Management of TB in migrants: questions and answers

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Conflict of interest disclosure

☑ **I have no real or perceived conflicts of interest that relate to this presentation.**

❑ **I have the following real or perceived conflicts of interest that relate to this presentation:**

Bibliography search

Key words:

((tuberculosis[Title/abstract]) AND treatment[Title/abstract]) AND (migrant*[Title/abstract] OR migration[Title/abstract] OR migrat*[Title/abstract])

No time limits: 6,185 documents

2015-2019: 373 documents

- Few with relevant information on *treatment results*
- Majority focused on *screening*

Introduction

Objectives

Questions and aswers on:

- Migration: ‘myths’ and reality
- History of migration and screening
- Screening options for TB and LTBI
- Migration and health
- Research priorities

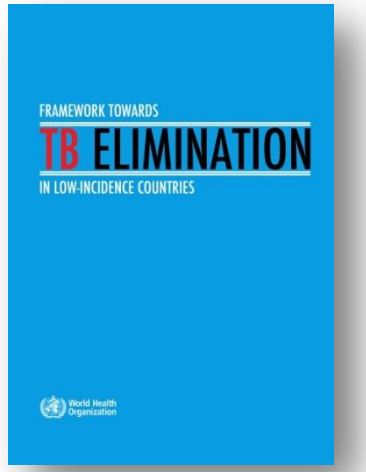
• Conclusions

ACTION FRAMEWORK

8 priority actions for elimination in low-incidence countries

Manage TB disease

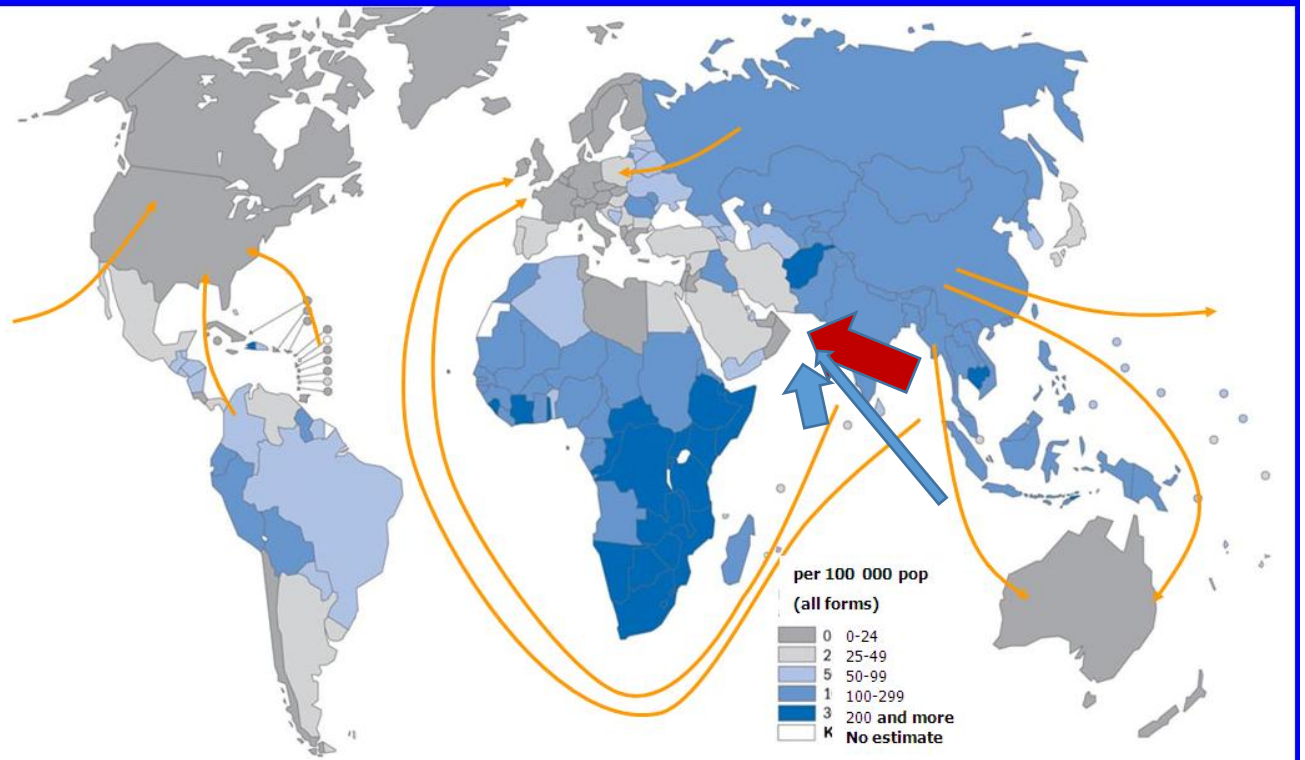
Manage LTBI



TB is poverty-related: the two faces of San Paulo

Migration is global

Re-import of TB into industrialized countries



Accord. WHO Report 2006

Migration Language
Migrant

- Any person who *is moving* or *has moved* across an *international* border or *within a state* (IDP) away from his/her habitual place of residence, regardless of:
  - The person's legal status;
  - Whether the movement is voluntary or involuntary;
  - What the causes for the movement are
  - What the length of the stay is.

Migration Language
Asylum-seeker & Refugee

Asylum-seeker*: individual seeking international protection.

In countries with individualized procedures, is someone whose claim has not yet been finally decided

Refugee*: a person who meets the eligibility criteria under the applicable definition (UNHCR's mandate or national legislation)

- **Every refugee is *initially* an asylum-seeker**
- **…but** not every asylum-seeker will *ultimately be recognized* as a refugee

**Master Glossary of Terms, UNHCR, June 2006*

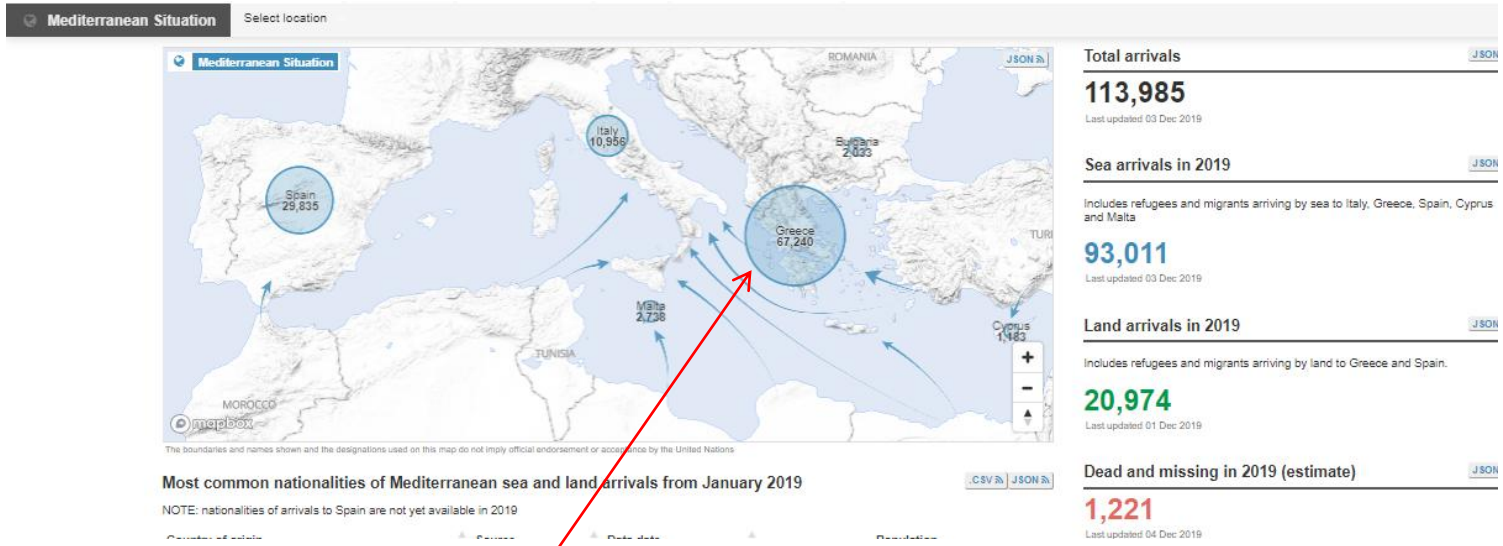
Migrants: questions and answers

QUESTION	ANSWER
Migrants keep increasing	Not true: peak in 2015/16
TB increases in Europe due to migration	TB declining in Europe, MDR increasing
	Foreign-born majority of cases in some countries (not all)
	Rates of TB x 100,000 stable in migrants
Foreign-born non adherent to treatment	In some countries: the opposite
Migrants transmit to local population	No evidence

Recent evidence on migrants' movements to Europe

(available at: https://data2.unhcr.org/en/situations/mediterranean)

Last updated **5 Dec 2019**

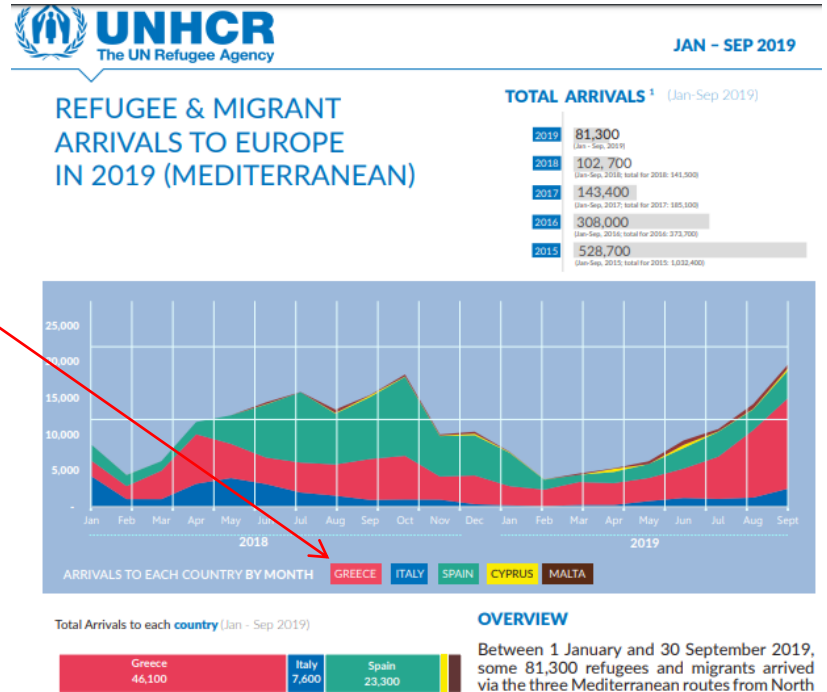


Myth: Migrants keep increasing

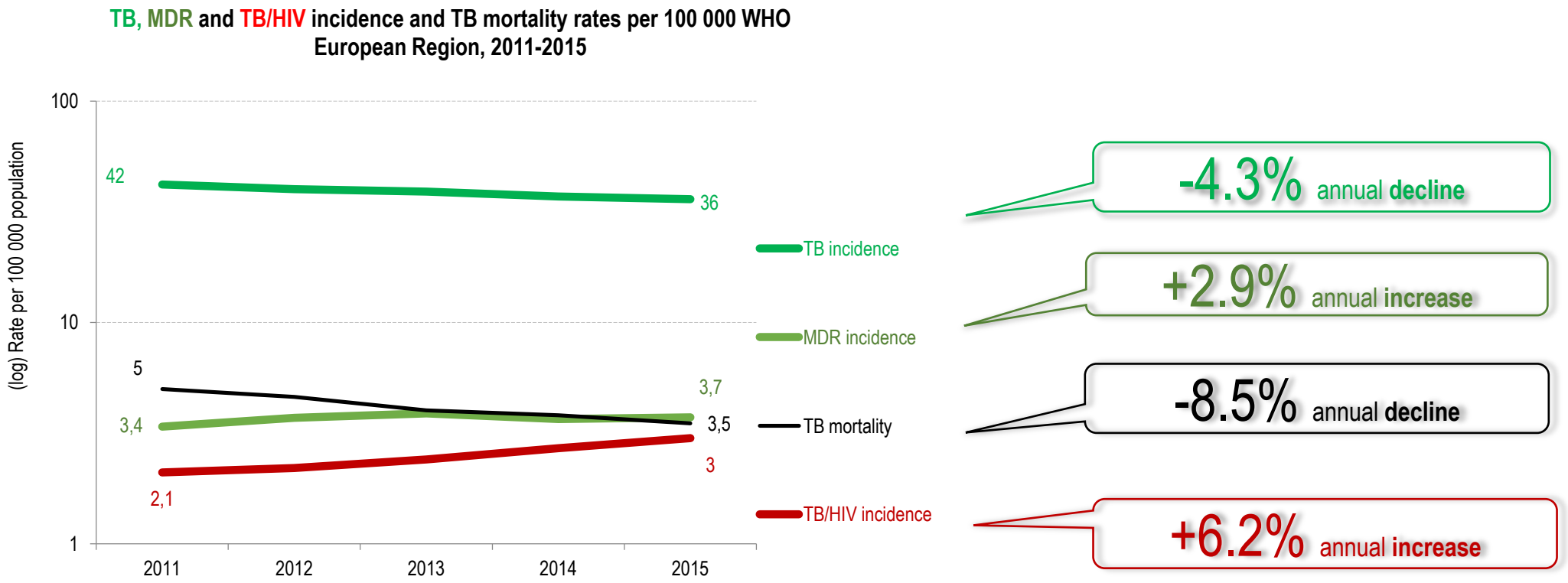
Most common nationalities of Mediterranean sea and land arrivals from January 2019

NOTE: nationalities of arrivals to Spain are not yet available in 2019

Country of origin	Source	Data date	Population	
Afghanistan		19 Nov 2019	20.5%	16,861
Syrian Arab Rep.		30 Nov 2019	16.8%	13,814
Others		30 Nov 2019	10.8%	8,908
Morocco		30 Nov 2019	8.8%	7,212
Algeria		30 Nov 2019	4.7%	3,854
Iraq		30 Nov 2019	4.7%	3,850
Tunisia		30 Nov 2019	4.1%	3,389
Guinea		30 Nov 2019	4.0%	3,328
Dem. Rep. of the Congo		31 Oct 2019	4.0%	3,316
Côte d'Ivoire		30 Nov 2019	4.0%	3,303



Myth: TB increases in Europe due to migration



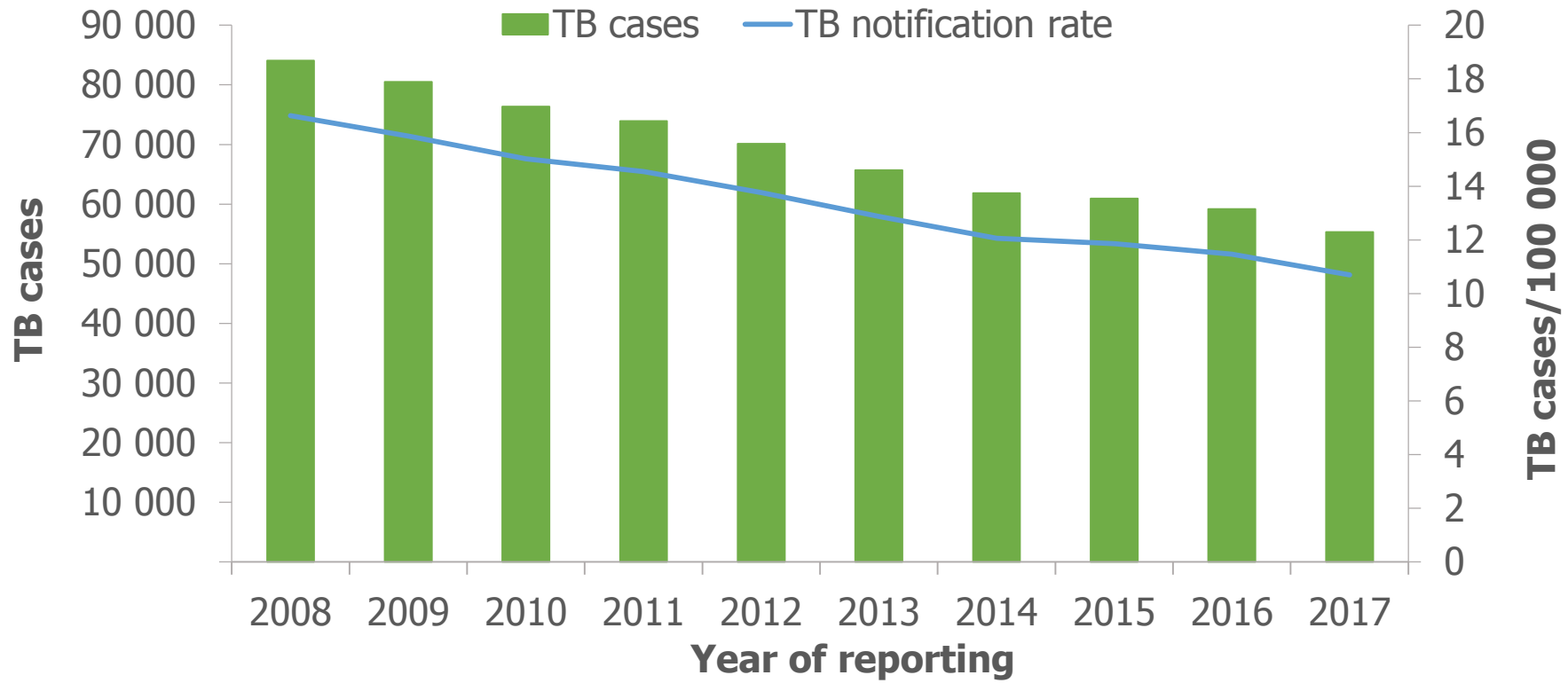
Source: WHO Europe / ECDC. Tuberculosis surveillance and monitoring in Europe 2017

