Early Detection and Integrated Management of Tuberculosis in Europe

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Early diagnosis of tuberculosis

D3.3
Migration Screening Evaluation in Italy

WP 3 – Evaluation

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History of the changes

Version	Date	Released by	Comments
0.1	27/07/2019	Ibrahim Abubakar	First version for submission: subject to further update

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Definitions and acronyms

Acronyms	Definitions
TB	Tuberculosis

1. Introduction

1.1. General context

The E-DETECT Tuberculosis (TB) consortium is a European Commission co-funded group which brings together world leading TB experts in national public health agencies (Sweden, United Kingdom, Dutch, Italy and Romania), with industry (Delft diagnostics) and major academic centres (UCL, Karolinska, SMI, OSR, UNIBS). The composition of the consortium also reflects the incidence of TB in different European countries.

The overall objective of the consortium is to contribute to a decline, and the eventual elimination of TB, in the EU. Specific objectives include:

1. To ensure **early diagnosis** in vulnerable populations- defined as **homeless individuals, Roma, those with a history of drug use** within the **community, and prisoners-** in two high incidence European countries (Romania and Bulgaria). This will be done by an outreach mobile digital x-ray screening van equipped with automated x-ray reading equipment and rapid molecular diagnostics.
2. To evaluate approaches to consolidate **migrant TB detection** and improve European **cross-border management** by:
    a. producing new feasibility data on **early detection and care integration** in individuals arriving via the Mediterranean sea in Italy using innovative molecular testing at immigration
    b. collating, analysing and evaluating multi country data on TB in **migrants** to low incidence countries to inform effective strategies for **early diagnosis** of active and latent TB in low incidence EU countries (Work Package [WP] 6).
    c. ensuring **cross-border** transfer of information and referral of patients, especially migrants dispersed through EU coordinated activity and patients with multi-drug resistant TB (WP 5 and 6).
3. To support the development of action plans in member states by taking best practice approaches from countries where E-DETECT TB partners have developed national and international strategies and evidence from this project and providing a framework, in

collaboration with ECDC, to support the adaptation and implementation of these measures across other EU member states.

Successful delivery of all programmes should result in a substantial impact on EU TB incidence; we are aiming to reduce the overall European incidence reducing the number of cases annually from about 67,000 to 54,000 over the programme implementation period and beyond due to earlier detection and integrated care in high-risk groups.

A key deliverable for this project is therefore the **implementation and evaluation migrant TB detection in Italy and early diagnosis of active and latent TB in migrants in low incidence countries.** In this setting, further decline of TB incidence can only be achieved by intervention in migrant populations who account for the majority of new TB notifications. Lessons would be identified that are applicable to low incidence countries with a high migrant TB burden in the EU. The screening of migrants immediately on arrival will have a direct effect of early diagnosis on the 20,000 migrants we plan to screen in Italy leading to an increase in quality of life with an estimated gain of 0.05 quality adjusted life years per person diagnosed early and nearly 1 quality adjusted life year for cases prevented. The work programme in Italy will help identify the optimal strategy for targeting vulnerable migrants arriving via the Mediterranean Sea, with particular emphasis on strengthening of cross-border interventions.

1.2. Deliverable objectives

The main objective of this deliverable is to undertake a cost-effectiveness analysis to inform an economic evaluation of the programme and assess value for money. The objective of the cost effectiveness analysis is the estimation of the cost per case of active TB detected.

2. Methodological approach

Around 3,000 Tuberculosis (TB) cases are diagnosed in Italy each year, of them more than 50% (mainly with MDR TB) occur in the foreign-born population. EDETECT-TB program in Sicily Italy aimed at implementing and evaluating active TB screening in the migrant population at point of entry in the

country. Between November 2016 and December 2017 newly arrived migrants at point of arrivals in Sicily, were screened for active TB using a smartphone application, and in symptomatic individuals followed by fast molecular test (Xpert MTB/RIF Ultra) on collected sputum samples.

For cost-effectiveness analysis, a decision tree model, which represents the screening and diagnosis pathway, was developed to estimate cost per case of active TB detected, compared to the status-quo or no screening. Data were fully anonymised. All analysis was carried-out in the software Microsoft Excel.

The cost analysis was conducted from the (programme) provider perspective. The costs included were the salaries of nurses and medical doctors involved in the administration of the symptom screening questionnaire, collection of the sputum samples and the clinical evaluation of tests results, transportation costs to deliver the samples from Sicily to the analysis lab in Milan and the Xpert test cost. Details of the cost data collected are reported in Table 1.

Table 1. Costs per sample and salaries per activity duration.

Activity	**Average time (minutes)**	**Average hourly rates (€)**
Nurse administering the questionnaire	5 minutes	13.04
Nurse collecting sputum sample	10 minutes	14.02
Medical doctor clinical evaluation of positive/information	30 minutes	35.90
Activity	**Average number of samples**	**Average rate per trip (€)**
Courier charges	60 per trip	50.00
Test	**Cost per test (€)**	
Xpert MTB	58.91	

Probabilities were calculated according to the trial pathway reported in Figure 1 and reported in Table 2.

