The European experience: Tuberculosis as a moving target

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Prof. Migliori Giovanni Battista

☐ I have no conflict of interest.
Introduction

AIMS: to discuss (briefly)

- Health problems in migrants
- TB Control & Elimination strategies and migration
- Migration flows
- Policies for refugees in Europe
- ERS/UNION-ER statement on refugees
- Conclusions
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Health problems in migrants/refugees

The commonest health conditions observed by health organizations are:

- Hypothermia
- Burns
- Gastrointestinal conditions
- Cardiovascular events
- Pregnancy and related complications
- Diabetes
- Hypertension
- Respiratory diseases
- Skin diseases (scabies, dermatitis...)
- Hepatitis A
The snow ocean!!!
The snow ocean!!!
<table>
<thead>
<tr>
<th>Disease</th>
<th>Indicator</th>
<th>Syria</th>
<th>Afghanistan</th>
<th>Iraq</th>
<th>Eritrea</th>
<th>Somalia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphtheria [3]</td>
<td>Cases reported to WHO in 2012, 2013, 2014</td>
<td>0, 0, and NA</td>
<td>0, 0, 0</td>
<td>3, 4, and 5</td>
<td>0, 0 and NA</td>
<td>65, 7 and NA</td>
</tr>
<tr>
<td>Typhoid fever</td>
<td>Risk of typhoid</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Cholera</td>
<td>Risk</td>
<td>No recent outbreak</td>
<td>Recurrent outbreaks</td>
<td>On-going outbreak in Baghdad, Babylon, Najaf, Qadisiyah, and Muthanna.</td>
<td>NA</td>
<td>Recurrent outbreaks</td>
</tr>
<tr>
<td>Hepatitis A†</td>
<td>Risk</td>
<td>High endemic</td>
<td>NA</td>
<td>High endemic</td>
<td>High endemic</td>
<td>High endemic</td>
</tr>
<tr>
<td>Hepatitis E†</td>
<td>Risk</td>
<td>NA</td>
<td>NA</td>
<td>High endemic</td>
<td>NA</td>
<td>High endemic</td>
</tr>
<tr>
<td>Helminthiasis³</td>
<td>Risk of soil transmitted helminthiasis</td>
<td>+</td>
<td>++</td>
<td>✓</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>(ascaris, whipworm, hookworm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leishmaniasis**</td>
<td>Risk of cutaneous leishmaniasis</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Risk of visceral leishmaniasis</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Hepatitis B**</td>
<td>Prevalence of chronic hepatitis B</td>
<td>Intermediate prevalence: 5.6%</td>
<td>High prevalence: 10.3%</td>
<td>Low prevalence: 1.3%</td>
<td>High prevalence: 15.9%</td>
<td>High prevalence: 12.4%</td>
</tr>
<tr>
<td>Hepatitis C**</td>
<td>Prevalence</td>
<td>High prevalence: 3.1%</td>
<td>High prevalence: 1.1%</td>
<td>High prevalence: 3.2%</td>
<td>High prevalence: 1%</td>
<td>NA</td>
</tr>
<tr>
<td>HIV</td>
<td>Prevalence</td>
<td>Low</td>
<td>NA</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
</tr>
<tr>
<td>Malaria†</td>
<td>Risk of malaria</td>
<td>Malaria-free</td>
<td>NA</td>
<td>Malaria-free</td>
<td>Risk of P. falciplarum &gt;&gt; P. vivax</td>
<td>Risk of P. falciparum</td>
</tr>
<tr>
<td>Measles</td>
<td>Incidence per 100 000 in 2013 and 2014</td>
<td>1.84 and 2.68</td>
<td>1.41 and 1.75</td>
<td>2.09 and 3.02</td>
<td>0.77 and 0.02</td>
<td>2.17 and 9.12</td>
</tr>
<tr>
<td>Polio</td>
<td>Cases reported to WHO in 2012, 2013 and 2014</td>
<td>0, 35 and NA</td>
<td>46, 17, and 28</td>
<td>0, 0, and 2</td>
<td>0, 0, and 0</td>
<td>1, 195 and 5</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>Incidence/100 000</td>
<td>Low: 17</td>
<td>High: 169</td>
<td>Low: 25</td>
<td>High: 40 to 499</td>
<td>High: 285</td>
</tr>
<tr>
<td>Antimicrobial resistance</td>
<td>Risk of carriage of multidrug-resistance Gram-negative bacteria</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Rabies</td>
<td>Risk level for humans contracting rabies</td>
<td>High</td>
<td>High</td>
<td>High</td>
<td>High</td>
<td>High</td>
</tr>
</tbody>
</table>
Protocolized Screening in Health Settings

