Η πρόληψη της Φυματίωσης στους μετανάστες- ειδικούς πληθυσμούς

Επίατρος Μαρία Κηπουρού
Επιμελήτρια Πνευμονολογικής κλινικής 424 ΓΣΝΕ
244 million international migrants in 2015 out of a global population of 7.3 billion: 1 in every 30 people.
International migrant: the broadest definition, used by the United Nations, is any individual who lives in a country temporarily or permanently apart from his or her usual place of residence for at least a year (25). In many cases, these individuals have migrated for reasons including family, work or education (24,26). However, migrants entering Europe also include forced migrants, who may include refugees, asylum seekers and some undocumented migrants (who may have initially entered countries with visas to work that have subsequently lapsed).

Asylum seeker: a migrant seeking asylum (e.g. under the 1951 United Nations Convention on the Status of Refugees), and who is specifically seeking protection from persecution in his or her country of origin due to factors such as race, religion or politics (26,27).

Refugee: an individual who has been granted asylum or has been successful in overturning a previous judgement that ruled against an asylum application (26,28).

Political instability: A unified, whole-of-government approach to noncommunicable disease prevention is the best way to ensure sustained and stable funding, resources and public health and research priorities (4). Therefore, political instability can threaten efforts to reduce the noncommunicable disease burden.

Undocumented migrant: an individual who is without legal status in the country to which he or she has migrated or who has overstayed after a visa/working permit has expired (29).

S. Hargreaves, WHO, 2018
Despite the high burden in TB in migrants in many countries, there is evidence that TB within migrant communities does not significantly influence the levels of TB within the native population, with migrants unlikely to spread TB to the wider population in receiving countries. Rather it appears that acquisition of TB among migrants is a result of local transmission within migrant communities themselves or from reactivation of LTBI.

S. Hargreaves, WHO, 2018
• Οι μετανάστες στην Ευρώπη υφίστανται δυσανάλογο φορτίο MDR TB

• MDR TB among foreign-born in Europe: 73.4%

• Σημαντική ετερογένεια ανάμεσα στις χώρες

S. Hargreaves, Clin Microb Inf, 2017
MDR/ XDR tuberculosis in Greece: predominance of Mycobacterium tuberculosis genotypes endemic in the Former Soviet Union countries

- 54 MDR/ XDR 2007-2011
- 16 / 38 μετανάστες ή επαναπατρισμένοι

MDR/XDR-TB in migrants is of key importance for TB control in Greece

The genotypes of 60.8% (28/46) of MDR-TB cases in Greece were phylogeographically specific for M. tuberculosis populations in FSU countries. Of them, Beijing and LAM lineages and, in particular, epidemic clonal clusters Beijing B0/W148 (#100-32) and #94-32 and LAM-RUS#843-52, actively circulating in FSU countries, were predominant. At the same time, it is noteworthy that imported MDR Beijing and LAM strains showed only limited transmission within Greece from immigrants to the autochthonous population.

P. Ioannidis, Clin Microbiol Infect, 2017
Παράγοντες κινδύνου για TB σε πρόσφυγες και μετανάστες

- Προ μετανάστευσης σε χώρα με υψηλή επίπτωση TB
- Προ μετανάστευσης σε χώρα σε διαμάχη- διακεκομένη παροχή υγείας
- Δυσκολίες κατά τη μετανάστευση
- Χρόνος σε χώρους φιλοξενίας
- Κοινωνικός αποκλεισμός στη χώρα μετανάστευσης
- Χωρίς πρόσβαση στο σύστημα υγείας

- Υψηλότερος κίνδυνος για τους μη νόμιμους μετανάστες

- Ασθένεια των φτωχών (40% των μη γεννημένων στην Ευρώπη ήταν σε κίνδυνο για φτώχεια και κοινωνικό αποκλεισμό vs 21% των γηγενών, Eurostat 2017)

S. Hargreaves, WHO, 2018
Screening ΤΒ στους μετανάστες: 1. ενεργή νόσος 2. LTBI

- Δημογραφικά στοιχεία του μεταναστεύοντος πληθυσμού
- ΤΒ επιδημιολογία στη χώρα υποδοχής
- Διαθέσιμοι πόροι

