Χαρακτηριστικά και έκβαση ασθενών με φυματίωση στην Ελλάδα και σύγκριση με την Ευρώπη

Κατερίνα Μανίκα
Επίκουρη Καθηγήτρια Πνευμονολογίας ΑΠΘ
Μονάδα Αναπνευστικών Λοιμώξεων
Πνευμονολογική Κλινική ΑΠΘ

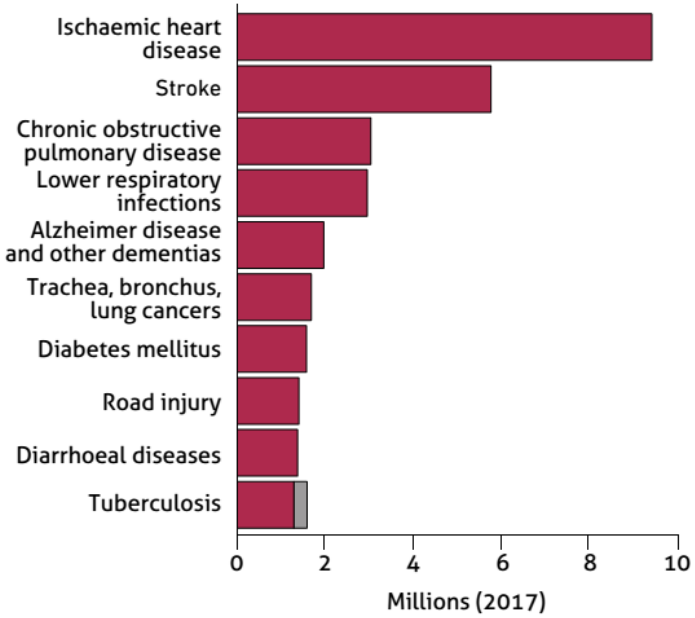
Η Φυματίωση στον κόσμο

GLOBAL TUBERCULOSIS REPORT 2019

- **10.000.000** νέες περιπτώσεις TB παγκοσμίως το 2018
- **Παγκόσμια επίπτωση: 132/100.000**
- Το 57% των ασθενών είναι άντρες, το 32% γυναίκες και το 11% παιδιά
- 8,6% των ασθενών με TB ζουν με HIV
- **500.000** νέες περιπτώσεις RR/MDR-TB

- **1.200.000 θάνατοι** από TB σε άτομα χωρίς HIV και επιπλέον 250.000 θάνατοι σε άτομα με HIV

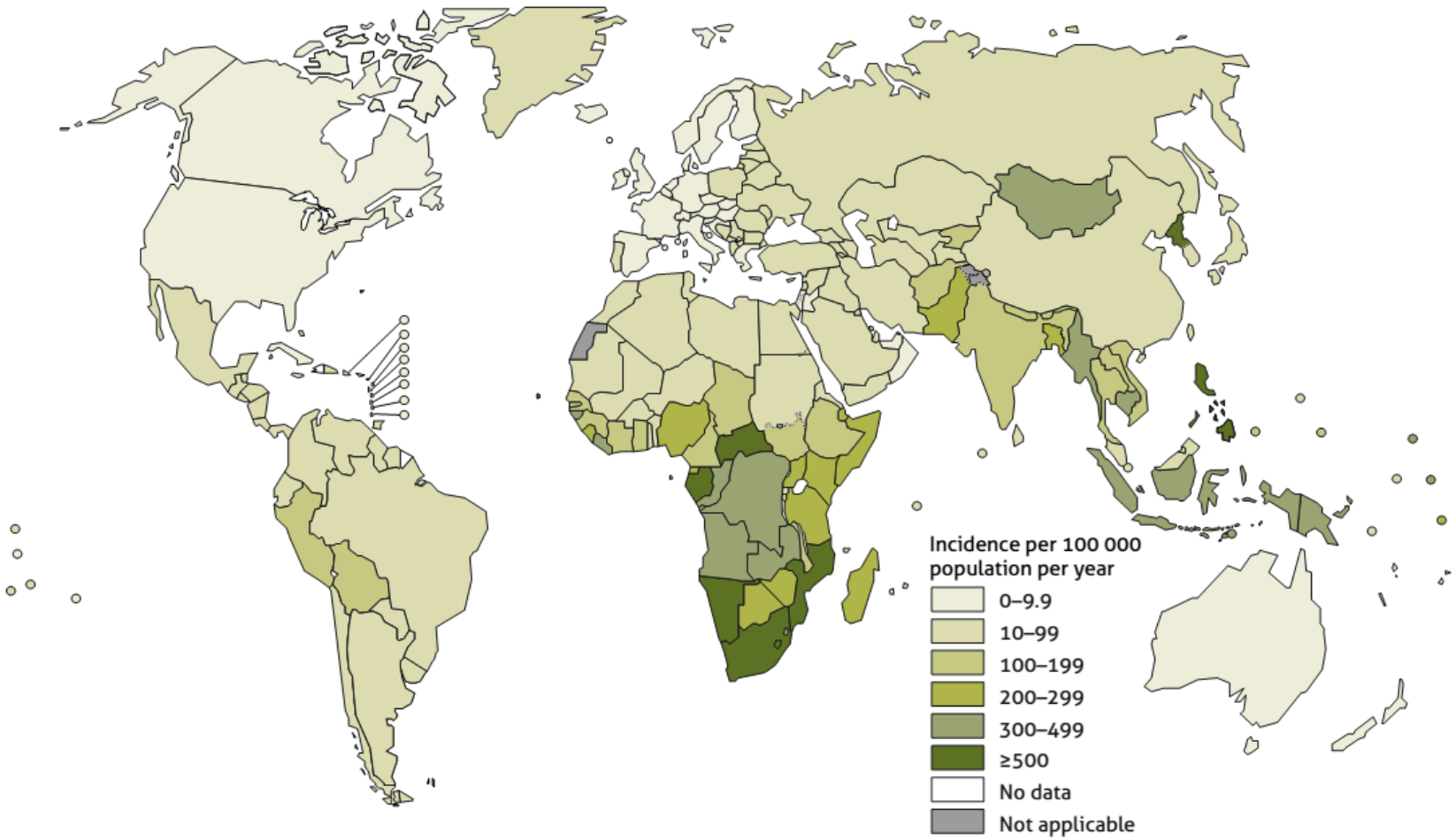
Top causes of death worldwide in 2017.[a,b] Deaths from TB among HIV-positive people are shown in grey.



Η Φυματίωση στον κόσμο

GLOBAL TUBERCULOSIS REPORT 2019

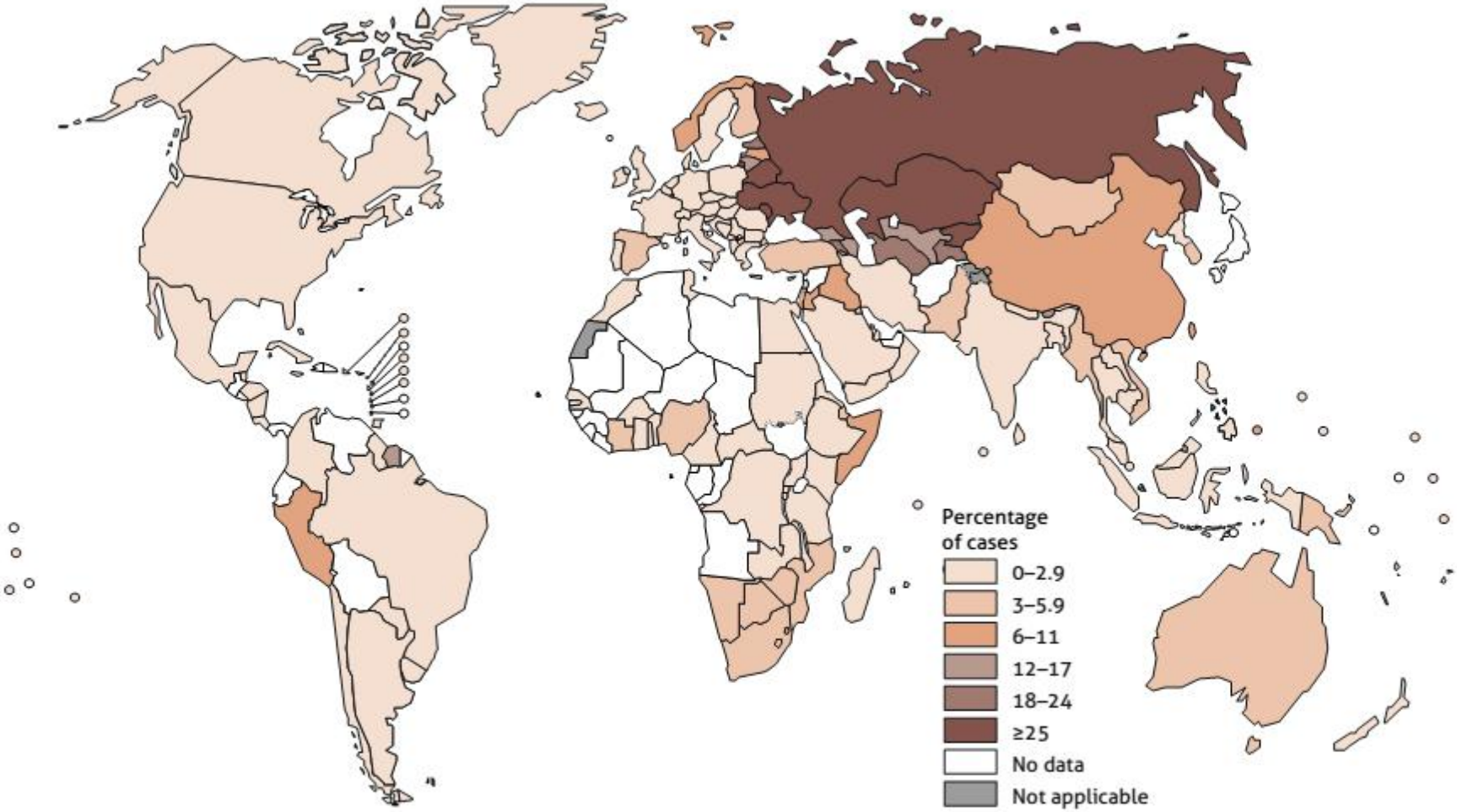
Estimated TB incidence rates, 2018



Η πολυανθεκτική Φυματίωση στον κόσμο

GLOBAL TUBERCULOSIS REPORT 2019

Percentage of new TB cases with MDR/RR-TB[a]



[a] Percentages are based on the most recent data point for countries with representative data from 2004 to 2019. Model-based estimates for countries with data before 2004 are not shown. MDR-TB is a subset of RR-TB.

Tuberculosis elimination: where are we now?

Alberto Matteelli[1], Adrian Rendon[2], Simon Tiberi[3], Seif Al-Abri[4], Constantia Voniatis[5], Anna Cristina C. Carvalho[6], Rosella Centis[7], Lia D'Ambrosio[7,8], Dina Visca[9], Antonio Spanevello[9,10] and Giovanni Battista Migliori[7]

Eur Respir Rev 2018; 27: 180035

Το παράδειγμα της Κύπρου

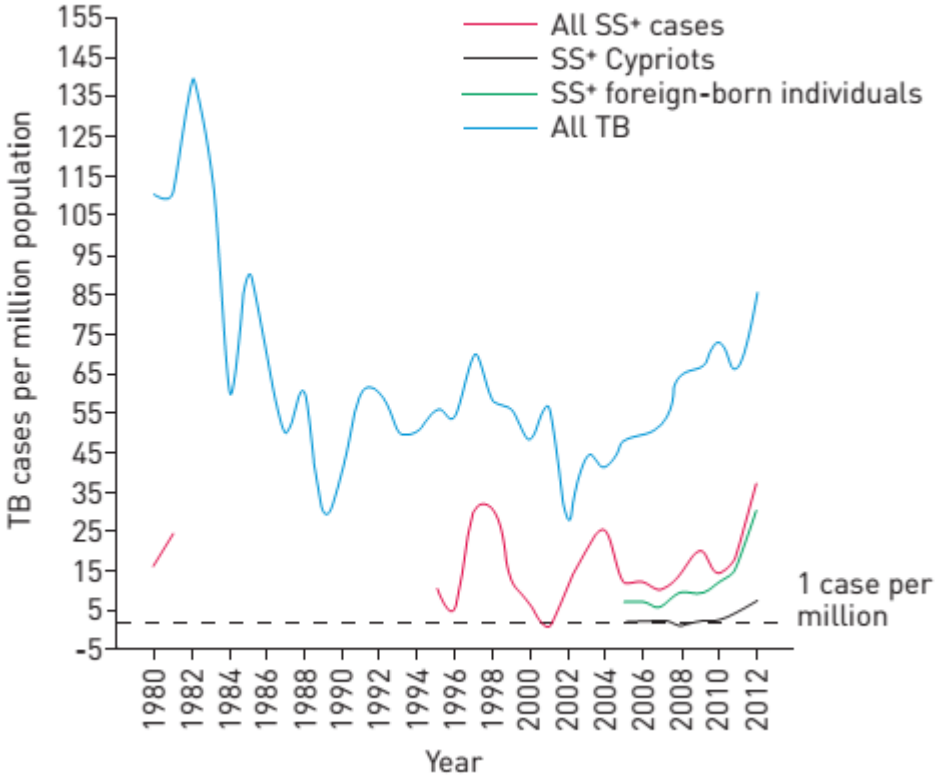
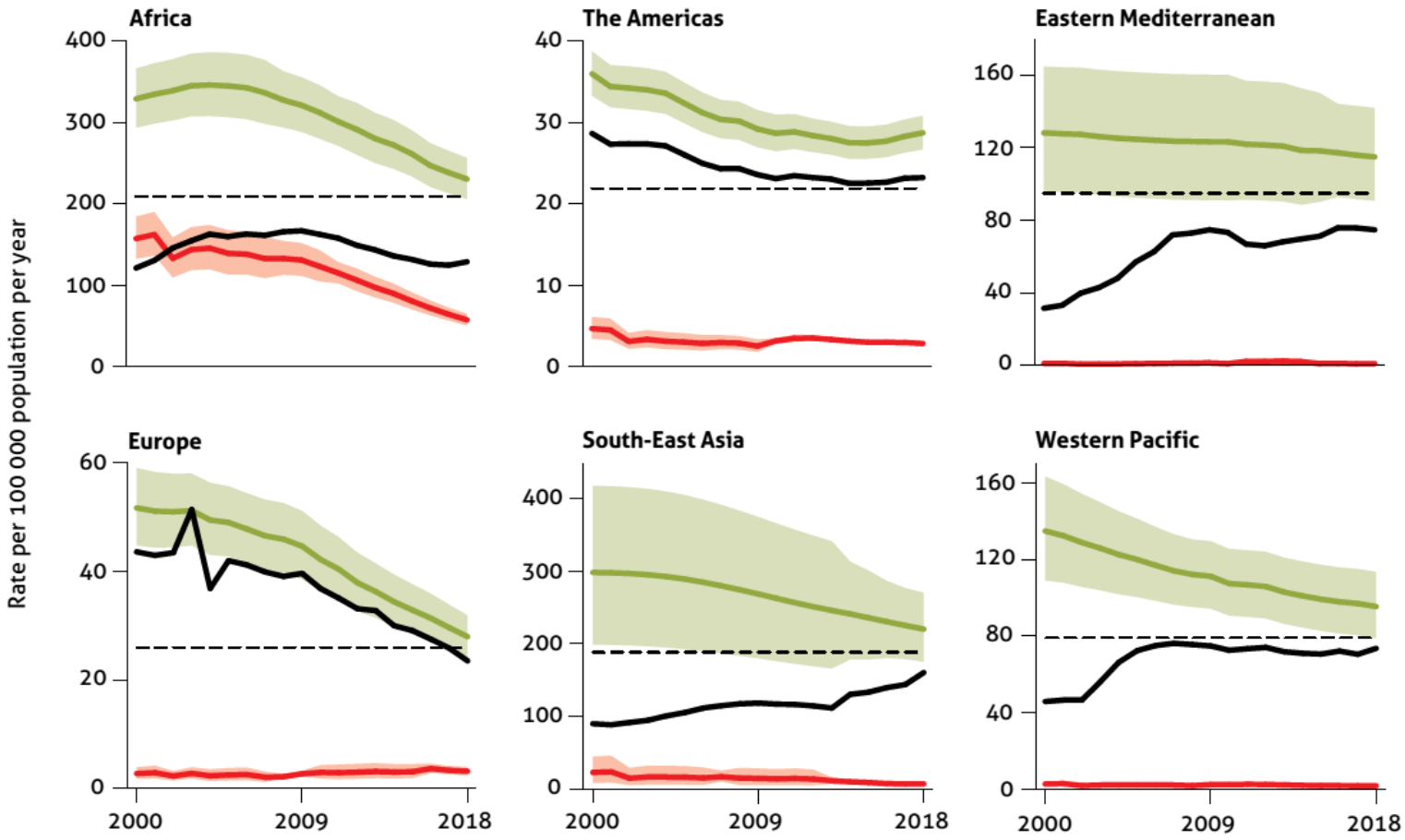


FIG. 3.11

Regional trends in estimated TB incidence rates by WHO region, 2000–2018. Total TB incidence rates are shown in green and incidence rates of HIV-positive TB are shown in red. The black solid lines show notifications of new and relapse cases for comparison with estimates of the total incidence rate. Shaded areas represent uncertainty intervals. The horizontal dashed line shows the 2020 milestone for incidence of the End TB Strategy.

GLOBAL TUBERCULOSIS REPORT 2019

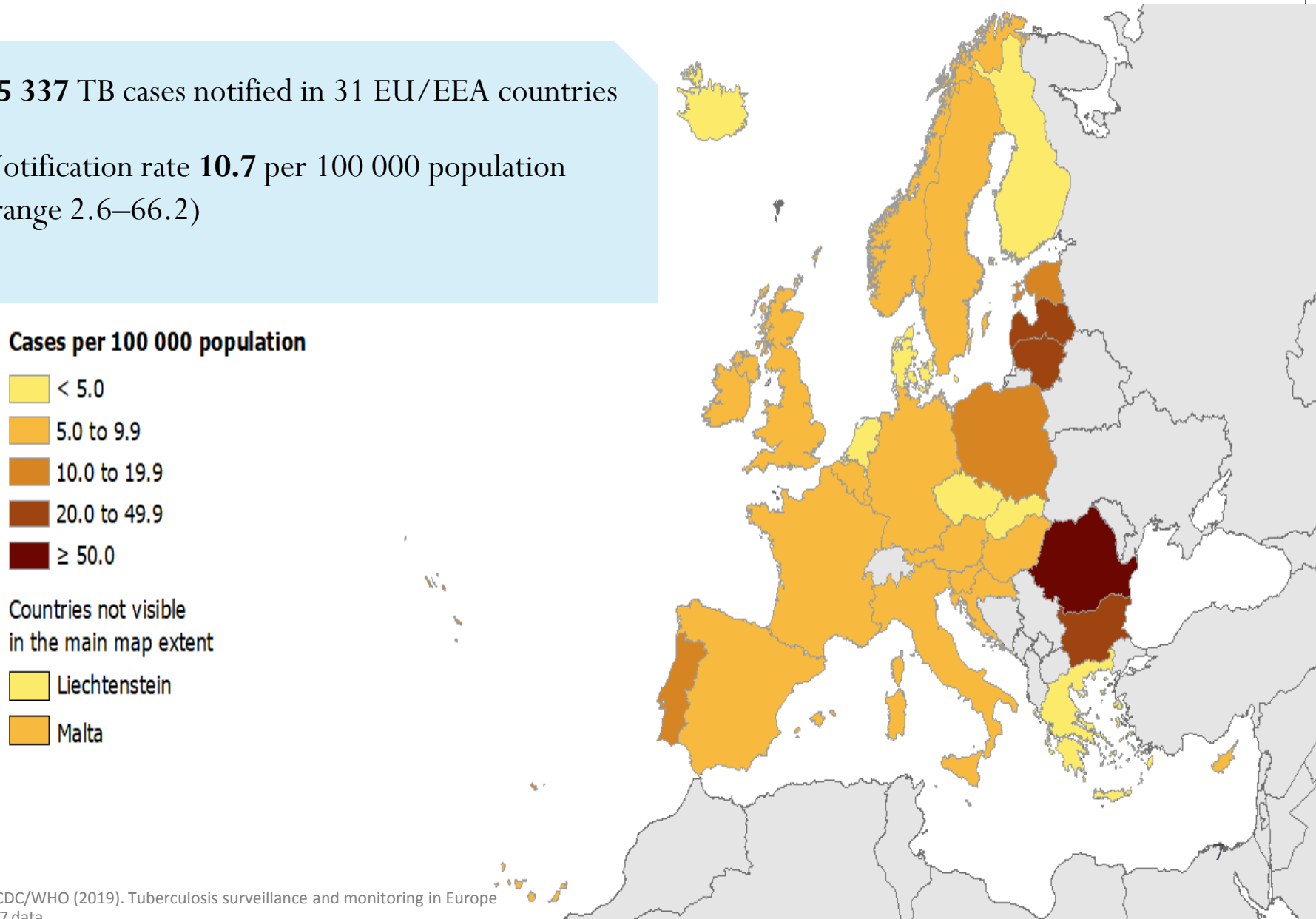


Η Ευρώπη εμφανίζει την ταχύτερη ελάττωση στην επίπτωση της ΤΒ στον κόσμο

TB notifications, EU/EEA, 2017

55 337 TB cases notified in 31 EU/EEA countries

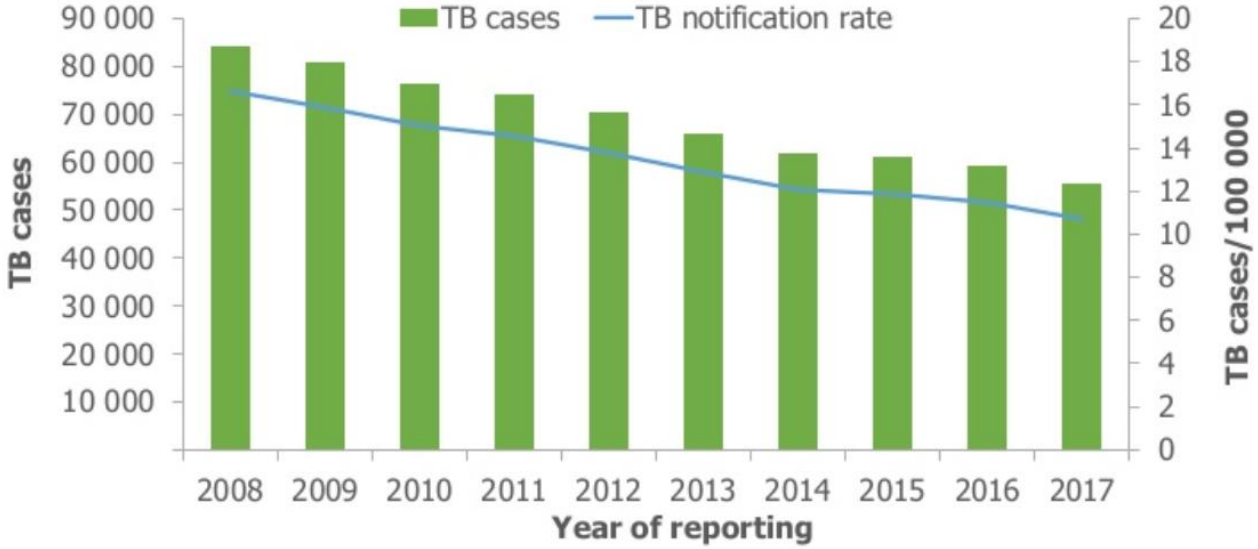
Notification rate **10.7** per 100 000 population (range 2.6–66.2)



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

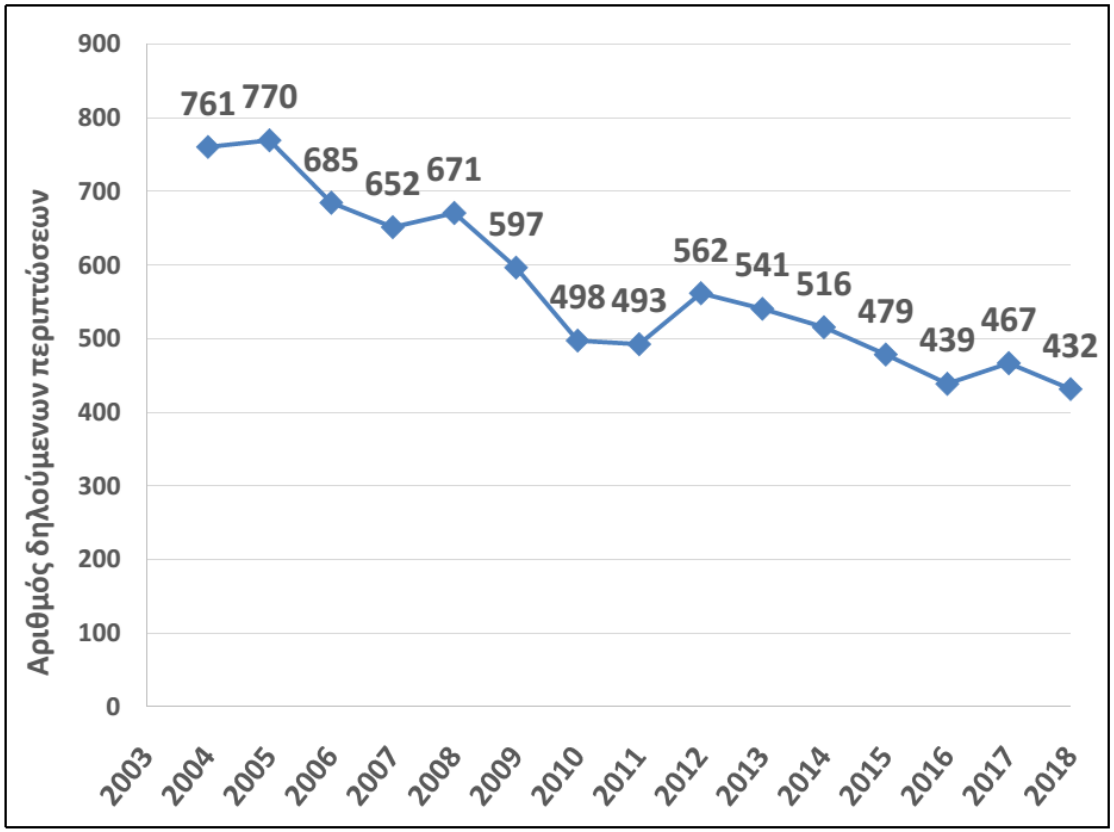
Notified TB cases, EU/EEA, 2008–2017

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

Δηλωθείσες περιπτώσεις φυματίωσης, Ελλάδα, 2004-2018



2019* : n = 377

Μεταξύ 2004 και 2018: ελάττωση αριθμού δηλούμενων περιπτώσεων ΤΒ κατά 43,2%
(Μέση ετήσια μείωση : 3,1%)
Μεταξύ 2012 και 2018 μείωση κατά 23,1 %

