



European policies in the management of tuberculosis among migrants



Lia D'Ambrosio^{a,b}, Rosella Centis^a, Masoud Dara^c, Ivan Solovic^d, Giorgia Sulis^e, Alimuddin Zumla^f, Giovanni Battista Migliori^{a,*}

^a World Health Organization Collaborating Centre for Tuberculosis and Lung Diseases, Maugeri Institute, IRCCS, Via Roncaccio 16, 21049, Tradate, Italy

^b Public Health Consulting Group, Lugano, Switzerland

^c World Health Organization Regional Office for Europe, UN City, Copenhagen, Denmark

^d National Institute for TB, Lung Diseases and Thoracic Surgery, Catholic University Ruzomberok, Vysoké Tatry, Slovakia

^e Department of Infectious and Tropical Diseases, WHO Collaborating Centre for TB/HIV and TB Elimination, University of Brescia, Brescia, Italy

^f Center for Clinical Microbiology, Division of Infection and Immunity, University College London and NIHR Biomedical Research Centre, UCL Hospitals NHS Foundation Trust, London, UK

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SUMMARY

Globally 10.4 million new tuberculosis (TB) incident cases were estimated to have occurred in 2015, of which 3% were reported in the World Health Organization European Region. Importantly, about 25% of the global multidrug-resistant TB (MDR-TB) cases are reported in the European Region, representing one of the greatest challenges to TB control; these are reported particularly in the countries of the Former Soviet Union. Over a quarter of TB cases in the European Union and European Economic Area (EU/EEA) are reported among foreign-born individuals. In line with the recent increase of migration flows towards Europe, TB among migrant populations is also on the rise, emphasizing the need for a better understanding of the TB trends at the regional and sub-regional levels, and of the existing policies on migrants and refugees. The present article is aimed at describing the policies and practices of European countries with a low and intermediate TB incidence with regard to the detection and management of TB and latent TB infection (LTBI) among refugees in Europe.

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1. Introduction: tuberculosis (TB) and migration

Out of the 10.4 million newly diagnosed tuberculosis (TB) cases estimated to have occurred globally in 2015, 3% were reported from the World Health Organization (WHO) European Region countries (11% being HIV-infected).^{1,2} According to the latest surveillance data, 25% of global multidrug-resistant TB (MDR-TB) cases are estimated to occur in the WHO European Region; they represent one of the top priorities for TB control (and eventually elimination), particularly in Eastern Europe.^{3,4}

Over a quarter of TB cases in the European Union and European Economic Area (EU/EEA) are reported among foreign-born individuals. Four countries (France, Germany, Spain, and the UK) account for 74.9% of all cases reported among migrants.² The recent increase of migration flows towards Europe further emphasizes the need for a better understanding of the TB trends

at regional and sub-regional levels, and of the existing policies on migrants and refugees. Discrimination, hostility, and economic adversity (here defined in agreement with the 1951 'Convention and Protocol relating to the status of Refugees' <http://www.unhcr.org/3b66c2aa10.html>) are factors afflicting the lives of many migrants and refugees across Europe.^{1–4} Several factors (including free movement within the EU and the Newly Independent States, for seasonal labour) have contributed to increase population mobility within and towards Europe,^{5–7} which poses new challenges for TB control and elimination. New efforts are therefore needed to make quality prevention, diagnosis, and treatment of both TB and latent TB infection (LTBI) possible.^{6,8}

Better coordination is necessary to ensure that individual human rights (independent of the legal or residential status of the subject) are preserved and that public health pre-requisites to control and ultimately eliminate TB are met. This includes proper prevention, diagnosis, and treatment of both MDR and extensively drug-resistant (XDR)-TB.^{9–11} In the interests of both the individual and the wider hosting community, unrestricted free access to TB diagnosis and treatment (with a guarantee of

* Corresponding author.