Figure 1. Screening pathway. From 3787 patients screened, a total of 18 active TB cases were detected.

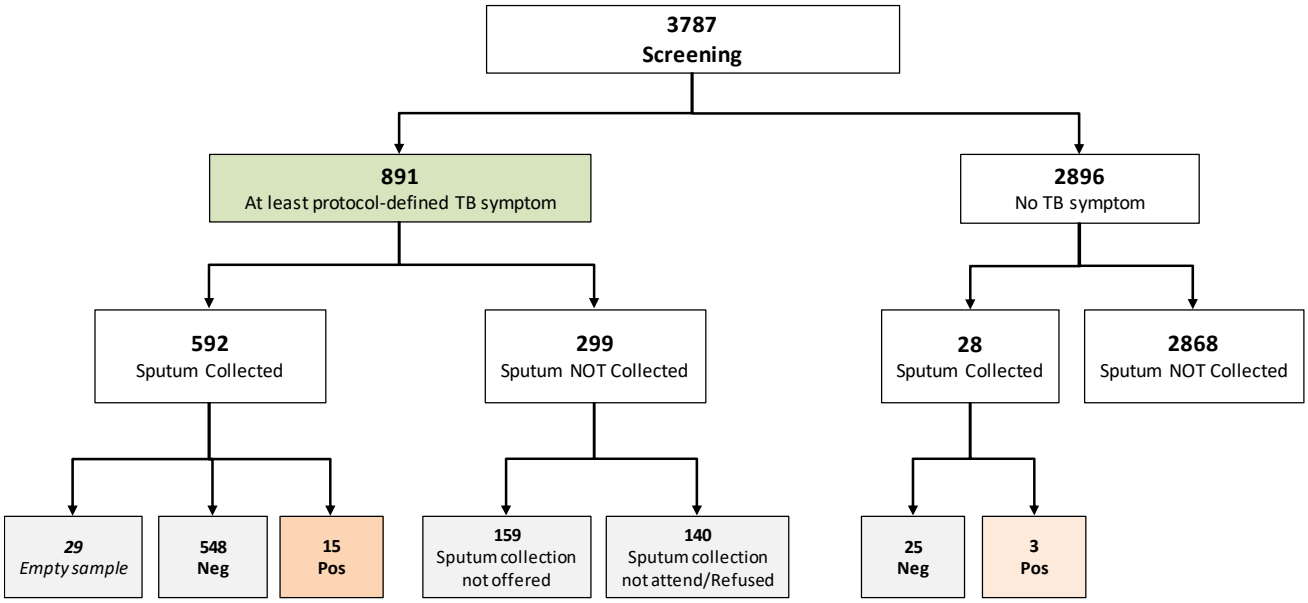
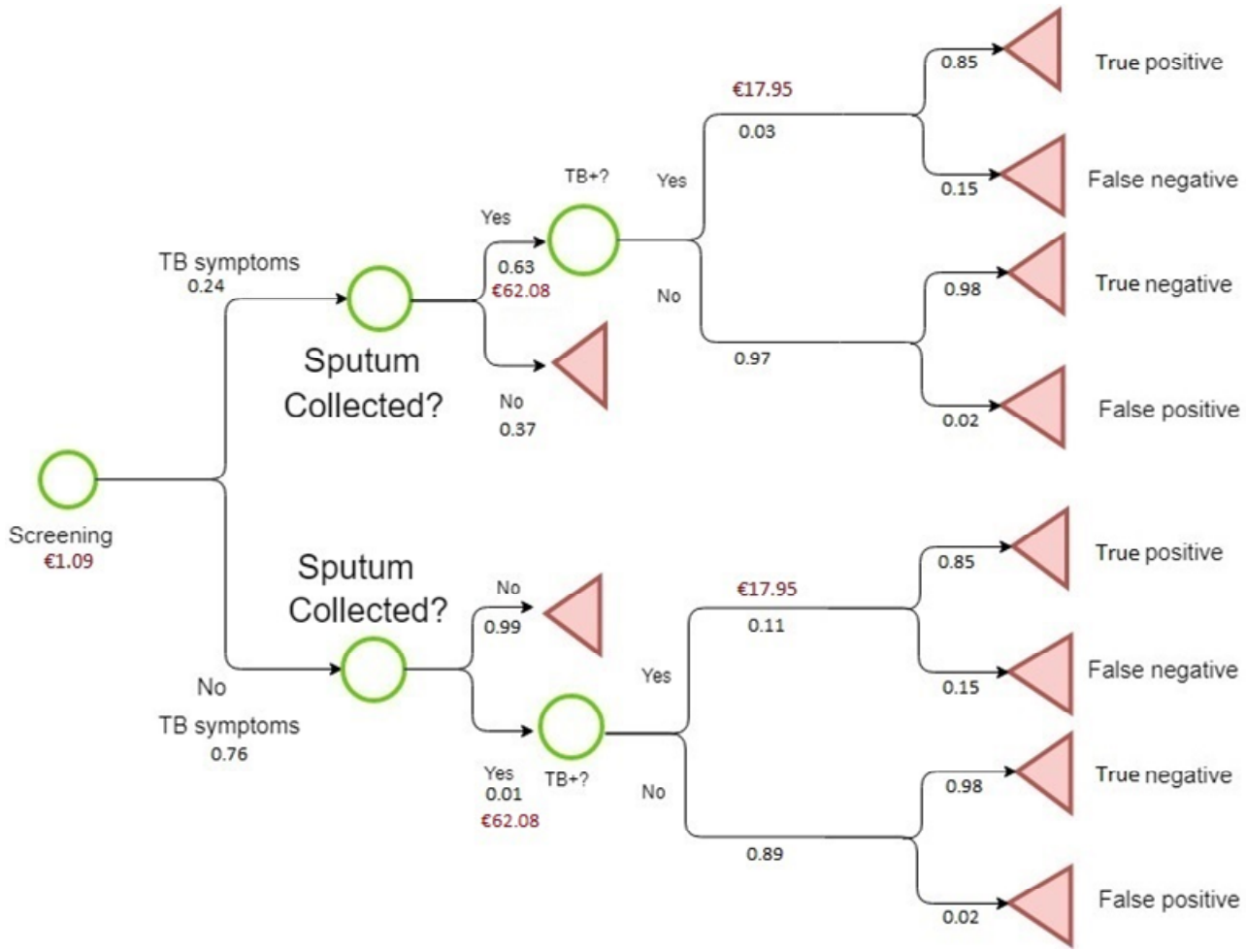