*δεδομένα έως και 22/11/2019

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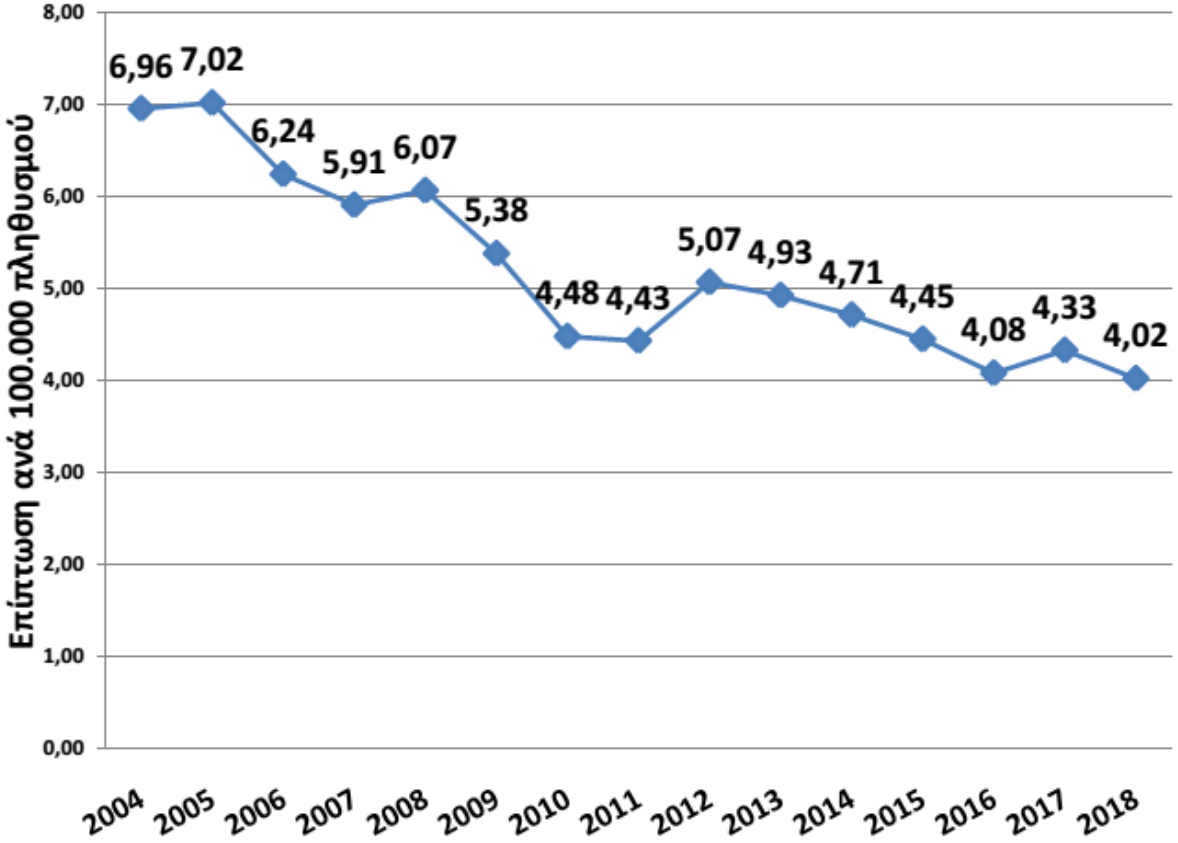
Δηλούμενη επίπτωση φυματίωσης, Ελλάδα 2004 - 2018



Μεταξύ 2004 και 2018 ελάττωση δηλούμενης επίπτωσης: 42,2%
(Μέση ετήσια μείωση 3 %)
Μεταξύ 2012 και 2018 μείωση κατά 20,7% %

Πηγές: ΕΟΔΥ και ΕΛΣΤΑ

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Ποια είναι η επίπτωση στην Ελλάδα?

OPEN ACCESS Freely available online

PLOS | ONE

Evaluation of Tuberculosis Underreporting in Greece through Comparison with Anti-Tuberculosis Drug Consumption

Theodore Lytras[1]*, Georgia Spala[2], Stefanos Bonovas[2], Takis Panagiotopoulos[1]

1 National School of Public Health, Athens, Greece, 2 Hellenic Centre for Disease Control and Prevention, Athens, Greece

Abstract

Surveillance is an integral part of tuberculosis (TB) control. Greece has a low TB notification rate, but there are doubts about underreporting. Examining anti-TB drug consumption is a way to validate the results of surveillance and estimate TB burden in the country. We used surveillance data from 2004 to 2008 to calculate the average prescribed treatment duration with the first-line anti-TB drugs isoniazid, rifampicin, ethambutol and pyrazinamide. We then obtained the best available data on consumption of these drugs, and calculated the number of treated cases to which these quantities correspond. We thus estimated underreporting at around 80% (77–81%), and annual TB incidence at about 30 cases per 100,000 population, five times over the notification rate. Underreporting was found to be constant over the study period, while incidence followed a decreasing trend. In addition we estimated that one person receives chemoprophylaxis for latent tuberculosis infection (LTBI) for every three TB cases. These results indicate the need for a comprehensive plan to improve TB surveillance and TB contact tracing in Greece, especially in light of the economic crisis affecting the country since 2009.

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Pilot study of the completeness of notification of adult tuberculosis in Athens, Greece

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*European Programme for Public Health Microbiology Training, European Centre for Disease Prevention and Control, Stockholm, Sweden; †National School of Public Health, Athens, ‡Hellenic Centre for Disease Control and Prevention, Athens, §Microbiology Laboratory & National Reference Laboratory for Mycobacteria, and ¶Infection Control Committee, Sotiria Chest Diseases Hospital, Athens, Greece

SUMMARY

SETTING: Sotiria Chest Diseases Hospital (SCDH), a referral hospital in Athens, Greece, 2012.

OBJECTIVE: To assess the completeness of the mandatory notification system for tuberculosis (TB) at the SCDH, and compare the observed and estimated annual incidence rates.

DESIGN: Record linkage and the capture-recapture method were applied. Data sources were the registers from the national mandatory notification register (Hellenic Centre for Disease Control and Prevention [HCDCP]), the National Reference Laboratory for Mycobacteria (NRLM) and SCDH records. The log-linear model with the lowest Akaike information criterion was selected as the most valid statistical model.

RESULTS: The observed and estimated TB under-reporting rates at the national level were respectively 55% (95%CI 49–60) and 75% (95%CI 71–78). The observed completeness of the HCDCP, NRLM and SCDH registers were respectively 45% (95%CI 40–51), 66% (95%CI 61–71) and 36.5% (95%CI 31–42). The estimated TB incidence rate was 15 cases per 100 000 (range 13–19/100 000), compared to the 4.9/100 000 rate officially notified.

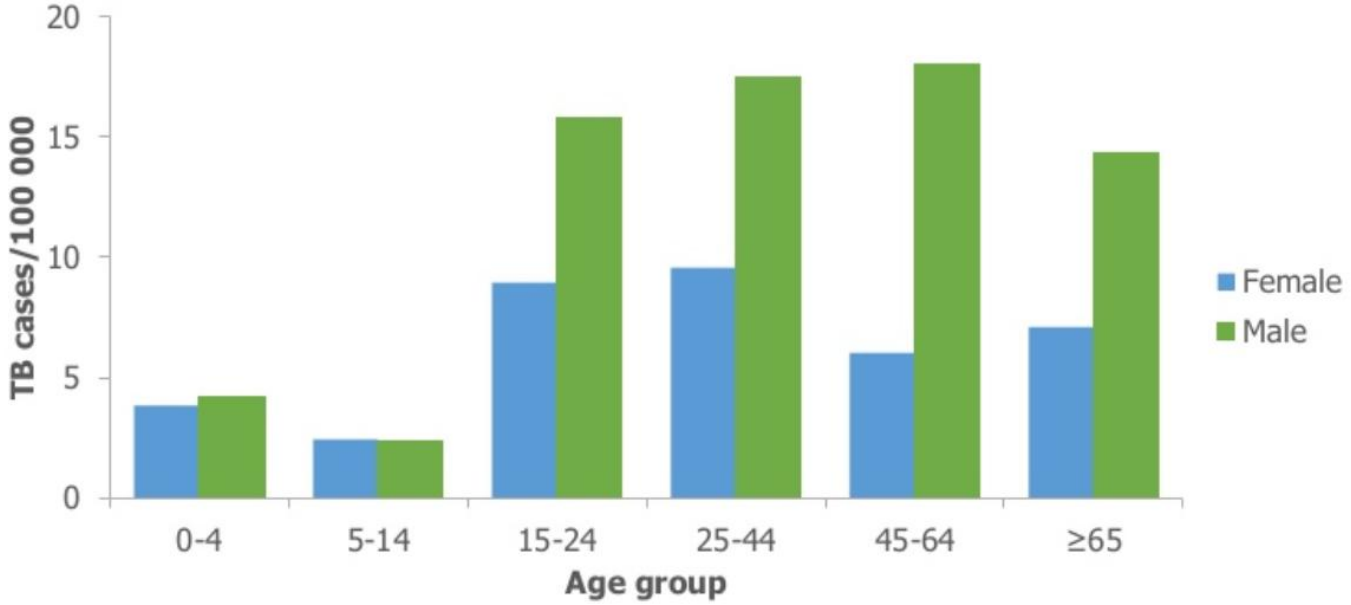
CONCLUSION: Adult TB incidence has been largely underestimated, and the TB burden is likely to be much higher than officially notified in our setting. A thorough review of the notification system should be carried out. The implementation of a network-based notification system and retraining of all relevant personnel is advised.

KEY WORDS: TB; surveillance; under-reporting; record linkage; capture-recapture; Greece

TB notification rate by sex and age group, EU/EEA, 2017

The highest notification rate was observed in the age group **25–44 years** (13.6 per 100 000)

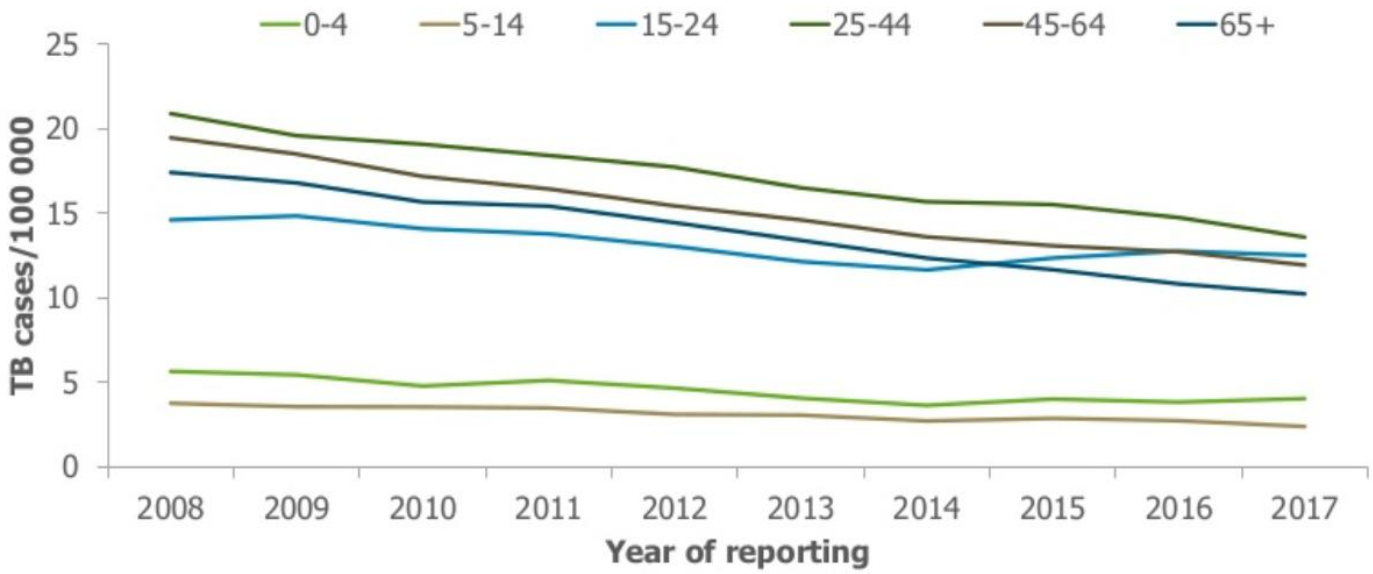
Males were over-represented in all age groups over 14 years



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

TB notification rate by age group, EU/EEA, 2008–2017*

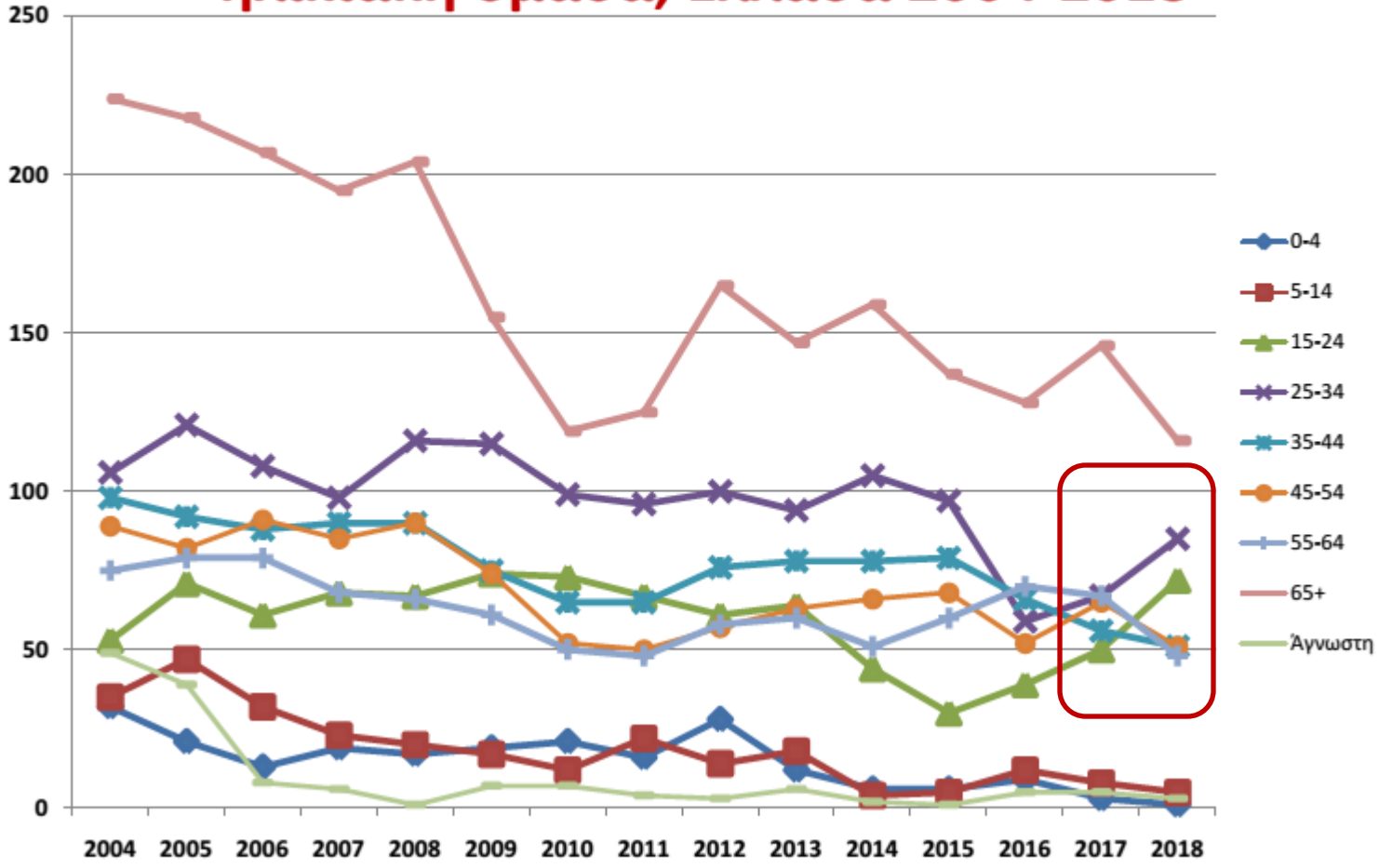
Annual average decrease by **2–6%** in all age groups



* Croatia is not included for the years prior to 2010

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

Δηλωθείσες περιπτώσεις ΤΒ ανά ηλικιακή ομάδα, Ελλάδα 2004-2018



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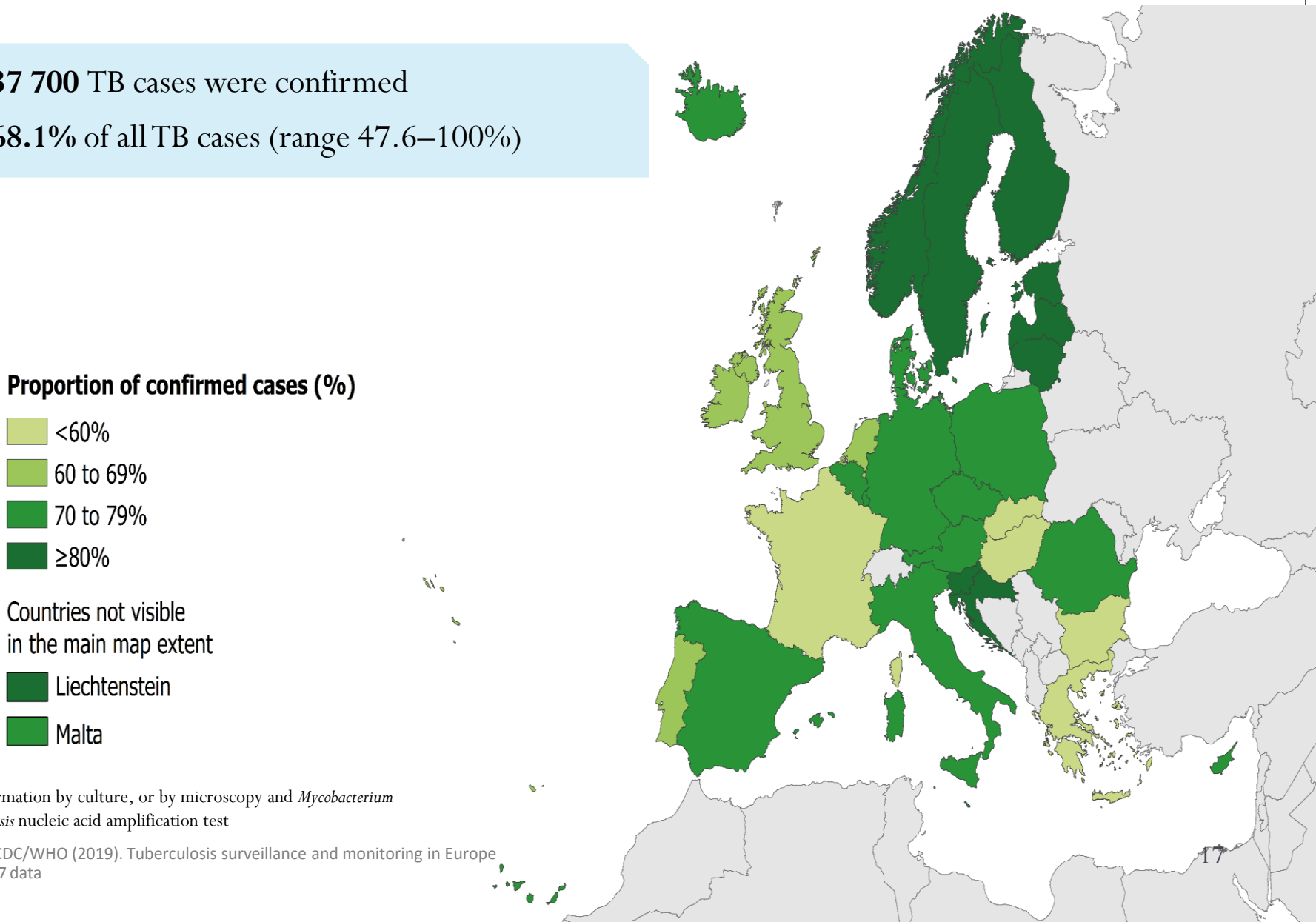
Confirmed TB cases*, EU/EEA, 2017

37 700 TB cases were confirmed

68.1% of all TB cases (range 47.6–100%)



* Confirmation by culture, or by microscopy and *Mycobacterium tuberculosis* nucleic acid amplification test

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

Εργαστηριακή επιβεβαίωση – Αποτελέσματα ευαισθησίας δηλωθέντων περιπτώσεων, Ελλάδα 2011-2017

	ΕΡΓ. ΕΠΙΒΕΒΑΙΩΜΕΝΑ	DST (%)	MDR	MDR %	XDR
2011	59,6%	57,2%	5	3,1%	2
2012	40,4%		1		0
2013	62,8%	68,7%	10	4,8%	0
2014	65,9%	48,5%	4	2,4%	1
2015	63,3%	69,2%	9	4,3%	0
2016	55,5%	50,4%	5	4,0%	0
2017	56,7%	72,1%	7	3,7%	2
Στόχοι	100% ή κ/α ≥90%	DST≥75 %			

2017

MDR EU/ΕΕΑ: 3,8 %

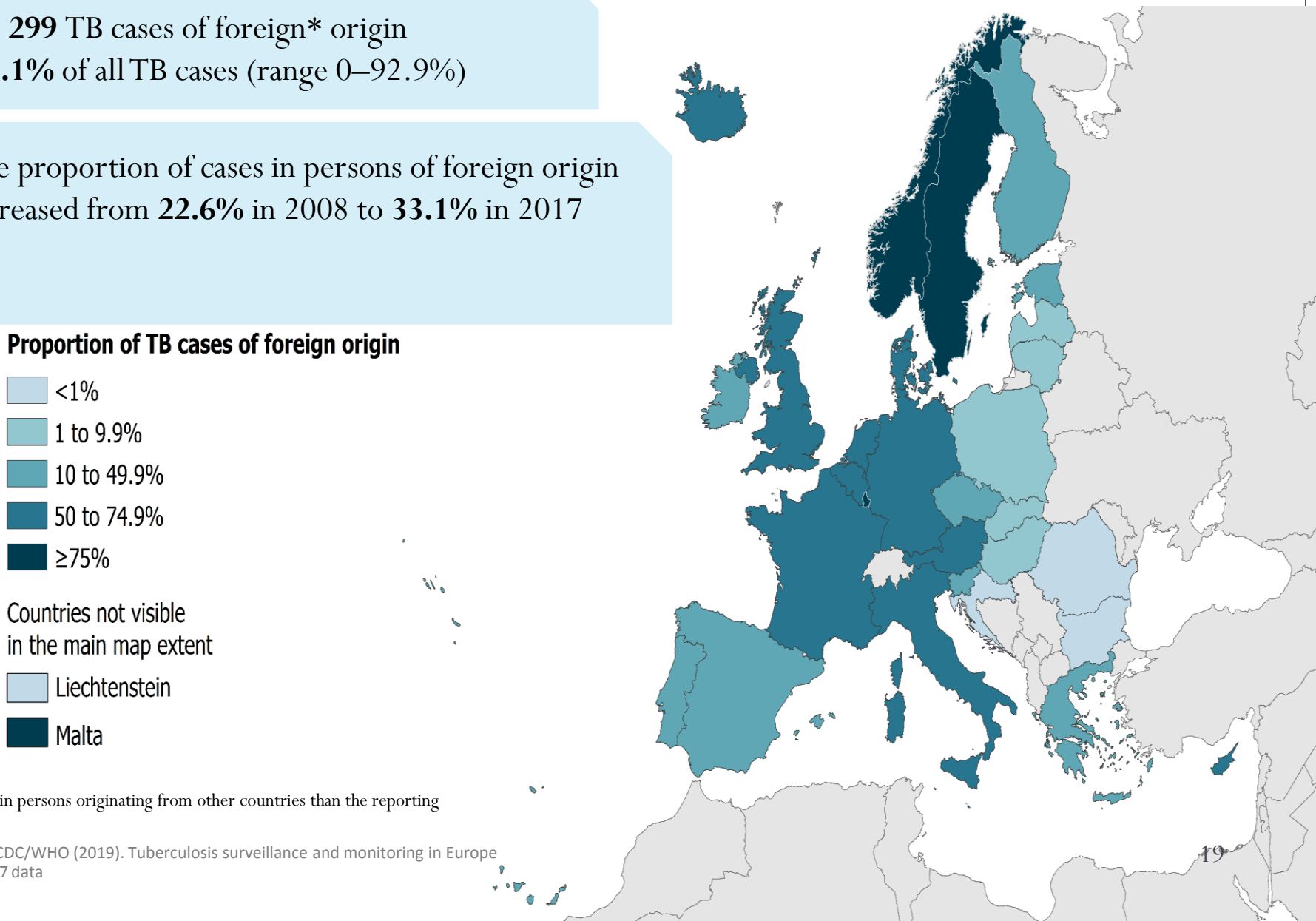
MDR ΕΛΛΑΔΑ: 3,7 %

Πηγή: ΕΟΔΥ

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%)