E-mail address: giovannibattista.migliori@fsm.it (G.B. Migliori).

protection from deportation until the end of treatment) has to be ensured to undocumented migrants as well, as recommended by the WHO.^{12–16}

2. TB and refugees

Over one million refugees and migrants entered Europe in 2015, while this was ‘only’ 216 000 in 2014.^{5,17} Between January 1 and September 30, 2016 an estimated 302 335 new migrants reached the Europe Region, with 3498 deaths/missing officially reported. Interestingly, over 60% of those landing in Europe after crossing the Mediterranean Sea were born in 10 countries, as summarized in Figure 1.¹⁷ As of today, the top four countries of origin for asylum seekers are the Syrian Arab Republic (28% of total arrivals), Afghanistan (14%), Iraq (9%), and Nigeria (8%).¹⁷

The aim of the present article is to describe the policies and practices of European countries with a low and intermediate TB incidence with regard to the detection and management of TB and LTBI among refugees in Europe.^{6,18}

3. The European survey on policies

The survey was performed between October 2015 and February 2016, and was coordinated by the TB Advocacy ad-hoc Working Group of the European Respiratory Society (ERS), in collaboration with the WHO Regional Office for Europe and the European Region of the International Union Against Tuberculosis and Lung Disease (The Union).¹⁹ The survey included multiple choice and open-ended questions concerning screening and management of TB and LTBI among refugees in Europe. It was completed by the

coordinators of national TB programmes of all EU/EEA countries of the WHO European Region, plus six additional EU candidate countries (Albania, Bosnia and Herzegovina, the former Yugoslav Republic of Macedonia, Montenegro, Serbia, and Turkey) and Switzerland.¹⁹

4. Results

All countries except two (36/38, 94.7%) answered the questionnaire. A summary of the core results is presented in Table 1.

Thirty-one countries (86.1%) reported that screening is performed for active TB and 19 for LTBI. Eight countries only (22.2%) collected data on LTBI treatment outcomes. Interestingly, about half of the countries not yet screening are developing TB and LTBI screening plans. National guidelines in force imply a legal obligation to screen for TB and/or LTBI in almost 60% of the surveyed countries (21/36).

Country representatives reported details on how screening practices are organized. Active TB screening is essentially based on diagnostic algorithms including different combinations of symptom-based questionnaires, bacteriological examinations, and chest radiography. LTBI screening is conducted through different combinations of interferon-gamma release assays (IGRAs) and/or the tuberculin skin test (TST).

Confirming previous findings,¹¹ LTBI screening was found to be performed by TST only in 22.2% of the countries (8/36), by TST plus IGRA in 30.5% of the countries, and by TST plus IGRA only in selected cases in 11% of the countries. Screening practices were found to be organized differently based on the setting- or country-specific organization of health services. In the majority of countries

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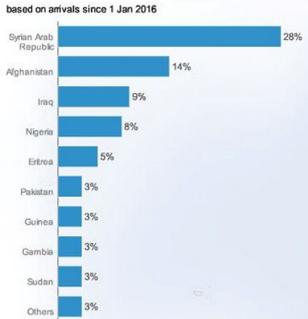
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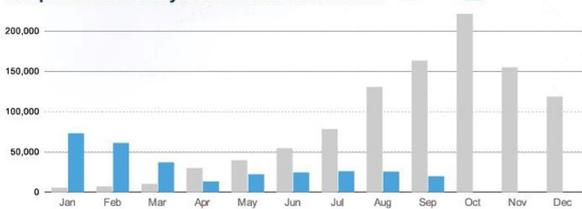
Increasing numbers of refugees and migrants take their chances aboard unseaworthy boats and dinghies in a desperate bid to reach Europe. The vast majority of those attempting this dangerous crossing are in need of international protection, fleeing war, violence and persecution in their country of origin. Every year these movements continue to exact a devastating toll on human life.

Top-10 nationalities of Mediterranean sea arrivals

Top-10 nationalities represent 79% of the sea arrivals based on arrivals since 1 Jan 2016