- Screening of migrant population for certain conditions should be considered in accordance with national guidelines.

- Specific infectious diseases should be considered depending on the symptoms presented during medical examination.

- Screening for multidrug-resistant Gram-negative bacteria (MDR-GNB) should be considered for migrants requiring hospitalization, in accordance with the standard national guidelines for persons at risk of carrying MDR-GNB (particularly from Asia and Africa).
## Differential diagnosis among newly arrived migrants

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

ECDC. Infectious diseases of specific relevance to newly-arrived migrants in the EU/EEA
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<table>
<thead>
<tr>
<th>Year</th>
<th>Organization</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>1980s</td>
<td>International Union against Tuberculosis and Lung Disease</td>
<td>Establishes a model program to control tuberculosis in Tanzania</td>
</tr>
<tr>
<td>1991</td>
<td>World Health Assembly</td>
<td>Establishes the “70/85” targets (detect 70% of infectious cases of tuberculosis and cure 85% of the detected cases)</td>
</tr>
<tr>
<td>1993</td>
<td>WHO</td>
<td>Declares that tuberculosis is a global emergency</td>
</tr>
<tr>
<td>1994</td>
<td>WHO</td>
<td>Launches a new framework for controlling tuberculosis</td>
</tr>
<tr>
<td>1995</td>
<td>WHO</td>
<td>Launches DOTS as the official WHO strategy</td>
</tr>
<tr>
<td>1998</td>
<td>First ad hoc Committee on the Tuberculosis Epidemic (London Committee)</td>
<td>Establishes the Stop TB Initiative</td>
</tr>
<tr>
<td>2000</td>
<td>Stop TB Initiative</td>
<td>Produces the Amsterdam declaration, a call for action from 20 countries with the highest burden of tuberculosis, and establishes targets to meet the United Nations’ Millennium Development Goals</td>
</tr>
<tr>
<td>2001</td>
<td>Stop TB Partnership (formerly the Stop TB Initiative)</td>
<td>Organizes six working groups and launches the Global Drug Facility</td>
</tr>
<tr>
<td>2001</td>
<td>Global Fund in collaboration with Stop TB Partnership</td>
<td>Launches the Global Fund activities, the Millennium Development Goals, and the Washington Commitment</td>
</tr>
<tr>
<td>2002</td>
<td>WHO</td>
<td>Launches its Expanded DOTS Framework for Effective Tuberculosis Control and establishes DOTS as a brand name</td>
</tr>
<tr>
<td>2006</td>
<td>WHO</td>
<td>Launches the Stop TB Strategy, consisting of six components, including the revised DOTS strategy as the first component</td>
</tr>
<tr>
<td>2006</td>
<td>WHO</td>
<td>Launches the Global Plan to Stop TB, 2006–2015</td>
</tr>
<tr>
<td>2012</td>
<td>WHO</td>
<td>Addresses the issue of elimination of tuberculosis after 2015 with the Scientific Technical Advisory Group</td>
</tr>
</tbody>
</table>

Migliori GB et al. NEJM 2010
The End TB Strategy: Snapshot

VISION
A world free of tuberculosis — zero deaths, disease and suffering due to tuberculosis