S. Hargreaves, WHO, 2018
Screening Tb στους μετανάστες: 1. ενεργή νόσος 2. LTBI

- **Pre-entry screening**
  - Active TB screening in country of origin for people who intend to migrate (Australia, Canada, United Kingdom, United States of America)

- **On arrival screening**
  - Active TB screening at borders or soon after entry
    - Airports
    - Receptions centres/holding camps
    - Migrant centres

- **Post-arrival screening**
  - Active TB and/or LTBI screening in settlement country
    - Active or passive screening
    - Various models (primary care, antenatal services, identification services, nonclinical settings)
    - Contact tracing

*M. Pareek, BMC Med, 2016*
A systematic review of the sensitivity and specificity of symptom- and chest-radiography screening for active pulmonary tuberculosis in HIV-negative persons and persons with unknown HIV status.

Summary Estimates

- CXR any abnormality
- CXR TB abnormality
- Prolonged Cough
- Any cough
- Any Symptom

Van Hoog, WHO, 2013
CHEST X-RAY: AN ESSENTIAL TOOL TO END TB

CXR IS A SENSITIVE TOOL FOR SCREENING FOR ACTIVE TB
Reference: Systematic screening for active tuberculosis: principles and recommendations (4)
- CXR has higher sensitivity for pulmonary TB than screening for TB symptoms.

AN ABNORMAL CXR IS AN INDICATION FOR FULL DIAGNOSTIC EVALUATION
Reference: International standards for tuberculosis care (20)
- All patients with unexplained findings suggestive of TB on CXR should be evaluated for TB with a bacteriological diagnostic test.
- CXR can be used as a supplementary diagnostic aid, although the specificity is low.
- A bacteriologically confirmed diagnosis is always preferred.

CXR CAN IMPROVE THE EFFICIENCY OF USING THE XPERT MTB/RIF ASSAY
Reference: implementation manual for the Xpert MTB/RIF assay (3)
- CXR and further clinical assessment can be used to triage who should be tested with the Xpert MTB/RIF assay to reduce the number of individuals tested and the associated costs, as well as to improve the pre-test probability for TB and, thus, the predictive value of the Xpert MTB/RIF assay.

+ Ερωτηματολόγιο (ευαισθησία 97.8%)
+ Xpert MTB/RIF (αύξηση κόστους)
Καθώς οι περισσότεροι πρόσφυγες δε μένουν σε ένα μέρος αλλά μπορεί συχνά να αλλάζουν τόπο, θα έπρεπε από το screening να προκύπτει ένα γρήγορο και αξιόπιστο αποτέλεσμα. Η καλλιέργεια πτυέλων ίσως να μην είναι η πιο αποτελεσματική παρέμβαση σε αυτό τον πληθυσμό. Αντίθετα, το GeneXpert MTB/RIF παρέχει το γρηγορότερο αποτέλεσμα (σε λιγότερο από 2 ώρες), έχει καλύτερη ευαίσθητη από το άμεσο παρασκεύασμα και ελέγχει την ευαίσθησια στην ριφαμπικίνη (C.C. Heuvelings, Int J Inf Dis, 2017)
Towards tackling tuberculosis in vulnerable groups in the European Union: the E-DETECT TB consortium

Ibrahim Abubakar¹, Alberto Matteelli², Gerard de Vries³, Dominik Zenner⁴, Daniela M. Cirillo⁵, Knut Lönnroth⁶, Gilda Popescu⁷, Lucia Barcellini⁸, Alistair Story⁹ and Giovanni Battista Migliori ¹⁰

<table>
<thead>
<tr>
<th>Work package</th>
<th>Interventions</th>
<th>Main outcome(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outreach activity in Romania and Bulgaria</td>
<td>Mobile digital radiography, computer-aided diagnostics, mobile provision of Xpert test, social support and integration with hospital care</td>
<td>Number of active TB cases detected using mobile radiography van in Romania and Bulgaria</td>
</tr>
<tr>
<td>Implement and evaluate migrant TB detection in Italy</td>
<td>Latent TB testing in settled migrants (tuberculin skin test, interferon gamma release assay)</td>
<td>Number of patients treated in Romania and Bulgaria Number of latent and active TB cases detected in migrants in Italy</td>
</tr>
<tr>
<td>Creating a database listing active and latent TB cases</td>
<td>Active TB screening in newly arrived migrants (questionnaire, Xpert ULTRA) Migrant TB screening database Data from multiple countries</td>
<td>Linkage to care among detected migrants in Italy Multi-country data platforms for migrant TB established and analysed</td>
</tr>
<tr>
<td>Supporting the strengthening of national TB programmes</td>
<td>Survey of national programme managers Review of existing policies</td>
<td>Synthesis of best practice for developing national action plans</td>
</tr>
</tbody>
</table>