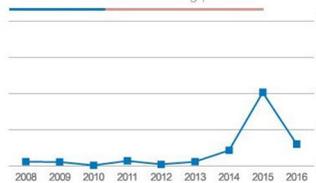


Comparison of monthly Mediterranean sea arrivals



Evolution - Mediterranean Sea

Sea arrivals | Dead/missing persons

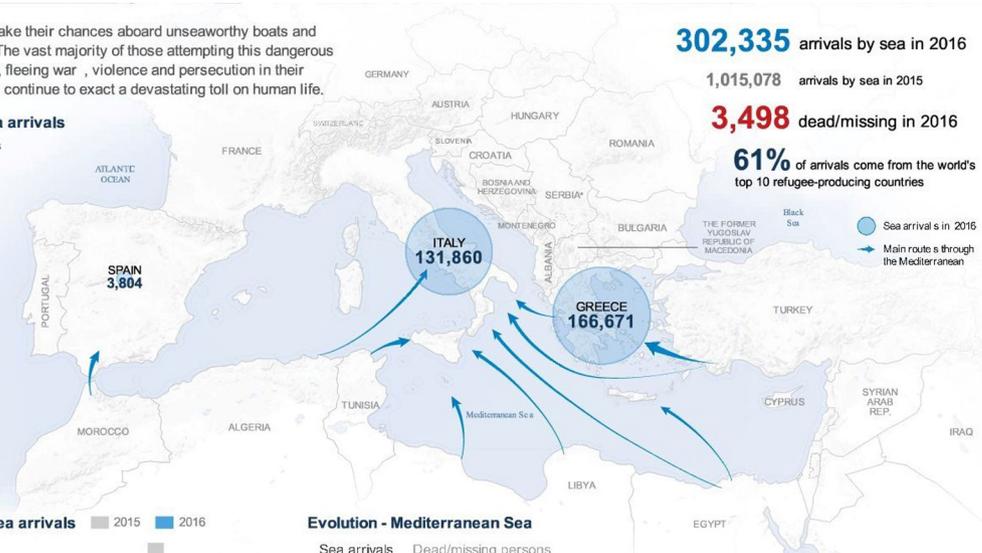


302,335 arrivals by sea in 2016

1,015,078 arrivals by sea in 2015

3,498 dead/missing in 2016

61% of arrivals come from the world's top 10 refugee-producing countries



Demographics based on arrivals since 1 Jan 2016



*Serbia (AND KOSOVO): SIRS/134 (1999) | Download excel data | The boundaries and names shown and the designations used on this map do not imply of endorsement or acceptance by the United Nations

<http://data.unhcr.org/mediterranean/regional.php>

1/1

Figure 1. Recent evidence on migrant movements to Europe (available at <http://data.unhcr.org/mediterranean/regional.php>, last accessed September 30, 2016).

Table 1
Summary of the core findings of the recently published survey on European policies and practices among refugees^a

Active TB	LTBI
Screening	Screening
Yes: 31/36 (86.1%)	Yes: 19/36 (52.7%)
No: 2/36 (5.2%)	No: 9/36 (25%)
Not systematic: 3/36 (8.3%)	Not systematic: 8/36 (22.2%)
Symptom-based questionnaires:	TST: 19/36 (52.7%)
Systematic: 20/36 (55.5%)	TST only: 8/36 (22.2%)
Not systematic: 1/36 (2.7%)	TST plus IGRA: 11/36 (30.5%)
Bacteriology	Not systematic TST plus IGRA: 4/36 (11.1%)
Systematic: 9/36 (25%)	Not applicable: 13/36 (36.1%)
For symptomatic individuals only: 9/36 (25%)	
Chest radiography	
Systematic: 25/36 (69.4%)	
Not systematic: 2/36 (5.5%)	
Other procedures ^b : 1/36 (2.7%)	
Not systematic screening: 5/36 (13.9%) ^c	
Procedures if diagnosis of active TB	Procedures if diagnosis of LTBI
No refusal of asylum: 34/36 (94.4%)	No refusal of asylum: 20/36 (55.5%)
Obligation to undergo treatment: 24/36 (66.6%)	Obligation to undergo preventive therapy: 8/36 (22.2%)
Other: 10/36 (27.7%)	Other: 18/36 (50%)
Not applicable: 2/36 (5.5%)	Not applicable: 8/36 (22.2%)
Data collection to assess treatment success rates	Data collection to assess completion rates
Yes: 19/36 (52.7%)	Yes: 8/36 (22.2%)
No: 10/36 (27.7%)	No: 20/36 (55.5%)
Not answered: 6/36 (16.6%)	Not answered: 6/36 (16.6%)
Not applicable: 1/36 (2.7%)	Not applicable: 2/36 (5.5%)
Screening and management according to national/international guidelines/legislation	Screening and management according to national/international guidelines/legislation
Yes: 27/36 (75%)	Yes: 19/36 (52.7%)
No: 3/36 (8.3%)	No: 7/36 (19.4%)
Not applicable: 1/36 (2.7%)	Not applicable: 5/36 (13.8%)
Not answered: 5/36 (13.8%)	Not answered: 5/36 (13.8%)
Place of screening	Refugee centres only: 10/36 (27.7%)
	On arrival only: 4/36 (11.1%)
	Community only: 1/36 (2.7%)
	National TB programme centre only: 1/36 (2.7%)
	On arrival and in refugee centres: 6/36 (16.6%)
	On arrival and pre-arrival: 1/36 (2.7%)
	On arrival and in the community: 1/36 (2.7%)
	On pre-arrival and in the community: 1/36 (2.7%)
	In refugee centres and in the community: 6/36 (16.6%)
	Not applicable: 5/36 (13.8%)
Legal requirement for screening	Yes: 21/36 (58.3%)
	No: 12/36 (33.3%)
	Not applicable: 3/36 (13.8%)
Plans to implement screening for active TB/LTBI	Yes: 8/17 ^d (47%)
	No: 5/17 ^d (29.4%)
	Not answered: 3/17 ^d (17.6%)
	Not applicable: 1/17 ^d (5.9%)
Special measures to deal with undocumented migrants	Yes: 22/36 (61.1%)
	No: 1/36 (2.7%)
	Not answered: 13/36 (36.1%)
Infection control measures for individuals with possible TB	Respirators used for staff and surgical masks for individuals with possible TB or other respiratory disease: 24/36 (66.6%)
	Only respirator used for staff in contact with refugees: 1/36 (2.7%)
	Other: 7/36 (19.4%)
	Not answered: 4/36 (11.1%)