Courtesy Dr. A. Dadu, WHO/EURO

Notified TB cases, EU/EEA, 2008–2017

Continuous decline between 2008 and 2017:

- Number of TB cases decreased by **34%**
- Notification rate decreased by **36%**



Source: ECDC/WHO (2019). Tuberculosis surveillance and monitoring in Europe 2019–2017 data

TB in persons of foreign origin, EU/EEA, 2017

18 299 TB cases of foreign* origin

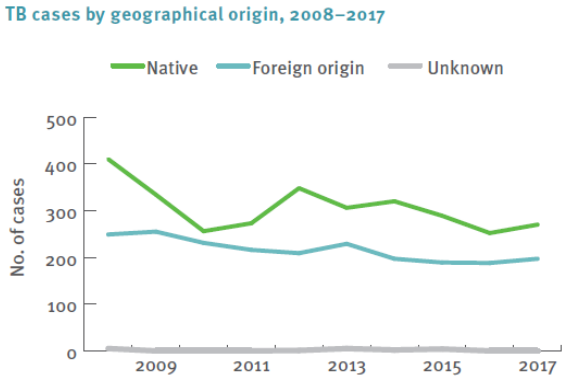
33.1% of all TB cases (range 0–92.9%)

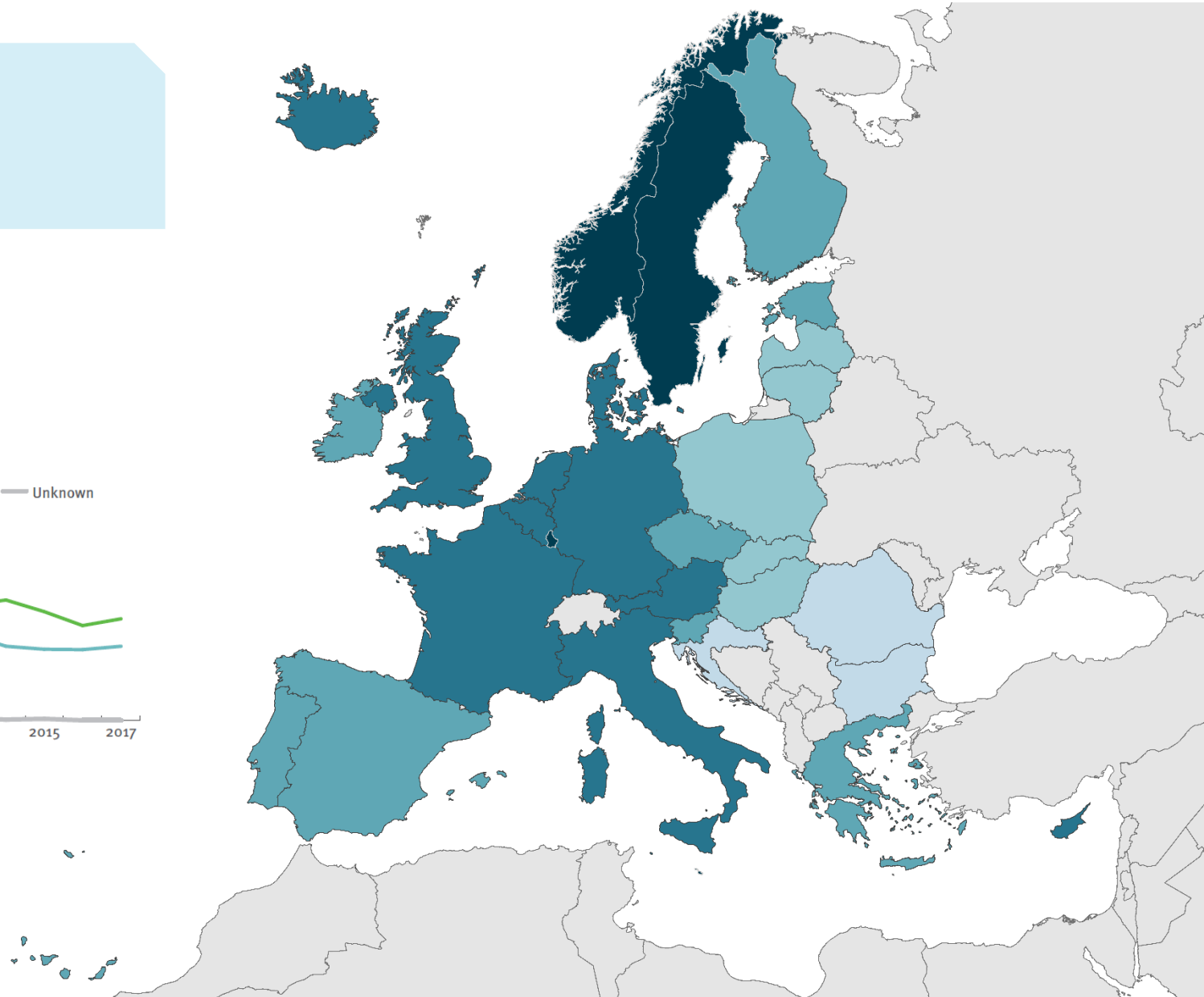
Proportion of TB cases of foreign origin

- <1%
- 1 to 9.9%
- 10 to 49.9%
- 50 to 74.9%
- ≥75%

Countries not visible in the main map extent

- Liechtenstein
- Malta





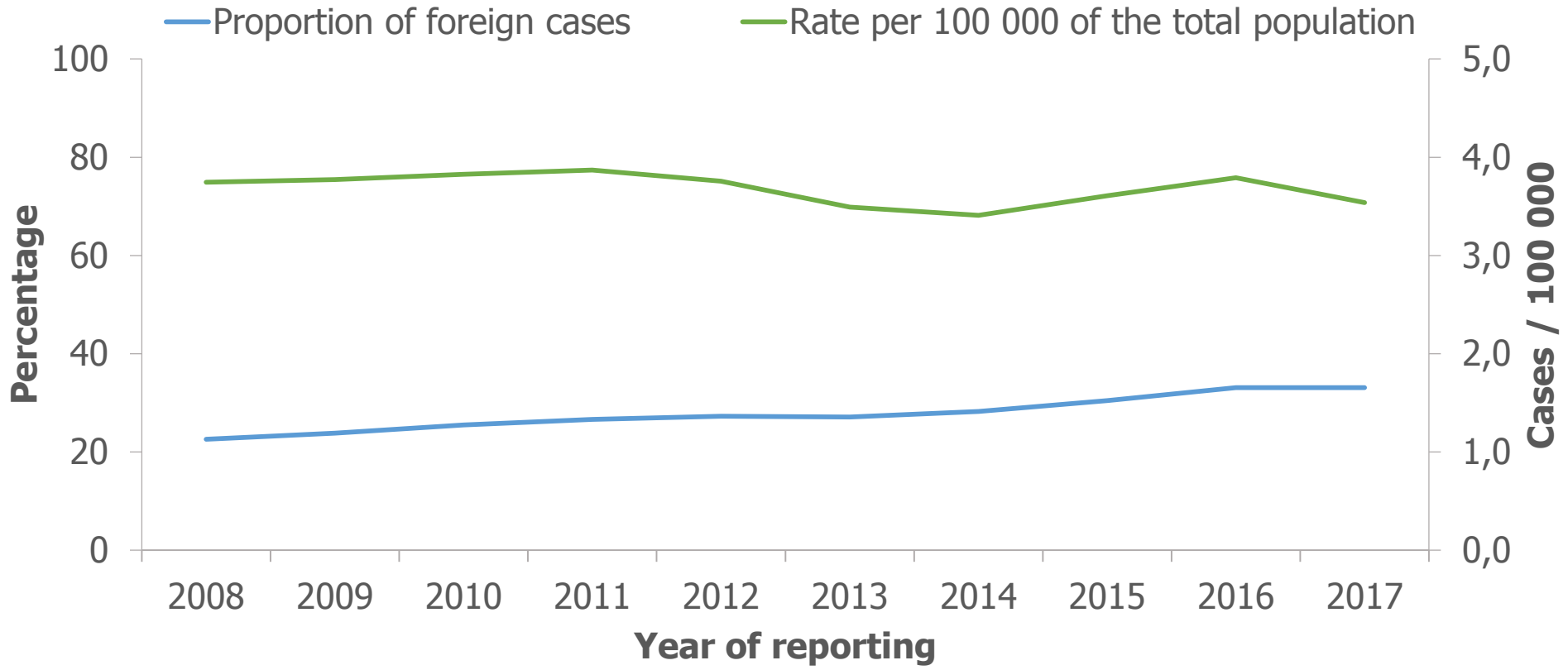
* Notified in persons originating from other countries than the reporting country

Source: ECDC/WHO (2019). Tuberculosis surveillance and monitoring in Europe 2019–2017 data

TB cases in persons of foreign origin, EU/EEA, 2008–2017*

The proportion of cases in persons of foreign origin increased from **22.6%** in 2008 to **33.1%** in 2017

The rate of TB cases of foreign origin per 100 000 of the total population was stable between **3.4** and **3.9**

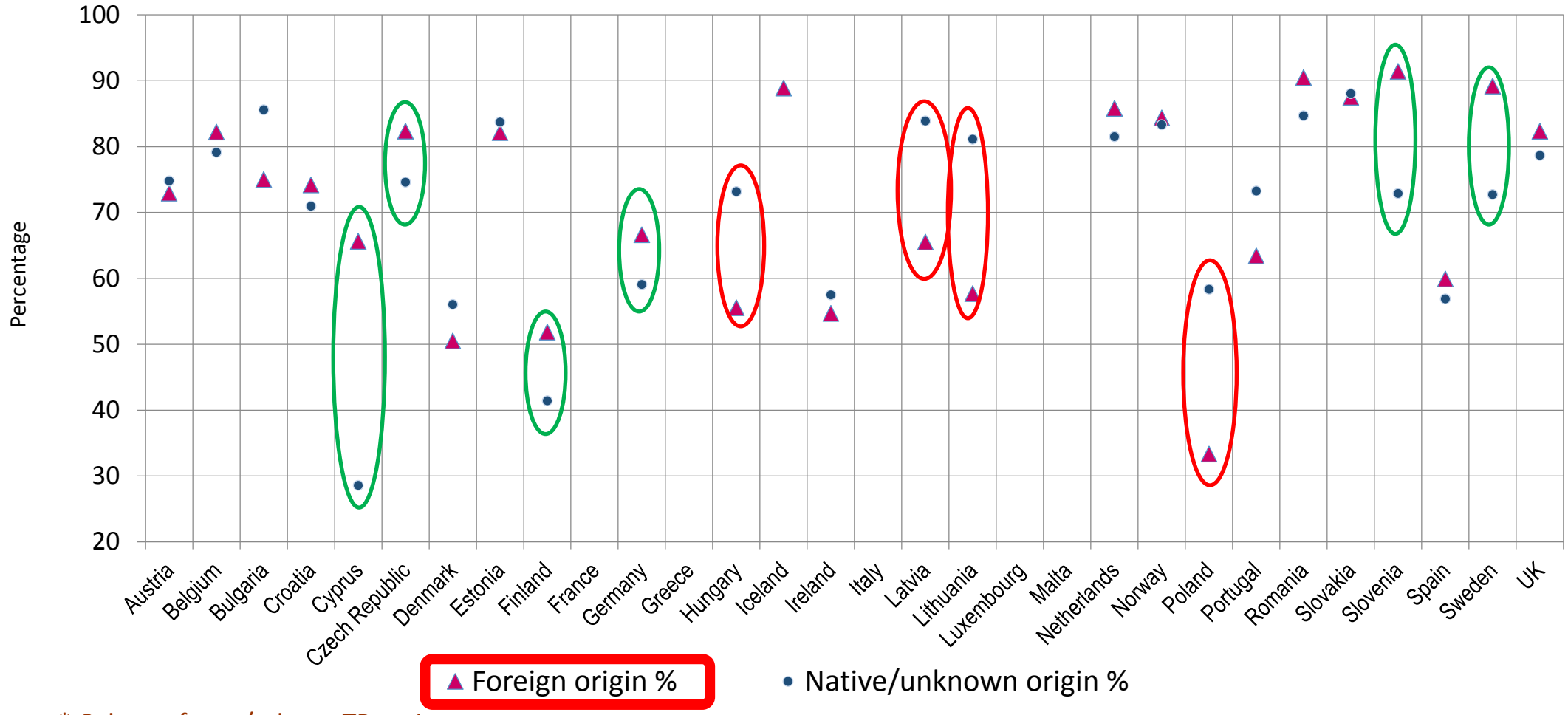


* Croatia is not included for the years prior to 2012

Source: ECDC/WHO (2019). Tuberculosis surveillance and monitoring in Europe 2019–2017 data

Myth: foreign born not adherent

*TB treatment success** by origin; EU/EEA, 2014



* Cohort of new/relapse TB patients

Tuberculosis surveillance and monitoring in Europe 2017. WHO/ECDC joined report

Nellums *et al. BMC Medicine* (2018) 16:27
DOI 10.1186/s12916-017-1001-7

BMC Medicine

RESEARCH ARTICLE Open Access

Multidrug-resistant tuberculosis treatment adherence in migrants: a systematic review and meta-analysis

Laura B. Nellums[†], Kieran Rustage[†], Sally Hargreaves[†] and Jon S. Friedland[*]

Abstract

Background: Multidrug-resistant tuberculosis (MDR-TB) is a growing concern in meeting global targets for TB control. In high-income low-TB-incidence countries, a disproportionate number of MDR-TB cases occur in migrant (foreign-born) populations, with concerns about low adherence rates in these patients compared to the host non-migrant population. Tackling MDR-TB in this context may, therefore, require unique approaches. We conducted a systematic review and meta-analysis to identify and synthesise data on MDR-TB treatment adherence in migrant patients to inform evidence-based strategies to improve care pathways and health outcomes in this group.

Methods: This systematic review and meta-analysis was conducted in line with PRISMA guidelines (PROSPERO 42017070756). The databases Embase, MEDLINE, Global Health and PubMed were searched to 24 May 2017 for primary research reporting MDR-TB treatment adherence and outcomes in migrant populations, with no restrictions on dates or language. A meta-analysis was conducted using random-effects models.

Results: From 413 papers identified in the database search, 15 studies reporting on MDR-TB treatment outcomes for 258 migrants and 174 non-migrants were included in the systematic review and meta-analysis. The estimated rate of adherence to MDR-TB treatment across migrant patients was 71% [95% confidence interval (CI) = 58–84%], with non-adherence reported among 20% (95% CI = 4–37%) of migrant patients. A key finding was that there were no differences in estimated rates of adherence [risk ratio (RR) = 1.05; 95% CI = 0.82–1.34] or non-adherence (RR = 0.97; 95% CI = 0.79–1.36) between migrants and non-migrants.

Conclusions: MDR-TB treatment adherence rates among migrants in high-income low-TB-incidence countries are approaching global targets for treatment success (75%), and are comparable to rates in non-migrants. The findings highlight that only just over 70% of migrant and non-migrant patients adhere to MDR-TB treatment. The results point to the importance of increasing adherence in all patient groups, including migrants, with an emphasis on tailoring care based on social risk factors for poor adherence. We believe that MDR-TB treatment targets are not ambitious enough.

Keywords: Tuberculosis, Drug resistance, Migration, Treatment adherence

15/413 studies included

- MDR outcomes: **258 migrants vs 171 non-migrants**
- **Estimated rate of adherence**: 71%
- **No difference between migrants and non-migrants**

Although there are standardized recommendations for treatment regimens, variation in access to treatment and treatment adherence impact on the effectiveness of care, and there is evidence in migrant populations of loss to follow-up at every stage of the screening and treatment pathway, plus challenges in linking screening with secondary care (43,108).

Pulmonol. 2018;24(2):99–105

REVIEW

Migration, TB control and elimination: Whom to screen and treat☆

A. Rendon[a,1], R. Centis[b], J.-P. Zellweger[c,1], I. Solovic[d], C.A. Torres-Duque[e], C. Robalo Cordeiro[f], F.C. de Queiroz Mello[g], D. Manissero[h,1], G. Sotgiu[i,*,1]

Abstract Tuberculosis (TB) in migrants represents an important clinical and public health threat, particularly in low TB incidence countries. The current review is aimed to assess issues related to screening and treatment of migrants with latent TB infection or TB disease.