<20 cases per 100,000 population

>20 cases per 100,000 population

Stockholm Sweden

Multi-city Netherlands

Multi-city UK

Multi-city Italy

Bucharest Romania

Sofia Bulgaria

ERJ, 2018
Διαγνωστική προσέγγιση LTBI

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

Similar to the findings described by a previous ERS/WHO Europe Region Study [10], LTBI screening is performed by using different combinations of tuberculin skin test (TST) and interferon-γ release assays (IGRAs) in 23 (63.8%) out of 36 different European countries (eight (22.2%) out of 36, TST only, 11 (30.5%) out of 36, TST plus IGRA, four (11.1%) out of 36, TST plus IGRA in selected cases (only in Bacillus Calmette–Guérin non-vaccinated children aged <12 years and after TB exposure in the Netherlands; and in case of recent exposure to TB in Portugal, Slovenia and Monaco).
The effectiveness and cost-effectiveness of screening for latent tuberculosis among migrants in the EU/EEA: a systematic review

Christina Greenaway¹,², Manish Pareek³, Claire-Nour Abou Chakra⁴, Moneeza Walji², Iuliiia Makarenko², Balqis Alabdulkarim², Catherine Hogan¹,³, Ted McConnell², Brittany Scarfo², Robin Christensen⁵,⁶, Anh Tran⁷, Nick Rowbotham⁷, Marieke J van der Werf⁸, Teymur Noori⁸, Kevin Pottie⁹, Alberto Matteelli¹⁰, Dominik Zenner¹¹,¹², Rachael L. Morton⁷

Different LTBI treatment regimens had low to moderate efficacy but were equivalent in preventing active TB. Rifampicin-based regimens may be preferred because of lower hepatotoxicity (risk ratio = 0.15) and higher completion rates (82% vs 69%) compared with isoniazid. Only 14.3% of migrants eligible for screening completed treatment because of losses along all steps of the LTBI care cascade. Limited economic analyses suggest that the most cost-effective approach may be targeting young migrants from high TB incidence countries. Discussion: The effectiveness of LTBI programmes is limited by the large pool of migrants with LTBI, poorly predictive tests, long treatments and a weak care cascade. Targeted LTBI programmes that ensure high screening uptake and treatment completion will have greatest individual and public health benefit.
Χρήση ερωτηματολογίου
1. Εμπύρετο > 1w
2. Βήχας >2w
3. Νυκτερινή εφίδρωση
4. Απώλεια ΒΣ
5. Αιμόπτυση

- 2567/ 2904 αιτούντεςάσυλο
- 87% Αφρική
- 63/2567 θετικό ερωτηματολόγιο
- 27 ολοκλήρωσαν τον έλεγχο σε 6 ημέρες- 4 ΤΒ, 1 ΤΒ σε 74 ημέρες στα ΤΕΠ
- LTBI: Ro σε 60ημέρες

Screening for active and latent tuberculosis among asylum seekers in Italy: A retrospective cohort analysis

Agostina Pontarelli, Valentina Marchese, Carla Scolari, Susanna Capone, Issa El-Hamad, Francesco Donato, Rolando Moioli, Enrico Girardi, Daniela Maria Cirillo, Francesco Castelli, Alberto Matteelli

Travel Medicine, 2018
Systematic Tuberculosis Screening in Asylum Seekers in Italy

Elisa Vanino,1 Marina Tadolini,1 Luciano Attard,1 Claudio Po,2 Fausto Francia,2 Adriana Giannini,2 and Pierluigi Viale1

1Infectious Diseases Unit, Department of Medical and Surgical Sciences, St Orsola-Malpighi Hospital, Alma Mater Studiorum University of Bologna; and 2Department of Public Health, Emilia Romagna Region, Italy

The preliminary findings of a tuberculosis (TB) screening of asylum seekers performed in a reception center located in northern Italy reveal a post-entry screening prevalence rate of 535 per 100 000 individuals screened. This result shows that systematic use of chest radiography is a useful tool for active TB screening among asylum seekers in Italy.