TB, tuberculosis; LTBI, latent tuberculosis infection; TST, tuberculin skin test; IGRA, interferon-gamma release assay.

^a From Dara et al.,¹⁹ modified; 36 countries surveyed.

^b Initial algorithm with tuberculin skin tests (TST) and blood examination.

^c Numerator includes countries that do not systematically perform any examination.

^d Denominator is the number of countries that do not (or do not systematically) screen for TB/LTBI.

($n = 22$, 61.1%), both TB and LTBI screening are done in devoted refugee centres. In 22 countries (61.1%), screening interventions are managed through a strict collaboration between governmental and private sector staff.

The majority of countries (75%) answered that screening practices are consistent with both national and international guidelines in force. The proportion decreased to 52.7% ($n = 19$) for LTBI screening. Several countries reported that infection control measures were considered suboptimal, although respirators were

reported to be available to protect health staff to complement administrative measures.

5. From evidence to recommendations

The results of the study are pivotal to coordinate future initiatives in favour of an improved management of refugees in Europe.¹⁹ The high response rate confirmed that the topic is of importance to the agenda of the different countries. The relevant

Table 2
Summary of the recommendations of the European Respiratory Society, the World Health Organization Europe Region, and The Union Europe Region on core actions for optimal management of tuberculosis among refugees^a

Recommendation	Comments
1 Ensure adequate prevention, diagnosis, and treatment of TB and LTBI based on the End TB Strategy	LTBI management is a core intervention to pursue TB elimination; diagnosis and treatment of LTBI might be not feasible in all countries
2 Provide quality surveillance, monitoring, and evaluation, coupled with operational research	Solid evidence is needed to guide public health interventions; operational research is necessary to guide rational introduction of the diagnostics and drugs
3 Ensure timely screening for TB among refugees born in middle and high TB incidence countries	Evidence on yield and the cost-effectiveness of screening practices is needed
4 Prevent stigmatization and stereotypes, of both TB infected people and vulnerable groups	The recommendation aims at encouraging unrestricted access to TB services
5 Promote universal access to LTBI (in the countries where these are offered) and TB services (prevention, diagnosis, and treatment)	Universal access includes adequate management of comorbidities
6 Ensure quality infection control in settings where refugees are hosted, screened, and treated	The package includes protective measures for staff, as well as HIV testing and counselling to detect HIV and TB–HIV co-infected individuals

TB, tuberculosis; LTBI, latent tuberculosis infection.

^a From Dara et al.,²⁷ modified.

inter-country variability in policies reflects the difficulty, at the European level, of coordinating complex interventions, which imply technical expertise, organization of different services, and important funding, as well as delicate legal and ethical issues.

As expected, more information was available on TB than on LTBI screening practices. Feasibility issues are clearly driving these results. In some countries, the large numbers of arrivals and the increased mobility make LTBI screening even more difficult to perform. Further research, providing data on the yield of different screening practices and on their cost-effectiveness, will provide better information to design rational and sustainable screening plans.