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



* 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 σε γηγενείς και αλλοδαπούς στην EU/EEA

% TB σε αλλοδαπούς

- Δυτική Ευρώπη (Βρετανία, Γερμανία, Γαλλία): 50%
- Βόρεια Ευρώπη (Σουηδία, Νορβηγία): 85-90%
- Ανατολική Ευρώπη (Ουγγαρία, Πολωνία, Σλοβακία): <5%

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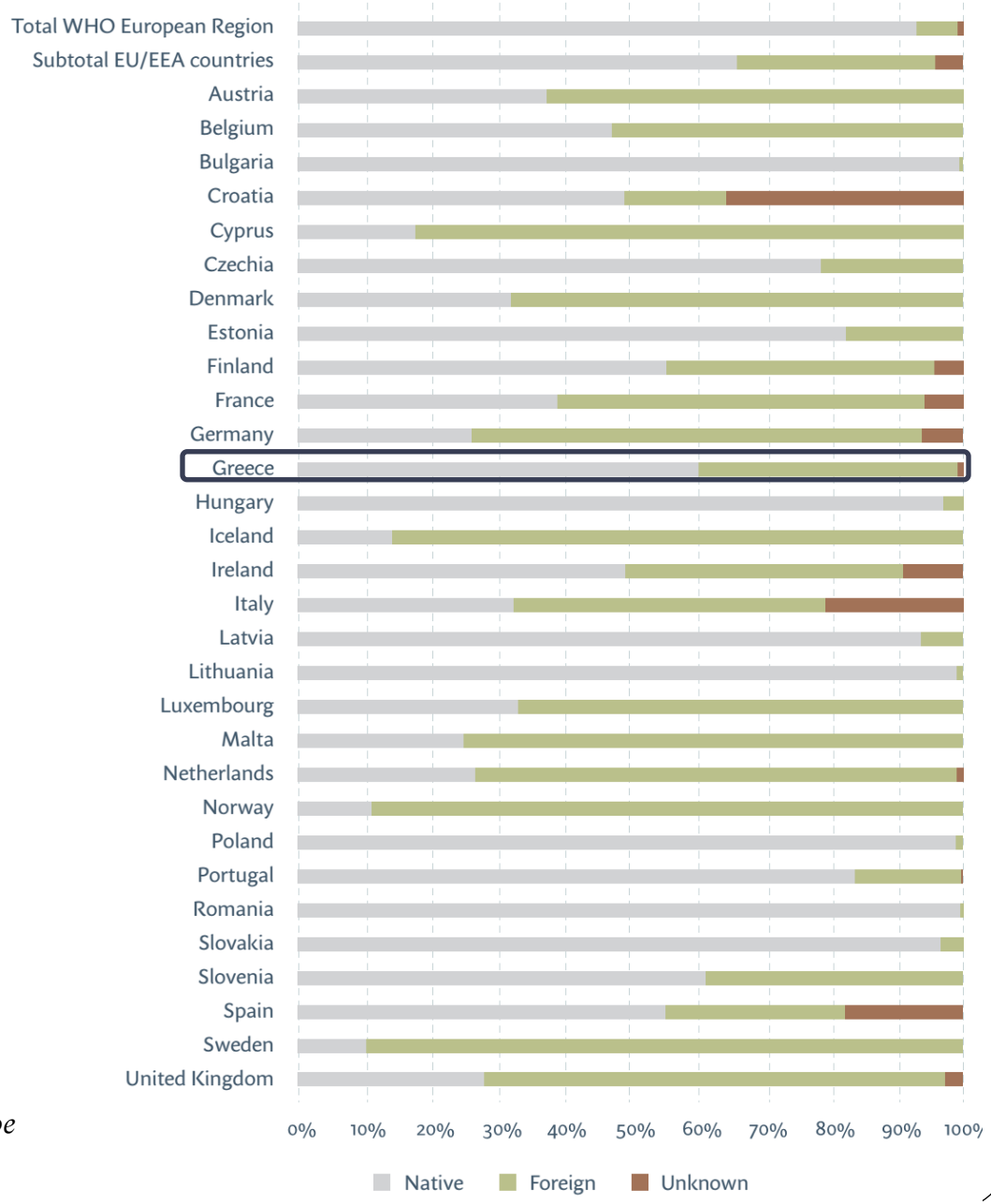
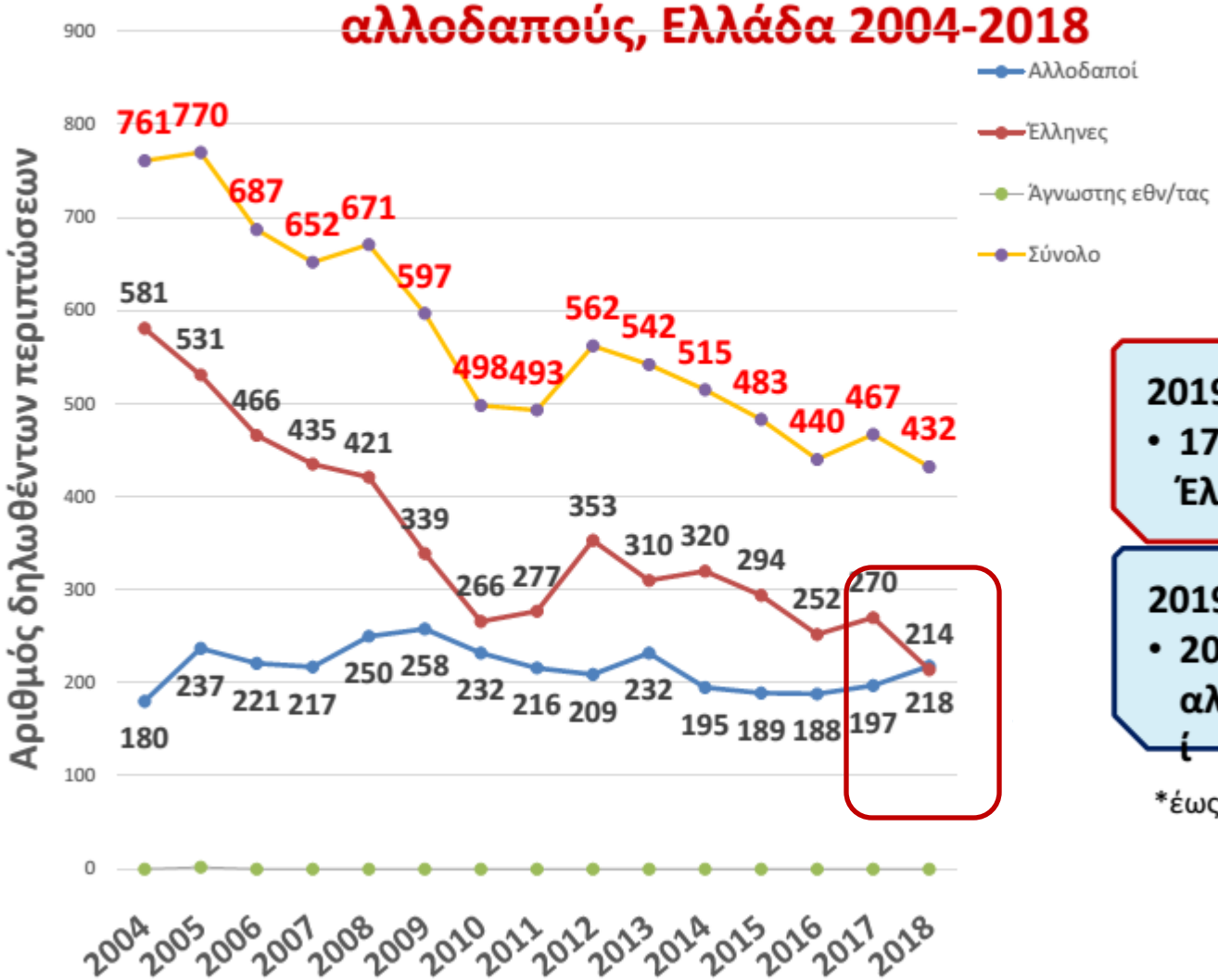
Hargreaves S.WHO Regional Office for Europe 2018, HEN synthesis report 56

Fig. 2. Active TB cases among native and foreign-born individuals in EU/EEA countries, 2015



Δηλωθείσες περιπτώσεις φυματίωσης σε Έλληνες & αλλοδαπούς, Ελλάδα 2004-2018



2019*
- **177 Έλληνες**

2019*
- **206 αλλοδαποί**

*έως και 22/11/2019

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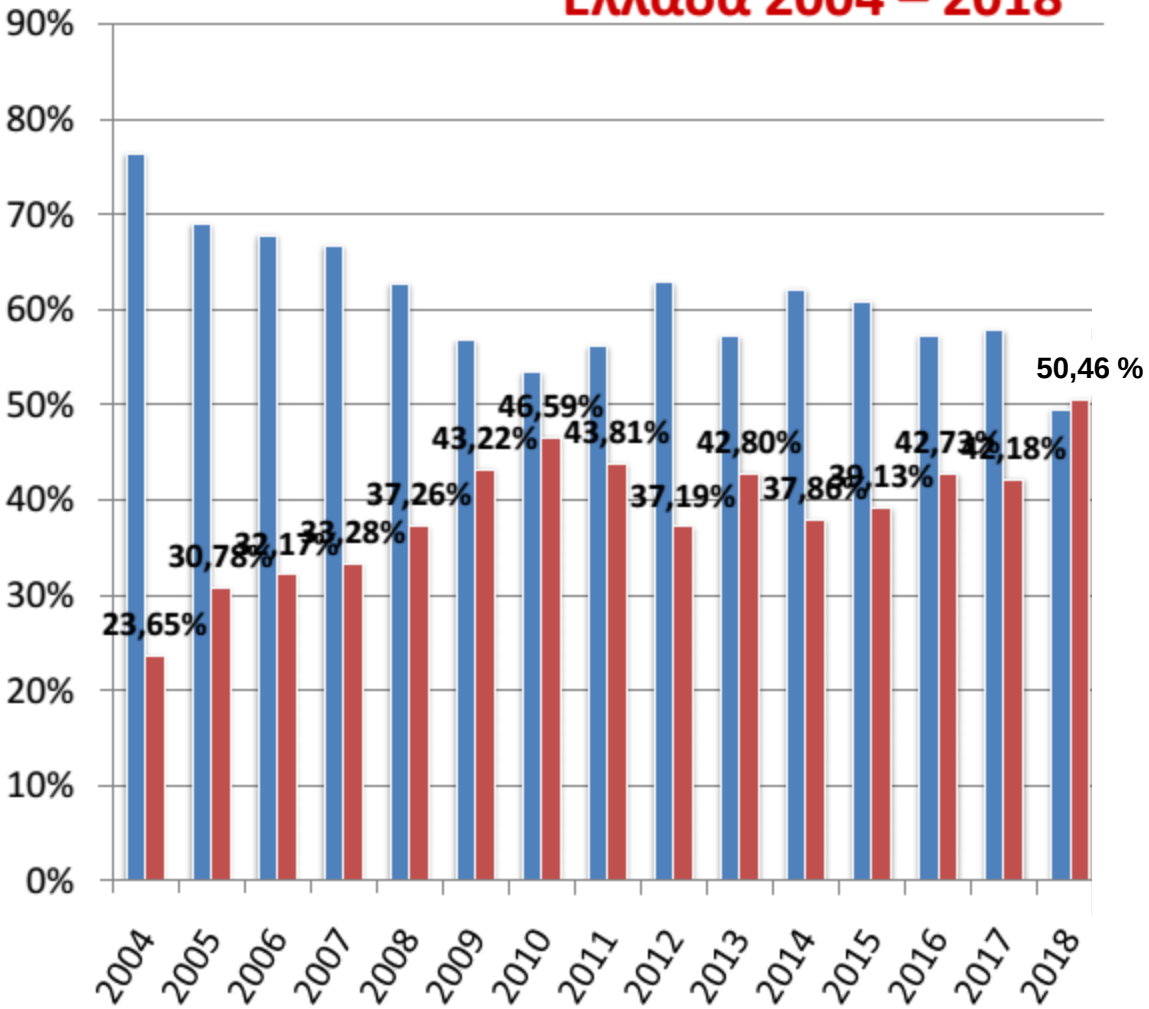
Κατανομή συχνότητας δηλωθέντων περιπτώσεων φυματίωσης ανά εθνικότητα, Ελλάδα 2004 – 2018



2019*

- Έλληνες: 45,4%
- Αλλοδαποί: 54,6 %

*δεδομένα έως και 22/11/2019

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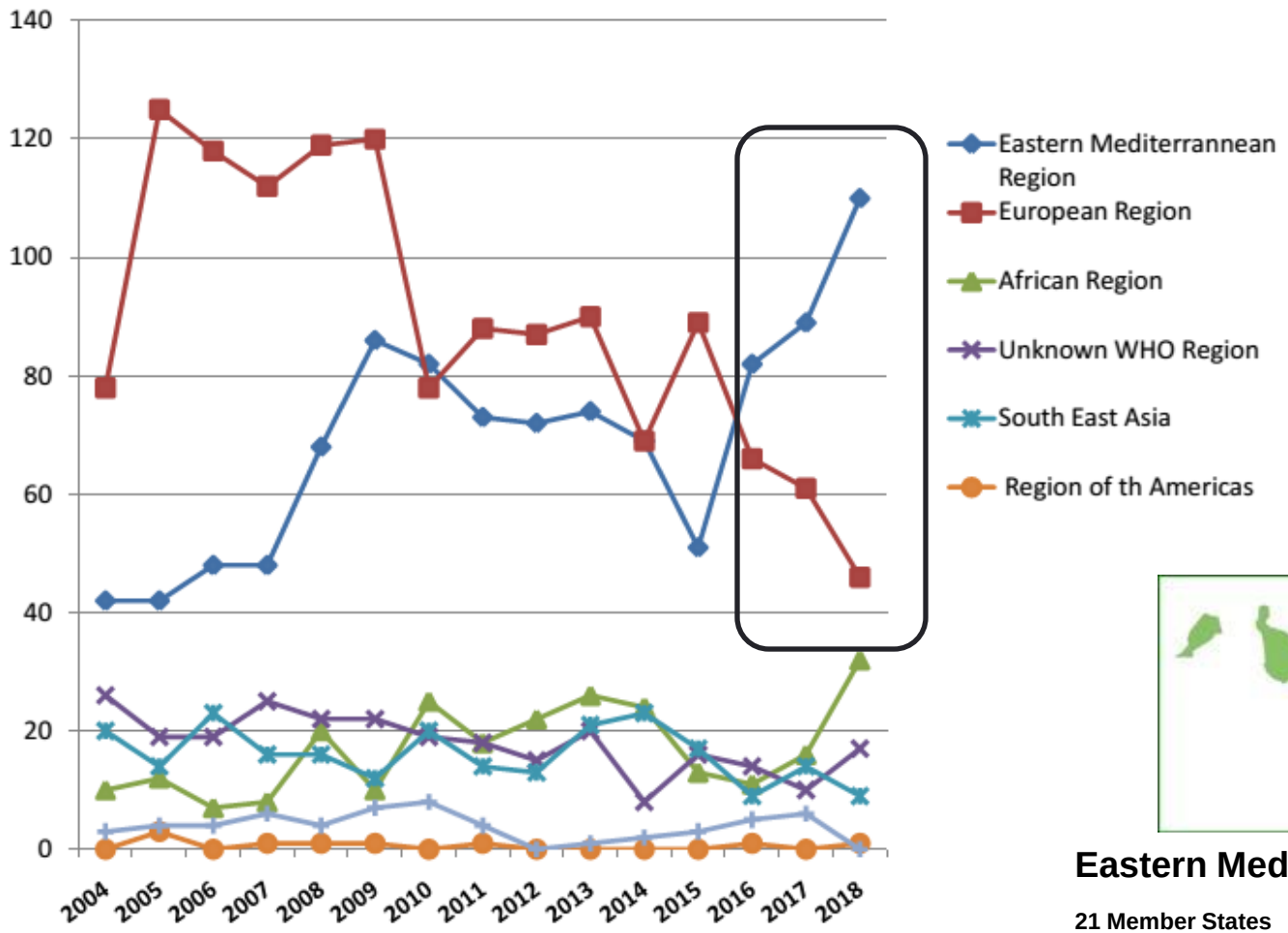
Δηλούμενος αριθμός περιπτώσεων TB σε αλλοδαπούς ασθενείς ανά WHO Region προέλευσης των ασθενών, Ελλάδα 2004-2018



Eastern Mediterranean Region

21 Member States
Afghanistan, Bahrain, Djibouti, Egypt, Iran (Islamic Republic of), Iraq, Jordan, Kuwait, Lebanon, Libyan Arab Jamahiriya, Morocco, Oman, Pakistan, Qatar, Saudi Arabia, Somalia, Sudan, Syrian Arab Republic, Tunisia, United Arab Emirates, Yemen

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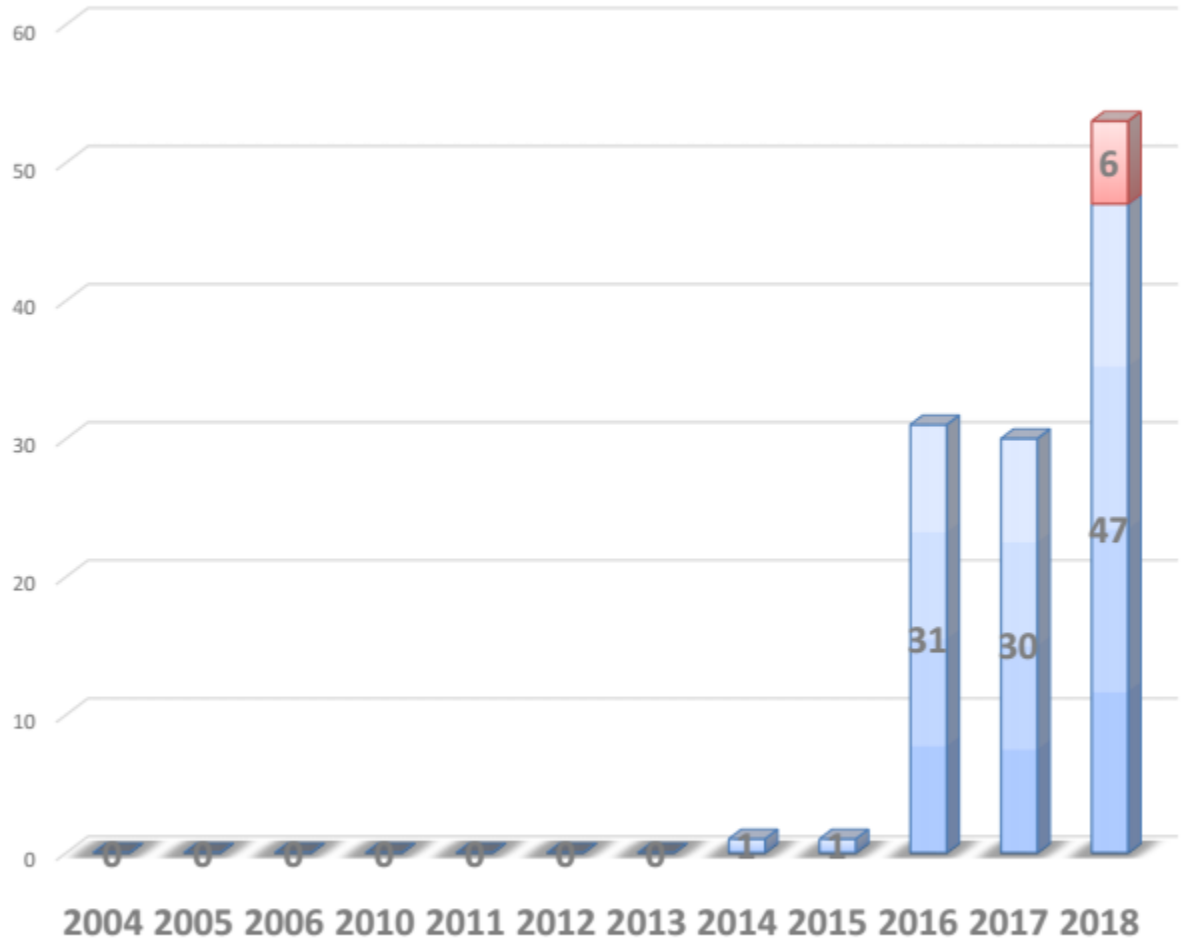
Δηλωθείσες περιπτώσεις ΤΒ σε ΚΥΤ/ΚΦ και ξενώνες προσφύγων/μεταναστών, Ελλάδα 2004-2018



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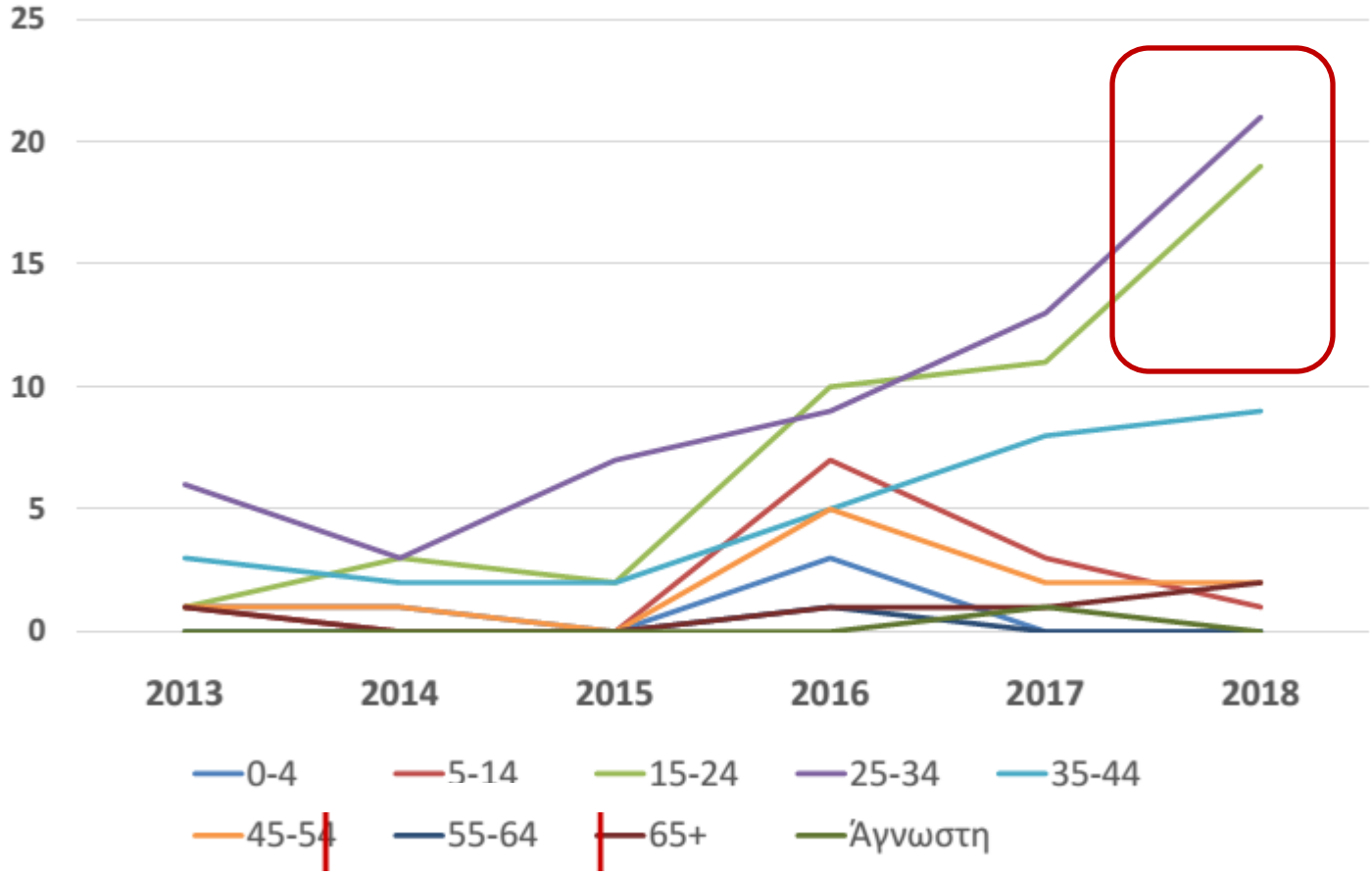
Δηλωθείσες περιπτώσεις ΤΒ σε ΚΥΤ/ΚΦ/Ξενώνες φιλοξενίας προσφύγων και μεταναστών ανά ηλικιακή ομάδα, Ελλάδα 2013-2018



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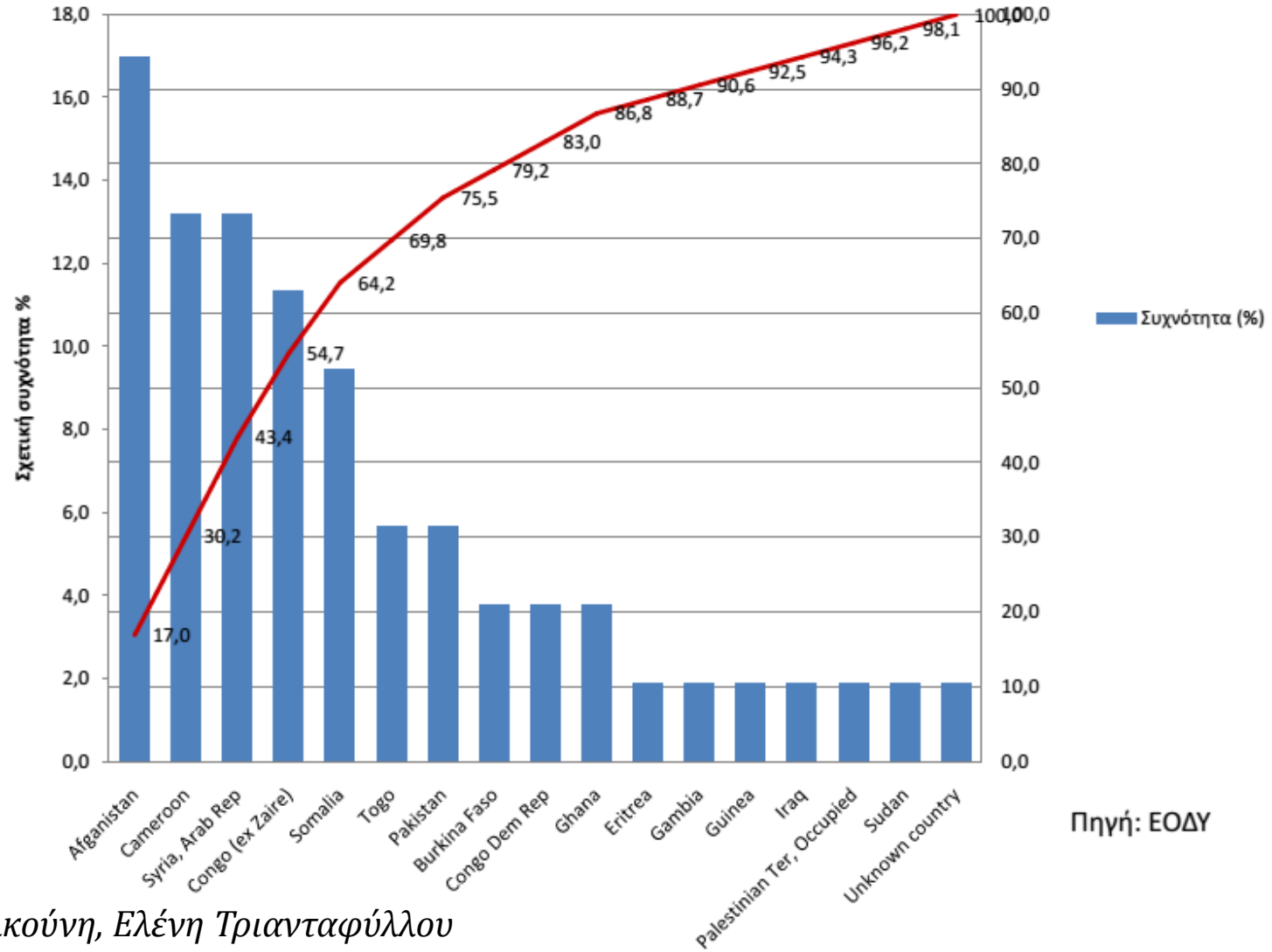
Χώρα προέλευσης δηλούμενων περιπτώσεων ΤΒ σε ΚΥΤ/ΚΦ και ξενώνες φιλοξενίας προσφύγων/μεταναστών, Ελλάδα 2018



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Αυξημένη επίπτωση ΤΒ στους μετανάστες- Γιατί?