RESEARCH ARTICLE

Find and treat or find and lose? Tuberculosis treatment outcomes among screened newly arrived asylum seekers in Germany, 2002 to 2014

Anna Kuehne[1,2], Barbara Hauer[1], Bonita Brodhun[1], Walter Haas[1], Lena Fiebig[1]
1. Robert Koch Institute, Department for Infectious Disease Epidemiology, Respiratory Infections Unit, Berlin, Germany
2. Postgraduate Training for Applied Epidemiology, Robert Koch Institute, Berlin, Germany affiliated to the European Programme for Intervention Epidemiology Training, ECDC, Stockholm, Sweden

Correspondence: Lena Fiebig (FiebigL@rki.de)

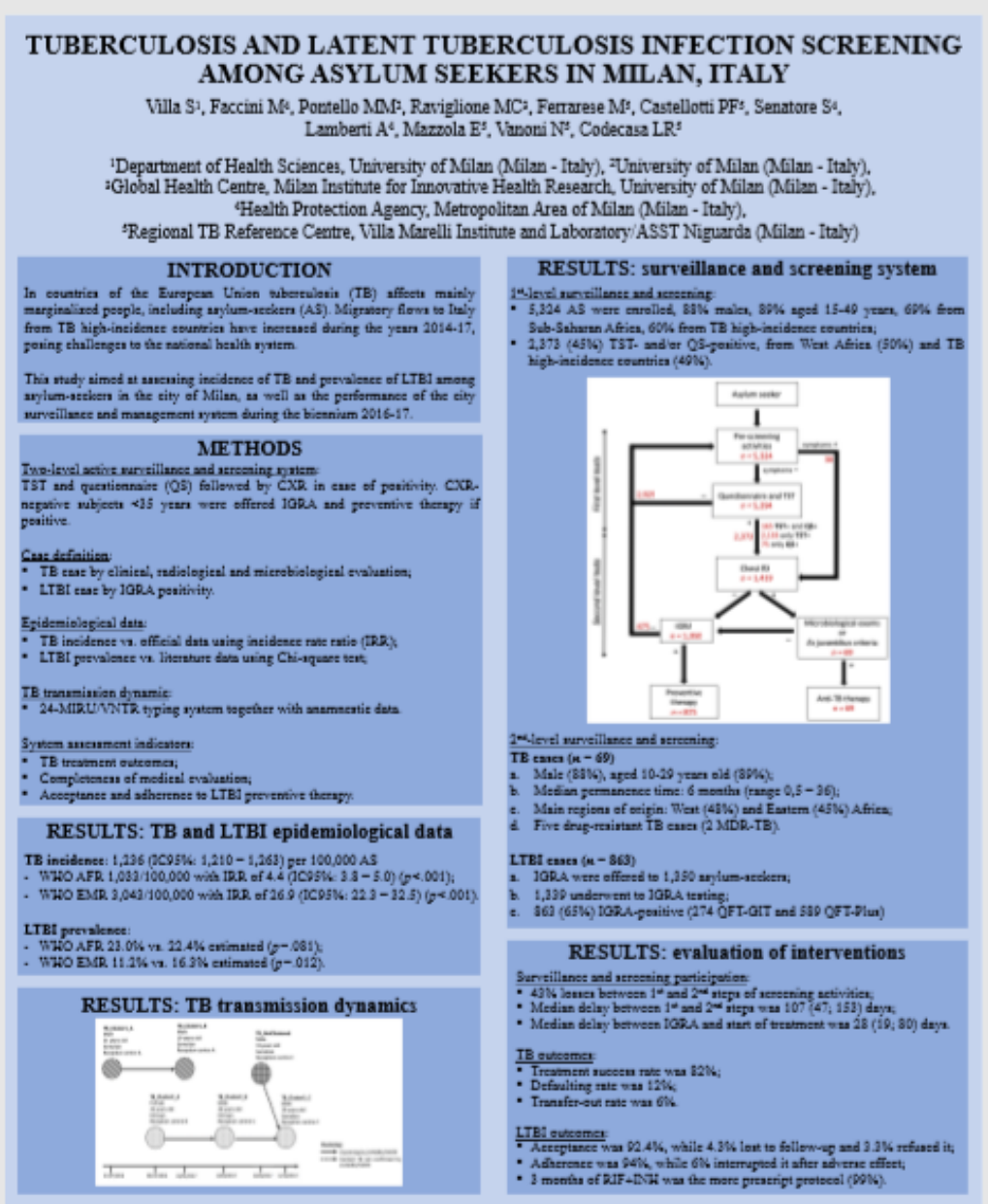
to follow-up. **Results:** TB treatment success was highest among cases identified by contact tracing (87%; 3,139/3,591), followed by passive case finding (74%; 28,804/39,019) and by screening asylum seekers (60%; 884/1,474). Cases identified by screening asylum seekers had 2.4 times higher odds of not having a successful treatment outcome as opposed to all other

While specific reasons for the higher odds of non-successful treatment among asylum seekers in Germany need to be studied further, available research suggests that patients need to be better linked to treatment facilities and structural barriers to treatment completion need to be addressed to secure screening benefits for asylum seekers and the communities.

Asylum seekers in Milan

- TB incidence is high among asylum seekers in Milan
- Transmission within reception centres is rare
- Within the system, attrition may occur frequently when different screening sites are involved
- TB treatment success (82%) is high although improvement is possible by reducing defaulting (12%) and transfer-out (6%)
- LTBI treatment acceptance (92.4%) and adherence (94% with 6% interrupting for AE) are high

If you really care, good results are guaranteed



TUBERCULOSIS AND LATENT TUBERCULOSIS INFECTION SCREENING AMONG ASYLUM SEEKERS IN MILAN, ITALY

Villa S[1], Faccini M[4], Pontello MM[2], Raviglione MC[3], Ferrarese M[5], Castellotti PF[5], Senatore S[4], Lamberti A[4], Mazzola E[5], Vanoni N[5], Codecasa LR[5]

[1]Department of Health Sciences, University of Milan (Milan - Italy), [2]University of Milan (Milan - Italy), [3]Global Health Centre, Milan Institute for Innovative Health Research, University of Milan (Milan - Italy), [4]Health Protection Agency, Metropolitan Area of Milan (Milan - Italy), [5]Regional TB Reference Centre, Villa Marelli Institute and Laboratory/ASST Niguarda (Milan - Italy)

INTRODUCTION

In countries of the European Union tuberculosis (TB) affects mainly marginalized people, including asylum-seekers (AS). Migratory flows to Italy from TB high-incidence countries have increased during the years 2014-17, posing challenges to the national health system.

This study aimed at assessing incidence of TB and prevalence of LTBI among asylum-seekers in the city of Milan, as well as the performance of the city surveillance and management system during the biennium 2016-17.

METHODS

Two-level active surveillance and screening system:
TST and questionnaire (QS) followed by CXR in case of positivity. CXR-negative subjects <35 years were offered IGRA and preventive therapy if positive.

Case definition:
- TB case by clinical, radiological and microbiological evaluation;
- LTBI case by IGRA positivity.

Epidemiological data:
- TB incidence vs. official data using incidence rate ratio (IRR);
- LTBI prevalence vs. literature data using Chi-square test;

TB transmission dynamic:
- 24-MIRU/VNTR typing system together with anamnestic data.

System assessment indicators:
- TB treatment outcomes;
- Completeness of medical evaluation;
- Acceptance and adherence to LTBI preventive therapy.

RESULTS: TB and LTBI epidemiological data

TB incidence: 1,236 (IC95%: 1,210 – 1,263) per 100,000 AS
- WHO AFR 1,033/100,000 with IRR of 4.4 (IC95%: 3.8 – 5.0) ($p<.001$);
- WHO EMR 3,043/100,000 with IRR of 26.9 (IC95%: 22.3 – 32.5) ($p<.001$).

LTBI prevalence:
- WHO AFR 23.0% vs. 22.4% estimated ($p=.081$);
- WHO EMR 11.2% vs. 16.3% estimated ($p=.012$).

RESULTS: TB transmission dynamics

RESULTS: surveillance and screening system

1st-level surveillance and screening:
- 5,324 AS were enrolled, 88% males, 89% aged 15-49 years, 69% from Sub-Saharan Africa, 60% from TB high-incidence countries;
- 2,373 (45%) TST- and/or QS-positive, from West Africa (50%) and TB high-incidence countries (49%).

2nd-level surveillance and screening:
TB cases (n = 69)
a. Male (88%), aged 10-29 years old (89%);
b. Median permanence time: 6 months (range 0,5 – 36);
c. Main regions of origin: West (48%) and Eastern (45%) Africa;
d. Five drug-resistant TB cases (2 MDR-TB).

LTBI cases (n = 863)
a. IGRA were offered to 1,350 asylum-seekers;
b. 1,339 underwent to IGRA testing;
c. 863 (65%) IGRA-positive (274 QFT-GIT and 589 QFT-Plus)

RESULTS: evaluation of interventions

Surveillance and screening participation:
- 43% losses between 1st and 2nd steps of screening activities;
- Median delay between 1st and 2nd steps was 107 (47; 153) days;
- Median delay between IGRA and start of treatment was 28 (19; 80) days.

TB outcomes:
- Treatment success rate was 82%;
- Defaulting rate was 12%;
- Transfer-out rate was 6%.

LTBI outcomes:
- Acceptance was 92.4%, while 4.3% lost to follow-up and 3.3% refused it;
- Adherence was 94%, while 6% interrupted it after adverse effect;
- 3 months of RIF+INH was the more prescript protocol (99%).

Courtesy Dr Simone Villa & Mario Raviglione, Milano 2018; ERJ 2019

Myth: migrants transmit TB to the native population

Assessing transmission dynamics from foreign-born to native European populations

Tuberculosis transmission between foreign- and native-born populations in the EU/EEA: a systematic review

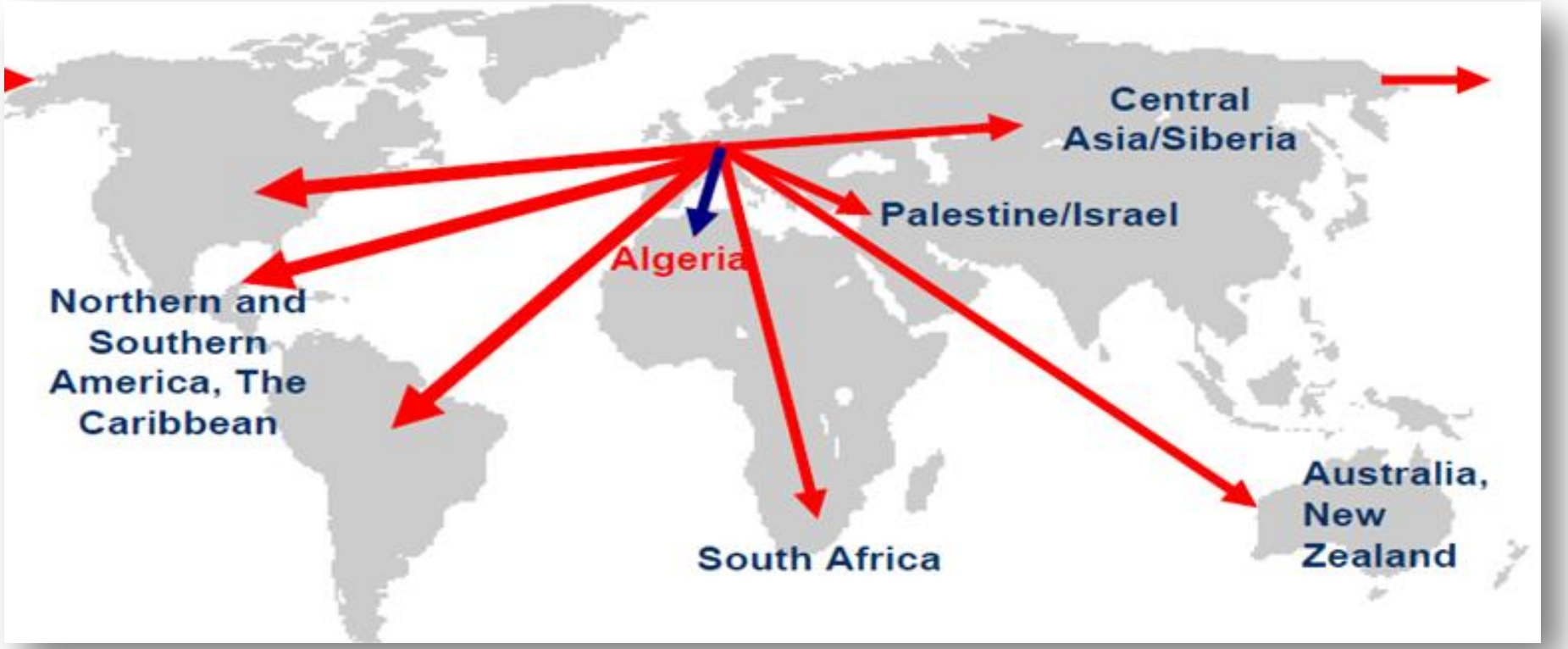
Andreas Sandgren[1,6], Monica Sañé Schepisi[2,6], Giovanni Sotgiu[3], Emma Huitric[1], Giovanni Battista Migliori[4], Davide Manissero[1,5], Marieke J. van der Werf[1] and Enrico Girardi[2]

Eur Respir J 2014; 43: 1159–1171

- Molecular epidemiology studies 1990-2012 (IS6110 RFLP and MIRU-VNTR (12&15 loci)
- **15 studies** (1992-2007) covering 12,366 cases, median 49% foreign born
- Countries: B, D, DK, F, I, E, S, N, UK
- Clustered isolates (=recent transmission) 8.5-49% of all TB case genotypes
- **Foreign-born cases were equally or more likely to have unique isolates**, but % of clustered cases not negligible, esp. in foreign clusters
- 1/3 of clusters were mixed (foreign/native) with 0-34% of all genotyped cases
- **Cross-transmission was bi-directional**
- **TB in foreigners has no significant influence on TB in native populations in Europe**