GOAL
End the global tuberculosis epidemic

INDICATORS

<table>
<thead>
<tr>
<th>INDICATORS</th>
<th>2020</th>
<th>SDG 2030</th>
<th>END TB 2025</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduction in number of TB deaths compared with 2015 (%)</td>
<td>35%</td>
<td>50%</td>
<td>95%</td>
</tr>
<tr>
<td>Reduction in TB incidence rate compared with 2025 (%)</td>
<td>20%</td>
<td>10%</td>
<td>5%</td>
</tr>
<tr>
<td>Tuberculosis deaths and catastrophic costs due to TB (%)</td>
<td>Zero</td>
<td>Zero</td>
<td>Zero</td>
</tr>
</tbody>
</table>

PRINCIPLES

1. Government stewardship and accountability, with monitoring and evaluation
2. Strong position with civil society organizations and community
3. Protection and promotion of human rights, dignity and equity
4. Adaptation of the strategy and targets at country level, with global collaboration

PILLARS AND COMPONENTS

1. UNAIDS PATHWAY TO CARE AND PREVENTION
   - Early diagnosis of tuberculosis in adults and children
   - Treatment of all people with tuberculosis
   - Complementary activities for TB control

2. PILLARS AND SUPPORTIVE SYSTEMS
   - Policy commitment with adequate resources for tuberculosis care and prevention
   - Engagement of communities, civil society organizations, and public and private care providers
   - Universal health coverage policy, and regulatory frameworks for access to medicines, and monitoring and evaluation
   - Equity, social security, and redressal of issues of discrimination and non-discrimination of patients

3. INTENSIFIED RESEARCH AND INNOVATION
   - Innovation, development and rapid uptake of new tools, interventions and strategies

GLOBAL TB STRATEGY
The global strategy and targets for tuberculosis prevention, care and control after 2015, were endorsed by all member states at the 2014 World Health Assembly.

REACHING THE TARGETS
To reach the targets set out in the End TB Strategy, the annual decline in global TB incidence rates must first accelerate from an average of 2% per year in 2015 to 3% per year by 2023. Second, the proportion of people with TB who die from the disease (the case-fatality rate) needs to decline from a projected 5% in 2015 to 4% by 2030. These declines in deaths and incidence by 2030 while still feasible with existing tools supplemented by universal health coverage and social protection.

ENDING THE TB EPIDEMIC
Ending the global TB epidemic is feasible with dramatic decline in TB deaths and cases, and elimination of epidemic and social burden of TB. Failure to do so will carry serious individual, and global public health consequences.

Achievement of this goal by 2030 requires:
1. Expanding the scope and reach of interventions for TB care and prevention, with a focus on high-risk, integrated and patient-centered approaches.
2. Blending full benefits of health and development policies and systems, through engaging a multi-sectoral initiative of all stakeholders working across the value chain.
3. Pursuing new scientific knowledge and innovations that can dramatically change TB prevention and care.

To ensure full impact, these actions must build on principles of government stewardship, engagement of civil society, human rights and equity, and adaptation to the unique context of diverse epidemics and settings.

KEY TB FACTS
- In 2012, 9 million people fell sick with TB and 1.3 million died from it, including 490,000 among people who were HIV positive.
- In 2013, there were an estimated 480,000 new cases of multidrug-resistant TB.

ACHIEVEMENTS
- 37 million lives saved since 2000
- 45% decrease in TB mortality rate since 1990
- 3 million people who fall sick with TB and are untreated every year

CHALLENGES
- MDR-TB crisis
- Access to drugs for treatment and quality
Targets

<100 cases per million

Current TB burden-2012
in low-incidence countries

<10 cases per million

Pre-elimination: 2035
in low-incidence countries

<1 case per million

Elimination: 2050
ACTION FRAMEWORK

8 priority actions for elimination in low-incidence countries

1. Ensure political commitment, funding and stewardship for planning and essential services of high quality
2. Address the most vulnerable and hard-to-reach groups
3. Address special needs of migrants and cross-border issues
4. Undertake screening for active TB and latent TB infection in TB contacts and selected high-risk groups, and provide appropriate treatment
5. Optimize the prevention and care of drug-resistant TB
6. Ensure continued surveillance, programme monitoring & evaluation, and case-based data management
7. Invest in research and new tools
8. Support global TB prevention, care and control
The formula of TB Elimination