- Διαμονή σε χώρα με υψηλή επίπτωση πριν την μετανάστευση
- Διαμονή σε περιοχή όπου το σύστημα υγείας έχει διαταραχθεί
- Δυσμενείς συνθήκες κατά τη μετανάστευση
- Παραμονή σε πολυπληθείς καταυλισμούς
- Κοινωνική απομόνωση στη χώρα υποδοχής
- Περιορισμένη πρόσβαση στο σύστημα υγείας στη χώρα υποδοχής

Hargreaves S.WHO Regional Office for Europe 2018, HEN synthesis report 56

World Health Organization
REGIONAL OFFICE FOR Europe

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STATE OF THE ART

Active case finding and treatment adherence in risk groups in the tuberculosis pre-elimination era

R. K. Gupta,* M. Lipman,†‡ A. Story,§ A. Hayward,¶ G. de Vries,#** R. van Hest,††‡‡ C. Erkens,# M. X. Rangaka,* I. Abubakar*

Η έγκαιρη διάγνωση και αντιμετώπιση της ΤΒ στις ευπαθείς ομάδες αποτελεί αναπόσπαστο τμήμα της στρατηγικής για την εξάλειψη της ΤΒ στις χώρες με χαμηλή επίπτωση

- Άστεγοι → 200-7700/100.000
- Φυλακισμένοι → 2800/100.000
- Χρήστες ουσιών → 354/100.000
- Μετανάστες → 350/100.000

Klinkenberg E, Eur Respir J 2009

Δηλούμενη επίπτωση ΤΒ σε κρατούμενους Ελλάδα 2018 :
34 Χ επίπτωση γεν.πληθυσμού

Μέση δηλούμενη επίπτωση ΤΒ σε κρατούμενους ΕΕ/ΕΟΧ 2017:
155/100.000
11,4 Χ επίπτωση γεν.πληθυσμού

Ουρανία Καλκούνη, Ελένη Τριανταφύλλου
Γραφείο Νοσημάτων που μεταδίδονται μέσω του αναπνευστικού
Τμήμα Επιδημιολογικής Επιτήρησης και Παρέμβασης, ΕΟΔΥ

Active case finding and treatment adherence in risk groups in the tuberculosis pre-elimination era

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INT J TUBERC LUNG DIS 22(5):479–487
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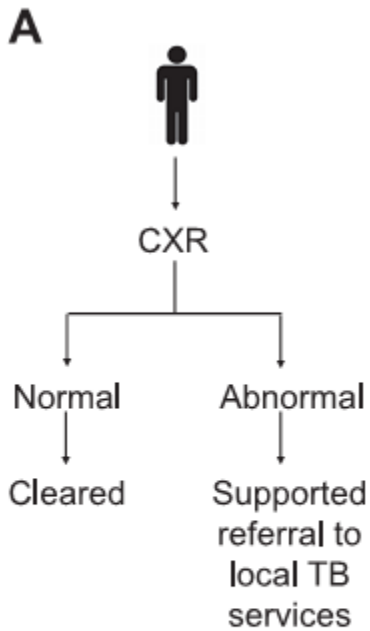
Κλασική μέθοδος με κινητή ακτινολογική μονάδα



Active case finding με κινητή ακτινολογική μονάδα σε άστεγους-αποτελέσματα

- Find and treat (Λονδίνο): μικρότερη πιθανότητα Z/N (+), cost effective
- Παρίσι: 179 TB σε 22.000
- Ρόττερνταμ: 28 (328/100.000)-ελάττωση μετάδοσης
- Συνολική απόδοση 16 μελετών: 931/100.000

Το παράδειγμα της Ολλανδίας

Van de Berg S, Eur Respir J 2017
DeVries G , EACCTB 2019

Μετανάστες

- Screening γίνεται σε μετανάστες από χώρες με επίπτωση TB >100/100.000
- α/α στους ≥ 18 ετών και έλεγχος για LTBI στους <18 ετών
- Σε άτομα ≥ 12 ετών από χώρες με επίπτωση > 200/100.000 follow up α/α
- Ο έλεγχος γίνεται στα κέντρα δημόσιας υγείας

Αιτούντες άσυλο

- Screening γίνεται στους αιτούντες άσυλο από χώρες με επίπτωση TB >50/100.000
- α/α σε ≥ 18 ετών (συζητείται ο έλεγχος για LTBI σε <18 ετών)
- Σε άτομα ≥ 12 ετών από χώρες με επίπτωση > 200/100.000 follow up α/α
- **Ο έλεγχος γίνεται στα κέντρα υποδοχής εντός 48 ωρών από την άφιξη**

Ο αλγόριθμος του screening αξιολογείται τακτικά- μία πληθυσμιακή ομάδα θεωρείται κατάλληλη για έλεγχο όταν ο αριθμός των ατόμων που πρέπει να ελεγχθούν για να βρεθεί θετικό αποτέλεσμα είναι ≤ 2000, δηλαδή επίπτωση TB ≥50/100.000

Evaluation screening regular migrants, 2011-2015

TB incidence country of origin	Number	TB found by screening	Yield per 100,000 (+ Conf. Interval)
~~≤50~~	~~26,101~~	~~7~~	~~27 (11-55)~~
51-100	37,787	11	29 (15-52)
101-200	36,548	41	112 (80-152)
>200 (+ Eritrea)	13,028	38	292 (206-400)
unknown	2,837	0	-
Total	**116,301**	**97**	**83 (67-100)**

- Screening migrants from countries with a TB incidence ≤50/100,000 was discontinued per 1/1/2015 (Van den Berg, ERJ 2017).
- In the Netherlands, a **cut-off of 50/100,000 (NNS=2000)** was arbitrarily set (De Vries, ERJ 2016).
- Based on this evaluation screening **(regular)** migrants from countries with a TB incidence ≤100/100,000 was discontinued per 1/4/2019.

DeVries G , EACCTB 2019

MDR TB, EU/EEA, 2017

1 107 MDR TB cases notified by 30 EU/EEA countries

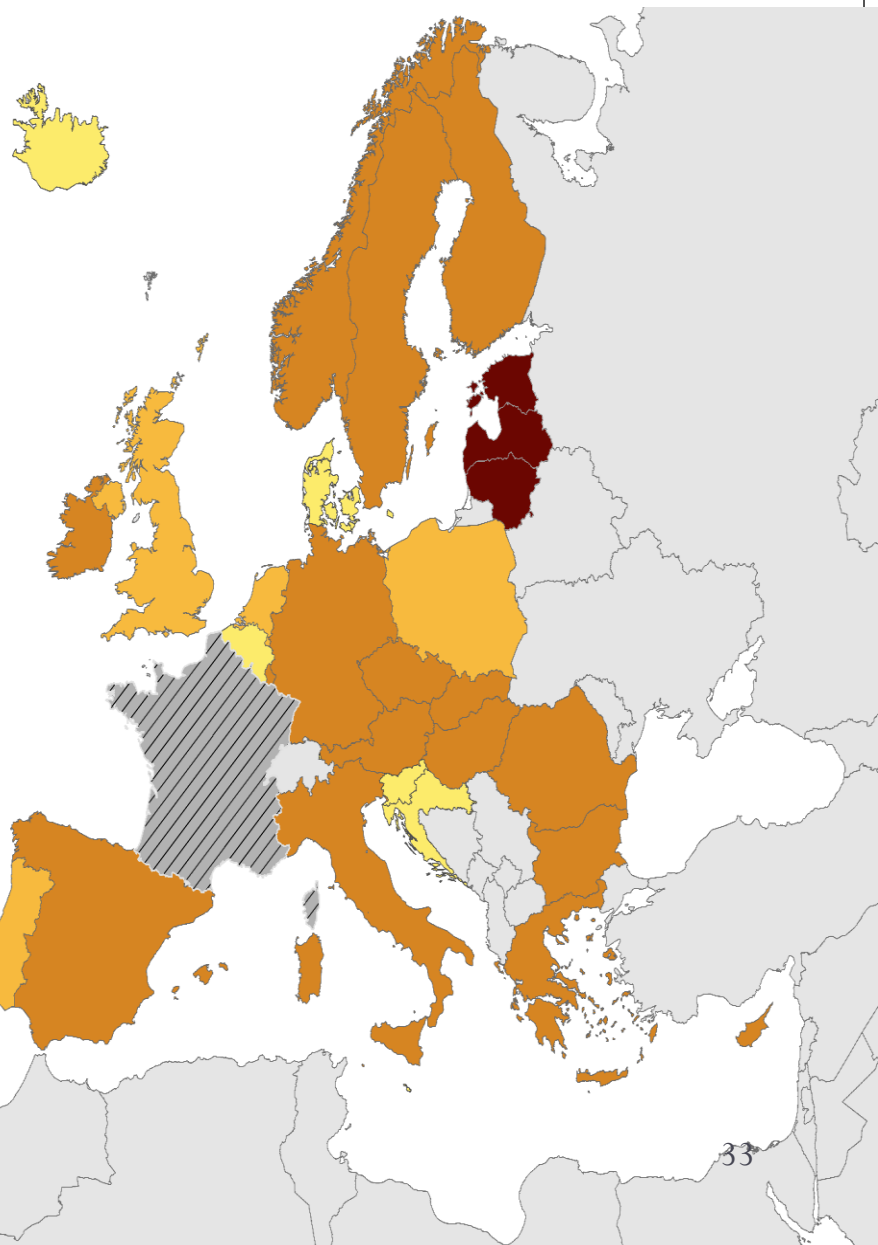
3.7% of all TB cases with available DST* results had MDR TB (range 0–25.4%)

Proportion of MDR TB cases among TB cases with available DST results

- <1%
- 1 to 1.9%
- 2 to 4.9%
- 5 to 9.9%
- ≥10%
- No data reported

Countries not visible in the main map extent

- Liechtenstein
- Malta

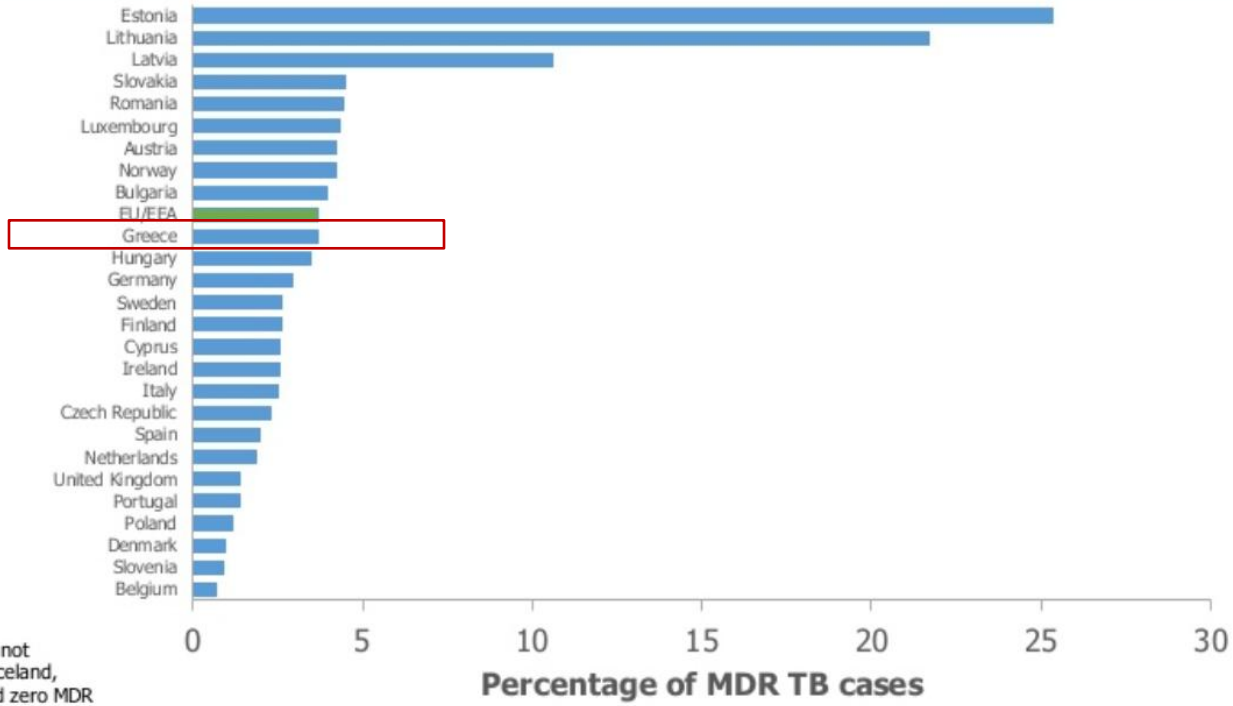


* DST – drug susceptibility test

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

Proportion of multidrug-resistant TB (MDR TB), EU/EEA, 2017*

1 107 MDR TB cases notified by 30 EU/EEA countries
3.7% of all bacteriologically-confirmed TB cases with available DST results had MDR TB (range 0–25.4%)



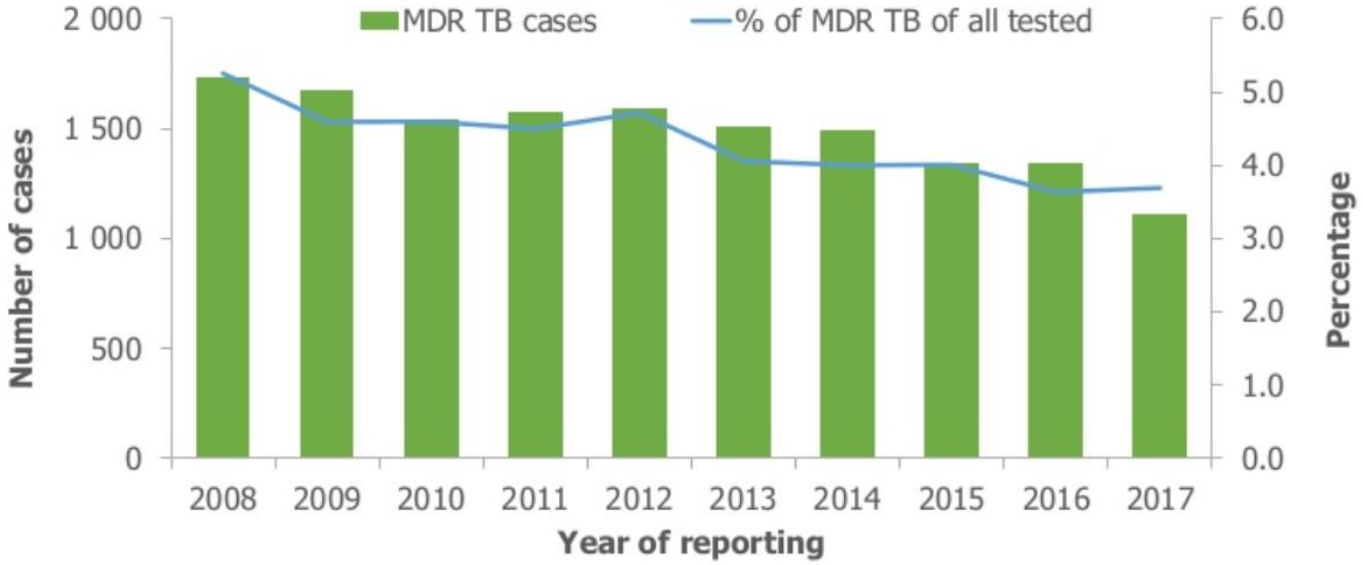
* MDR TB data from France are not included in the graph. Croatia, Iceland, Liechtenstein and Malta reported zero MDR TB cases for 2017

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

MDR TB cases and proportions of all TB cases tested for drug resistance, EU/EEA, 2008–2017*

The total number of notified MDR TB cases decreased from **1 733** in 2008 to **1 107** in 2017

Proportion of MDR TB cases among all TB cases tested for drug resistance decreased from **5.3%** in 2008 to **3.7%** in 2017



* Countries and the years they are not included due to reporting discrepancies: Croatia (2008, 2010), France (2012, 2015, 2017), Greece (2008), Luxembourg (2008)

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

XDR TB (% των MDR) EU/EEA, 2017

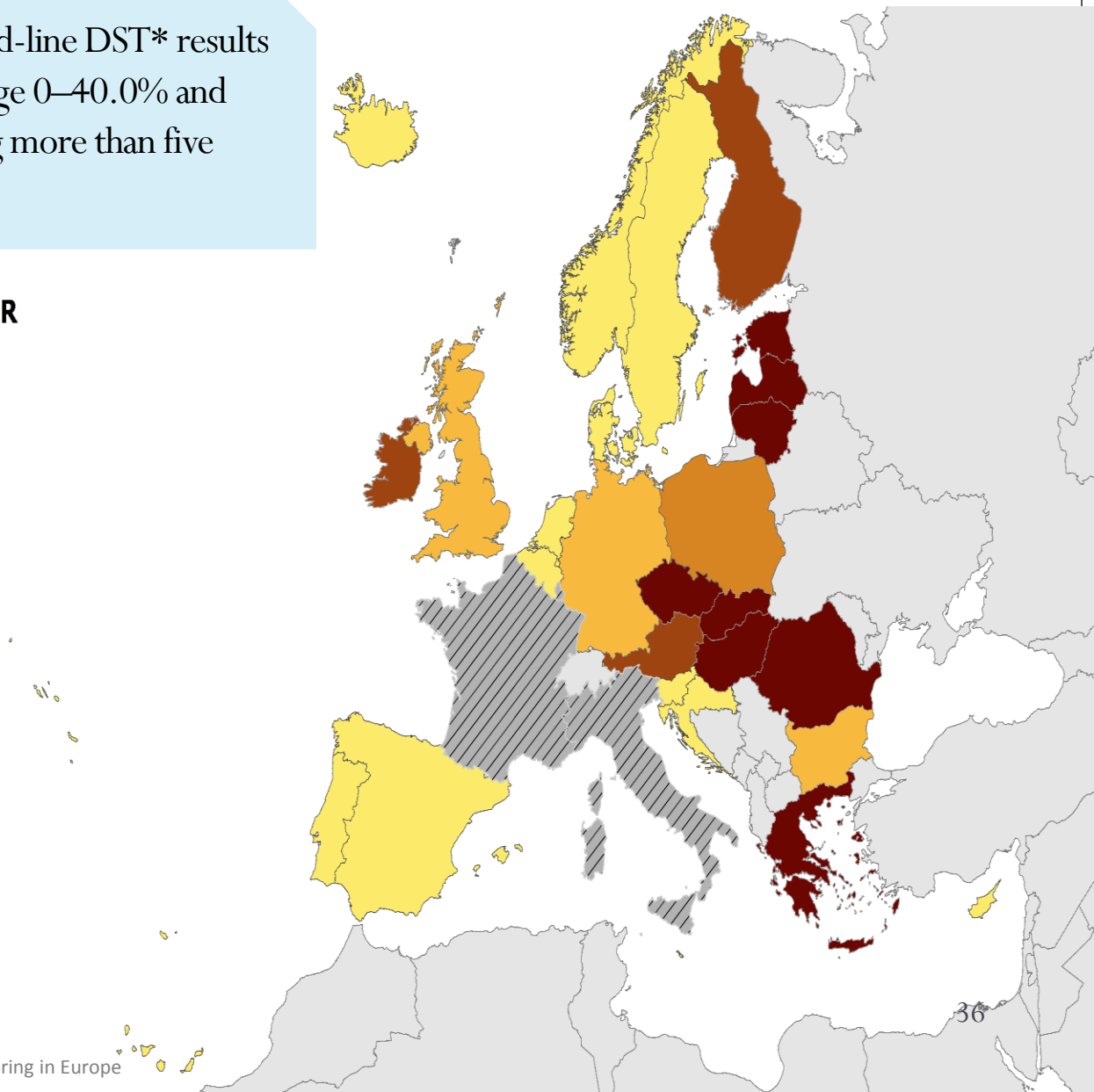
24.3% of MDR TB cases with second-line DST* results were extensively drug-resistant (range 0–40.0% and 26.5–39.1% for countries reporting more than five XDR TB cases)

Proportion of XDR TB cases among MDR TB cases with second-line DST results

- <1%
- 1 to 9.9%
- 10 to 14.9%
- 15 to 24.9%
- ≥25%
- No data reported

Countries not visible in the main map extent

- Liechtenstein
- Malta



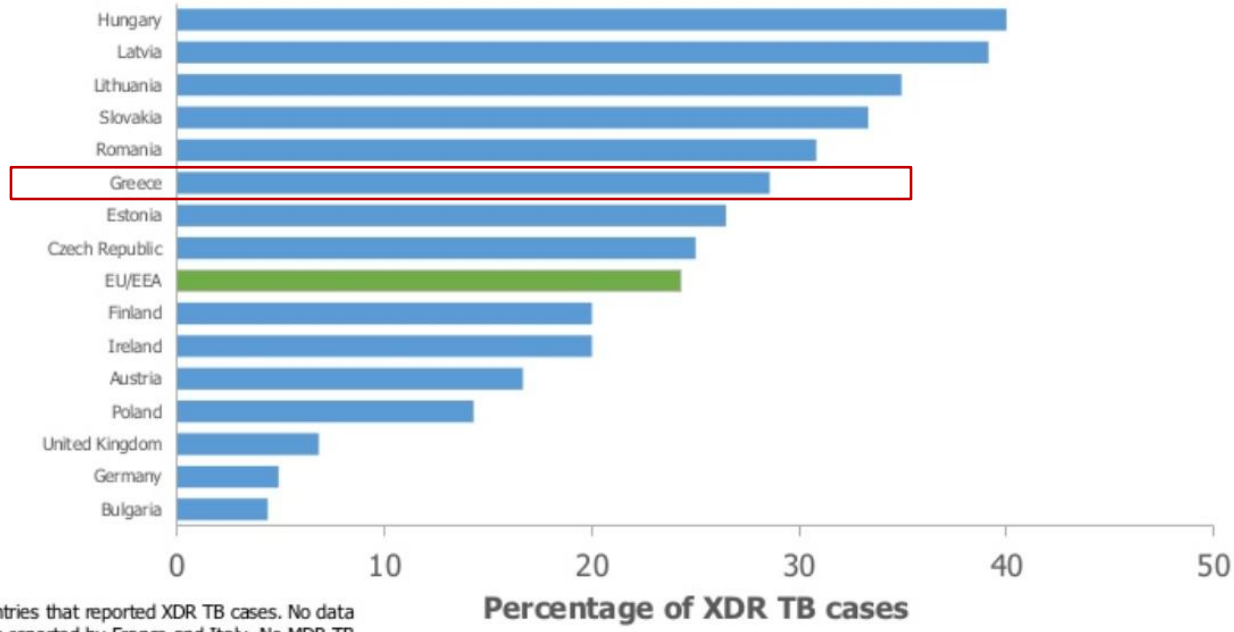
* DST – drug susceptibility test

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

Proportion of extensively drug-resistant TB (XDR TB), EU/EEA, 2017

187 XDR TB cases notified in 15 EU/EEA countries*

24.3% of all MDR TB cases with second-line drug susceptibility test results (range 0–40.0%)