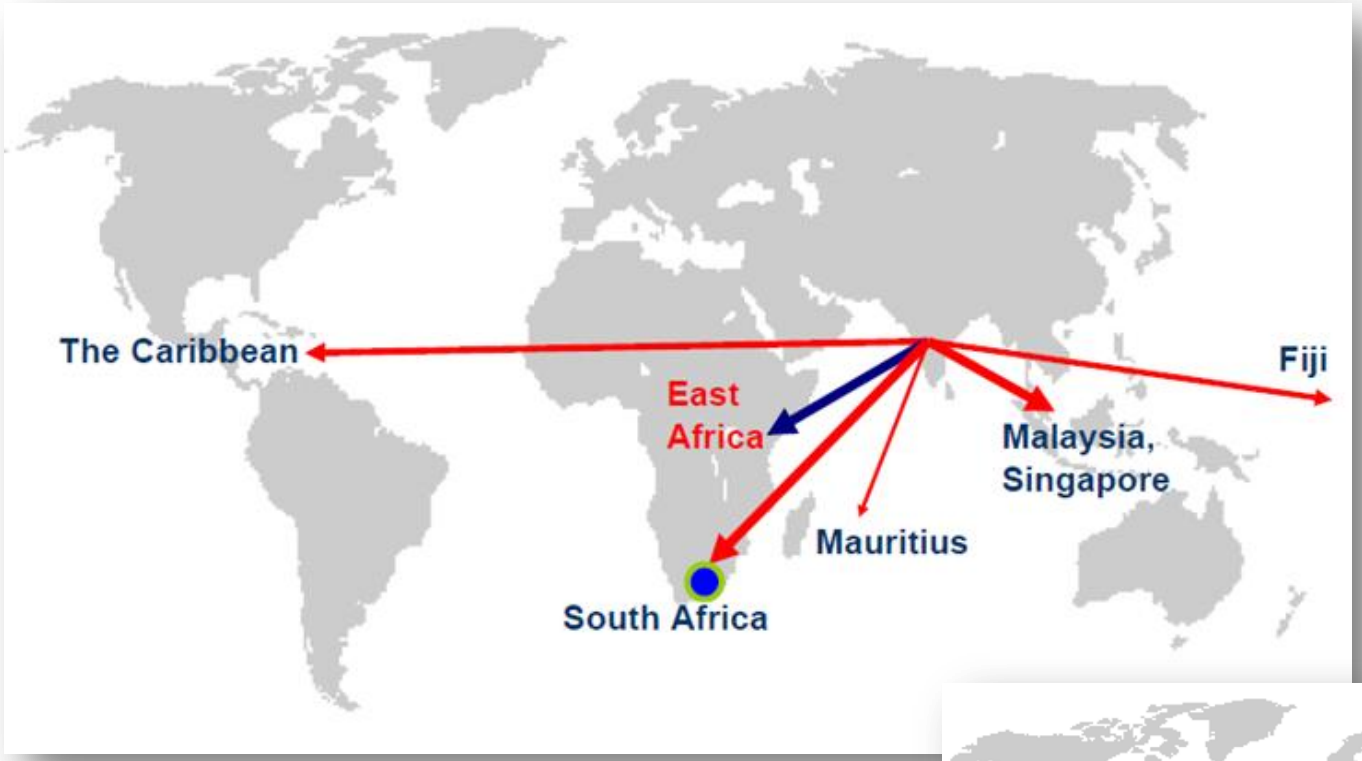
History of migration

History of migration
120 years ago, 70 million to overseas



Source: Rainer Münz-Erste group

1870-1940 South-South Emigration

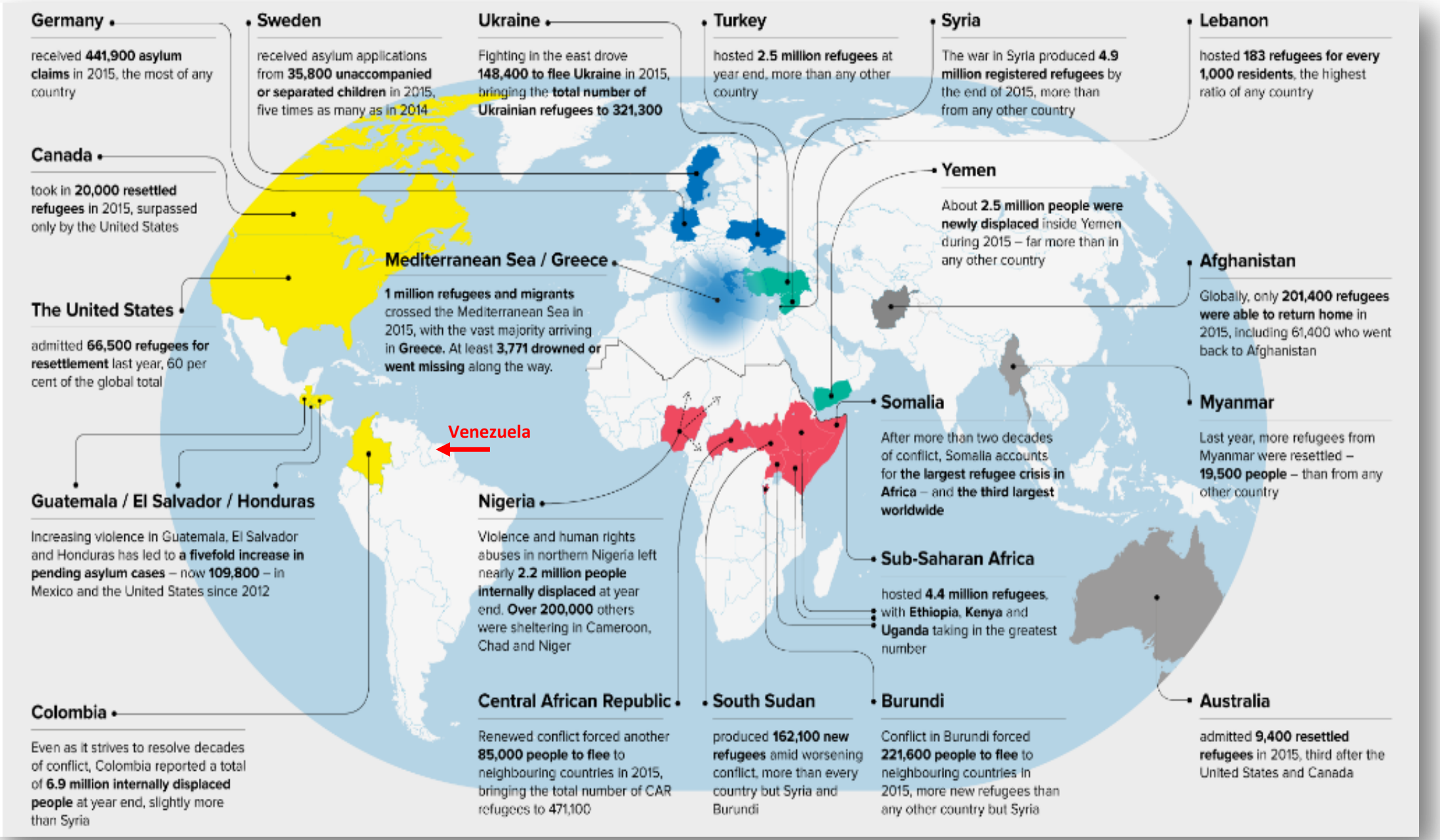


Source: Rainer Münz-Erste group

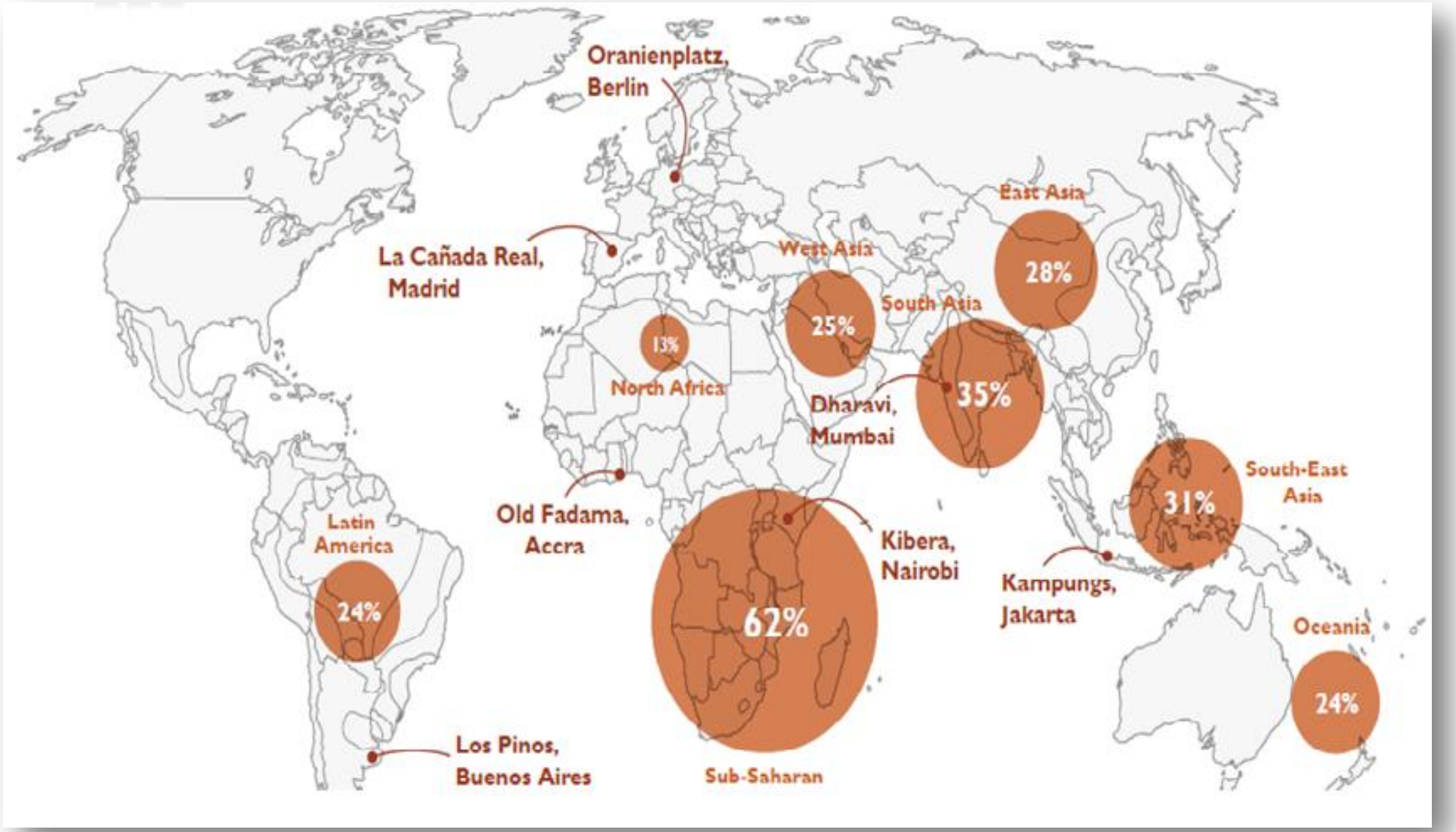
1945-1950: World Migration

Source: Rainer Münz-Erste group

Highest record for Forced Displacement



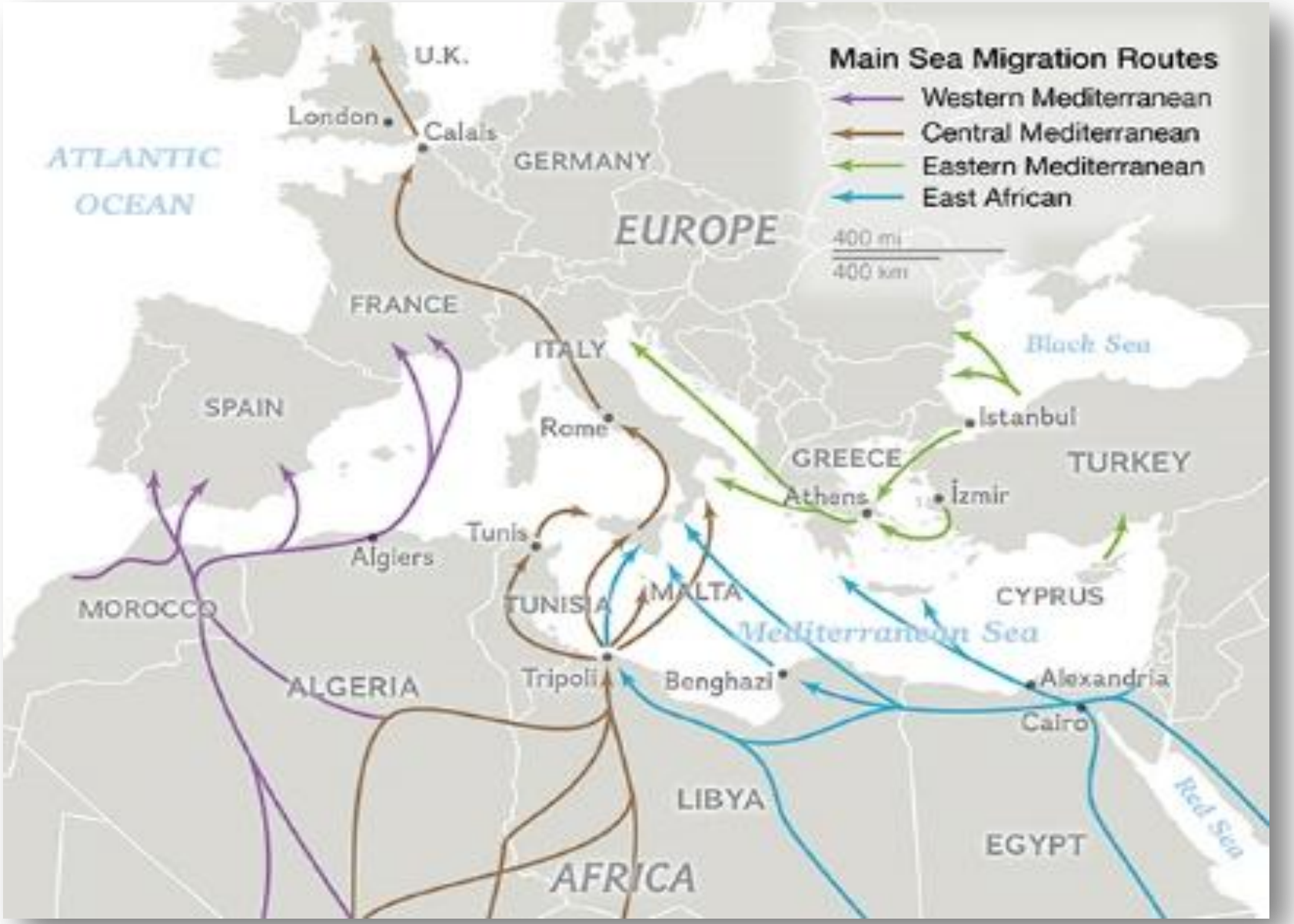
Informal Settlement and Slums



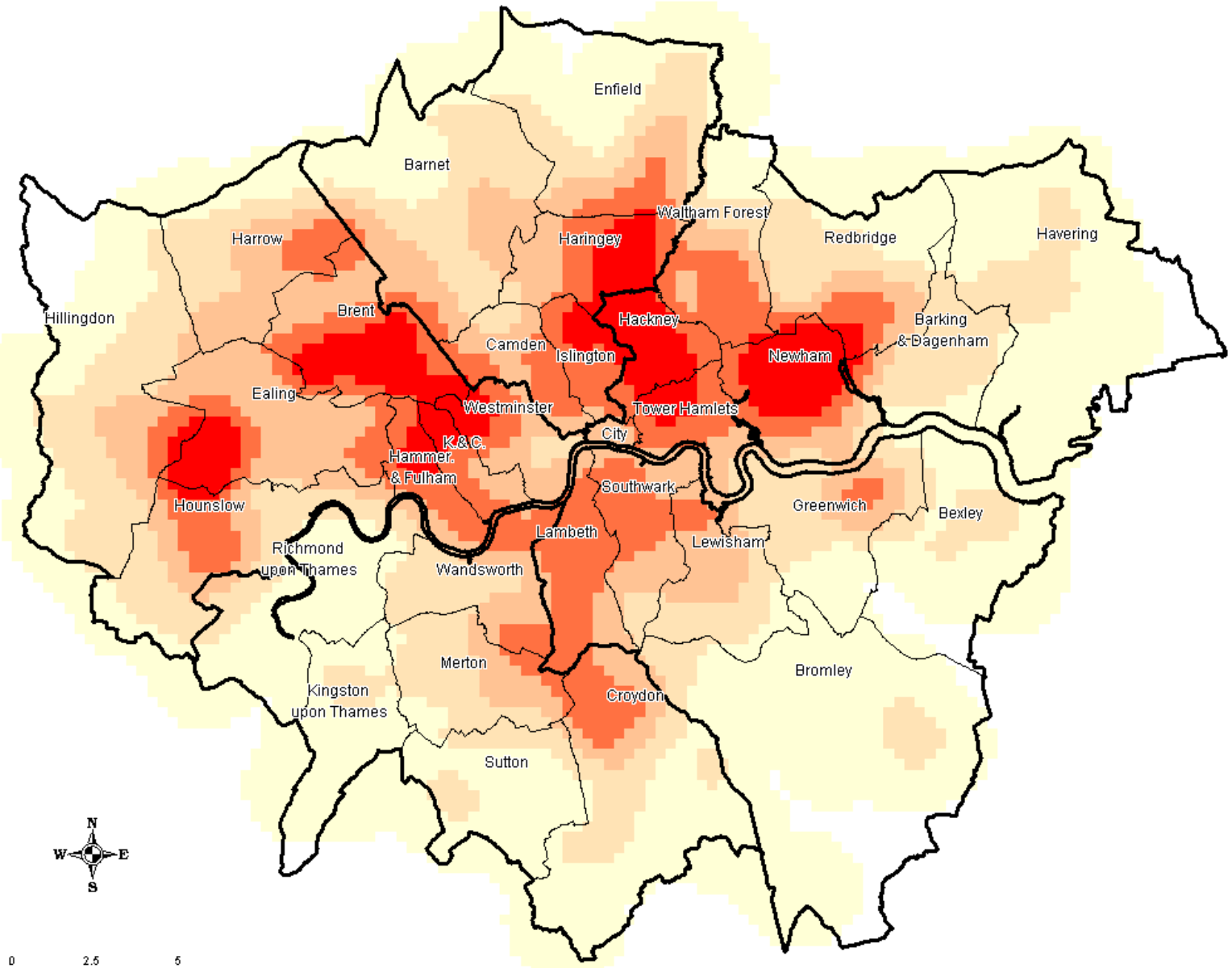
Transit cities: Africa

Source: Adapted from the 2014 Mediterranean Transit Migration (MTM) Map on Mixed Migration Routes in the MTM Region (i-Map).