However, our findings suggest that travel history by itself (length and conditions) might play an independent role in the risk of developing active TB and should be taken into account beside the estimated WHO TB incidence rate, which is often used as a demarcation line to decide if screening should be performed.

• 3366 άτομα 2014-2015
• 82% Αφρική, 17% ινδική χερσόνησο, 5 Συρία
• 18 TB, 1 εξωπνευμονική
• ‘Όλες οι ακτινογραφίες ενδεικτικές ΤΒ (πύκνωση, όζοι, κοιλότητες)
• 33% ασυμπτωματικοί στη διάγνωση
• ‘Όχι νέα κρούσματα μετά το screening
• Post-entry screening prevalence: 535/ 100000 vs 6.7/100.000
• Number needed to screen: 187

Table 1. Number of Symptomatic and Asymptomatic Individuals Affected by Microbiologically Confirmed or Not Confirmed Tuberculosis

<table>
<thead>
<tr>
<th></th>
<th>TB Bacteriologically Confirmed Cases</th>
<th>TB Bacteriologically Not Confirmed Cases</th>
<th>Total</th>
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</thead>
<tbody>
<tr>
<td>Symptomatic individuals</td>
<td>8</td>
<td>4</td>
<td>12</td>
</tr>
<tr>
<td>Asymptomatic individuals</td>
<td>4</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td>12</td>
<td>6</td>
<td>18</td>
</tr>
</tbody>
</table>
Άστεγοι και χρήστες ουσιών

- η μετάδοση διευκολύνεται λόγω καθυστερημένης αναζήτησης ιατρικής βοήθειας, συγχωνωτισμού, φτωχών συνθηκών αερισμού και υγιεινής
- Πρόοδος σε ενεργή νόσο: HIV, κακή διατροφή, αλκοόλ, κατάχρηση ουσιών

προκλήσεις:
- Υψηλής ευαισθησίας στρατηγική για πρώιμη ανίχνευση της TB
- ποιός, πώς και πόσο συχνά θα ελεγχθεί
- Ελάττωση νοσηρότητας και θνητότητας σε ατομικό επίπεδο και ελάττωση μετάδοσης σε επίπεδο δημόσιας υγείας


R. Van Hest, ERJ, 2016
Molecular epidemiology of tuberculosis in England, 1998


SUMMARY


OBJECTIVE: To investigate the proportion of tuberculosis (TB) cases attributable to recent transmission and factors associated with clustering.

DESIGN: Demographic, clinical and microbiological surveillance data were collated from all new culture-confirmed cases in 1998. Using insertion sequence (IS) 6110 restriction fragment length polymorphism (RFLP) typing, strains were classified as clustered (identical patterns) or unique and risk factors were determined using multivariable logistic regression.

RESULTS: RFLP patterns were available for 2265 of 3713 (61%) cases: 1808 had ≥5 IS6110 copies, while 372 cases were in 152 clusters, giving an estimated proportion due to recent transmission of 12.2%. Pulmonary disease (aOR 1.6; 95%CI 1.1–2.2), previous treatment (aOR 3.7; 2.2–6.5) and homelessness (aOR 5.5; 1.2–24.1) were independent risk factors for clustering. Fourteen per cent of patients of Indian subcontinent origin were clustered compared with 27% of white patients. Many clusters spanned ethnic groups (45%) and geographical regions (47%).

CONCLUSION: The calculated proportion of TB cases due to recent transmission is low. Adjusting for missed cases and study duration, it increases to 27.6%. Many cases may arise from reactivation or acquisition outside England. Transmission within England accounted for approximately one in four cases and occurred over wide geographic areas, between ethnic groups and among the homeless. Molecular epidemiology can inform local and national public health action.

KEY WORDS: tuberculosis; molecular; transmission; typing; England