A core research priority, given the increased breakdown risk (LTBI progressing to TB disease because of the prevalent unhealthy travel conditions), is represented by the management of LTBI.^{1,10,11} This intervention is, in fact, crucial if the TB elimination strategy is taken into consideration.^{10,11}

From the organizational point of view, inter-sectoral collaboration involving governmental and private services is key to increase the cultural sensitivity of TB services. The importance of ensuring quality infection control measures whenever TB patients are hosted needs also to be underlined.²⁰ The results of this and similar studies will support the proper implementation of the End TB Strategy, the TB Action Plan for the WHO European Region 2016–2020,²¹ and the Health 2020 Policy Framework²² to address inequity. The final goal of these strategies is to end TB and ultimately eliminate TB.^{10,11,23–25} Additional evidence is obviously necessary.²⁶

The ERS and the WHO Regional Office for Europe have proactively launched a new branch of the TB Consilium (an internet-based and cost-free platform supporting clinicians managing difficult-to-treat TB cases) to allow better cross-border TB control among refugees and migrants. The new function is presently live and accessible at the TB Consilium website (<http://www.tbconsilium.org>). The hope is to contribute to improve prevention, diagnostic, and treatment services for migrants and refugees. Furthermore, the same ERS TB Advocacy ad-hoc Committee, in collaboration with the WHO Office for Europe and The Union Europe Region have developed recommendations for the better management of migrants and refugees²⁷(Table 2).

In conclusion, the new interest raised among politicians and policymakers on these delicate issues needs to be channelled into concrete actions promoting unrestricted access of migrants and refugees to TB prevention, diagnosis, and treatment services, while ensuring that individual human rights are met and that the community is protected from further transmission of *Mycobacterium tuberculosis*.

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References

- World Health Organization. Global tuberculosis report 2016. WHO/HTM/TB/2016.13. Geneva: WHO; 2016.
- European Centre for Disease Prevention and Control/WHO Regional Office for Europe. Tuberculosis surveillance and monitoring in Europe 2016. Stockholm: ECDC; 2016.
- Falzon D, Mirzayev F, Wares F, Baena IG, Zignol M, Linh N, et al. Multidrug-resistant tuberculosis around the world: what progress has been made? *Eur Respir J* 2015;**45**:150–60.
- Jenkins HE, Crudu V, Soltan V, Ciobanu A, Domete L, Cohen T. High risk and rapid appearance of multidrug resistance during tuberculosis treatment in Moldova. *Eur Respir J* 2014;**43**:1132–41.
- Matteelli A, Lönnroth K, Mosca D, Getahun H, Centis R, D'Ambrosio L, et al. Cameroon's multidrug-resistant tuberculosis treatment programme jeopardised by cross-border migration. *Eur Respir J* 2016;**47**:686–8.
- Dara M, Solovic I, Goletti D, Sotgiu G, Centis R, D'Ambrosio L, et al. Preventing and controlling tuberculosis among refugees in Europe: more is needed. *Eur Respir J* 2016;**48**:272–4.
- de Vries G, van Rest J, Meijer W, Wolters B, van Hest R. Low yield of screening asylum seekers from countries with a tuberculosis incidence of less than 50 per 100,000 population. *Eur Respir J* 2016;**47**:1870–2.
- Dara M, de Colombani P, Petrova-Benedict R, Centis R, Zellweger J, Sandgren A, et al., on behalf of the members of the Wolfheze Transborder Migration Task Force. The minimum package for cross-border TB control and care in the WHO European Region: a Wolfheze Consensus Statement. *Eur Respir J* 2012;**40**:1081–90.
- Dara M, Kluge H. Roadmap to prevent and combat drug-resistant tuberculosis. Copenhagen: World Health Organization, Regional Office for Europe; 2011. Available at: http://www.euro.who.int/__data/assets/pdf_file/0014/152015/e95786.pdf (accessed September 30, 2016).
- Lönnroth K, Migliori GB, Abubakar I, D'Ambrosio L, de Vries G, Diel R, et al. Towards tuberculosis elimination: an action framework for low-incidence countries. *Eur Respir J* 2015;**45**:928–52.
- D'Ambrosio L, Dara M, Tadolini M, Centis R, Sotgiu G, van der Werf MJ. European National Programme Representatives. Tuberculosis elimination: theory and practice in Europe. *Eur Respir J* 2014;**43**:1410–20.
- International Union against Tuberculosis and Lung Disease. Recommendations to ensure the diagnosis and treatment of tuberculosis in undocumented migrants. A statement of the International Union against Tuberculosis and Lung Disease. IUATLD; 2008. Available at: http://www.theunion.org/get-involved/join-the-union/body/RESS_undocumented-migrants-Statement_2008.pdf (accessed September 30, 2016).
- Migliori GB, Zellweger JP, Abubakar I, Ibraim E, Caminero JA, De Vries G, et al. European Union standards for tuberculosis care. *Eur Respir J* 2012;**39**:807–19.
- van der Werf MJ, Sandgren A, D'Ambrosio L, Blasi F, Migliori GB. The European Union standards for tuberculosis care: do they need an update? *Eur Respir J* 2014;**43**:933–42.
- Migliori GB, Sotgiu G, D'Ambrosio L, Centis R, Lange C, Bothamley G, et al. TB and MDR/XDR-TB in the EU and EEA countries: managed or mismanaged? *Eur Respir J* 2012;**39**:619–25.
- Veen J, Migliori GB, Raviglione MC, Reider HL, Dara M. Harmonisation of TB control in the WHO European region: the history of the Wolfheze Workshops. *Eur Respir J* 2011;**37**:950–9.
- UNHCR – The UN Refugee Agency. Refugees and migrants crossing the Mediterranean to Europe. Overview of arrival trends as of September 30, 2016.