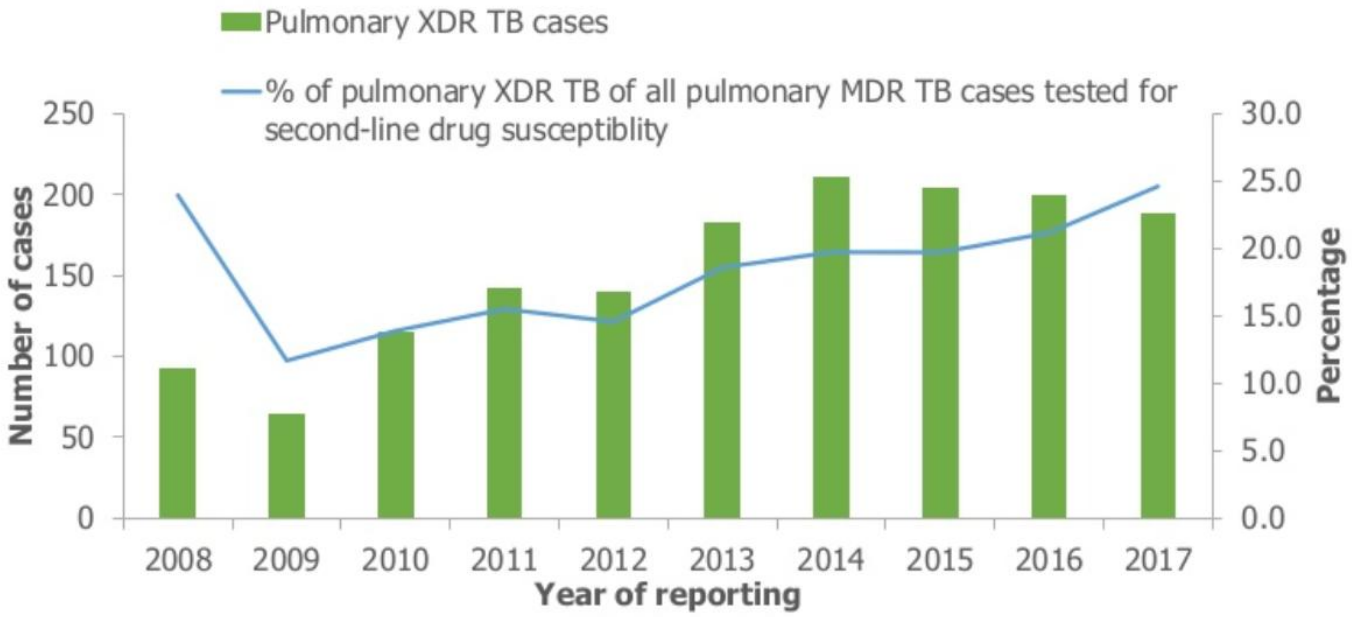
* The graph shows countries that reported XDR TB cases. No data on MDR or XDR TB were reported by France and Italy. No MDR TB cases were reported by Croatia, Iceland, Liechtenstein and Malta

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

Pulmonary XDR TB cases and proportions of all pulmonary MDR TB cases tested for second-line drug resistance, EU/EEA, 2008–2017*

The total number of pulmonary XDR TB cases increased from **64** in 2009 to **188** in 2017

The proportion of XDR TB cases among pulmonary MDR TB cases increased from **11.7%** in 2009 to **24.6%** in 2017

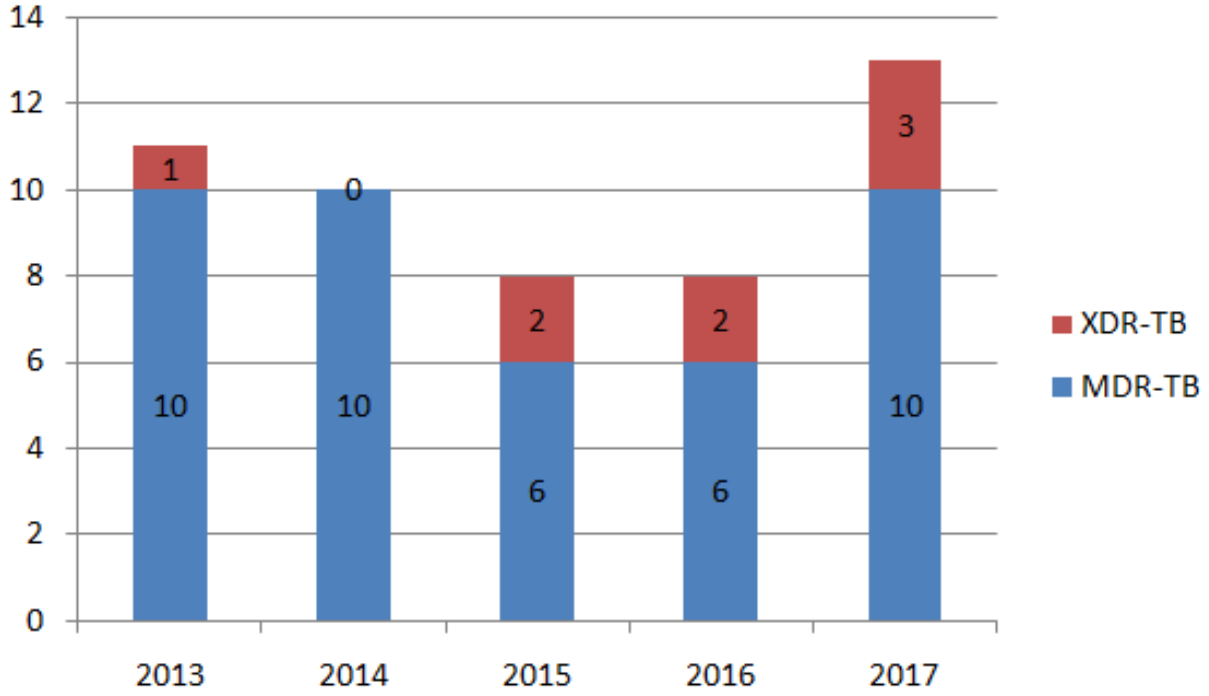


* Countries and the years for which they are not included due to reporting discrepancies or no data: Croatia (2008-2012), France (2008-2012, 2017), Greece (2008), Luxembourg (2008), Italy (2008-2012), Spain (2008-2012)

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

ΓΕΝΙΚΟ ΝΟΣΟΚΟΜΕΙΟ ΝΟΣΗΜΑΤΩΝ ΘΩΡΑΚΟΣ ΑΘΗΝΩΝ Η ΣΩΤΗΡΙΑ

Ετήσιος αριθμός MDR/XDR-TB Αντιφυματικό Τμήμα- Μονάδα Πολυανθεκτικής Φυματίωσης



Multidrug-resistant/extensively drug-resistant tuberculosis in Greece: predominance of *Mycobacterium tuberculosis* genotypes endemic in the Former Soviet Union countries

CMI CLINICAL MICROBIOLOGY AND INFECTION
ESCMID

Clinical Microbiology and Infection 23 (2017) 1002–1004

- MDR-TB στην Ελλάδα <2,5% του συνολικού αριθμού TB
- 2007-2011: 54 στελέχη MDR-TB (10 XDR-TB) - 16 Έλληνες και 38 μετανάστες ή επαναπατρισθέντες
- VNTR- profiles για 46
- Το 60,8% των MDR-TB στην Ελλάδα οφείλονται σε στελέχη ενδημικά στις χώρες της πρώην ΕΣΣΔ
- Τα εισαγόμενα στελέχη MDR Bejing και LAM εμφάνισαν περιορισμένη μεταδοτικότητα από αλλοδαπούς σε γηγενείς

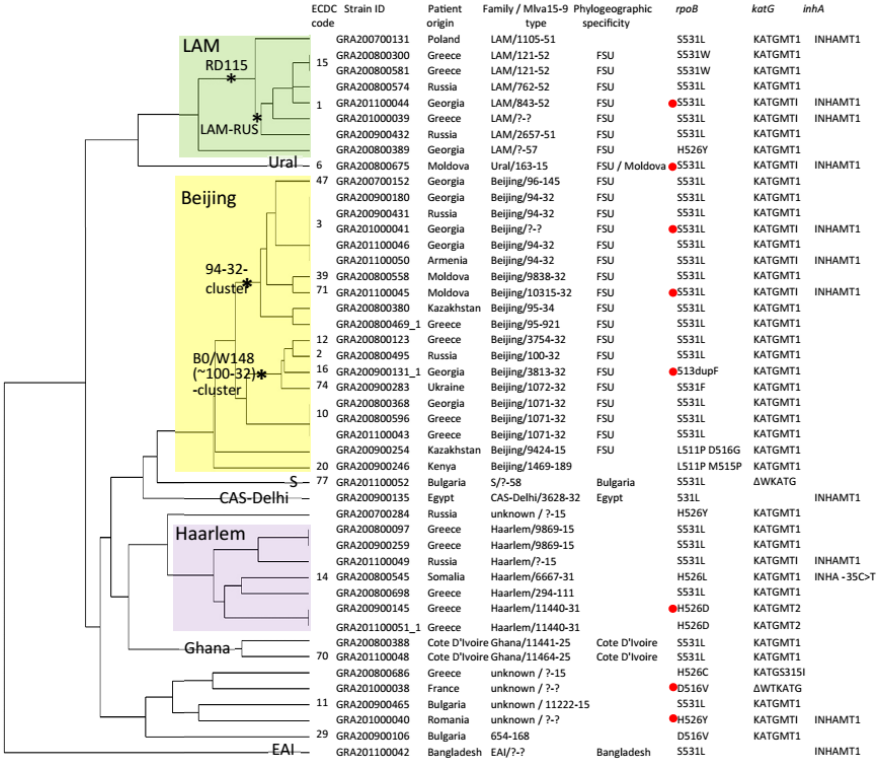
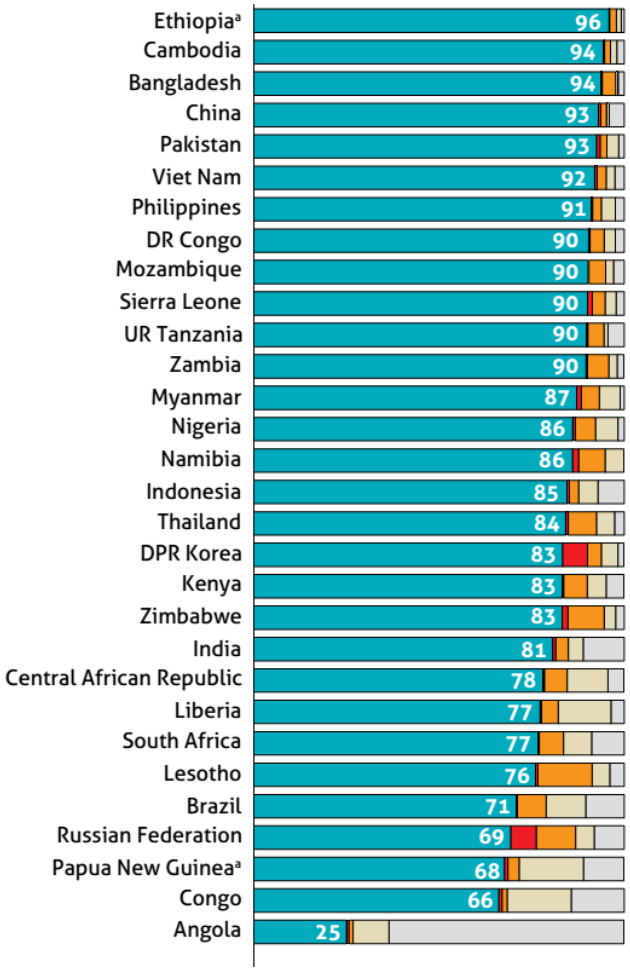


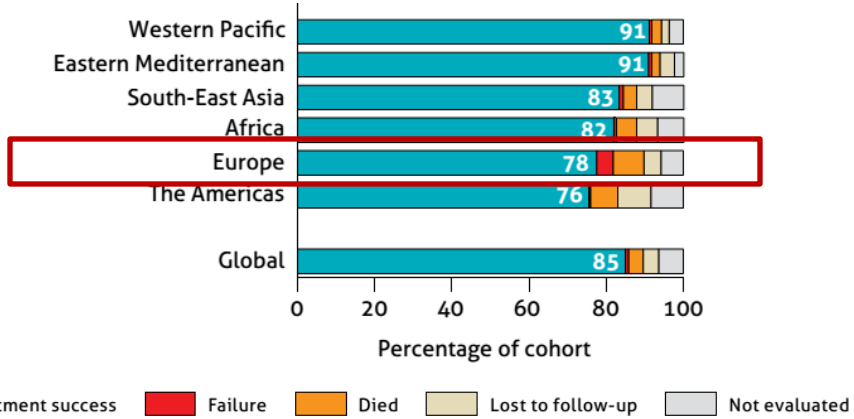
Fig. 1. The UPGMA dendrogram of the 24-MIRU-VNTR digital profiles of multidrug-resistant *Mycobacterium tuberculosis* isolates from Greece. ECDC codes and Mlva15-9 types refer to the European clusters [2] and MIRU-VNTR*plus*.org types, respectively. Extremely drug-resistant strains are depicted by a red dot. Information on phylogeographic specificity of strains is given in the Supplementary material (Table S3).

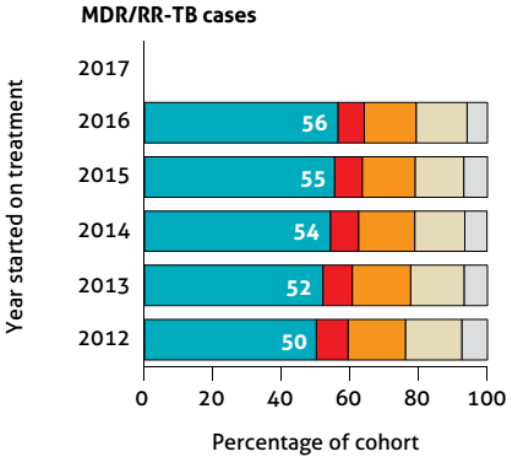
Έκβαση

FIG. 4.25

Treatment outcomes for new and relapse TB cases in 2017, 30 high TB burden countries, WHO regions and globally





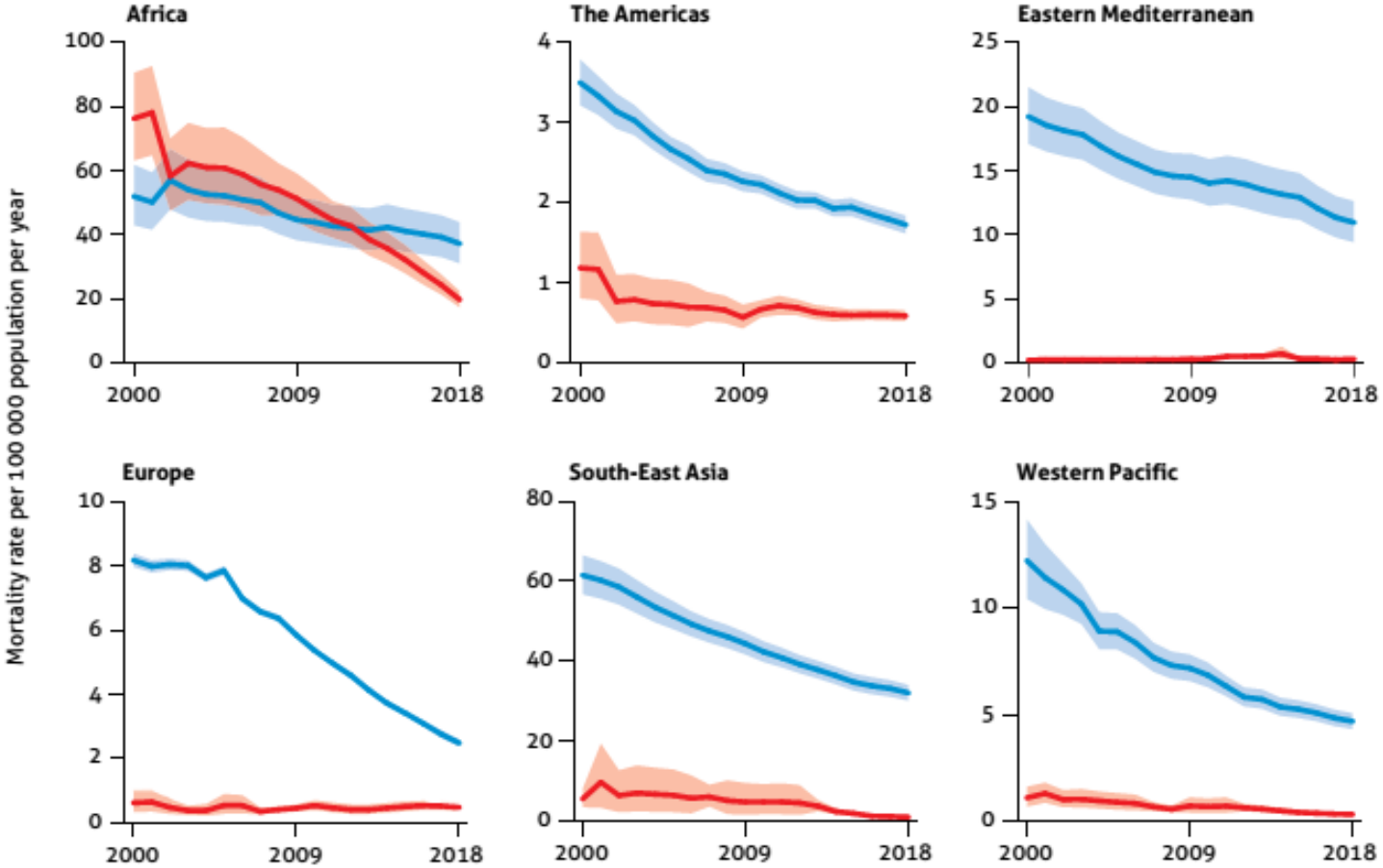


GLOBAL TUBERCULOSIS REPORT 2019

GLOBAL TUBERCULOSIS REPORT 2019

FIG. 3.22

Regional trends in estimated TB mortality rates by WHO region, 2000–2018. Estimated TB mortality rates among HIV-negative people are shown in **blue** and estimated mortality rates among HIV-positive people are shown in **red**. Shaded areas represent uncertainty intervals.

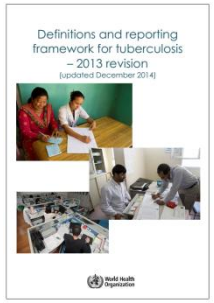


Η WHO European region εμφανίζει την ταχύτερη μείωση στους θανάτους στον κόσμο και φαίνεται ότι θα πετύχει το στόχο για το 2020

A.2.1 Treatment outcomes for TB patients (excluding patients treated for RR-TB or MDR-TB)

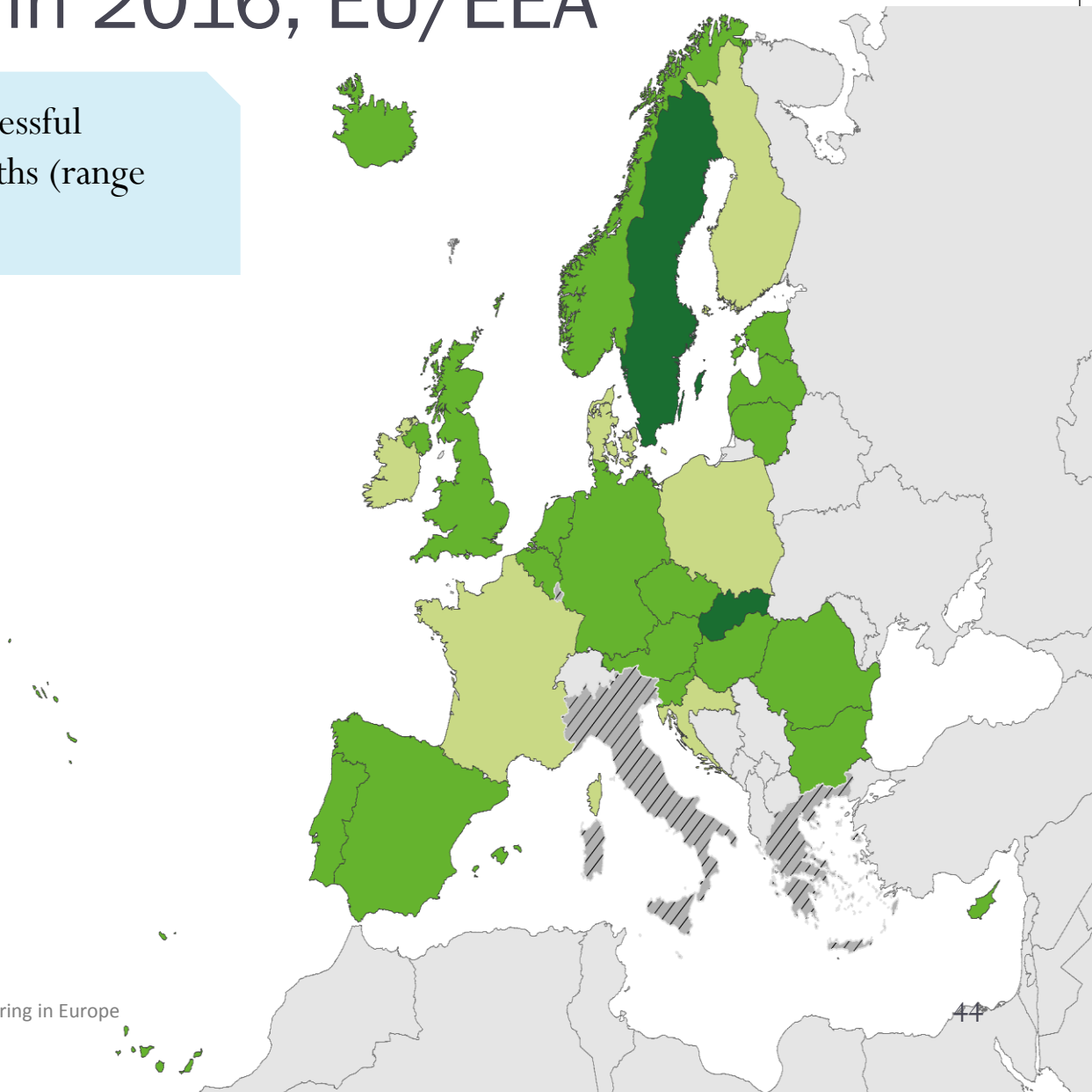
All bacteriologically confirmed and clinically diagnosed TB cases should be assigned an outcome from this list **except** those with RR-TB or MDR-TB, who are placed on a second-line drug regimen (see section A.2.2).