TB Control = diagnosis + treatment of infections cases

TB Elimination = TB Control + TB prevention = TB Control + (LTBI diagnosis + LTBI treatment)
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Vulnerable and hard-to-reach groups/migrants/cross-border issues

Major migration and movements routes, 2015

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ERS TB Advocacy activities

ERS statement on refugees

Tuberculosis care among refugees arriving in Europe: a ERS/WHO Europe Region survey of current practices

1. Implement End TB Strategy (adequate prevention, diagnosis, treatment)
2. Surveillance M&E
3. Timely screening
4. Avoid stigma
5. Universal access
6. Infection control
Support the refugees: The European Respiratory Society and the European Lung Foundation are calling for refugees traveling across Europe to have better access to TB diagnostics and treatments to prevent a rise in the disease on the continent.

ERS marks World TB Day

World TB Day is marked across the world today under the theme of ‘Unite to End TB’ and in 2014, it is 8 million people contracted TB. A key issue in the field is the need for urgent action on the care of TB among refugees. Writing in the European Respiratory Journal today, experts are calling for refugees traveling across Europe to have better access to TB diagnostics and treatments to prevent a rise in the disease. This call coincides with the launch of a new online platform to facilitate better communication between clinicians in different countries.

Health experts call for coordinated European response on tuberculosis

WHO meeting with Health attaches of all the Permanent Representations of EU Member States

TB, HIV and hepatitis C workshop opens discussion on gaps and options moving forward

A European Parliament workshop focusing on TB, HIV and hepatitis C was held this month providing a forum for discussion and assessment of existing tools, challenges and gaps, as well as possible ways forward in these disease fields.

Read more
Target: 38 low and intermediate incidence countries of WHO European Region (EU/EEA, Switzerland + Albania, Bosnia and Herzegovina, the former Yugoslav Republic of Macedonia, Montenegro, Serbia and Turkey)

Methods: A simple questionnaire (multiple choice and open-ended questions) developed by the ERS TB Advocacy ad-hoc Committee (in collaboration with WHO EURO & WHO CC, Tradate, Italy) Sept-Oct 2015

Four sections:
1. Screening for TB and LTBI
2. Management of TB and LTBI
3. Guidelines, legislation and evidence on the results of screening and treatment of TB and LTBI in Europe
4. Organizational aspects and infection control issues
• 36/38 (94.7%) target countries responded
• Quantitative and qualitative data
• Active TB screening is conducted in 31/36 countries (86.1%) except Italy, Monaco and Portugal where a non-systematic screening is performed (only in symptomatic individuals); no screening is performed in Former Yugoslavia Republic of Macedonia (length of stay in holding centre is not long enough for screening to take place) and Serbia (insufficient governmental funding).
• There is a legal obligation to screen for TB and/or LTBI in 21 of the 36 countries (58.3%)
SCREENING 2

- Chest radiography (26/36, 72.2% of which 2 not systematically);
- Symptom-based questionnaires in 21/36 countries (58.3%)
- Bacteriology (18/36, 50% sputum smear/culture collection of which 9 for symptomatic individuals only)
- 6 countries do not systematically perform any TB specific examination
- 1 country starts the algorithm with tuberculin skin tests (TST) and blood test.
- 19 (52.7%) screen systematically for LTBI
- 9 (25%) do not screen at all for LTBI
- 8 countries do LTBI screening under specific conditions
The decision to perform TB/LTBI screening is determined by the TB incidence rate in the country of origin of refugees in 14/36 (38.8%) of the countries. No single threshold was provided.
SUMMARY OF TB AND LTBI SCREENING
MANAGEMENT OF TB AND LTBI

• 30/36 (83.3%) the public sector services are in charge of managing refugees for TB-related issues, complemented by international organizations.