- UNHCR; 2016, Available at: <http://data.unhcr.org/mediterranean/regional.php> (accessed September 30, 2016).
18. World Health Organization. Sixty-Seventh World Health Assembly. Global strategy and targets for tuberculosis prevention, care and control after 2015. A67/11. Geneva: WHO; 2014, Available at: http://apps.who.int/gb/ebwha/pdf_files/WHA67/A67_11-en.pdf (accessed September 30, 2016).
 19. Dara M, Solovic I, Sotgiu G, D'Ambrosio L, Centis R, Tran R, et al. Tuberculosis care among refugees arriving in Europe: a ERS/WHO Europe Region survey of current practices. *Eur Respir J* 2016;**48**:808–17.
 20. Sotgiu G, D'Ambrosio L, Centis R, Bothamley G, Cirillo DM, De Lorenzo S, et al. TB and M/XDR-TB infection control in European TB reference centres: the Achilles' heel? *Eur Respir J* 2011;**38**:1221–3.
 21. World Health Organization, Regional Office for Europe. Tuberculosis action plan for the WHO European Region 2016–2020. WHO; 2015, Available at: http://www.euro.who.int/__data/assets/pdf_file/0007/283804/65wd17e_Rev1_TBActionPlan_150588_withCover.pdf?ua=1 (accessed September 30, 2016).
 22. World Health Organization, Europe Regional Office. Health 2020 policy framework. WHO; 2013, Available at: <http://www.euro.who.int/en/health-topics/health-policy/health-2020-the-european-policy-for-health-and-well-being/about-health-2020> (accessed September 30, 2016).
 23. Diel R, Loddenkemper R, Zellweger JP, Sotgiu G, D'Ambrosio L, Centis R, et al. European Forum for TB Innovation. Old ideas to innovate tuberculosis control: preventive treatment to achieve elimination. *Eur Respir J* 2013;**42**:785–801.
 24. World Health Organization. Systematic screening for active tuberculosis: principles and recommendations. WHO/HTM/TB/2013.04. Geneva: WHO; 2013.
 25. Uplekar M, Weil D, Lonnroth K, Jaramillo E, Lienhardt C, Dias HM, et al. WHO's Global TB Programme. WHO's new end TB strategy. *Lancet* 2015;**385**:1799–801.
 26. Bothamley GH, Ditiu L, Migliori GB, Lange C. Active case-finding in Europe: a TBNET (Tuberculosis Network European Trials group) survey. *Eur Respir J* 2008;**31**:1023–30.
 27. Dara M, Solovic I, Sotgiu G, D'Ambrosio L, Centis R, Goletti D, et al. Statement of the European Respiratory Society (ERS) and the European Region of the International Union Against TB and Lung Disease (The Union): call for urgent actions to ensure access to early diagnosis and care of TB among refugees. *Eur Respir J* 2016;**47**:1345–7.