Outcome	Definition
Cured	A pulmonary TB patient with bacteriologically confirmed TB at the beginning of treatment who was smear- or culture-negative in the last month of treatment and on at least one previous occasion.
Treatment completed	A TB patient who completed treatment without evidence of failure BUT with no record to show that sputum smear or culture results in the last month of treatment and on at least one previous occasion were negative, either because tests were not done or because results are unavailable.
Treatment failed	A TB patient whose sputum smear or culture is positive at month 5 or later during treatment.
Died	A TB patient who dies for any reason before starting or during the course of treatment.
Lost to follow-up	A TB patient who did not start treatment or whose treatment was interrupted for 2 consecutive months or more.
Not evaluated	A TB patient for whom no treatment outcome is assigned. This includes cases "transferred out" to another treatment unit as well as cases for whom the treatment outcome is unknown to the reporting unit.
Treatment success	The sum of *cured* and *treatment completed.*



Treatment success as of 2017 in all TB cases notified in 2016, EU/EEA

70.7% of all TB cases* had a successful treatment outcome after 12 months (range 31.3–100%)



Proportion of treatment success

- <60%
- 60 to 84.9%
- ≥85%
- No data reported

Countries not visible in the main map extent

- Liechtenstein
- Malta

* Four EU/EEA countries did not report treatment outcome data

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

Treatment success as of 2017 in MDR TB cases notified in 2015*, EU/EEA

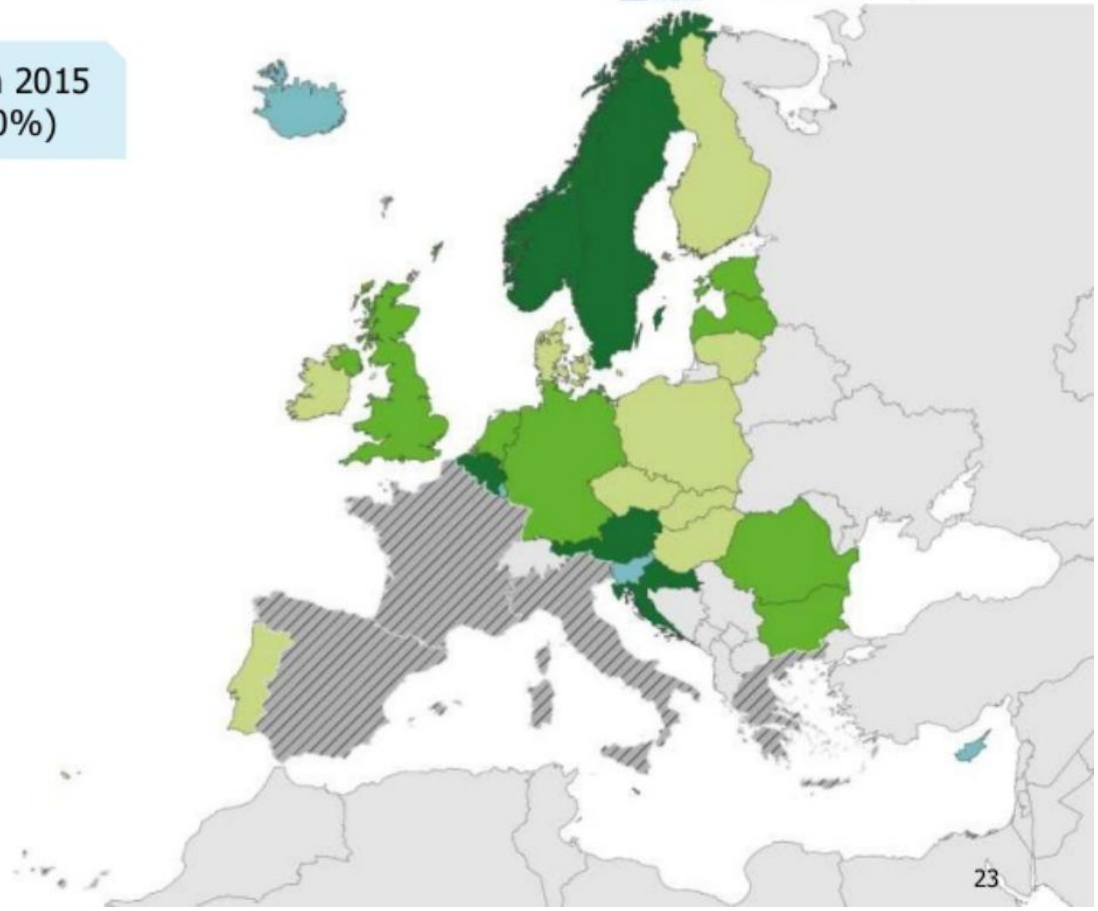
44.8% of all MDR TB cases notified in 2015 were successfully treated (range 0–100%)

Proportion of treatment success among MDR TB cases

- Zero cases
- <40%
- 40 to 69.9%
- ≥70%
- No data reported

Countries not visible in the main map extent

- Liechtenstein
- Malta



* Cyprus, Iceland, Liechtenstein, Luxembourg and Slovenia reported zero MDR TB cases in 2015. Treatment outcome and, or DST data were not available for France, Greece, Italy and Spain

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

Treatment success as of 2017 in XDR TB cases notified in 2014*, EU/EEA

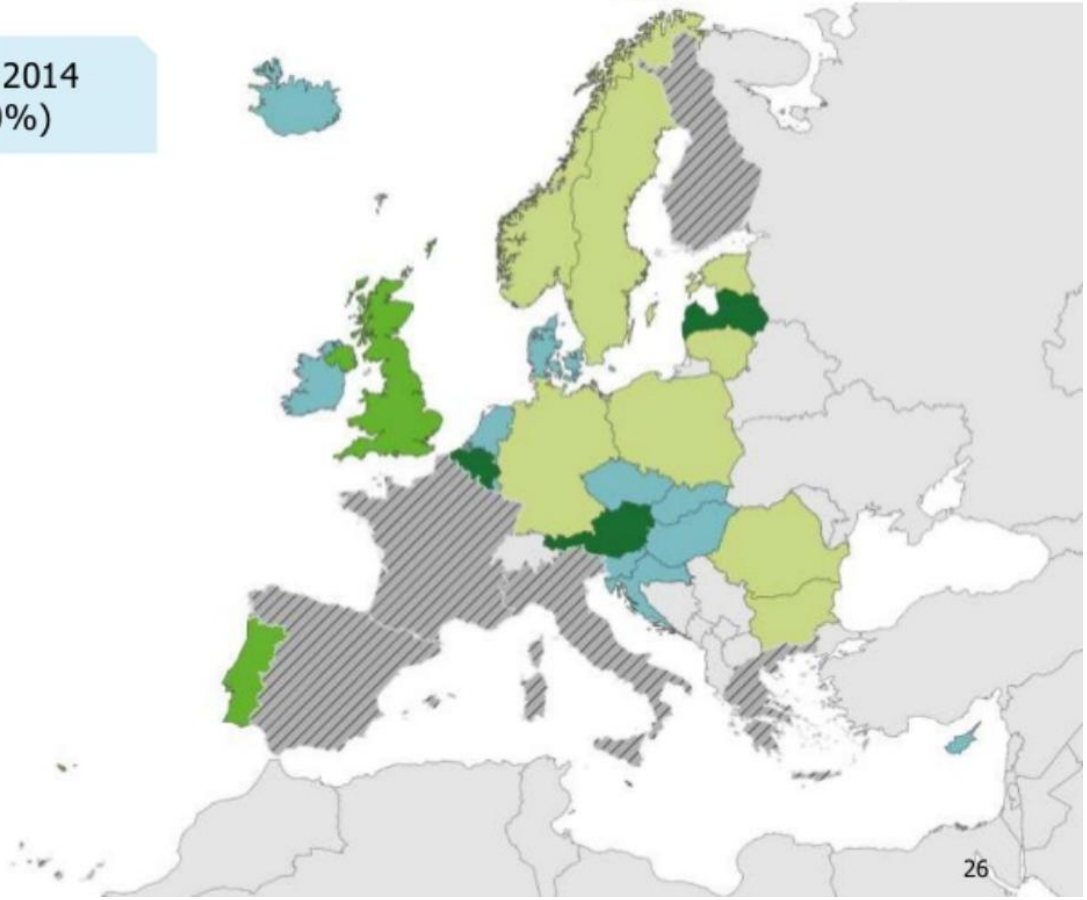
27.6% of all XDR TB cases notified in 2014 were successfully treated (range 0–100%)

Proportion of treatment success among XDR TB cases

- Zero cases
- <40%
- 40 to 69.9%
- ≥70%
- No data reported

Countries not visible in the main map extent

- Liechtenstein
- Malta



* Croatia, Cyprus, Czech Republic, Denmark, Hungary, Iceland, Ireland, Liechtenstein, Luxembourg, Malta, Netherlands, Slovakia and Slovenia reported zero XDR TB cases in 2014. Treatment outcome and, or DST data were not available for Finland, France, Greece, Italy and Spain

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

Παράγοντες κινδύνου για θάνατο σε ασθενείς με TB

- 4732 pts (52,5±19,9 έτη) – treatment success 83,9%
- Θάνατοι 8%- παράγοντες κινδύνου: ηλικία ≥75, PTB με Z/N (+), αναφορά έκβασης από νοσοκομείο

Mok J, BMC Infect Dis 2018

Table 4 Summary of risk factors for TB case fatality, according to TB incidence and HIV prevalence

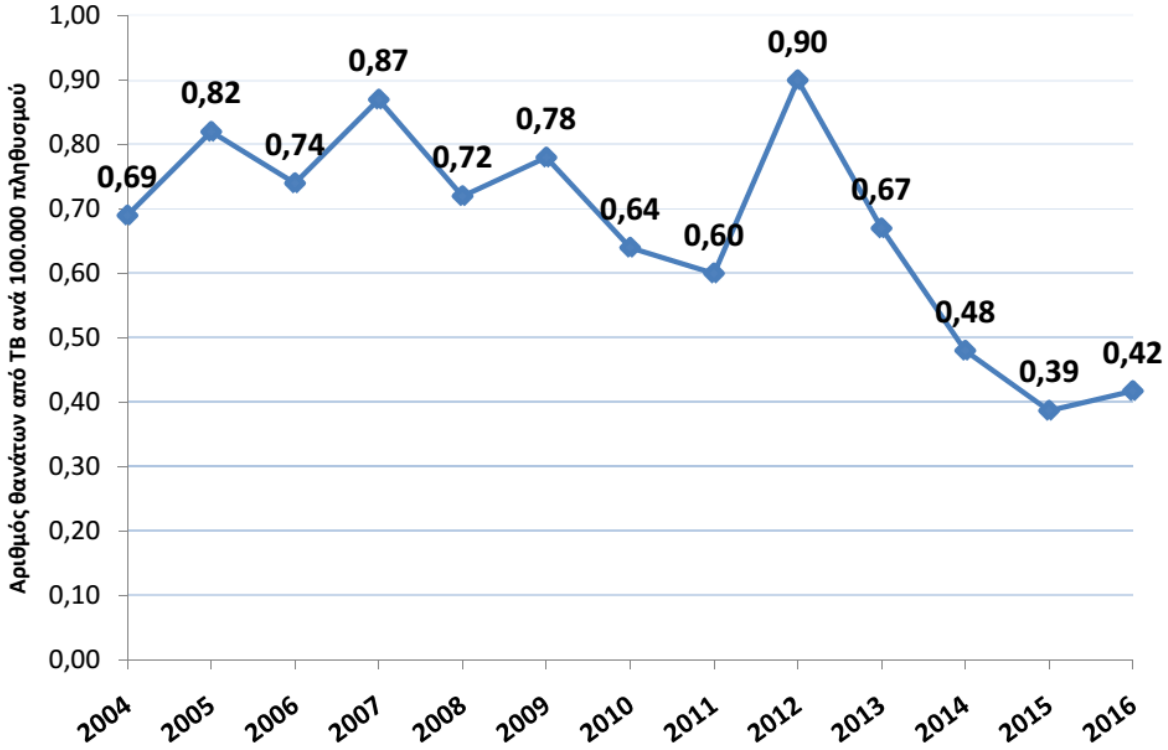
Risk factor	References
Regions of high TB incidence and high HIV prevalence	
Older age (mostly >35 years)	25, 59, 63, 93
HIV positivity	13, 25, 27, 31, 38, 59, 63
Features of advanced HIV	29, 31, 32, 99
Smear-negative disease	27, 29, 36, 38, 59
Malnutrition	31, 63, 93
Regions of low TB incidence and low HIV prevalence	
Older age (mostly >50 years)	16, 24, 28, 35, 37, 40, 53, 56, 91
Non infective comorbidities	16, 18, 22, 37, 53, 56, 91, 100
Smear-positive disease	16, 24, 37
Organ failure	55, 56, 100
Alcohol or drug misuse	24, 52
Extensive or cavitatory disease on CXR	16, 18, 24, 28, 52
Symptoms >4 weeks	37, 55, 52

TB = tuberculosis; HIV = human immunodeficiency virus; CXR = chest X-ray.

- Συστηματική ανασκόπηση μελετών για παράγοντες κινδύνου θνητότητας σε ασθενείς με TB 1966-2010
- Οι περισσότερες αναφέρονται σε θανάτους από κάθε αίτιο στη διάρκεια της θεραπείας

Waitt CJ, Int j Tuberc Lung Dis 2011

Αδρή θνησιμότητα από φυματίωση, Ελλάδα 2001-2016



Πηγή: ΕΟΔΥ- ΕΛΣΤΑΤ

Ουρανία Καλκούνη, Ελένη Τριανταφύλλου
Γραφείο Νοσημάτων που μεταδίδονται μέσω του αναπνευστικού
Τμήμα Επιδημιολογικής Επιτήρησης και Παρέμβασης, ΕΟΔΥ

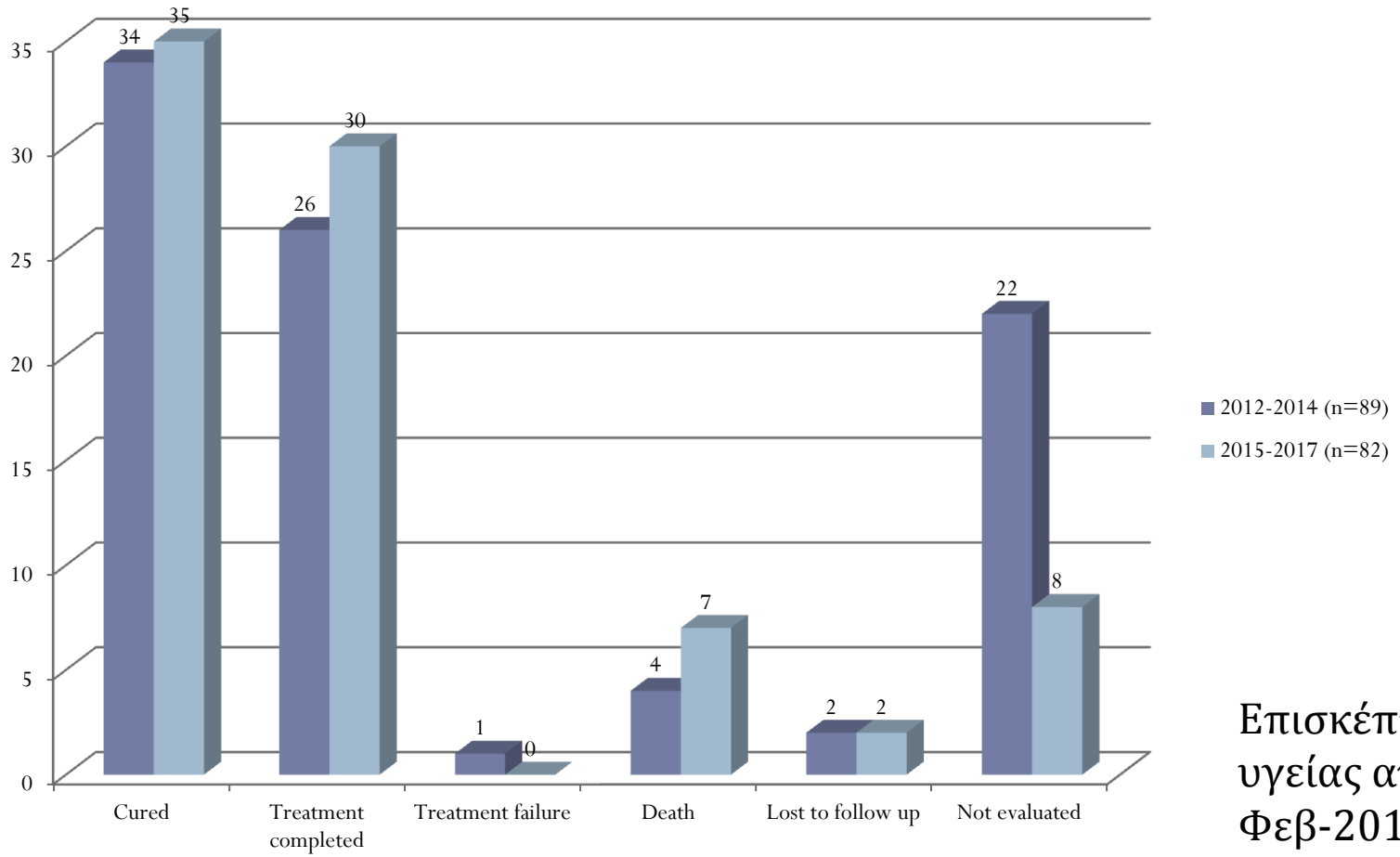
Ιατρείο Φυματίωσης Πνευμονολογικής Κλινικής ΑΠΘ

Ασθενείς με ενεργό TB

	2012-2014 (n=89)	2015-2017 (n=82)	Σύνολο (n=171)	p
Ηλικία	49,5±19,2	53,8±15,6	51,6±17,8	0,130
Άρρεν φύλο (%)	60 (67,5)	48 (58,5)	108 (63,2)	0,229
Αλλοδαποί (%)	28 (31,5)	22 (26,8)	50 (29,2)	0,476
Z/N (+) (%)	46 (51,7)	36 (43,9)	82 (48)	0,592
Καλλιέργεια (+) (%)	61 (68,5)	61 (74,4)	122 (71,4)	0,205
Πνευμονική προσβολή (%)	81 (91)	68 (82,9)	149 (87,1)	0,115
Θετική έκβαση (%)	**60 (67,4)**	**65 (79,3)**	**125 (73,1)**	0,081
Θετική έκβαση * (%)	**56 (66,7)**	**58 (84,1)**	**114 (74,5)**	**0,014**

* Εξαιρώντας τους ανοσοκατασταλμένους ασθενείς

Έκβαση ασθενών Πνευμονολογικής ΑΠΘ



Επισκέπτρια υγείας από Φεβ-2015

11 θάνατοι: 4 ηλικία > 80, 3 ανοσοκατεσταλμένοι, 4 από άγνωστο ή άσχετο αίτιο

Ιατρείο Φυματίωσης Πνευμονολογικής Κλινικής ΑΠΘ

Αλλοδαποί ασθενείς με ενεργό ΤΒ

Χώρα προέλευσης	2012-2014 (n=28)	2015-2017 (n=22)	2018 (n=13)
Ευρώπη	20 (71,4)	18 (82)	3 (23,1)
Ασία	6 (21,4)	2 (9)	8 (61,5)
Αφρική	1 (3,6)	1 (4,5)	2 (15,4)
Άγνωστη	1 (3,6)	1 (4,5)	

Το 2017 από σύνολο 29 ασθενών, 1 ήταν πρόσφυγας
Το 2018 από σύνολο 21 ασθενών, 10 ήταν πρόσφυγες
Το 2019 από σύνολο 20 ασθενών, 7 ήταν πρόσφυγες

Διαμονή σε: δομές φιλοξενίας προσφύγων, κέντρα κράτησης, κέντρα φιλοξενίας, δομές φιλοξενίας ανηλίκων, διαμερίσματα προσφύγων, δομές φιλοξενίας ΜΚΟ, άστεγοι……

Ιατρείο Φυματίωσης Πνευμονολογικής Κλινικής ΑΠΘ

Active screening

2017-2019:

- **57 άτομα** (9Γ, 48Α)
- Μέση ηλικία 26 έτη (25 ανήλικοι)
- Αφγανιστάν 16, Πακιστάν 10, Αλγερία 7, Αλβανία 6, Συρία 5 και … Λιβύη, Μολδαβία, Μπαγκλαντές, Ιράκ, Μαρόκο, Κογκό, Σιέρα Λεόνε
- Ευρώπη 7 (12,3%), Αφρική 14 (24,6%), Ασία 36 (63,1%)

- 11 απάντησαν θετικά σε τουλάχιστον μία ερώτηση του ερωτηματολογίου
- Σε 8 ζητήθηκε Ct θώρακα (4 δεν επανήλθαν) και σε 6 πτύελα (όλα αρνητικά)
- **Σε 2 διαγνώστηκε ΤΒ**, ο ένας με παθολογική α/α από μηνών….

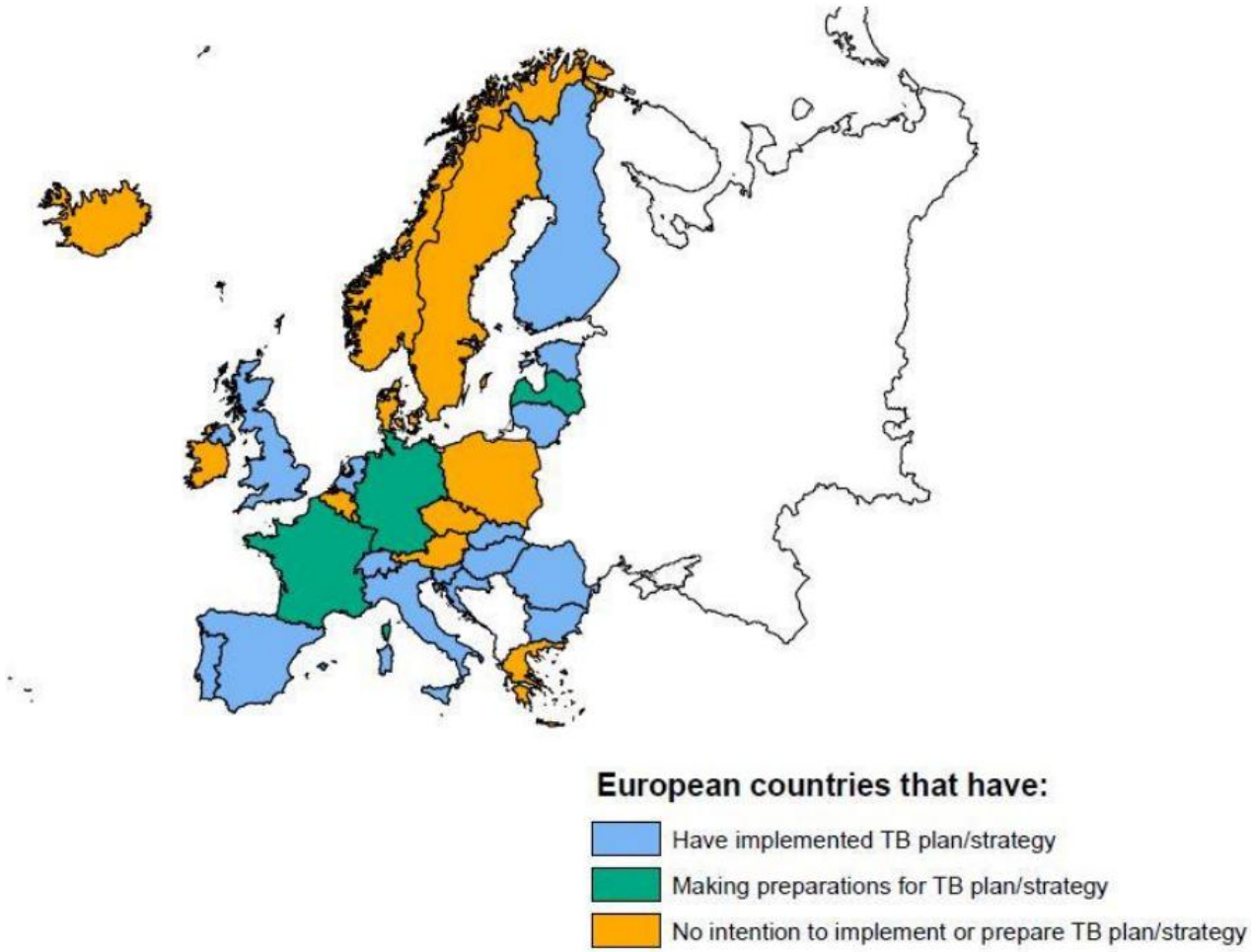
Ιατρείο Αναπνευστικών Λοιμώξεων
Πνευμονολογική Κλινική ΑΠΘ

- Παναγιώτα Κυρέλτση
- Μαρία Σιωνίδου
- Ευδοκία Σούρλα

- Πέτρος Πουλιόπουλος
- Marija Hatzi-Mitrova
- Μαρία Κηπουρού
- Ελένη Παπαδάκη
- Τάνια Κωσταντά

Tuberculosis in the European Union and European Economic Area: a survey of national tuberculosis programmes

Figure 1: National TB control plans or strategies in EU/EEA countries



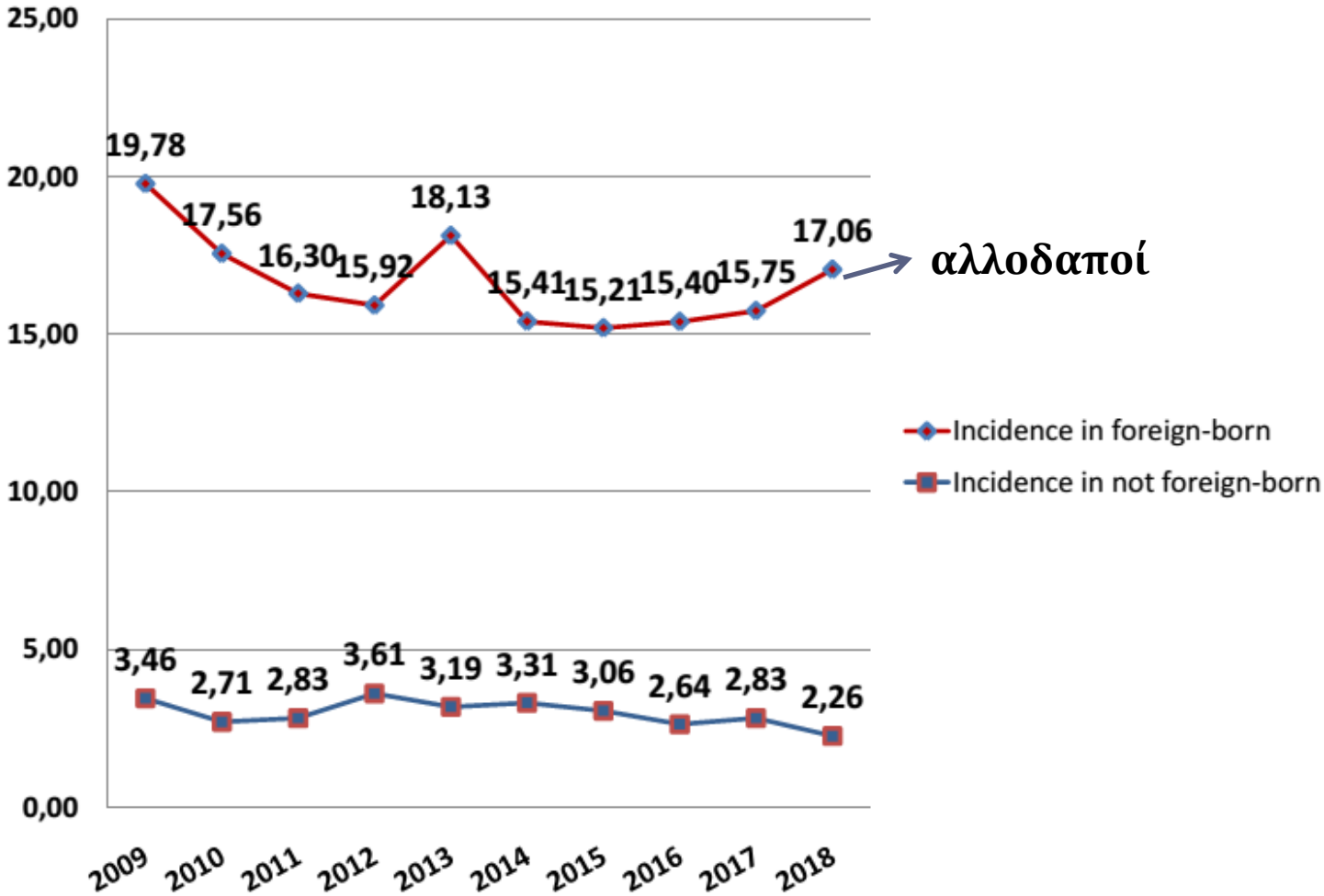
Η Ελλάδα δεν έχει και δε σχεδιάζει να αποκτήσει εθνικό πρόγραμμα κατά της φυματίωσης

Collin S,
Eur Respir J 2018

Screening migrants for tuberculosis and latent TB infection: the reward will come later

Jean-Pierre Zellweger

TB incidence rate in foreign-born and not foreign-born, Greece 2009-2018

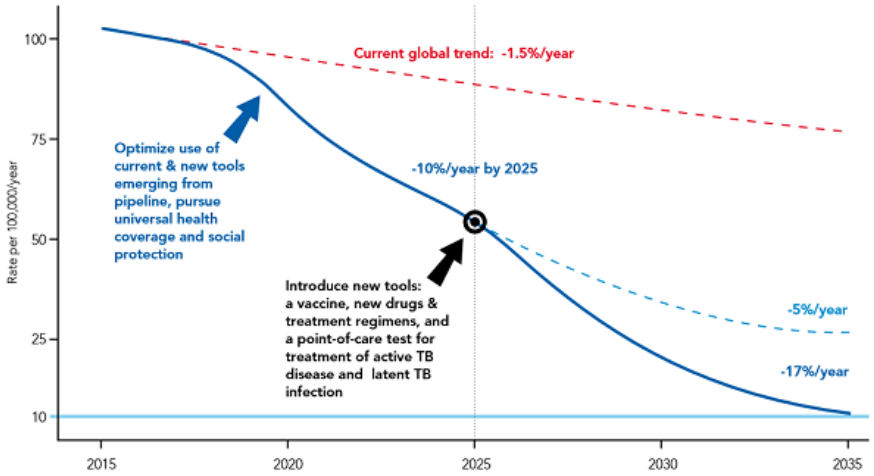


Πηγές: ΕΟΔΥ και EUROSTAT

Ουρανία Καλκούνη, Ελένη Τριανταφύλλου
Γραφείο Νοσημάτων που μεταδίδονται μέσω του αναπνευστικού
Τμήμα Επιδημιολογικής Επιτήρησης και Παρέμβασης, ΕΟΔΥ

THE END TB STRATEGY

Figure 2. Projected acceleration in the decline of global tuberculosis incidence rates to target levels



New cases

80%

drop in new TB cases by 2030

TB deaths

90%

drop in people dying of TB by 2030

Reducing poverty

100%

of TB-affected families protected from catastrophic costs by 2030

A paradigm shift: from TB control to TB elimination

TB elimination, defined as less than one TB case per million population, is seen as a scenario where TB is not eradicated but rather kept at such a low level that it no longer constitutes a public health problem [18].