Migration routes through the Mediterranean Sea

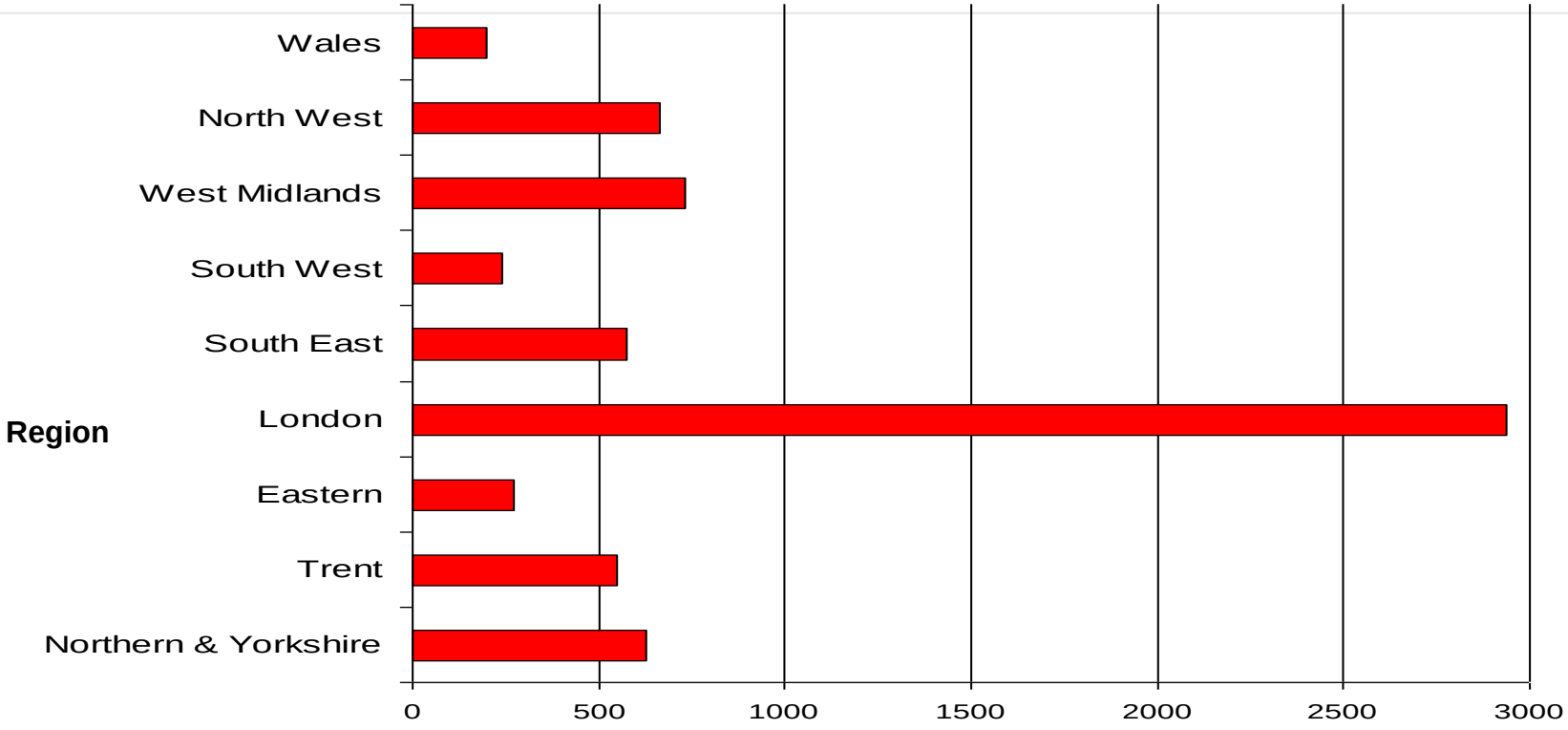


Density map of TB cases resident in Greater London



Source: Enhanced TB surveillance dataset, 2000
Surface created using kernel estimator with 1km bandwidth

Tuberculosis notifications - England and Wales by region



Data excludes chemoprophylaxis and Port Health Authorities
RHO boundaries as at April 1999
Source: Statutory notifications to the Communicable Disease Surveillance Centre
2000 data provisional

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History of screening

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EXPERT REVIEWS

The history and evolution of immigration medical screening for tuberculosis

Expert Rev. Anti Infect. Ther. 11(2), 137–146 (2013)

Masoud Dara[1], Brian D Gushulak[2], Drew L Posey[3], Jean-Pierre Zellweger[4] and Giovanni B Migliori*[5]

[1]*WHO Regional Office for Europe, Copenhagen, Denmark*
[2]*Migration Health Consultants, BC, Canada*
[3]*Division of Global Migration & Quarantine, National Center for Emerging & Zoonotic Infectious Diseases, Centers for Disease Control & Prevention, Atlanta, GA, USA*
[4]*Swiss Lung Association, Berne, Switzerland*
[5]*WHO Collaborating Centre for TB & Lung Diseases, S. Maugeri Foundation, Care & Research Institute, Via Roncaccio 16, 21049, Tradate, Italy*
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Identifying and managing TB in immigrating populations has been an important aspect of immigration health for over a century, with the primary aim being protecting the host population by preventing the import of communicable diseases carried by the arriving migrants. This review describes the history and development of screening for TB and latent TB infection in the immigration context (describing both screening strategies and diagnostic tests used over the last century), outlining current practices and considering the future impact of new advances in screening. The recent focus of the WHO, regarding their elimination strategy, is further increasing the importance of diagnosing and treating latent TB infection. The last section of this review discusses the latest public health developments in the context of TB screening in immigrant populations.

KEYWORDS: chest radiography • control • elimination • immigrants • screening • tuberculosis

The identification and management of diseases of public health importance in new arrivals is a relevant component of immigration health programs [1]. These programs were originally focused on protecting the health of the host population by excluding the arrival of those with communicable diseases.

Lazarettos were created in Europe since the 16th century to control prevalent epidemics

considers the future impact of new advances in screening.

The history of immigration medical screening

Evolving with quarantine and border health practices, immigration medical screening was a clinical process where new arrivals were assessed, inspected and examined by border or quarantine

Figure 1. Screening for tuberculosis, mental illness and syphilis, Ellis Island (USA), 1917. Upon arrival, migrants were asked to climb the steep stairs carrying with them their heavy luggage. On the top of the stairs, those coughing were examined for TB, while those smiling or looking happy were examined for mental illness and/or syphilis (which being often localized in the brain, was clinically diagnosed through psychiatric disturbances). The pictures were kindly provided by JP Zellweger.

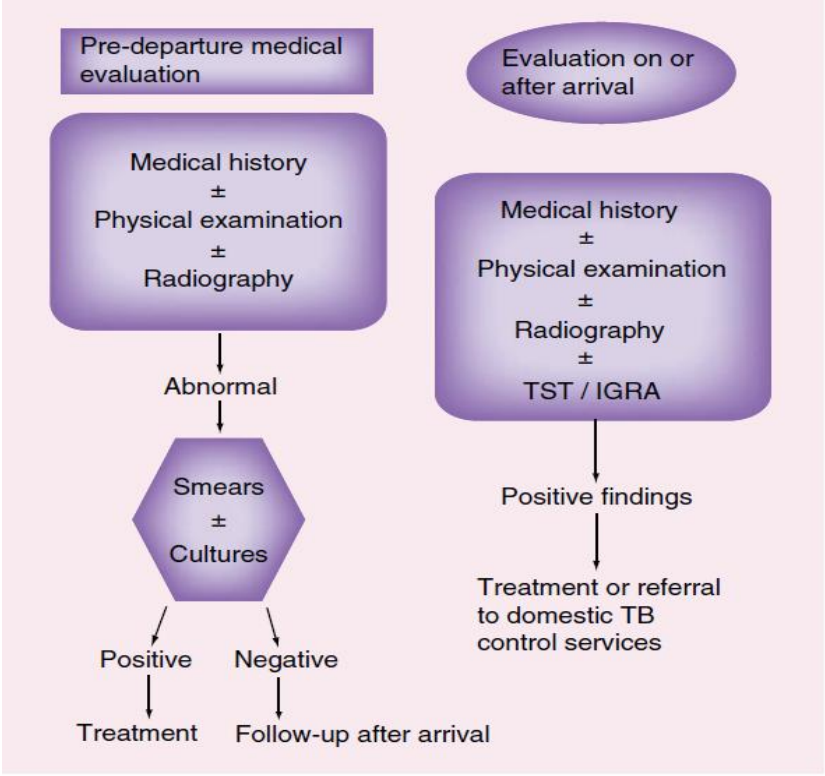


Figure 3. Examples of national practices.

At the same time, the improved understanding of the factors behind the reactivation of LTBI will allow better and more specific targeting of new diagnostic methodologies. Integrating immigration screening with programs to specifically identify LTBI at risk of reactivation and coupling that with domestic short course preventive therapy can be expected to be elements of widely applied best practices for managing TB in the foreign born in the future.

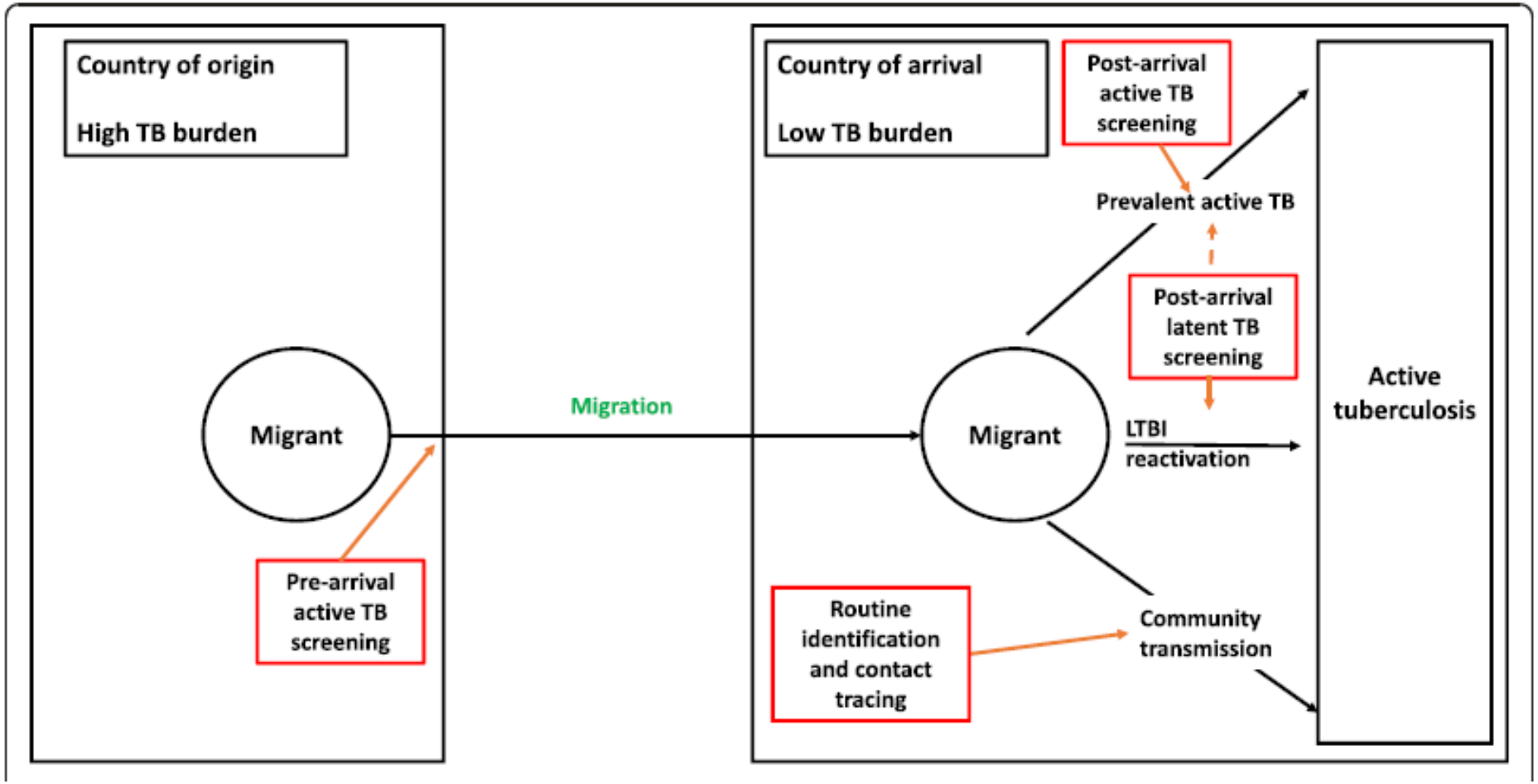
There is also a growing discussion about how screening programs can benefit broader control efforts. A recent analysis suggested that investments in TB infrastructure within a country will in the long run reduce the TB burden entering a receiving country greater than improvements in screening algorithms [70].

Key issues

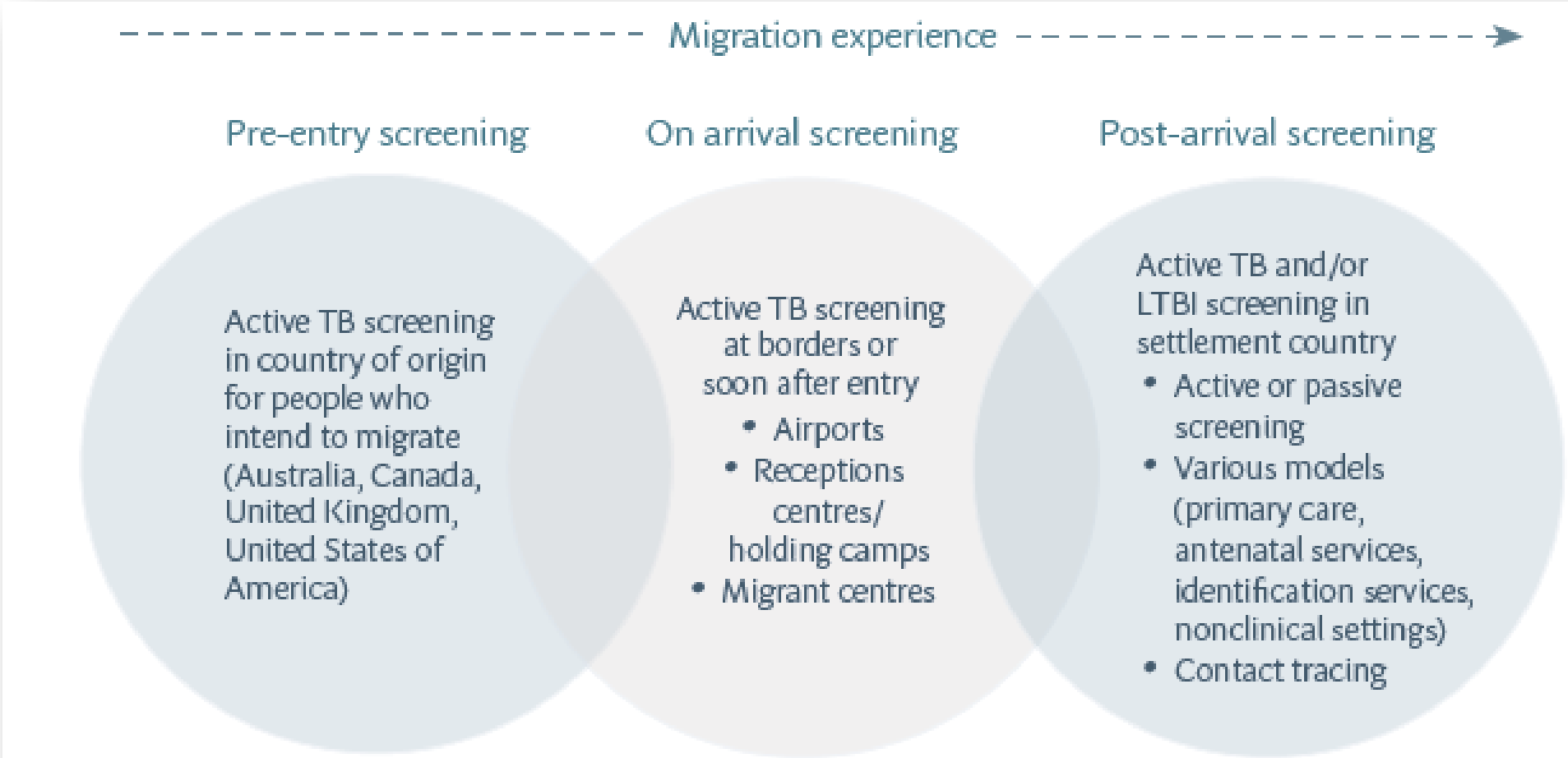
- Quarantine health practices and screening aimed at identifying transmissible diseases to protect host populations started before the 18th century.
- As the science and understanding of TB developed, programs and practices began to focus on the identification and management of diseases in a manner that supported organized immigration.
- While initially organized at the port of entry, screening practices were gradually integrated with predeparture investigations as requested by legislation in force in some countries.
- Initial immigration medical screening for TB is commonly undertaken through a combination of clinical and radiological methods. Individuals applying for permanent residence, temporary workers and long-staying visitors are often required to undergo a medical evaluation.
- The possibility to identify individuals in need of further investigation through scores and thresholds tuned on the country of origin of the migrants demonstrated significant advantages in terms of flexibility, cost and burden of medical procedures on the screened population, while maintaining approximately the same yield in terms of infectious TB cases detected.
- In the perspective of eliminating TB from low incidence countries, identification and treatment of latent infection is gaining more and more interest.

Screening practices for TB and LTBI

Schematic diagram of migration, factors determining how incident active tuberculosis occurs and methods of screening migrants



Pareek et al. BMC Medicine, 2016



Source: Modified from Pareek et al., 2016 (3).

Different approaches for the migrant screening process methods

Table 3 Potential strengths and weaknesses of different migrant screening methods

	Screening methodology	
	Screening for active tuberculosis	Screening for latent tuberculosis infection
Screening tool used	Chest x-ray	Tuberculin skin test
		Interferon gamma release assay
Screening location	Pre-arrival	Post-arrival
	At arrival	
	Post-arrival	
Strengths	Able to identify active TB	Identifies latent TB before reactivation occurs
	Able to identify infectious individuals	Can be built into community programmes
	Can be integrated into immigration processes	Targeted screening likely to be cost-effective
Weaknesses	Low yields for active TB	Programmatically difficult to implement
	Uncertain cost-effectiveness (unless screening targeted)	Numbers accepting and completing treatment may be suboptimal
	Does not identify patients with latent TB who can go on to reactivate	

Table 1. Immigration medical examination options.

