidating cost-effective approaches to decrease TB morbidity among asylum seekers in EU countries. Italy was selected as the country of implementation as it acts as the point of entry for a significant proportion of immigrants entering Europe.
We performed interventions to test different approaches for the screening of TB and LTBI in a relocation centre in Brescia, Lombardy (North of Italy).

We initially measured, in a retrospective study, the efficiency of the system in place and we found low completion rates for the screening process and low initiation and completion rates for preventive therapy.
In an interventional phase of the project we comparatively assessed the performance of a "centralized" screening system for TB and LTBI. In a preliminary analysis, this intervention allowed for a very significant increase in the proportion of asylum seekers completing screening, and initiating and completing preventive therapy.
We finally adopted an original e-health device for registration of project activities, as a prototype for a regional LTBI surveillance system (currently not available) and we found it acceptable and efficient in our pilot project.

5. Publications resulting from the work described

1. Pontarelli A, Marchese V, Scolari C, Capone S, El-Hamad I, Donato F, Moioli R, Girardi E, Cirillo DM, Castelli F, Matteelli A. Screening for active and latent tuberculosis among asylum seekers in Italy: A retrospective cohort analysis. Travel Med Infect Dis. 2019 Jan - Feb;27:39-45. doi: 10.1016/j.tmaid.2018.10.015.

2. Barcellini L, Borroni E, Cimaglia C, Girardi E, Matteelli A, Marchese V, Stancanelli G, Abubakar I; members of the E-Detect TB Consortium, Cirillo DM. App-based symptoms screening with Xpert MTB/RIF Ultra assay used for active tuberculosis detection in migrants at point of arrivals in Italy: The E-DETECT TB intervention analysis. PLoS One. 2019 Jul 1;14(7):e0218039.