Matteelli A, Eur respir Rev 2018

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,*]

CMI CLINICAL MICROBIOLOGY AND INFECTION
ESCMID

Clinical Microbiology and Infection 23 (2017) 141–146

- Σημαντικό ποσοστό της MDR-TB στους μετανάστες προκύπτει από αναζωπύρωση LTBI
- Πρόσφυγες και αιτούντες άσυλο έχουν αυξημένο κίνδυνο MDR-TB και χειρότερη έκβαση
- Ιατρικός τουρισμός
- Στις χώρες της Δυτικής Ευρώπης η συντριπτική πλειονότητα των MDR-TB αφορά αλλοδαπούς

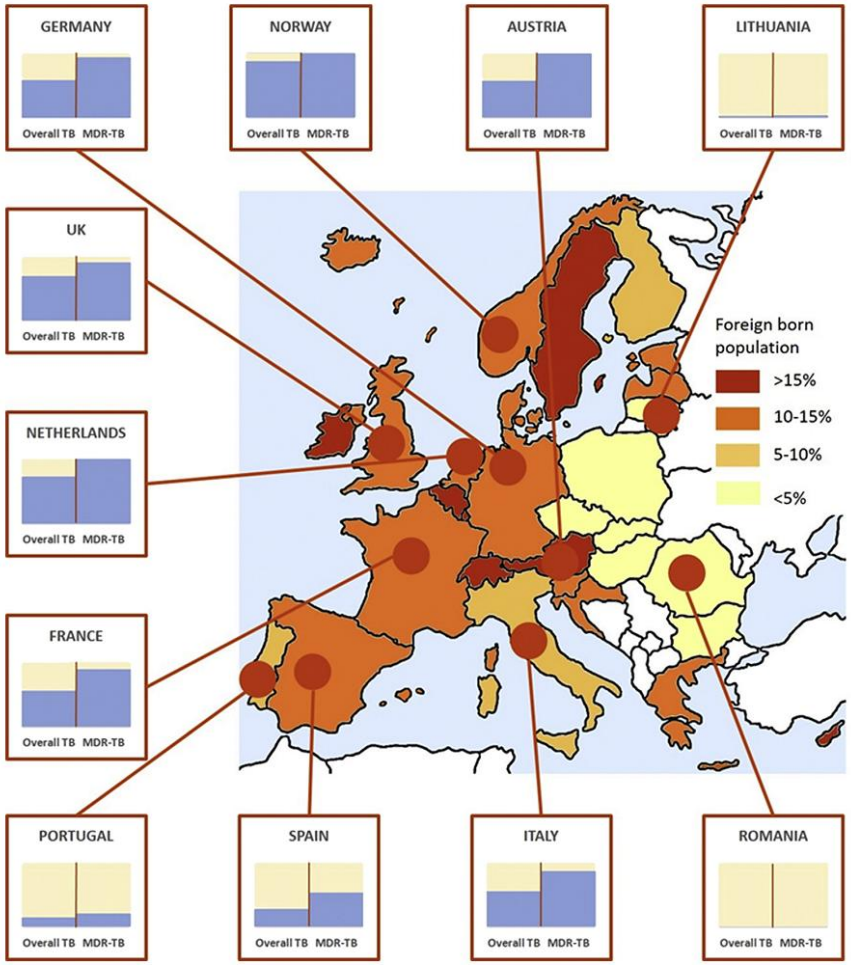
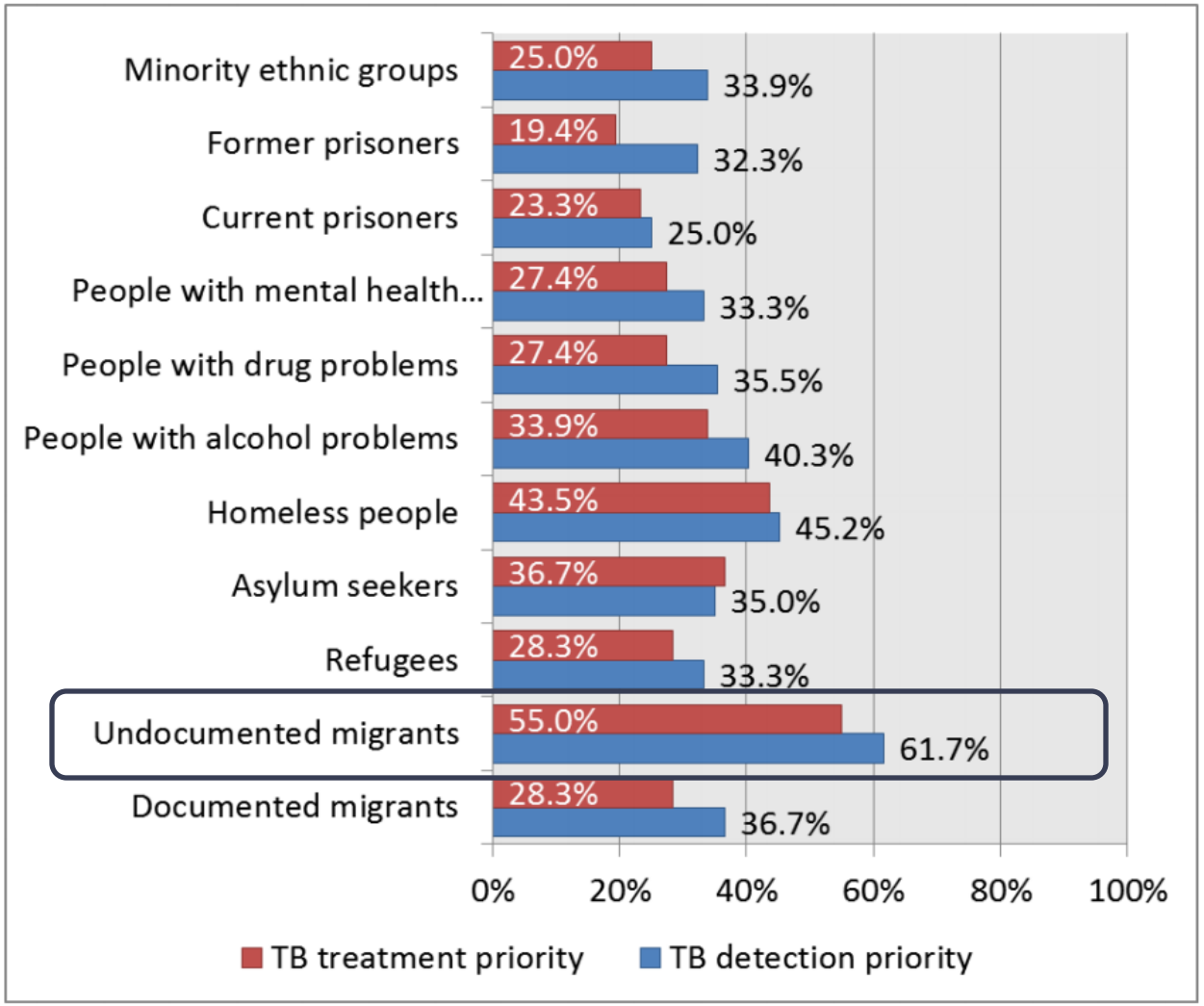


Fig. 1. Multi-drug-resistant tuberculosis (MDR-TB) and migration in Europe. The boxes in this figure illustrate the proportion of TB cases and MDR-TB cases that occur in migrants (blue stacks) in each country. Columns in the boxes represent the percentage of foreign-born overall, among the total TB and 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].

Tuberculosis in the European Union and European Economic Area: a survey of national tuberculosis programmes

Figure 3: Priority populations – *"In relation to TB control in your country, which population groups do you think have the highest unmet need for TB detection and treatment?"*



Η πληθυσμιακή ομάδα με τη μεγαλύτερη ανάγκη για τη διάγνωση και θεραπεία της φυματίωσης είναι οι παράτυποι μετανάστες

Collin S,
Eur Respir J 2018

Greece

Total population at 23 April 2018 by EUROSTAT: 10 768 193

TB case notifications, 2017

Total number of cases	467	
Notification rate per 100 000	4.3	
New[a] and relapses	434	
New[a] and relapses notification rate per 100 000	4.0	
Pulmonary	391	(83.7%)
of which microscopy-positive	227	(58.1%)
of which laboratory-confirmed	233	(59.6%)
Laboratory-confirmed TB cases	265	(56.7%)
Mean age of new native TB cases	62.8 years	
Mean age of new foreign TB cases	34.7 years	
Foreign origin of all TB cases	197	(42.2%)
New (not previously treated)	414	(88.7%)

[a] Cases with unknown previous treatment included in new cases.

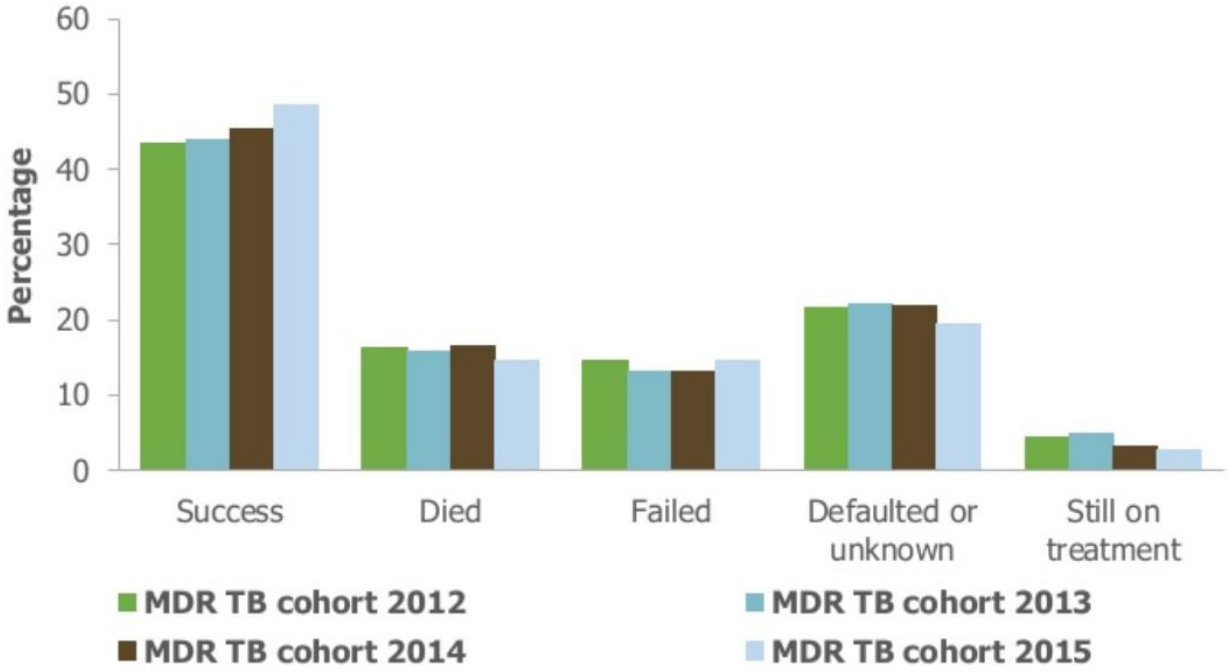
Drug resistance surveillance and TB/HIV coinfection, 2017

Completeness of DRS data[a]	Yes	
Completeness of HIV data[b]	Yes	
Case-linked data reporting	Yes	
Cases with DST results	191	(72.1%)
Estimated RR-TB among notified pulmonary cases N, (best–low–high)	10–0–24	
Pulmonary MDR-TB cases notified	6	(3.6%)
of which XDR-TB cases	1	(16.7%)
Notified MDR-TB	7	(3.7%)
of which XDR-TB cases	2	(28.6%)
TB cases tested for HIV	389	(83.3%)
HIV-positive TB cases	13	(3.3%)
of these on ART	–	–

[a] National coverage 100% or culturing ≥ 90%, C+/all TB cases > 50%, DST done for C+ > 75%, EQA ≥ 95%.
[b] More than 50% of TB cases with reported HIV status.

Treatment outcomes of MDR TB cases notified in 2012–2015, EU/EEA, 2017

The treatment success rate increased from **43.3** in 2012 to **48.5%** in 2015*



* XDR TB cases are not included

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

Greece

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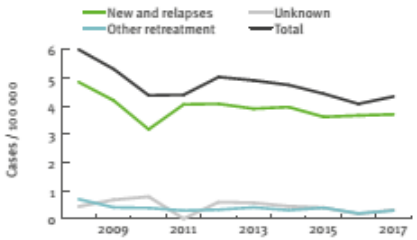
of these on ART	–	–

* National coverage 100% or culturing ≥ 90%, C+/all TB cases > 50%, DST done for C+ > 75%, EQA ≥ 95%.
* More than 50% of TB cases with reported HIV status.

Treatment outcome monitoring

Data not available

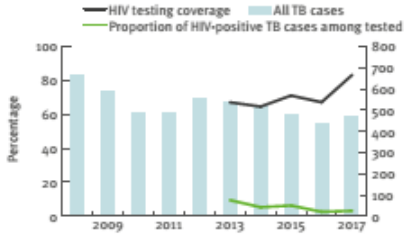
TB notification rates by treatment history, 2008–2017



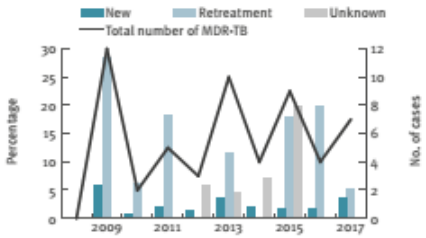
New and relapsed TB cases – notification rates by age group, 2008–2017

TB cases by geographical origin, 2008–2017

TB/HIV coinfection, 2008–2017



MDR-TB cases by previous treatment history, 2008–2017



Treatment outcome, new culture-confirmed pulmonary TB cases 2007–2016

Data not available

Χώρες χωρίς δεδομένα έκβασης : Ιταλία, Λουξεμβούργο, Μάλτα

Albania

Population estimate 2017 by UN Statistical Database: 2 930 187

TB case notifications, 2017

Total number of cases	503	
Notification rate per 100 000	17.2	
New* and relapses	503	
New* and relapses notification rate per 100 000	17.2	
Pulmonary new and relapse:	346	(68.8%)
of which smear-positive	–	–
of which laboratory-confirmed	210	(60.7%)
Laboratory-confirmed TB cases	210	(41.7%)
Mean age of new and relapse TB cases	44.1	years
Mean age of new foreign TB cases	–	years
Foreign origin of all TB cases	0	(0.0%)
New (not previously treated)	479	(95.2%)

* Cases with unknown previous treatment included in new cases.

Drug resistance surveillance and TB/HIV coinfection, 2017

Completeness of DRS data*	No	
Completeness of HIV data*	No	
Case-linked data reporting	Yes	
Cases with DST results	79	(37.6%)
Estimated RR-TB among notified pulmonary cases N, (best–low–high)	9–1–17	
Pulmonary MDR-TB cases notified	1	(0.0%)
of which XDR-TB cases	0	(0.0%)
Notified MDR-TB	4	(5.1%)
of which XDR-TB cases	0	–
TB cases tested for HIV	235	(46.7%)
HIV-positive TB cases	6	(1.7%)
of these on ART	6	(100.0%)

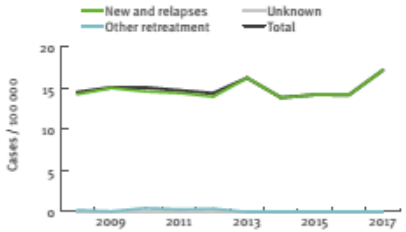
* National coverage 100% or culturing ≥ 90%. C+/all TB cases 50%. DST done for C+ > 75%. EQA ≥ 95%.
* More than 50% of TB cases tested for HIV.

Treatment outcome monitoring

Geographical coverage	National			
Outcome cohort	New and relapsed TB cases notified in 2016*		All RR/MDR-TB cases enrolled into second-line treatment in 2015*	
Case-linked data reporting	Yes			
Cases notified	409		3	
Success	357	(87.3%)	3	(100.0%)
Died	10	(2.4%)	0	–
Failed	3	(0.7%)	0	–
Lost to follow-up	20	(4.9%)	0	–
Not evaluated	19	(4.6%)	0	–

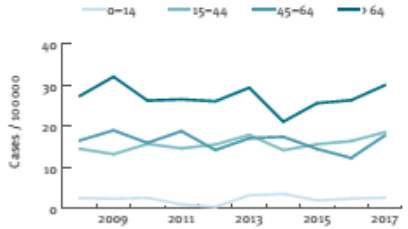
* Treatment outcome as presented is treatment outcome after 12 months.
* Treatment outcome as presented is treatment outcome after 24 months.

TB notification rates by treatment history, 2008–2017*



* Starting from 2013 onward, cases with unknown history are included in new and relapses.

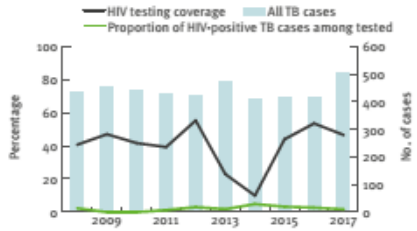
New and relapsed TB cases – notification rates by age group, 2008–2017*



* Data up to 2012 include new TB cases only.

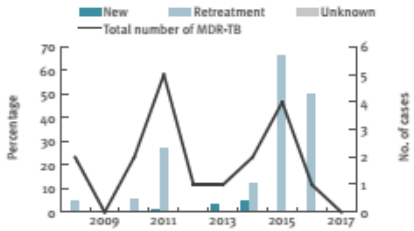
TB cases by geographical origin, 2008–2017

TB/HIV coinfection, 2008–2017*

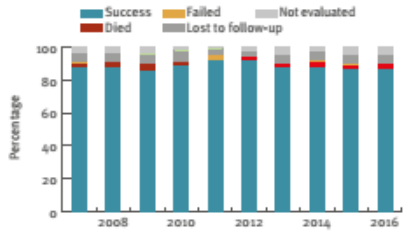


* Data up to 2014 include all TB cases.

MDR-TB cases by previous treatment history, 2008–2017



Treatment outcome, new and relapsed TB cases, 2008–2017*



* 2007–2011 cohorts include new cases only.

TB/HIV co-infection, EU/EEA, 2017

1 006 HIV-positive TB cases were notified by 23 EU/EEA countries in 2017

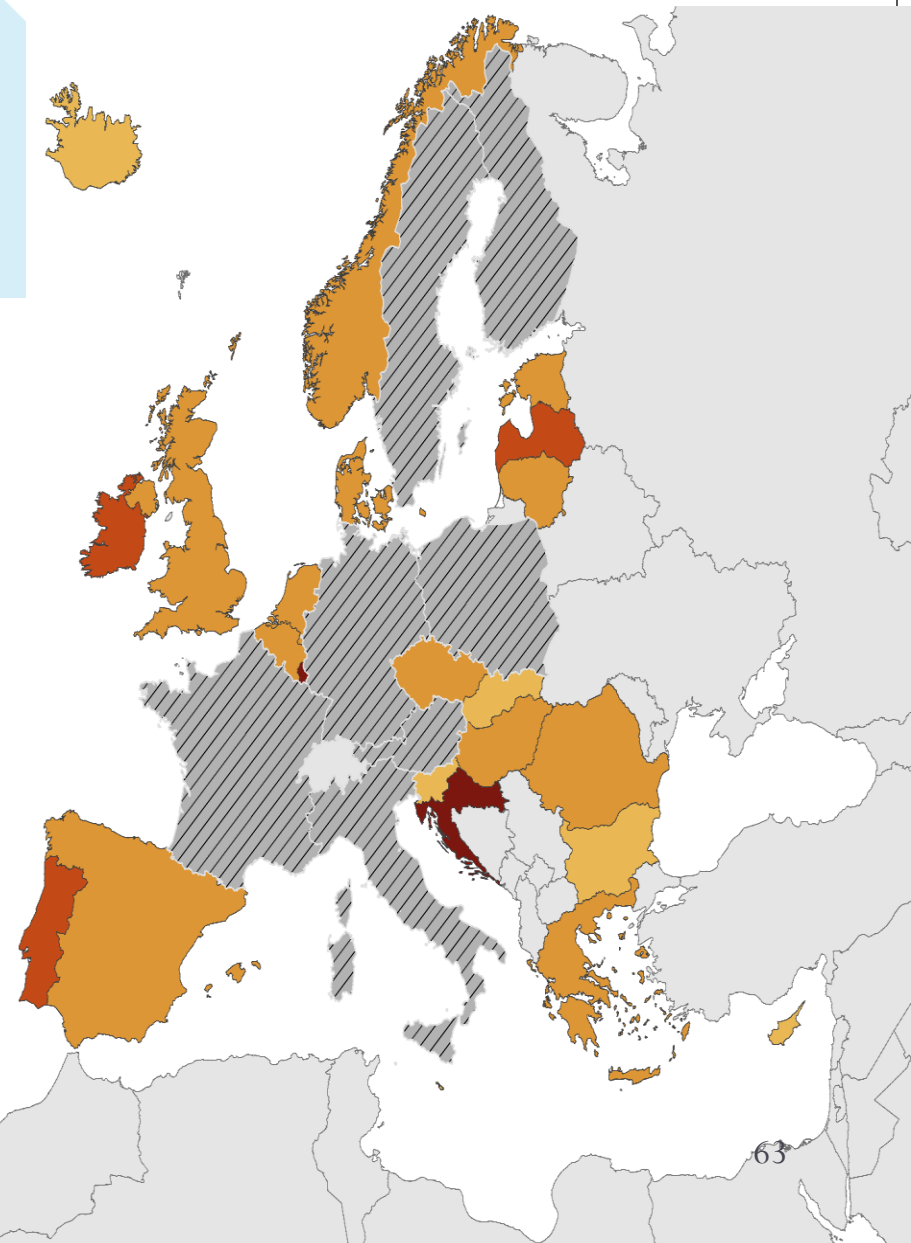
3.9% of TB cases with known HIV status were HIV-positive (range 0–13.7%*)

Proportion of co-infected TB cases among TB cases with known HIV status

- <1%
- 1 to 9.9%
- 10 to 14.9%
- ≥15%
- No data reported

Countries not visible in the main map extent

- Liechtenstein
- Malta



* Among countries reporting more than five TB cases with known HIV status

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

Tuberculosis in migrants in low-incidence countries: epidemiology and intervention entry points