Screening option	Location	Examples
Predeparture screening	Prior to the migrants' departure for the destination country	Australia, Canada, New Zealand and the USA
Immediate on-arrival screening	Examination at port of entry	UK and Switzerland
Postarrival screening	Screening after arrival and transit through the port of entry	Several European nations and Israel

Pareek et al. BMC Medicine, 2016
Dara M et al, Expert Review Anti Infect Therapy 2013

Yields for active tuberculosis from previous meta-analyses

Author	Year	Yield for active tuberculosis (%)		
		Overall	Pre-arrival	At/post-arrival
Klinkenberg [19]	2009	0.35	1.21	0.31
		0.51		
Arshad [18]	2010	0.35	-	0.35
Aldridge [71]	2014	0.22	0.22	-

Pareek et al. BMC Medicine, 2016

Yield of TB screening: Switzerland

INT J TUBERC LUNG DIS 14(11):1388–1394

Screening for tuberculosis in asylum seekers: comparison of chest radiography with an interview-based system

S. Schneeberger Geisler,* P. Helbling,* J. P. Zellweger,† E. S. Altpeter*

*Division of Communicable Diseases, Federal Office of Public Health, Berne, †Swiss Lung Association, Berne, Switzerland

SUMMARY

SETTING: Mandatory initial screening of asylum seekers for tuberculosis (TB) in Switzerland, 2004–2005 and 2007–2008.

OBJECTIVE: To compare the yield of screening by chest radiography with an individual assessment based on geographic origin, personal history and symptoms.

DESIGN: Cross-sectional retrospective comparison of two 2-year periods.

RESULTS: The prevalence of detected TB cases was defined as the proportion of screenees starting anti-tuberculosis treatment for culture-confirmed pulmonary TB within 90 days. TB prevalence was 14.3 per 10 000 asylum seekers screened (31/21 727) using chest radiography and 12.4 (29/23 402) using individual assessment. The sensitivity of radiography was 100% vs. 55% for individual assessment, but its specificity was lower (89.9% vs. 96.0%, respectively). The higher sensitivity of radiography meant shorter delays between screening and start of treatment (median 6 vs. 25 days). Its lower specificity led to a larger proportion of screenees needing further investigations for suspicion of TB (12% vs. 4%).

CONCLUSION: The interview-based system initially missed more cases, but the ultimate 90-day yield was comparable for the two periods. The main difference is the delay until start of treatment, which potentially increases transmission and secondary cases. The radiograph system was more burdensome to both the health care system and the screenees, as more suspects required further investigations.

KEY WORDS: tuberculosis; screening; immigrants; asylum seekers

Yield of screening for LTBI: Switzerland

Sarivalasis *et al. BMC Infectious Diseases* 2012, **12**:285
http://www.biomedcentral.com/1471-2334/12/285

BMC Infectious Diseases

RESEARCH ARTICLE Open Access

Factors associated with latent tuberculosis among asylum seekers in Switzerland: a cross-sectional study in Vaud County

Apostolos Sarivalasis[1*], Jean - Pierre Zellweger[2], Mohamed Faouzi[3], Oscar Daher[4], Charlotte Deslarzes[5] and Patrick Bodenmann[1]

Abstract

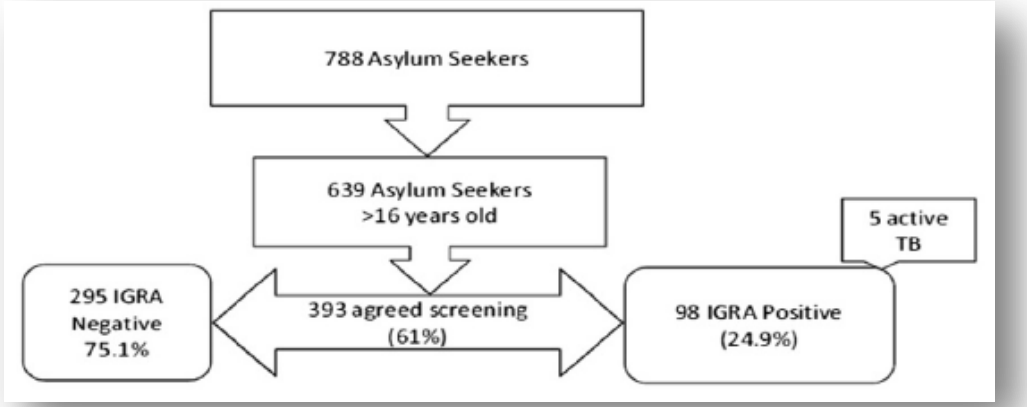
Background: Screening and treatment of latent tuberculosis infection (LTBI) in asylum seekers (AS) may prevent future cases of tuberculosis. As the screening with Interferon Gamma Release Assay (IGRA) is costly, the objective of this study was to assess which factors were associated with LTBI and to define a score allowing the selection of AS with the highest risk of LTBI.

Methods: In across-sectional study, AS seekers recently arrived in Vaud County, after screening for tuberculosis at the border were offered screening for LTBI with T-SPOT.TB and questionnaire on potentially risk factors. The factors associated with LTBI were analyzed by univariate and multivariate regression.

Results: Among 393 adult AS, 98 (24.93%) had a positive IGRA response, five of them with active tuberculosis previously undetected. Six factors associated with LTBI were identified in multivariate analysis: origin, travel conditions, marital status, cough, age and prior TB exposure. Their combination leads to a robust LTBI predictive score.

Conclusions: The prevalence of LTBI and active tuberculosis in AS is high. A predictive score integrating six factors could identify the asylum seekers with the highest risk for LTBI.

Keywords: Asylum seeker, Latent tuberculosis infection, Tuberculosis, Risk factors, Predictive score, Interferon gamma release assay



Conclusions

This study highlights the factors associated with LTBI among asylum seekers entering Vaud County, Switzerland. The observed prevalence of LTBI (24.9%) matches with the prevalence from the literature. The prevalence of TB previously undetected at the border in asylum seekers with LTBI was also high (5.1%). The factors associated with LTBI identified in this population (age, origin from FSU, Asian and African countries, ground transportation; married status; prior TB exposure and cough) were combined to create a predictive score of LTBI for asylum seekers which could be used at border screening. The application of this score to an asylum seeker population could help discriminating those most at risk for LTBI permitting a limitation of the number of IGRA to be performed in a border screening setting.

Latent tuberculosis screening and treatment among asylum seekers: a mixed-methods study

Ineke Spruijt[1,2], Dawit Tesfay Haile[2], Jeanine Suurmond[2], Susan van den Hof[1,3], Marga Koenders[4], Peter Kouw[5], Natascha van Noort[6], Sophie Toumanian[7], Frank Cobelens[8], Simone Goosen[9] and Connie Erkens[1]

@ERSpublications
LTBI screening and treatment among asylum seekers is feasible and effective when high quality of care is provided, including special attention for culture-sensitive education about TB and LTBI and collaboration with partner organisations http://bit.ly/2Lf6Y1I

Cite this article as: Spruijt I, Tesfay Haile D, Suurmond J, *et al.* Latent tuberculosis screening and treatment among asylum seekers: a mixed-methods study. *Eur Respir J* 2019; 54: 1900861 [https://doi.org/10.1183/13993003.00861-2019].

ABSTRACT

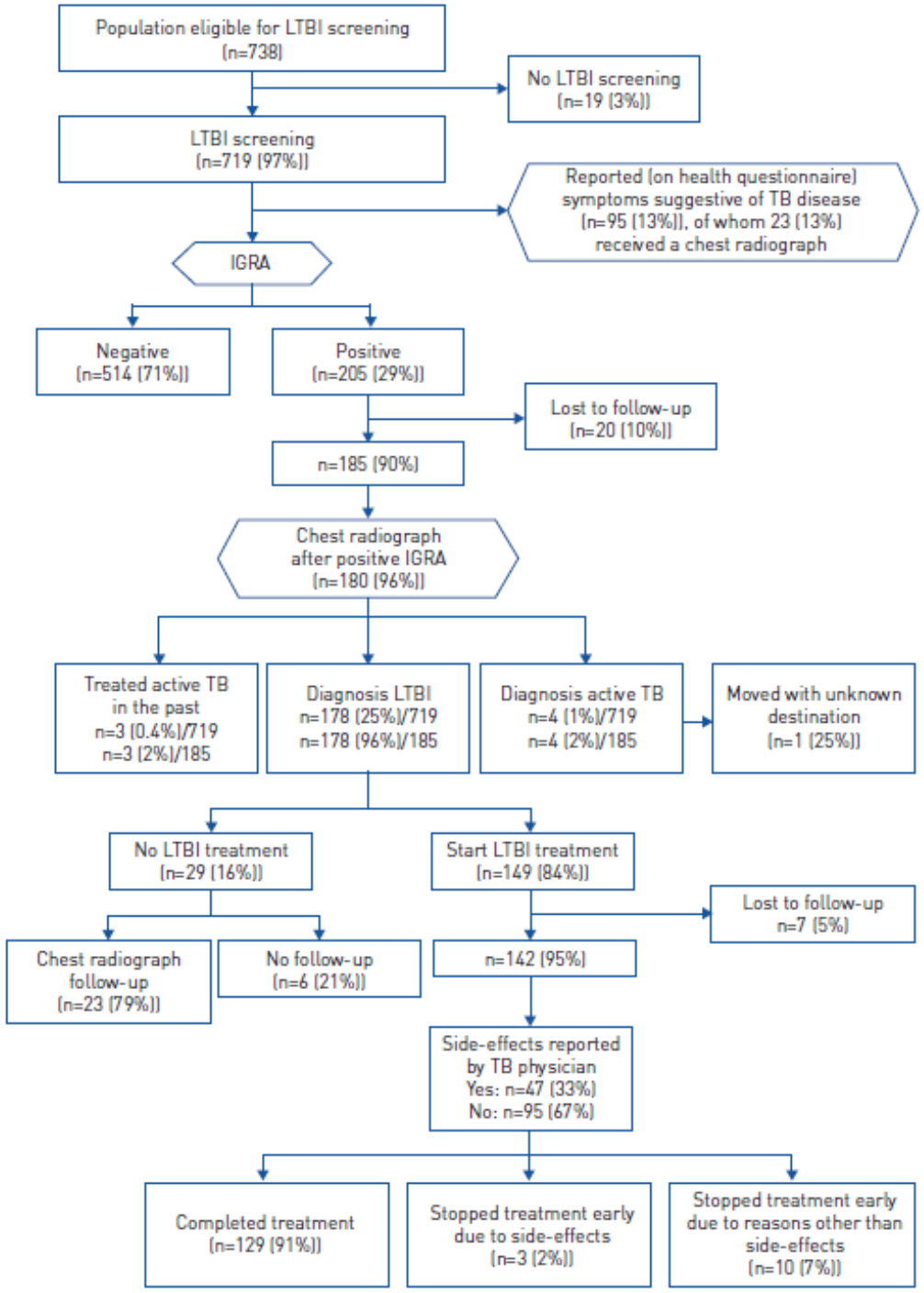
Introduction: Evidence on conditions for implementation of latent tuberculosis infection (LTBI) screening and treatment among asylum seekers is needed to inform tuberculosis (TB) control policies. We used mixed-methods to evaluate the implementation of an LTBI screening and treatment programme among asylum seekers in the Netherlands.

Methods: We offered voluntary LTBI screening to asylum seekers aged ⩾12 years living in asylum seeker centres from countries with a TB incidence >200 per 10 000 population. We calculated LTBI screening and treatment cascade coverage, and assessed associated factors with Poisson regression using robust variance estimators. We interviewed TB care staff (seven group interviews) and Eritrean clients (21 group and 21 individual interviews) to identify programme enhancers and barriers.

Results: We screened 719 (63% of 1136) clients for LTBI. LTBI was diagnosed among 178 (25%) clients; 149 (84%) initiated LTBI treatment, of whom 129 (87%) completed treatment. In-person TB and LTBI education, the use of professional interpreters, and collaboration with partner organisations were enhancers for LTBI screening uptake. Demand-driven LTBI treatment support by TB nurses enhanced treatment completion. Factors complicating LTBI screening and treatment were having to travel to public health services, language barriers and moving from asylum seeker centres to the community during treatment.

Conclusion: LTBI screening and treatment of asylum seekers is feasible and effective when high quality of care is provided, including culture-sensitive TB education throughout the care cascade. Additionally, collaboration with partner organisations, such as agencies responsible for reception and support of asylum seekers, should be in place.

719 screened for LTBI
178 (25%) with LTBI
149 (84%) initiated LTBI treatment
129 (87%) completed LTBI tretament



Migrants and health

Cross-border migration and tuberculosis care: the settings

- Migrants crossing borders have health problems, which may be pre-existing or discovered after arrival
- In case of further migration, some chronic or long-term diseases may need a further treatment in another country
- Continuity of care needs (ideally)
  - understanding the migrant's history, needs and priorities
  - search for prior medical documents
  - addressing the legal problems with local authorities
  - contacts with foreign structures in charge of further treatment
  - comprehensive information of the migrants

Infectious diseases to consider according to country of origin

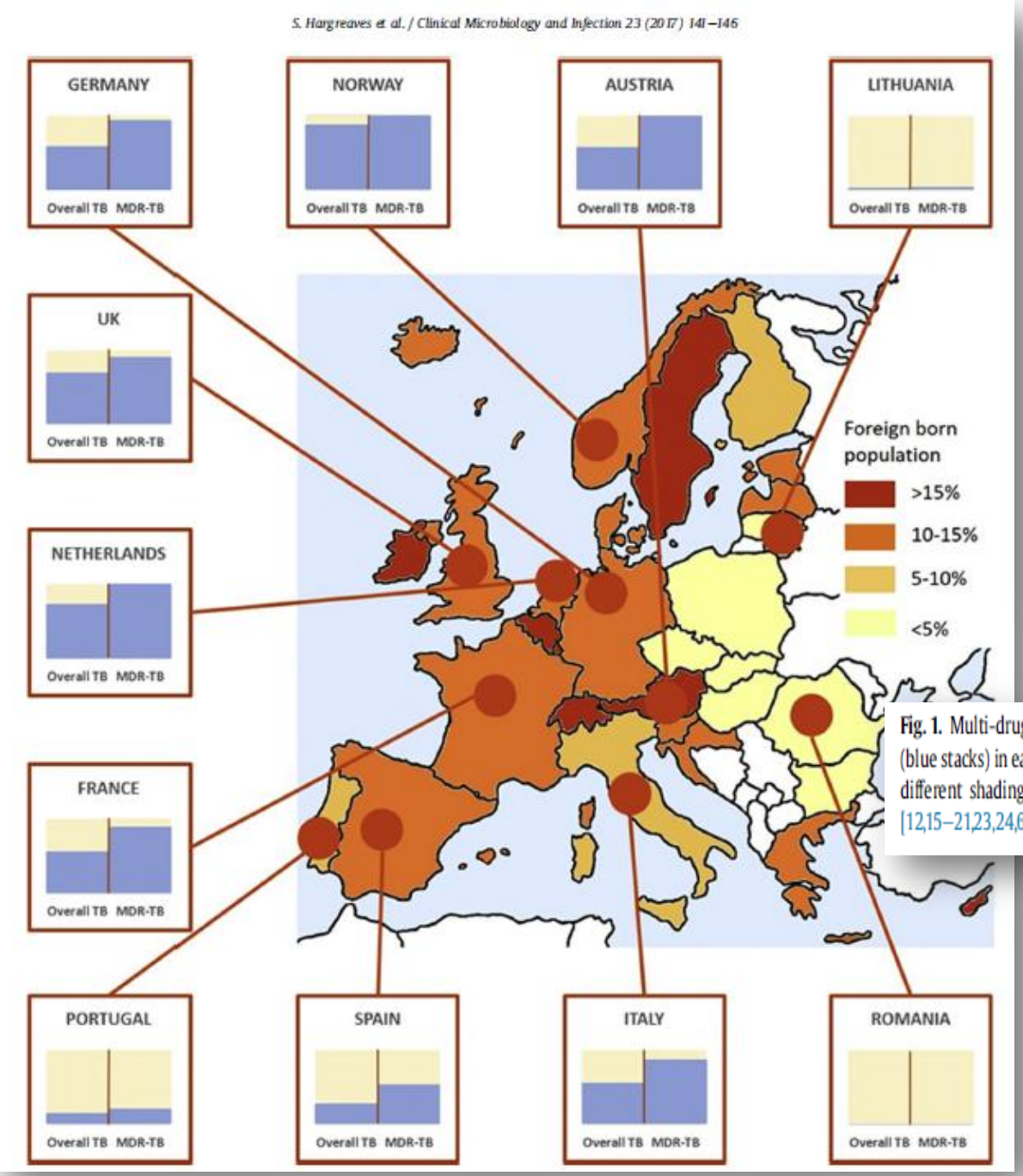
Disease	Indicator	Syria	Afghanistan	Iraq	Eritrea	Somalia
Diphtheria [3]	Cases reported to WHO in 2012, 2013, 2014	0, 0, and NA	0, 0, 0	3, 4, and 5	8, 0 and NA	65, 7 and NA
Typhoid fever	Risk of typhoid	✓	✓	✓	✓	✓
Cholera*	Risk	No recent outbreak	Recurrent outbreaks	On-going outbreak in Baghdad Babylon, Najaf, Qadisiyyah, and Muthanna.	NA	Recurrent outbreaks
Hepatitis A†	Risk	High endemicity	NA	High endemicity	High endemicity	High endemicity
Hepatitis E‡	Risk	NA	NA	High endemicity	NA	High endemicity
Helminthiasis§	Risk of soil transmitted helminthiasis (ascaris, whipworm, hookworm)	+	++	+	++	++
	Risk of urinary schistosomiasis	✓	Non-endemic country	✓	✓	✓
Leishmaniasis**	Risk of cutaneous leishmaniasis	✓	✓	✓	✓	✓
	Risk of visceral leishmaniasis	✓	✓	✓	✓	✓
Hepatitis B††	Prevalence of chronic hepatitis B	Intermediate prevalence: 5.6%	High prevalence: 10.5%	Low prevalence: 1.3%	High prevalence: 15.5%	High prevalence: 12.4%
Hepatitis C‡‡	Prevalence	High prevalence: 3.1%	High prevalence: 1.1%	High prevalence: 3.2%	High prevalence: 1%	NA
HIV	Prevalence	Low	NA	Low	Low	Low
Malaria§§	Risk of malaria	Malaria-free	Risk of *P. vivax* >> *P. falciparum*	Malaria-free	Risk *of P. falciparum* >> *P. vivax*	Risk *of P. falciparum*
Measles*	Incidence per 100 000 in 2013 and 2014	1.84 and 2.68	1.41 and 1.75	2.09 and 3.02	0.77 and 0.02	2.17 and 9.12
Polio***	Cases reported to WHO in 2012, 2013 and 2014	0, 35 and NA	46, 17, and 28	0, 0, and 2	0, 0, and 0	1, 195 and 5
Tuberculosis†††	Incidence/100 000	Low: 17	High: 189	Low: 25	High: 40 to 499	High: 285
Antimicrobial resistance	Risk of carriage of multidrug-resistance Gram-negative bacteria	NA	NA	NA	NA	NA
Rabies	Risk level for humans contracting rabies	High	High	High	High	High

