

## Towards tackling tuberculosis in vulnerable groups in the European Union: the E-DETECT TB consortium

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Tuberculosis in the European Union (EU) is increasingly a public health problem that disproportionately and increasingly affects risk groups. The 30 EU/EEA countries reported 60,195 cases of tuberculosis (TB) in 2015; 4.1% was multidrug resistant (MDR) TB.(1) The European Respiratory Society, the World Health Organization (WHO) European Region, European Centre for Disease Prevention and Control (ECDC) and other partners have articulated potential solutions, that are embedded into the new global approach for TB control – the End TB strategy.(2)(3)(4)(5) Within the context of the TB elimination framework for low incidence countries in Western Europe,(5) and the Tuberculosis action plan for the WHO European Region 2016–2020 that addresses the whole region with greater emphasis for high burden countries,(6) it is apparent that concrete trans-national evidence based interventional projects are needed. To address the high disease burden of TB in vulnerable EU populations we have formed the Early DETECTION of tuberculosis consortium (E-DETECT TB). It brings together world leading TB experts in national public health agencies, with industry and major academic centres and its membership reflects incidence of TB in different EU countries (figure). E-DETECT TB utilises evidenced-based approaches to target vulnerable populations, including migrants to the EU, homeless persons, prisoners, problem drug users and those with MDR TB (table). Here we outline key objectives and progress on this major European tuberculosis initiative with a special focus on migrant screening in Italy and active case finding in vulnerable groups in Romania.

Romania has the highest TB burden in the EU/EEA with more than one quarter (15195) of the reported patients, and with the highest rate of 76 per 100,000 population, which is seven times higher than the EU/EEA average. The number of patients declined dramatically in Romania since 2005 when almost 30000 patients were notified. The decline, however, is not observed among vulnerable populations, such as prisoners, homeless individuals, those with a history of drug use or in the Roma population. The E-DETECT TB project aims to apply innovative diagnostics tools such as digital radiography with computer-automated reading and rapid bacteriological tests such as Xpert MTB/RIF to improve early detection and diagnosis of TB in these vulnerable populations. The project also aims to strengthen care integration using an outreach strategy within the same vulnerable populations by providing a one-stop “shop” (clinic) which brings together all required procedures, social support to vulnerable groups, peer support, and close links to the national TB programme to ensure treatment completion. A pilot will be conducted in Bulgaria to assess and demonstrate the feasibility of the intervention; selected due to intermediate TB incidence and geographical proximity to Romania. This, together with the evaluation of effectiveness and cost-effectiveness will inform policy makers on the potential for sustainability and scale-up in Romania and other Eastern European countries.

TB cases of foreign origin constitute about a third of all cases in the EU/EEA.(1) In low incidence countries, trends in TB incidence are driven largely by international migration dynamics and TB incidence rates among the foreign-born are usually several times higher than among non-foreign-born people. For example, in northern European countries such as Sweden and Norway over 4 in 5 cases are of foreign origin. Consequently, tackling TB in migrants, especially migrant groups with additional vulnerabilities is a priority.(7–9) Important vulnerable populations in Western Europe includes asylum seekers and other migrants who arrive through routes that preclude pre-arrival TB screening. Most published evidence currently originated from countries of resettlement of these migrants: there are reasons to predict that the yield of screening interventions as well as the determinants of screening completion will be different in countries of first arrival, such as Italy, Greece and Spain. The E-DETECT TB project aims at acquiring new

insight of screening strategies in these vulnerable groups arriving in Italy. A two-pronged approach is adopted: early detection of those arriving with symptoms is the main priority as an early diagnosis is instrumental to start the appropriate treatment and prevent transmission.(10) Under these conditions, the screening for active disease using a mobile fast, sensitive and specific molecular assay such the Xpert ULTRA is an interesting approach that warrants evaluation to determine its accuracy and cost effectiveness. Recent data suggests that Xpert Ultra assay has an increased sensitivity compared to the previous versions of Xpert MTB/RIF and retains the specificity.(11) A complementary approach is detection and treatment of latent tuberculosis infection, which represents the main source of TB cases in immigrants. While probing new testing tools (i.e. new versions of the Interferon Gamma Release assays) we particularly focus on health care delivery system that can maximize screening and treatment completion rates. Monitoring and evaluation of TB screening among migrants is another important asset of the intervention. An electronic-health (eHealth) system called E-DETECT-TB has been developed to address the need of a user-friendly, fast, mobile tool to register screening results among migrants directly at the point of arrival and at relocation sites. The E-DETECT TB system includes a smart phone application for mobile data recording, a java-based software and a synchronized electronic database, offering the opportunities of standardizing screening practice and collecting good-quality data. The E-DETECT TB provides the opportunity to evaluate the public health use of this strategy in migrants and to investigate the potential for subsequent scale-up. However, the exchange of health information for individual migrants within a country and between countries remains a largely unresolved issue.