Lonnroth K, Int J Tuberc Lung Dis 2017

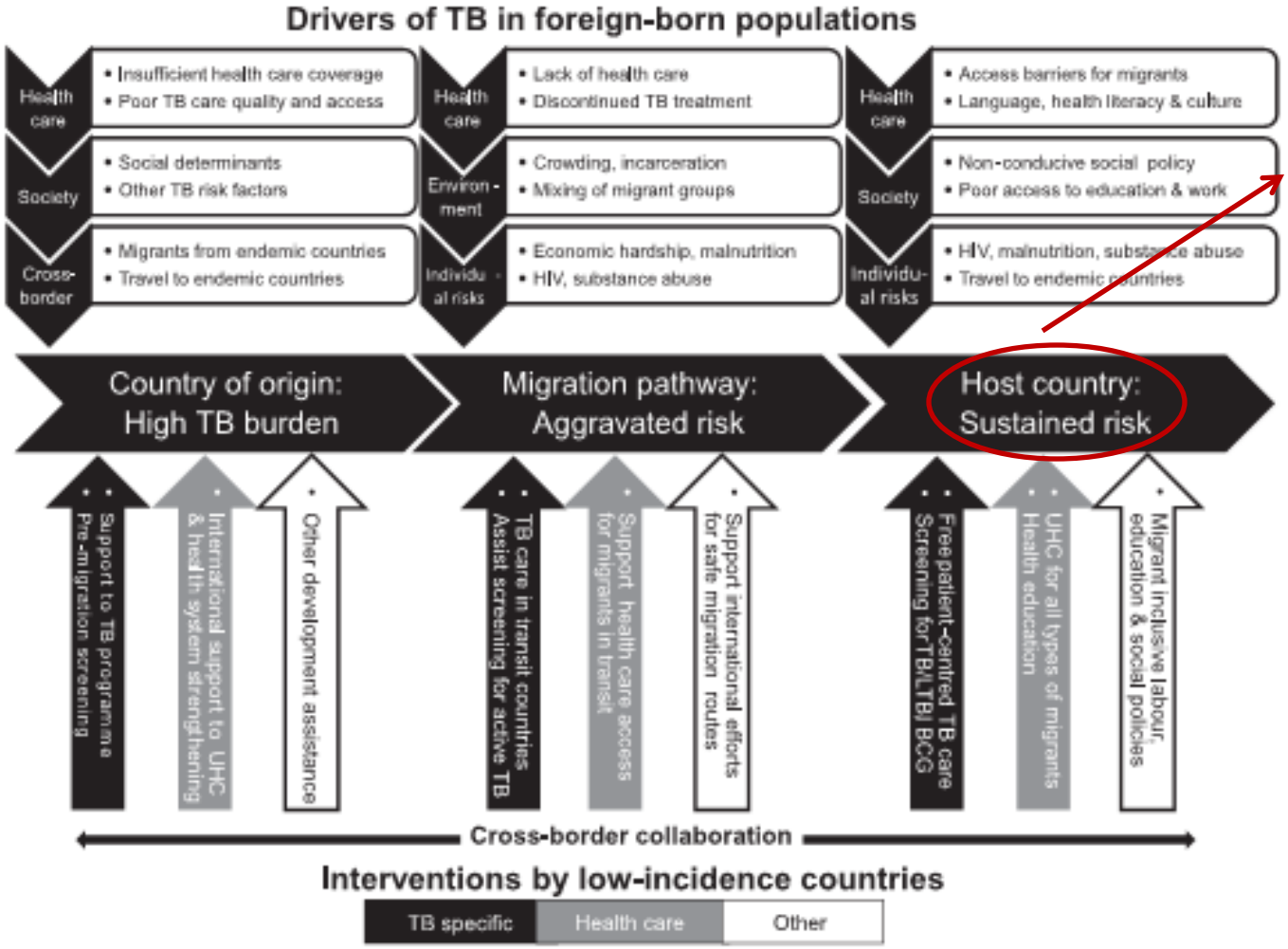


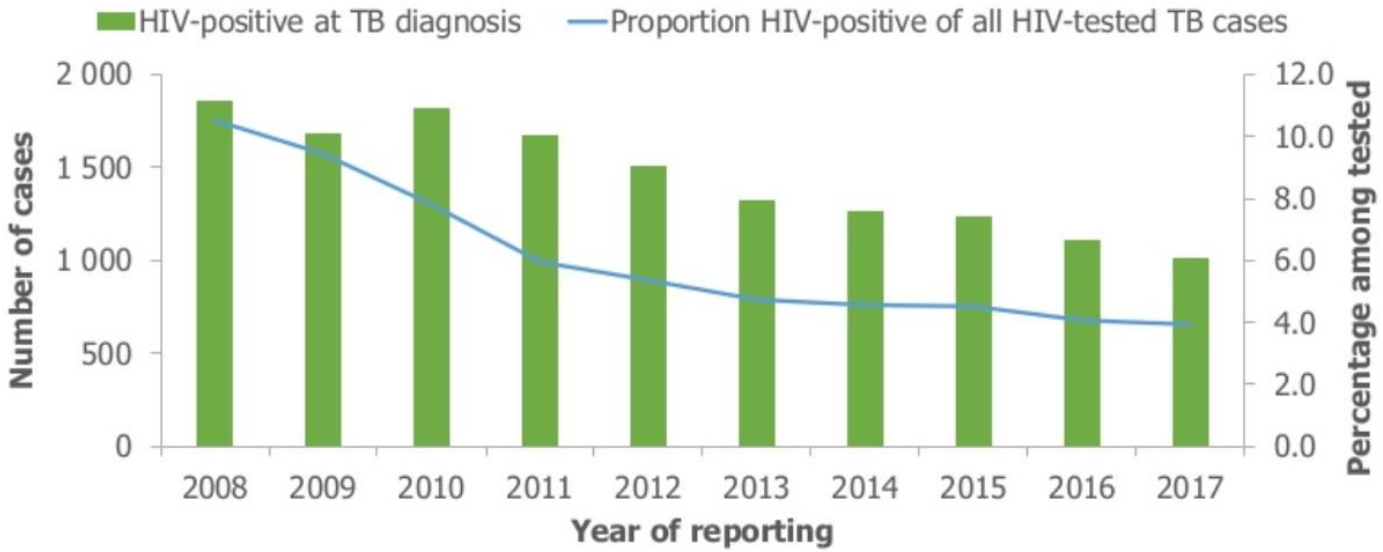
Figure 6 Drivers of TB in migrants to low-incidence countries and interventions for TB care and prevention along the migration pathway. TB = tuberculosis; HIV = human immunodeficiency virus; UHC = universal health coverage; LTBI = latent tuberculous infection; BCG = bacille Calmette-Guérin

Οι αιτούντες άσυλο και οι πρόσφυγες έχουν ιδιαίτερα υψηλό κίνδυνο TB λόγω της επιβαρυμένης κατάστασης από την οποία προσπαθούν αν ξεφύγουν αλλά και **λόγω των επικίνδυνων συνθηκών κατά τη μετανάστευση-** συνωστισμός, φυλάκιση, υποσιτισμός, έκθεση σε μετανάστες από χώρες υψηλότερης επίπτωσης

HIV-positive TB cases and proportions among all those tested, EU/EEA, 2008–2017*

The total number of HIV-positive TB cases decreased from **1 855** in 2008 to **1 006** in 2017

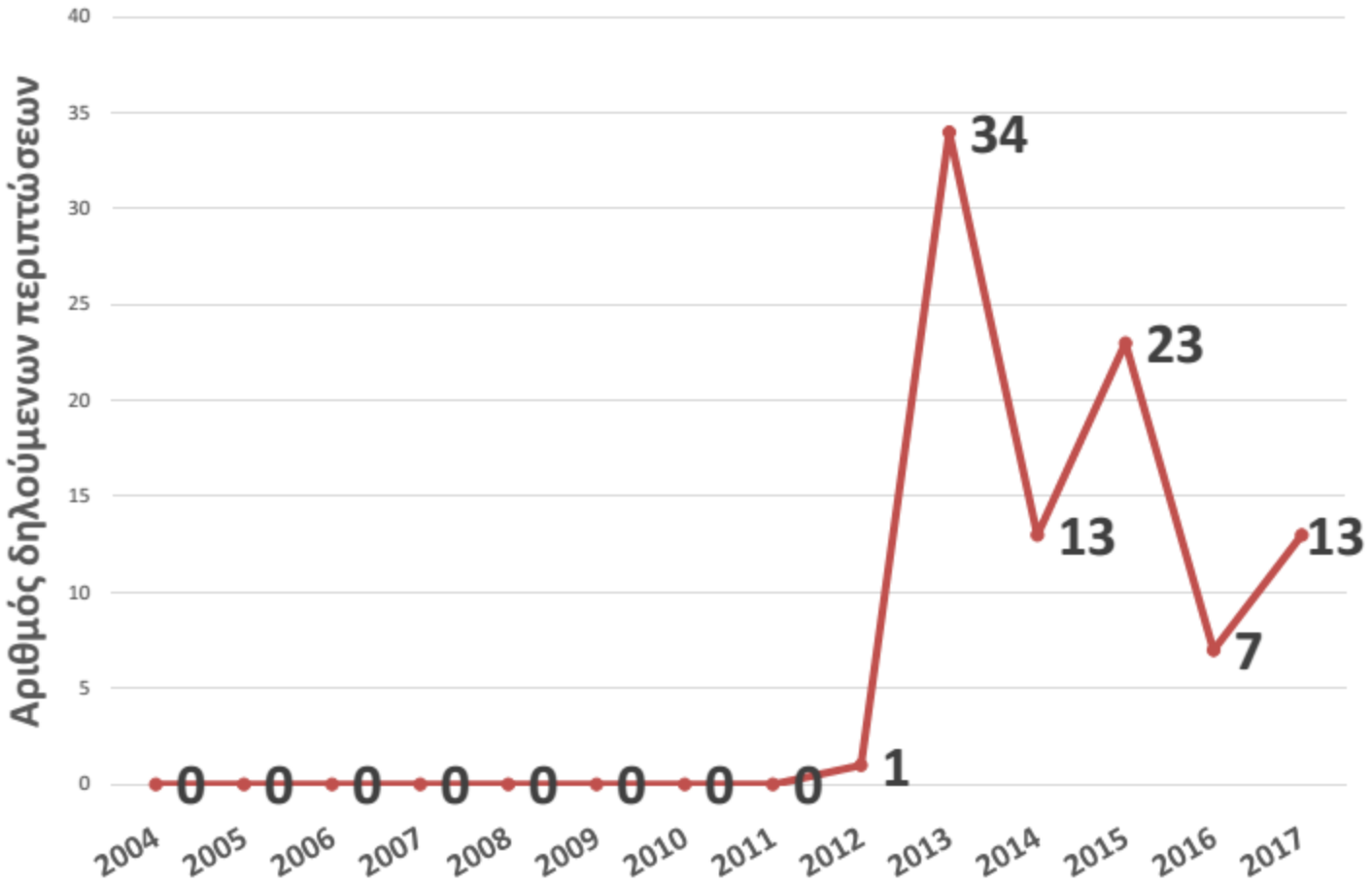
The proportion of HIV-positive TB cases among those tested decreased from **10.5%** in 2008 to **3.9%** in 2017



* Countries and the years for which they are not included due to reporting discrepancies or no data: Austria (2008-2017), Croatia (2008-2015), Cyprus (2009-2010, 2013), Finland (2008-2009, 2012-2017), France (2008-2012, 2017), Germany (2008-2017), Greece (2008-2012), Hungary (2008-2009, 2012-2013), Italy (2008-2017), Liechtenstein (2008-2017), Lithuania (2008-2009), Luxembourg (2008-2009, 2015), Norway (2008-2011), Poland (2008, 2012-2017), Sweden (2008-2017)

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

Ασθενείς με HIV λοίμωξη μεταξύ των δηλωθέντων περιπτώσεων φυματίωσης, Ελλάδα, 2004-2017



Πηγή: ΕΟΔΥ

Δηλωθείσες περιπτώσεις TB σε αλλοδαπής εθνικότητας ασθενείς σε δομές φιλοξενίας, Ελλάδα 2016 και 2017

	2016		2017	
	Αριθμός (n)	Ποσοστό (%)	Αριθμός (n)	Ποσοστό (%)
Σύνδεση με άλλο κρούσμα	12	34%	2	7,1%
Πνευμονική εντόπιση	32	91%	22	78,5%
Παρουσία σπηλαίου	11	31%	12	42,8%
Θετική μικροσκοπική	12	34%	13	46,4%
Ιστορικό προηγ.θεραπείας	10	29%	10	35,7%
MDR/TB	0	0%		

Πηγή: ΕΟΔΥ

Ουρανία Καλκούνη, Ελένη Τριανταφύλλου
Γραφείο Νοσημάτων που μεταδίδονται μέσω του αναπνευστικού
Τμήμα Επιδημιολογικής Επιτήρησης και Παρέμβασης, ΕΟΔΥ

Μετανάστες και MDR-TB

World Health Organization
REGIONAL OFFICE FOR Europe

- Το φορτίο της MDR-TB στους μετανάστες στην Ευρώπη είναι δυσανάλογο σε σχέση με το γηγενή πληθυσμό
- Πολλοί μετανάστες προέρχονται από χώρες εκτός WHO European Region με υψηλή επίπτωση MDR-TB
- Επιπλέον μέσα στη WHO European Region υπάρχει μετανάστευση από χώρες με υψηλή προς χώρες με χαμηλή επίπτωση MDR-TB
- Στην EU/EEA οι αλλοδαποί αποτελούν το 73,4% των MDR-TB - σημαντική ετερογένεια

Hargreaves S.WHO Regional Office for Europe 2018, HEN synthesis report 56

A.2.2 Outcomes for RR-TB/MDR-TB/XDR-TB patients treated using second-line treatment

Outcome	Definition
Cured	Treatment completed as recommended by the national policy without evidence of failure AND three or more consecutive cultures taken at least 30 days apart are negative after the intensive phase.[a]
Treatment completed	Treatment completed as recommended by the national policy without evidence of failure BUT no record that three or more consecutive cultures taken at least 30 days apart are negative after the intensive phase.[a]
Treatment failed	Treatment terminated or need for permanent regimen change of at least two anti-TB drugs because of: – lack of conversion[b] by the end of the intensive phase[a], *or* – bacteriological reversion[b] in the continuation phase after conversion[b] to negative, *or* – evidence of additional acquired resistance to fluoroquinolones or second-line injectable drugs, *or* – adverse drug reactions (ADRs).
Died	A patient who dies for any reason during the course of treatment.
Lost to follow-up	A patient whose treatment was interrupted for 2 consecutive months or more.
Not evaluated	A patient for whom no treatment outcome is assigned. (This includes cases "transferred out" to another treatment unit and whose treatment outcome is unknown)
Treatment success	The sum of *cured* and *treatment completed*

[a] For *Treatment failed*, lack of conversion by the end of the intensive phase implies that the patient does not convert within the maximum duration of intensive phase applied by the programme. If no maximum duration is defined, an 8-month cut-off is proposed. For regimens without a clear distinction between intensive and continuation phases, a cut-off 8 months after the start of treatment is suggested to determine when the criteria for *Cured*, *Treatment completed* and *Treatment failed* start to apply.

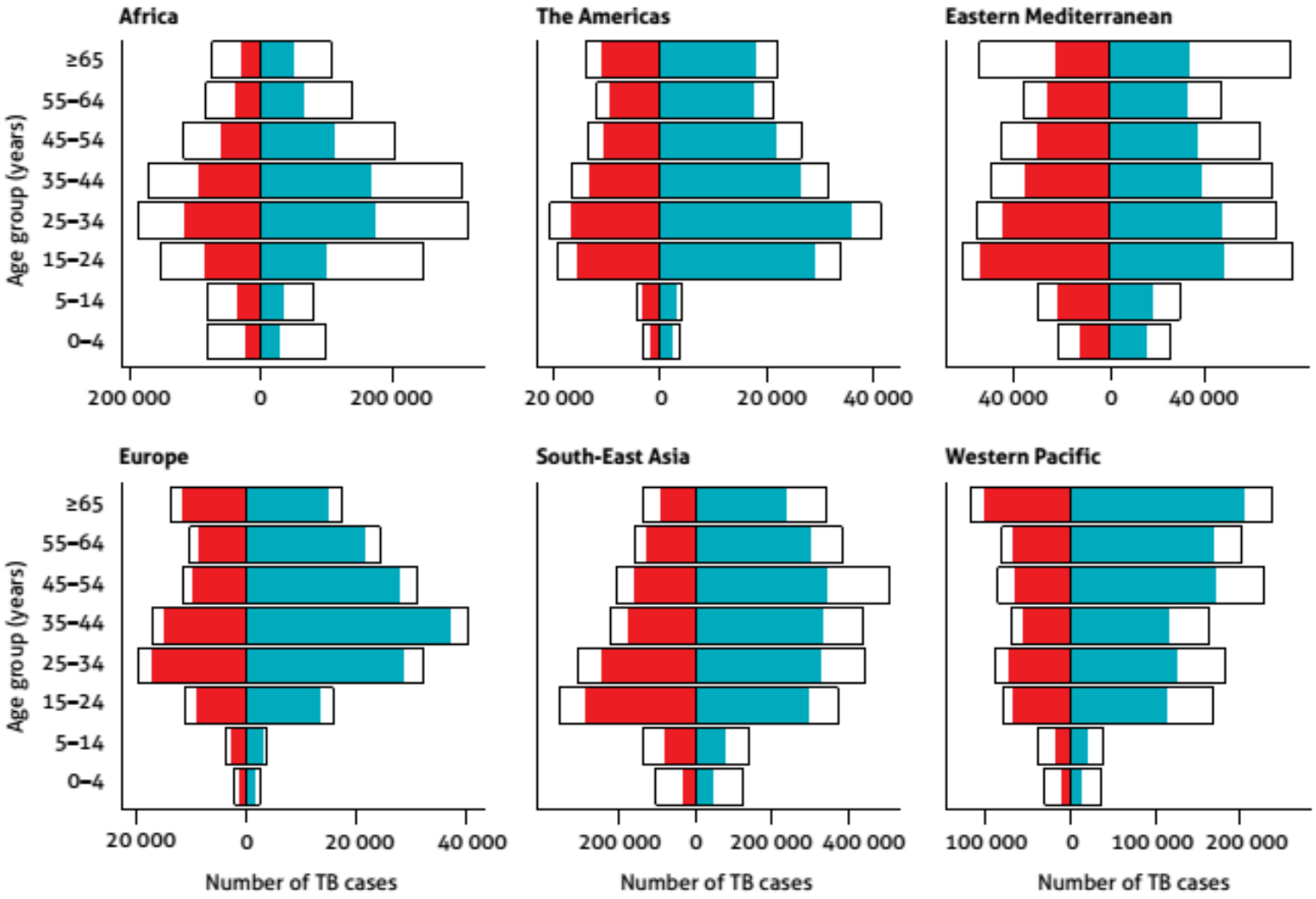
[b] The terms "conversion" and "reversion" of culture as used here are defined as follows:

Conversion (to negative): culture is considered to have converted to negative when two consecutive cultures, taken at least 30 days apart, are found to be negative. In such a case, the specimen collection date of the first negative culture is used as the date of conversion.

Reversion (to positive): culture is considered to have reverted to positive when, after an initial conversion, two consecutive cultures, taken at least 30 days apart, are found to be positive. For the purpose of defining *Treatment failed*, reversion is considered only when it occurs in the continuation phase.

FIG. 3.7

Regional estimates of TB incidence (black outline) and case notifications disaggregated by age and sex (female in red; male in turquoise), 2018

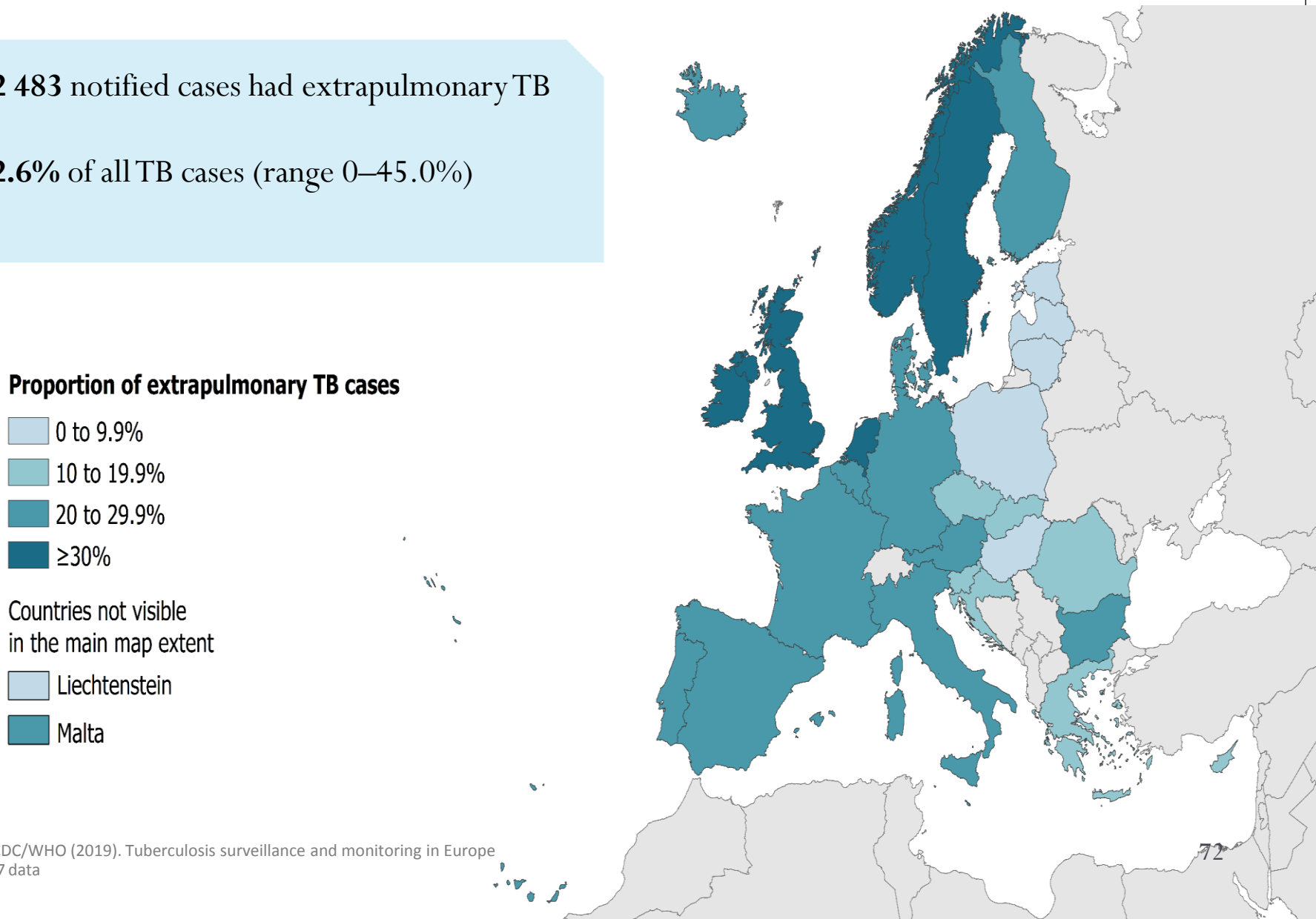


Παγκοσμίως από τις 10.000.000 περιπτώσεις TB δηλώνονται οι 7.000.000

Extrapulmonary TB, EU/EEA, 2017

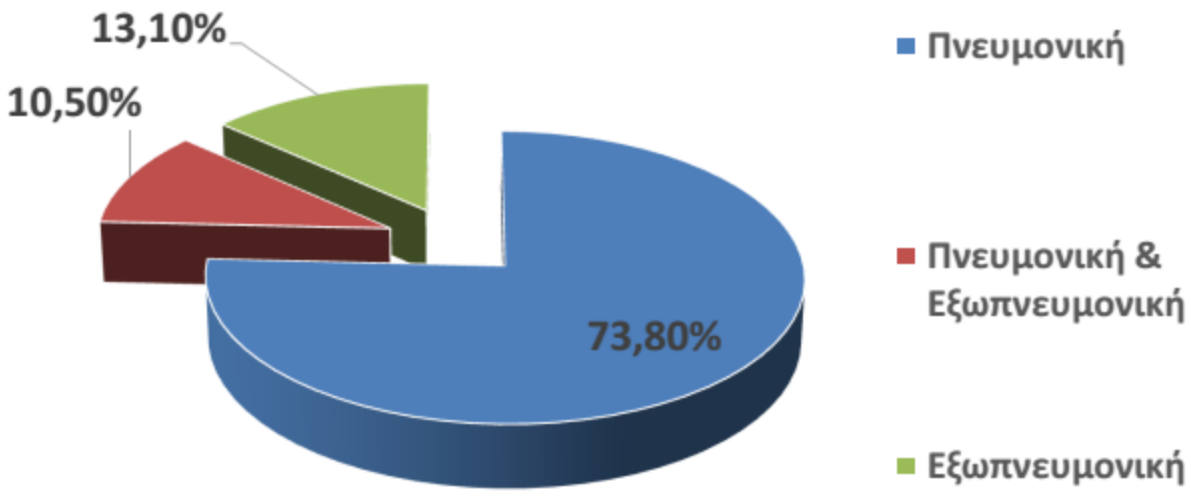
12 483 notified cases had extrapulmonary TB

22.6% of all TB cases (range 0–45.0%)



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

Εντόπιση νόσου, σύνολο περιπτώσεων, Ελλάδα 2004-2017



58% θετική μικροσκοπική αναπνευστικού δείγματος στους ενήλικες με πνευμονική ΤΒ

Πηγή: ΕΟΔΥ

Evaluation screening regular migrants, 2011-2015

TB incidence country of origin	Number	TB found by screening	Yield per 100,000 (+ Conf. Interval)
~~≤50~~	~~26,101~~	~~7~~	~~27 (11-55)~~
51-100	37,787	11	29 (15-52)
101-200	36,548	41	112 (80-152)
>200 (+ Eritrea)	13,028	38	292 (206-400)
unknown	2,837	0	-
Total	**116,301**	**97**	**83 (67-100)**

- Screening migrants from countries with a TB incidence ≤50/100,000 was discontinued per 1/1/2015 (Van den Berg, ERJ 2017).
- In the Netherlands, a **cut-off of 50/100,000 (NNS=2000)** was arbitrarily set (De Vries, ERJ 2016).
- Based on this evaluation screening **(regular)** migrants from countries with a TB incidence ≤100/100,000 was discontinued per 1/4/2019.

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Evaluation screening asylum seekers, 2011-2015

TB incidence country of origin	Number	TB found by screening	Yield per 100,000 (+ Conf. Interval)
≤50	49,142	16	33 (19-53)
51-100	5,833	11	189 (94-337)
101-200	10,385	34	327 (227-457)
>200 (+Eritrea)	23,966	65	271 (205-337)
unknown	10,180	0	-
Total	**99,506**	**126**	**127 (105-148)**

- Screening asylum seekers from countries with a TB incidence ≤50/100,000 was stopped in September 2015 (De Vries, ERJ 2016).

DeVries G , EACCTB 2019