ECDC 2015. Infectious diseases of specific relevance to newly-arrived migrants in the EU/EEA

Differential diagnosis among newly arrivad migrants

Clinical presentation	Differential diagnosis to consider
Fever	Typhoid fever Malaria Louse-borne diseases Visceral leishmaniasis Amoebic abscess Arboviruses
Respiratory symptoms	Tuberculosis Influenza
Gastrointestinal symptoms	Cholera Typhoid fever Shigellosis Amoebic colitis Helminthiasis: ascaris, whipworm, hookworm
Sores	Scabies Cutaneous leishmaniasis Cutaneous diphtheria
Skin rash	Measles Rubella Louse-borne diseases
Meningitis or other neurological symptoms	Rabies Invasive bacterial diseases (*Neisseria meningitidis, Haemophilus influenza type b and Streptococci pneumoniae*) Polio Dengue and other arboviruses

ECDC 2015. Infectious diseases of specific relevance to newly-arrived migrants in the EU/EEA



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journal homepage: www.clinicalmicrobiologyandinfection.com

Review

Multidrug-resistant tuberculosis and migration to Europe

S. Hargreaves [1], K. Lönnroth [2, 3], L.B. Nellums [1], I.D. Olaru [4, 5], R.R. Nathavitharana [1, 6], M. Norredam [7, 8], J.S. Friedland [1, *]

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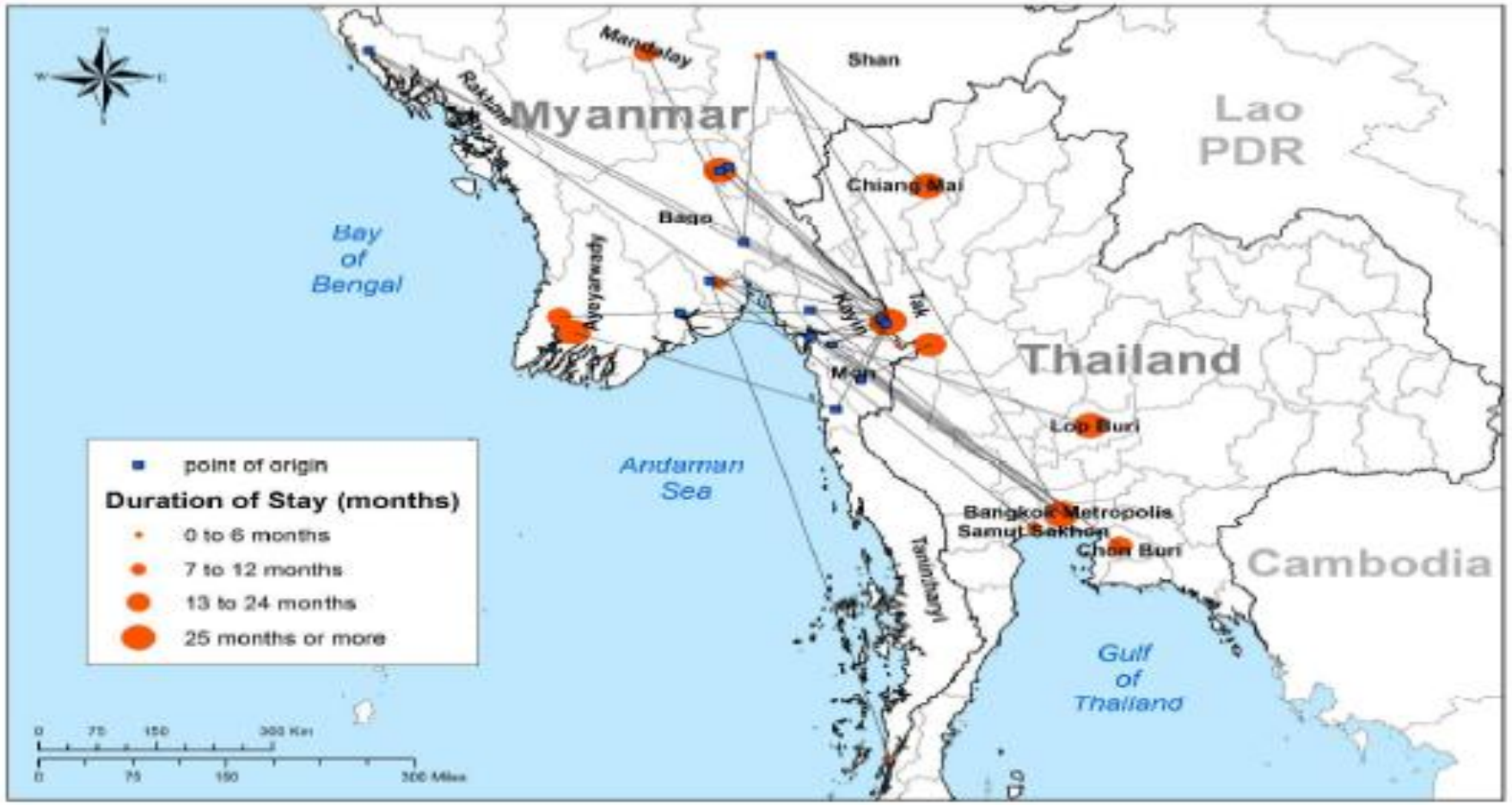
[8] Section of Immigrant Medicine, Department of Infectious Diseases, University Hospital, Hvidovre, Denmark

Fig. 1. Multi-drug-resistant tuberculosis (MDR-TB) and migration in Europe. The boxes in this figure illustrate the proportion of TB cases and MDR-TB cases that occur in migrants (blue stacks) in each country. Columns in the boxes represent the percentage of foreign-born overall, among the total TB and MDR-TB cases reported in that country. On the map, the different shadings of the countries represent the proportions of foreign-born individuals living in that country that are comprised by migrants. Data taken from references [12,15–21,23,24,61].

MDR-TB and migration in Europe

Migration from Myanmar to Thailand



Sein Sein Thi et al., Int J Tuberc Lung Dis. 2017

A cluster of multidrug-resistant *Mycobacterium tuberculosis* among patients arriving in Europe from the Horn of Africa: a molecular epidemiological study

Timothy M Walker, Matthias Merker*, Astrid M Knoblauch*, Peter Helbling, Otto D Schoch, Marieke J van der Werf, Katharina Kranzer, Lena Fiebig, Stefan Kröger, Walter Haas, Harald Hoffmann, Alexander Indra, Adrian Egli, Daniela M Cirillo, Jérôme Robert, Thomas R Rogers, Ramona Groenheit, Anne T Mengshoel, Vanessa Mathys, Marjo Haanperä, Dick van Soolingen, Stefan Niemann†, Erik C Böttger†, Peter M Keller†, and the MDR-TB Cluster Consortium‡*

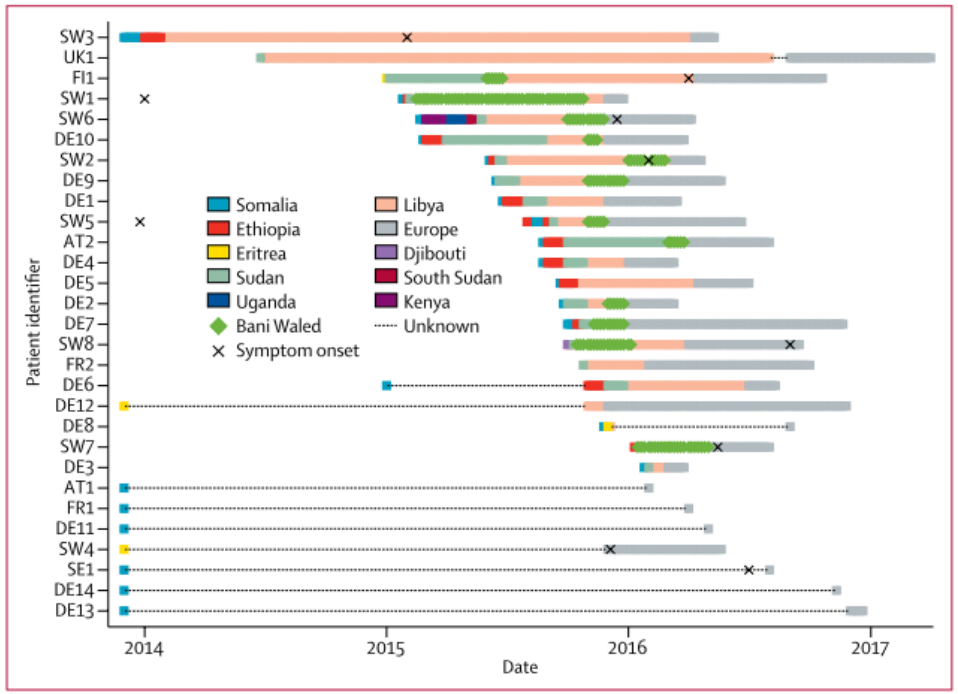


Figure 2: **Timeline of patient journeys until diagnosis**
The 1st of each month is shown as the country entry date. Subsequent countries visited in the same month are presented at 5-day intervals.

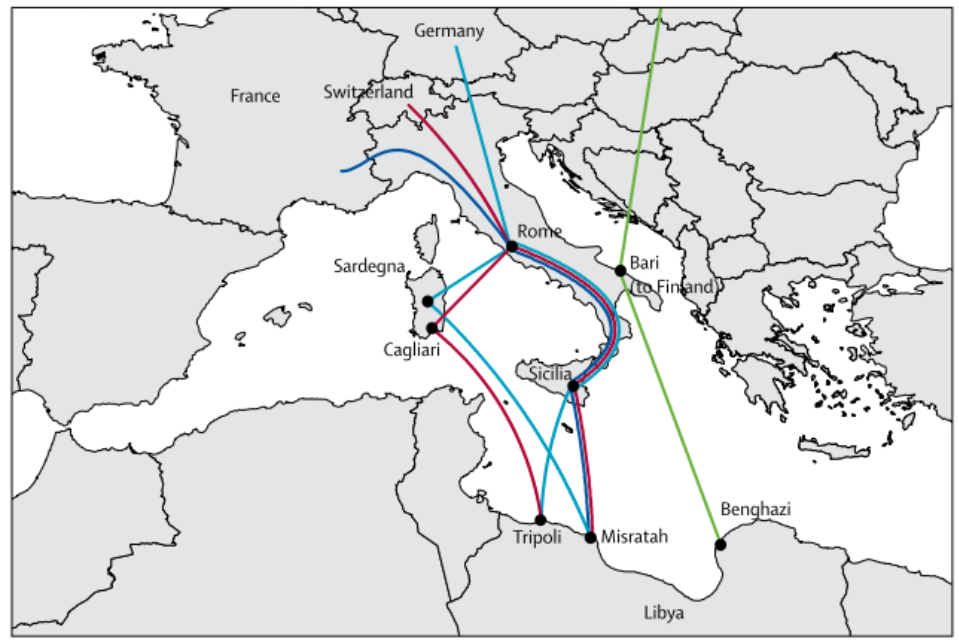


Figure 3: **Reported migration routes through Italy of 29 outbreak patients with a documented migration route, August, 2014, to February, 2017**

EUROPEAN LUNG CORN
ERS/THE UNION STATEMENT ON TUBERCULOS

Statement of the European Respiratory Society and the European region of the International Union Against Tuberculosis and Lung Disease: call for urgent actions to ensure access to early diagnosis and care of tuberculosis among refugees

Masoud Dara[1], Ivan Solovic[2], Giovanni Sotgiu[3], Lia D'Ambrosio[4,5], Rosella Centis[4], Delia Goletti[6], Raquel Duarte[7], Stefano Aliberti[8], Fernando Maria de Benedictis[9], Graham Bothamley[10], Tom Schaberg[11], Ibrahim Abubakar[12], Brian Ward[13], Vitor Teixeira[13], Christina Gratziou[14] and Giovanni Battista Migliori[4]

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Correspondence: Giovanni Battista Migliori, WHO Collaborating Centre for TB and Lung Diseases, Fondazi S. Maugeri IRCCS, Via Roncaccio 16, Tradate, Varese 21049, Italy. E-mail: giovannibattista.migliori@fsm.it

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ERS and the European region of The Union call for prioritisation of TB care, prevention a control among refugees http://ow.ly/YYCL8

Tuberculosis (TB) is a major cause of mortality from an infectious disease, globally affecting 9.6 mill cases, with 1.5 million deaths in 2014 [1]. In 2014, there were 273 381 TB cases reported in the Wo Health Organization (WHO) European region, and an estimated 33 000 deaths [2]. Vulnerable populati (*i.e.* individuals affected by discrimination, hostility or economic adversity), which often include migra and refugees, have an increased risk of suffering from TB disease [1, 3, 4]. If this is not efficiently address the exposure of these groups to *Mycobacterium tuberculosis* strains may lead to a rise in the number cases of disease and related deaths, as well as contributing to a further increase in drug-resistant TB cases

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Christina Gratziou is the European Respiratory Society Advocacy Council Chair and Secretary for European Un Affairs 2015–2018.

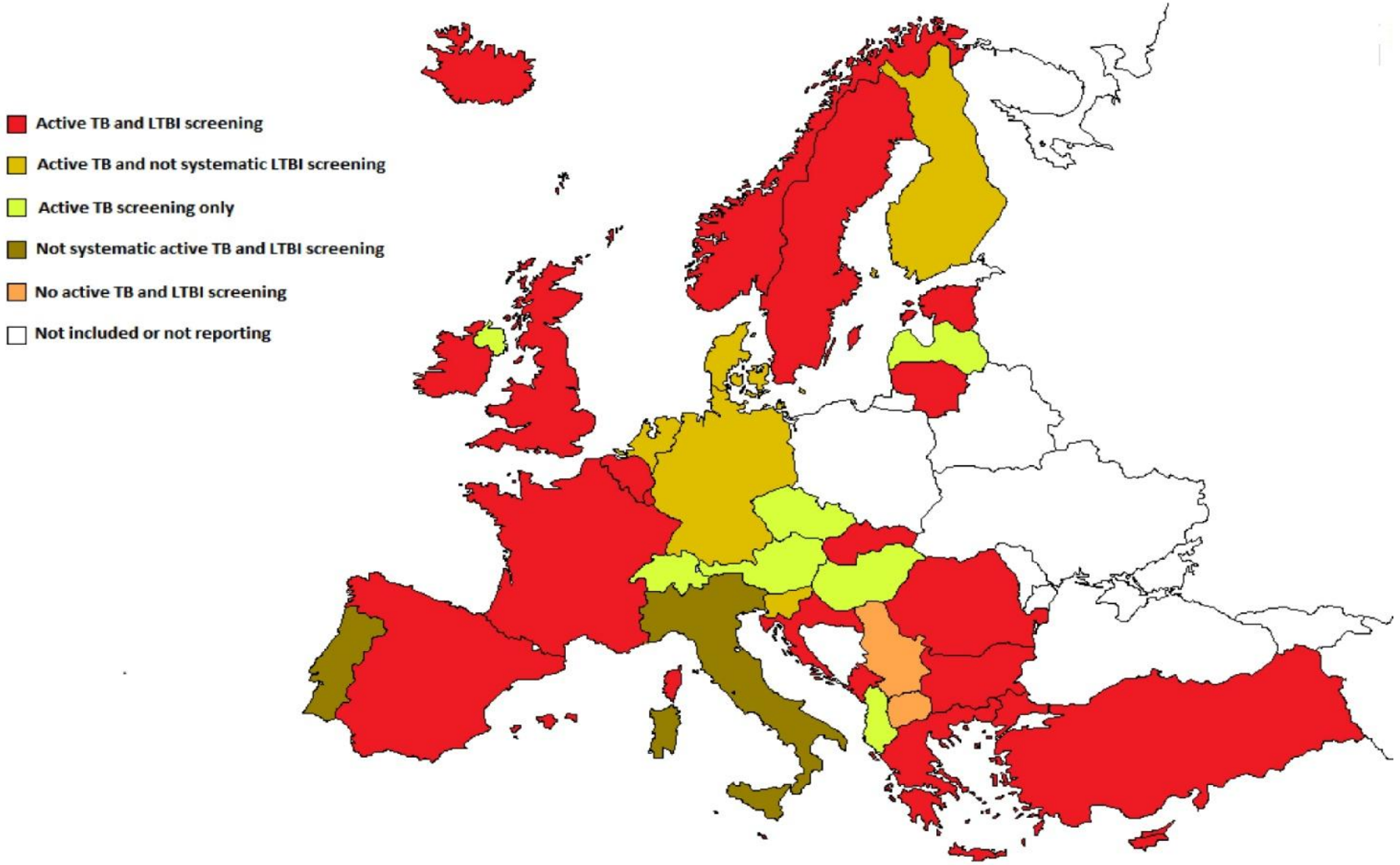
Conflict of interest: Brian Ward and Vitor Teixeira are employees of the European Respiratory Society. Disclosures be found alongside the online version of this article at erj.ersjournals.com

Recommendations ERS, UNION-ER (+WHO Euro)

- **Refugees to benefit from End TB Strategy principles**
- **Improve surveillance M&E, research on TB/LTBI**
- **Timely screening**
- **Avoid stigma & steroetypes**
- **Universal access TB/LTBI services**
- **Infection control**

The European Respiratory Society and the European region of the International Union Against TB and Lung Disease urge health authorities, national and international technical agencies and civil society organisations, as well as donor agencies, to prioritise TB care, prevention and control. They strongly recommend: 1) adapting and implementing the principles of the WHO End TB Strategy to ensure adequate prevention, diagnosis and treatment of TB (and of LTBI in the countries where these are offered) among refugees [1, 5]; 2) providing quality surveillance, monitoring and evaluation, and operational research to enhance TB prevention, control and care among refugees; 3) ensuring timely screening for active TB among refugees coming from middle or high TB incidence countries; 4) avoiding stigmatisation and stereotypes of both TB-infected people and vulnerable groups; 5) promoting universal access to prevention, diagnosis and treatment services for LTBI (in the countries where these are offered) and TB, as well as to the necessary care of existing comorbidities [1, 5]; and 6) ensuring quality infection control, including protective measures for staff, and providing HIV testing and counselling to detect HIV and TB/HIV co-infected individuals [18, 19].