Table 2. Probabilities of model parameters.

Parameter	Probability (uncertainty)	Source/Reference
Presence of TB symptoms	0.24	EDETECT study
Xpert MTB/RIFsensitivity	0.85 (95% CI 0.82–0.88)	(Shiying et al. 2017)
Xpert MTB/RIF specificity	0.98 (95% CI 0.96–0.98)	(Shiying et al. 2017)
Offer and acceptance to TB screening if symptomatic	0.63	EDETECT study
Offer and acceptance to TB screening if asymptomatic	0.01	EDETECT study
TB positive in symptomatic screened	0.03	EDETECT study
TB positive in asymptomatic screened	0.11	EDETECT study

The TB screening pathway was modelled as a probabilistic decision tree, see Figure 2.

Figure 2. Active TB screening decision tree schematic. Individuals terminate in this model in either an TB or not-TB state, indicated on the right-hand side as True positive/False negative and True negative/False positive respectively.



The cost-effectiveness of the scenario was determined comparing against status-quo using the incremental cost-effectiveness ratio (ICER). Denoting $c_{screening}$ as the expected cost incurred and $\#TP$ as the number of true positive LTBI diagnoses due to the screening programme, then

$$ICER = \frac{cscreening}{\#TP}$$

3. Summary of activities and research findings

Table 3. Main Results.

Total cost (€)	Total TB TP	Compared with status-quo		
		Incremental cost per patient (€)	Incremental cost per single TB diagnosis (€)	ICER (€/TB TP)
41828.2	15.3	11.05	81.12	2733.87

3.1. Cost Effectiveness Results

Table 3 shows the main results of the analysis. The incremental cost-effectiveness ratio was calculated comparing against the status quo of no intervention. The total cost of the program was 41,828.2€ and the average cost per recruited patient 11.05€. The number of true positive cases was 15.3 and the average cost per true positive case 2,733.87€.

4. Conclusions and future steps

In this work we calculated the costs incurred when screening for active TB a migrant population at point of entry in Italy. In particular, we performed a cost-effectiveness analysis by calculating the cost per correct diagnosis of a true positive case, and compared it against the status quo of no screening.

Next steps include the extension of this work to the cost and cost-effectiveness analysis of TB treatment in the same population by collecting costs of hospital admissions and treatment regimens.

Future work will also focus on the analysis of the epidemiological impact of this strategy on the whole Italian population by estimating the possible number of secondary infections averted.

5. Publications resulting from the work described

None but there will be peer reviewed publications

6. Bibliographical references

Li, Shiying, Bin Liu, Mingli Peng, Min Chen, Wenwei Yin, Hui Tang, Yuxuan Luo, Peng Hu, and Hong Ren. "Diagnostic accuracy of Xpert MTB/RIF for tuberculosis detection in different regions with different endemic burden: A systematic review and meta-analysis." *PLoS One* 12, no. 7 (2017): e0180725.