• The sheer volume of refugees cited as a challenge in eight (22.2%) countries.

• 23/36 (63.8%) report that efforts are ongoing to adapt TB services to refugees’ specific needs.

• 22/36 (61.1%) provide access to TB services for undocumented refugees.
DATA COLLECTION

• 22/36 (61.1%) countries collect data on active TB and 11/36 (30.5%) on LTBI

• TB treatment outcomes is available in 19/36 (52.7%) countries,

• Treatment completion rates for LTBI therapy available in only 8 (22.2%)

GUIDELINES ADHERENCE

• 27/36 (75%) countries answered that screening for TB is done as per national and international guidelines (offering the same services to refugees and nationals)
• Treatment provided in all countries
• No deportation due to being diagnosed with TB
• If the patient refuses treatment, 6 countries have involuntary isolation and one country only for MDR-TB cases involuntary isolation is considered.
The National representatives who contributed to collect the survey data were: Donika Mema Bardhi (Albania); Alina Virsa (Austria); Maryse Wanlin and Wouter Arrazola de Oñate (Belgium); Mariya Zamfirova (Bulgaria); Aleksandar Simunovic (Croatia); Constantia Voniatis (Cyprus); Peter Henrik Andersen and Annette Hartvig Christiansen (Denmark); Piret Viiklepp, Manfred Danilovitš (Estonia); Hanna Soini (Finland); Thierry Comolet (France); Barbara Hauer (Germany); Ourania Kalkouni (Greece); Gábor Kovács (Hungary); Joan O Donnell and Sarah Jackson (Ireland); Thorsteinn Blöndal (Iceland); Maria Grazia Pompa and Francesco Paolo Maraglino (Italy); Irina Lucenko (Latvia); Edita Davidaviciene (Lithuania); Pierre Weicherding (Luxembourg); Biljana Ilievka Poposka (Republic of Macedonia); Analita Pace-Asciak (Malta); Jean Lorenzi (Monaco); Olivera Bojovic and Stevan Lucic (Montenegro); Gerard de Vries (The Netherlands); Trude Arnesen and Karine Nordstrand (Norway); Raquel Duarte (Portugal); Georgeta Gilda Popescu and Chiotan Domnica Ioana (Romania); Violeta Mihailovic-Vunicin (Serbia); Ivan Solovic (Slovakia); Petra Svetina (Slovenia); Elena Andradas Aragonés (Spain); Jerker Jonsson (Sweden); Peter Helbling (Switzerland); Erhan Kabasakal (Turkey); Dominik Zenner and Alison Smith-Palmer (United Kingdom).
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TB Elimination is possible if proper strategy implemented: the case of Cyprus

Migliori GB et al. ERJ 2014
TB Elimination is possible: the case of Oman (ERJ 2018)

Figure 1: Decline of the case notification rate of tuberculosis towards the elimination threshold (1 case per million population) in Oman
TB Elimination is possible: the case of Oman (ERJ 2018)

If LTBI is managed among foreign-born

![Graph showing the decline of tuberculosis notifications in Oman from 2010 to 2016 for different categories: all SS+, National SS+, Expatriate SS+, All TB cases, and 1 case per million population. The graph indicates a declining trend over the years.](image)

Figure 1: Decline of the case notification rate of tuberculosis towards the elimination threshold (1 case per million population) in Oman

- Born abroad
- Born in Oman
Conclusions

• Several health issue are importants among migrants
• Migration flows are major determinants for TB control and elimination
• Important country-specific differences on management policies in Europe
• More is known on TB than on LTBI
• There are obvious implications for advocacy and research
• A coordinated effort of all stakeholders is necessary
If you want to go fast, go alone.

If you want to go far, go together.

-african proverb