SUMMARY OF TB AND LTBI SCREENING



Conclusions 1

- High response rate; TB screening considered important public health intervention
- Country-specific algorithms (questionnaire/CXR +bacteriology)
- Lack of analysis on yield of screening (workload?)
- >TB <LTBI: implications for TB Elimination?
- 11/36 countries ‘equipped’ to collect info on LTBI, but 3 do collect (Finland, Norway, UK)

Minimum package for cross border TB control and care

Eur Respir J 2012; 40: 1081–1090
DOI: 10.1183/09031936.00053012

PERSPECTIVE

Minimum package for cross-border TB control and care in the WHO European region: a Wolfheze consensus statement

Masoud Dara, Pierpaolo de Colombani, Roumyana Petrova-Benedict, Rosella Centis, Jean-Pierre Zellweger, Andreas Sandgren, Einar Heldal, Giovanni Sotgiu, Niesje Jansen, Rankica Bahtijarevic and Giovanni Battista Migliori on behalf of the members of the Wolfheze Transborder Migration Task Force

ABSTRACT: **The World Health Organization (WHO) European region estimates that more than 400,000 tuberculosis (TB) cases occur in Europe, a large proportion of them among migrants.**

A coordinated public health mechanism to guarantee TB prevention, diagnosis, treatment and care across borders is not in place. A consensus paper describing the minimum package of cross-border TB control and care was prepared by a task force following a literature review, and with input from the national TB control programme managers of the WHO European region and the Wolfheze 2011 conference. A literature review focused on the subject of TB in migrants was carried out, selecting documents published during the 11-yr period 2001–2011.

Several issues were identified in cross-border TB control and care, varying from the limited access to early TB diagnosis, to the lack of continuity of care and information during migration, and the availability of, and access to, health services in the new country.

The recommended minimum package addresses the current shortcomings and intends to improve the situation by covering several areas: political commitment (including the implementation of a legal framework for TB cross-border collaboration), financial mechanisms and adequate health service delivery (prevention, infection control, contact management, diagnosis and treatment, and psychosocial support).

KEYWORDS: **Control, Europe, human rights, immigration, multidrug-resistant tuberculosis, tuberculosis**

AFFILIATIONS
Author affiliations and a full list of task force members can be found in the Acknowledgements section.

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May 31 2012

ERJ Open

Management, human rights and finance	Governance	Legal framework	Commitment to cross-border TB control and care Ensure legal basis for cross-border TB control and care within EU and non-EU, and between EU and non-EU
		Funding	Ensure funding from government resources, health insurance and/or bilateral and multilateral funding mechanisms
		Intercountry correspondence	Create and maintain a live list of TB service providers in the region
	Service delivery	Prevention	Diagnosis and treatment of LTBI
		TB infection control	Administrative measures, environmental measures and personal protection
		Diagnosis	Early diagnosis including drug-resistant TB
		Treatment	Prompt and effective treatment
		Continuity of care	No deportation before the end of treatment or at least until the end of intensive phase and ensuring continuation phase treatment will be followed
	Surveillance and monitoring	Individual patient data	Effective transfer of patient's record
			Feedback to the centre sending patients
		Programme performance	Relevant indicators at country and regional level measure progress
	Supportive environment	Enablers and incentives	Counselling Psychosocial support to patients
		Advocacy communication and social mobilisation	Empower communities for providing migrant-sensitive services Improve communication with migrant communities Advocate for full engagement of health authorities and stakeholders

Defining a migrant-inclusive tuberculosis research agenda to end TB

Operational and implementation research	
Prevention and screening	Evaluate feasibility of LTBI targeted testing and treatment algorithms on migrants at key points along the migration pathway
	Assess the use of mobile health (mHealth) and digital health technologies to support linkage to care and treatment adherence in migrant populations
	Evaluate the operational impact of LTBI screening tools (both pre- and post-arrival)
Diagnostics	Evaluate specific evidence-based diagnostic guidelines in migrant populations compared to native populations
	Identify health systems and patient barriers to implementation of diagnostic testing strategies in migrants
Treatment	Establish the comparative effectiveness of treatment strategies (e.g., DOT vs. SAT)
	Evaluate the impact of novel treatment regimens, including short-course treatment, in migrants when implemented in programmatic settings
	Identify core components of interventions needed to maximize treatment adherence
	Pilot mechanisms to ensure that culture and drug susceptibility results are communicated to providers treating a patient along the migration pathway
Health systems and health economics research	Evaluate the cost and cost-effectiveness of migrant-focused TB interventions
	Analyze gaps in health system access specific to documented and undocumented migrants along the migration pathway
	Establish critical components necessary for operationalizing cross-border collaborations
Social protection research	Identify context-specific social and economic vulnerabilities in migrants
	Identify targetable socio-economic barriers to TB care for migrants
	Evaluate the effectiveness and impact of social protection strategies on reducing vulnerabilities and improving public health and TB outcomes in migrants
	Understand the contextual requirements for including migrants in social protection schemes
	Identify and evaluate TB-sensitive and TB-specific interventions on migrant health
Health and human rights research	Document infringements on human rights by TB programs
	Develop TB-specific interventions that support the human rights of migrants

TB = tuberculosis; LTBI = latent tuberculous infection; MDR-TB = multidrug-resistant TB; DOT = directly observed therapy; SAT = self-administered therapy.

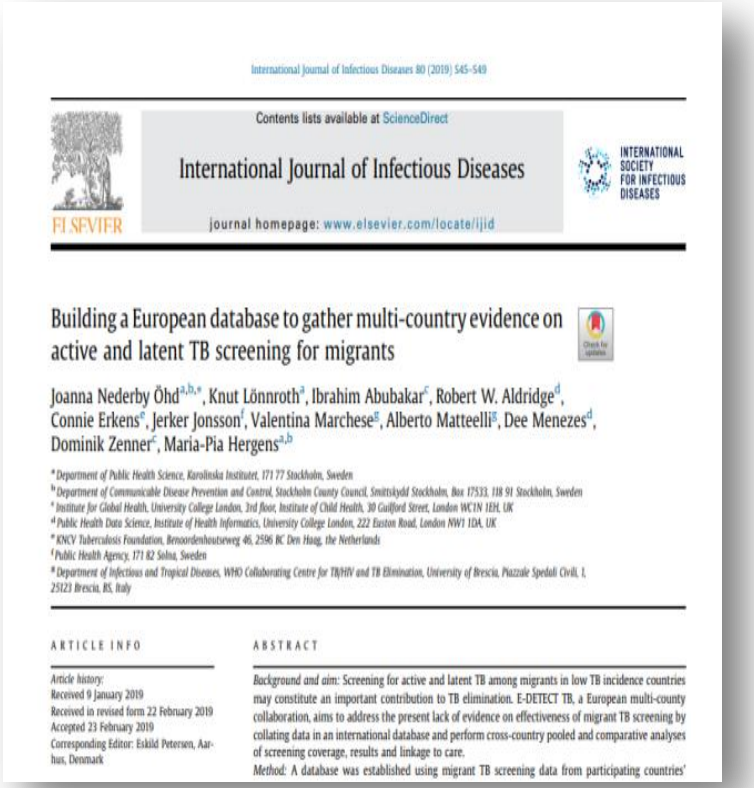
Shete P.B et al. Int J Tuberc L Dis 2018

Some answers

Factsheets for World TB Day 2019

E DETECT TB: a research consortium for the early detection and integrated management of tuberculosis in Europe (Link: https://e-detecttb.eu/)

EUROPEAN MIGRANT TB SCREENING DATABASE PUBLISHED IN IJID
(MARCH 2019)



International Journal of Infectious Diseases 80 (2019) 545–549

Contents lists available at ScienceDirect

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journal homepage: www.elsevier.com/locate/ijid

Building a European database to gather multi-country evidence on active and latent TB screening for migrants

Joanna Nederby Öhd[a,b,*], Knut Lönnroth[a], Ibrahim Abubakar[c], Robert W. Aldridge[d], Connie Erkens[e], Jerker Jonsson[f], Valentina Marchese[g], Alberto Matteelli[g], Dee Menezes[d], Dominik Zenner[c], Maria-Pia Hergens[a,b]

ARTICLE INFO

ABSTRACT

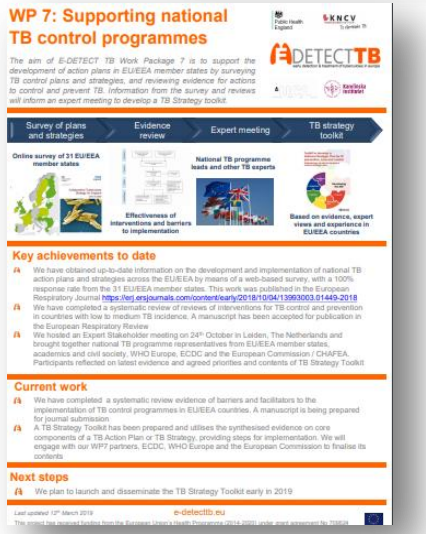
E-DETECT TB's projects

Outreach for early diagnosis (work package 4): WHO recommends systematic screening for active TB in subpopulations that have poor access to healthcare. Romania and Bulgaria are countries in transition from a high to intermediate incidence and are experiencing high TB rates among certain populations. In this work package we're using a mobile diagnostic unit equipped with digital radiography and molecular point of care tests to improve early diagnosis in these populations. (https://gallery.mailchimp.com/d405cdce217c79417c4a85931/files/7b29ec18-23c3-4b06-98cc-f9362a082c04/fact_sheet_WP4_WTBD_2019.pdf)

Migrant TB detection, prevention and treatment (work package 5): In Italy, we are actively screening new and settled migrants for active and latent TB respectively, ensuring that those testing positive are appropriately managed and generating the evidence to support future European policy (https://gallery.mailchimp.com/d405cdce217c79417c4a85931/files/63b2d415-3ce0-4008-80ea-fb707dfbfdce/fact_sheet_WP5_WTBD_2019.pdf.)

Establishing a database on migrant TB screening in Europe (work package 6): Many low-incidence EU countries have a high TB burden in migrants from endemic countries. Migrant TB screening policies vary widely across EU countries. This work package is establishing a multi-country database on migrant TB screening that will be used to inform the identification and harmonisation of cost-effective screening strategies in the EU. (https://gallery.mailchimp.com/d405cdce217c79417c4a85931/files/810d65f4-45a4-49ee-84d8-f10a6d83466d/fact_sheet_WP6_WTBD_2019.pdf.)

Supporting national TB control programmes (work package 7): The aim of E-DETECT TB work package 7 is to support the development of action plans in EU/EEA member states by surveying TB control plans and strategies, and reviewing evidence for actions to control and prevent TB. Information from the survey and reviews will inform an expert meeting to develop a TB Strategy toolkit. (https://gallery.mailchimp.com/d405cdce217c79417c4a85931/files/989c1ae6-f29e-4329-b59c-6d3504417add/Fact_sheet_WP7_WTBD_2019.pdf.)



Consultation with a TB Expert tbconsilium@gmail.com

The clinical service is active within the GTN "Global TB Network" (hosted by Waidid)

- FREE COST
- Top rapid procedure (48 h)
- >40 global TB experts
- in 4 languages (ENG, RU, SPA, PORT)
- easy to use (simplified collection data form)
- new e-platform available soon (Waidid website)
- indipendent & audited technical body for compassionate/expanded use of new drugs (outcomes)

- **CONTACT US : tbconsilium@gmail.com**

GTbN
the Global Tb Network
fighting Tb together

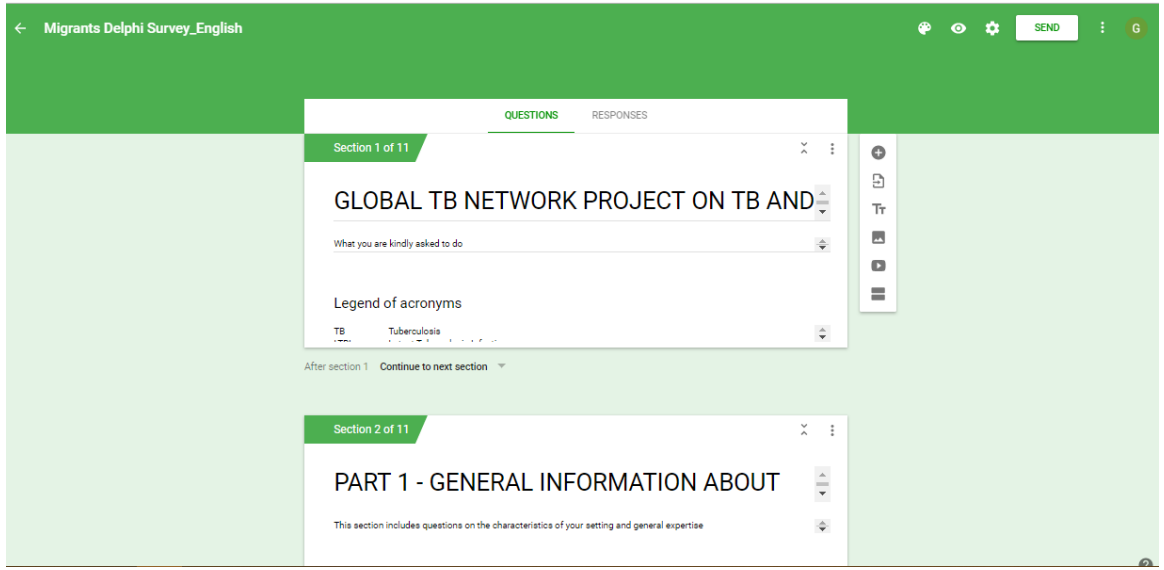
WAidid
World Association for Infectious Diseases and Immunological Disorders

Global TB Network (project on TB and migration)

- **Global effort: > 3,000 HCW in all continents**
- **Delphi questionnaire**
- **Educational & research objectives**
- **5 languages (ENG, FRE, SPA, POR, CHIN)**

GTbN
the Global Tb Network
fighting Tb together

The questionnaire



- **Easy**
- **Short (<10 min)**
- **To support a large project**
- **Investigating prevention, diagnosis and treatment of TB & LTBI in migrants**

The link to access the Questionnaire (English version) is:

https://docs.google.com/forms/d/1YqGZR1gdr8o0ChNpk4kfS0Zl1lSSVzE8Bo75tjsUAzE/edit

Ask Katerina Manika and Apostolos Papavasileiou to receive the link

Conclusions (2)

- We have discussed some of the ‘myths’ (migrants keep increasing and increase TB rates; *are not adherent to treatment* and transmit to local populations)
- We have briefly discussed pre- and post-entry screening options for TB and LTBI, their yield as well as the existing policies in Europe
- Migrants have several health issues beyond TB
- *Diagnosis and treatment of LTBI* are the core activities for TB elimination
- Among research *priorities related to treatment*, continuity of care is one of the core ones
- Free access, sensitivity of services, trans-border collaborations are some of the ingredients necessary to improve *adherence to treatment and treatment outcomes*

Thank you! ευχαριστίες!!!