More broadly, the E-DETECT TB assists the development of a robust regional monitoring and evaluation mechanism underpinned by the best quality operational data to support the identification of optimal approaches to diagnose latent and active TB and to ensure treatment completion. Many European TB programmes generate data on screening, however, the limited number of cases in each member state prevents the investigation of measures especially within subgroups. The E-DETECT TB project will provide a platform for the pooling of latent and active tuberculosis screening data from multiple countries to support future research into the best approaches for screening and evaluation of strategies to target risk groups. We have selected E-DETECT TB partner countries (Sweden, Netherlands, Italy and the UK) as the initial countries to contribute data and have secured agreement to include additional EU/EEA countries in due course. This new data platform should complement existing ECDC surveillance systems and provide useful data to inform future policy by member states.

A robustly designed and well implemented national TB strategy is regarded as key to successful national TB control.(12) One component of the E-DETECT TB aims to collate best evidence from published literature and national experts to inform a TB strategy prioritisation, action and support plan as a toolkit to aid national efforts to develop and implement national TB plans. To do so, we collect evidence through two systematic reviews, a pan-European survey and an expert consultation exercise aimed at weighing the evidence and identifying specific barriers and facilitators to strategy implementation. In addition, we can also include relevant emerging evidence from other E-DETECT TB actions, including evidence on TB screening and tackling TB in vulnerable populations. After a pilot phase, we are hoping to make the resulting toolkit available to all EU/EEA member states.

In conclusion, all countries, even in the rich Europe, have a north and a south. National and international movement of populations have always existed, although the phenomenon has been increasingly visible over the last decade. This new media-driven attention needs to be properly oriented as to ensure prevention of stigma and respect of human rights. Indeed, while some migrant groups are vulnerable populations, **others also** need attention: homeless, Roma, drug addicts and prisoners-among others- need free-cost, rapid and quality diagnosis and treatment for TB and for any other disease or co-morbidity. The E-DETECT TB project has been designed to test novel outreach approaches supporting quality TB management in different countries and populations. By bringing together these multiple strands of activity,

the consortium will play a key role in exploiting existing expertise among stakeholders in Europe, collaborating with the European Respiratory Society in its dissemination efforts, to maximize the impact of the intervention.

Although government commitment is a clear pre-requisite to control and eliminate TB, and no elimination effort can work without the support of national TB programmes, the fight against the white plague is driven by multi-factorial forces requiring multiple partners to join forces. National public health agencies, academia, the private sector including industry, civil society and professional organisations - in Europe the European Respiratory Society acts as a magnet for national associations - all need to collaborate closely to implement the End TB Strategy and to support and protect vulnerable populations.



Figure: Map of Europe showing E-DETECT TB partner countries and burden of tuberculosis.

Work Package	Interventions	Main Outcome
Outreach activity in Romania and Bulgaria	Mobile digital radiography, Computer aided diagnostics, mobile provision of Xpert test, social support and integration with hospital care	–Number of active TB cases detected using mobile x-ray van in Romania and Bulgaria –Number of patients treated in Romania and Bulgaria
Implement and evaluate migrant	Latent TB testing in settled migrants	–Number of latent and active TB

TB detection in Italy	(tuberculin skin test, Interferon Gamma Release Assay) Active TB screening in newly arrived migrants (questionnaire, Xpert ULTRA)	cases detected in migrants in Italy –Linkage to care among detected migrants in Italy
Creating a database listing active and latent TB cases	Migrant TB screening database Data from multiple countries	–Multi-country data platforms for migrant TB established and analysed
Supporting the strengthening of national TB programmes	Survey of national programme managers Reviewing existing policies	Synthesis of best practice for developing national action plans

Table. Summary table of E-DETECT TB interventions and outcomes.

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