RESEARCH ARTICLE

Migration-related tuberculosis: epidemiology and characteristics of tuberculosis cases originating outside the European Union and European Economic Area, 2007 to 2013

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Citation style for this article:

Ködmön C, Zucs P, van der Werf MJ. Migration-related tuberculosis: epidemiology and characteristics of tuberculosis cases originating outside the European Union and European Economic Area, 2007 to 2013. Euro Surveill. 2016;21(12):pii=30164. DOI: http://dx.doi.org/10.2807/1560-7917.ES.2016.21.12.30164

Article submitted on 03 February 2015 / accepted on 05 November 2015 / published on 24 March 2016

Migrants arriving from high tuberculosis (TB)incidence countries may pose a significant challenge to TB control programmes in the host country. TB surveillance data for 2007-2013 submitted to the European Surveillance System were analysed. Notified TB cases were stratified by origin and reporting country. The contribution of migrant TB cases to the TB epidemiology in EU/EEA countries was analysed. Migrant TB cases accounted for 17.4% (n = 92,039) of all TB cases reported in the EU/EEA in 2007-2013, continuously increasing from 13.6% in 2007 to 21.8% in 2013. Of 91,925 migrant cases with known country of origin, 29.3% were from the Eastern Mediterranean, 23.0% from south-east Asia, 21.4% from Africa, 13.4% from the World Health Organization European Region (excluding EU/EEA), and 12.9% from other regions. Of 46,499 migrant cases with known drug-susceptibility test results, 2.9% had multidrug-resistant TB, mainly (51.7%) originating from the European Region. The increasing contribution of TB in migrants from outside the EU/EEA to the TB burden in the EU/EEA is mainly due to a decrease in native TB cases. Especially in countries with a high proportion of TB cases in non-EU/EEA migrants, targeted prevention and control initiatives may be needed to progress towards TB elimination.

Introduction

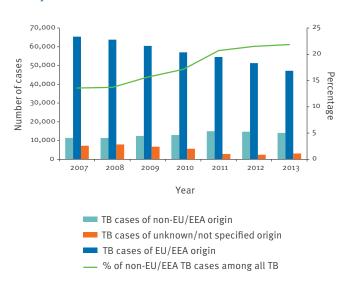
The tuberculosis (TB) notification rate in the European Union and European Economic Area (EU/EEA) declined from 16.8 per 100,000 population in 2007 to 12.7 per 100,000 in 2013 [1]. However, in some low-incidence countries, the decline in TB notification rate has slowed down, especially in countries reporting a high proportion of TB cases in individuals of foreign origin, i.e. migrants. In general, migration is influenced by socioeconomic and political factors [2]. Economic, social and political stability is relatively high in the

EU/EEA which thus attracts immigrants from many low-income countries around the world [3]. On average (years 2007-2012), 1.5 million migrants from outside the EU/EEA were registered annually in EU and EEA countries [4]. A considerable proportion of these migrants are coming from countries with a high TB burden such as Bangladesh, Brazil, China, India, Morocco, Pakistan, Russian Federation, Somalia and Ukraine [5]. They may arrive in the EU/EEA with active TB disease, or with latent TB infection (LTBI). To detect TB disease in migrants, several EU/EEA countries have introduced (pre-)entry screening programmes [6-8]. Screening of migrants for LTBI is also being explored by some countries, such as the Netherlands [9]. However, screening programmes will not identify all TB or LTBI cases among migrants, due to the limited sensitivity of the current screening tests (mainly chest x-ray and tuberculin skin test or interferon gamma release assay). Also, not all migrant groups are covered by the screening programme, e.g. undocumented migrants are often not included. In addition, migrants frequently travel back to their country of origin where they may be (re-) infected with TB [10].

Migrants developing TB may pose a challenge to TB programmes in the EU/EEA due to language and cultural differences [11]. Also, undocumented migrants may not access the healthcare system due to fear of deportation, and migrants whose stay is legal may be unfamiliar with the healthcare system and therefore encounter problems in seeking healthcare [12]. Since countries with low TB notification rates report high numbers of TB cases in migrants in particular, it is important to study this phenomenon because addressing TB in migrants will be essential to achieving the goal of TB programmes, i.e. TB elimination [13]. Therefore, the aim of this study is to quantify and to geographically

FIGURE 1

Number of tuberculosis cases by year and origin, and percentage of non-European Union/European Economic Area cases among all tuberculosis cases, European Union/European Economic Area, 2007–2013



EEA: European Economic Area; EU: European Union; TB: tuberculosis.

and epidemiologically characterise migration-related importation of TB to EU/EEA countries.

Methods

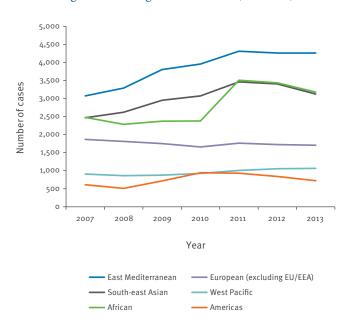
The European Centre for Disease Prevention and Control (ECDC) has collected case-based TB surveillance data from EU and EEA countries since 2007 and stored them in a common database (The European Surveillance System, TESSy) hosted by ECDC. Designated national surveillance institutions are responsible for data reporting to TESSy and for data validation.

The detailed data collection methods and definitions are described elsewhere [1]. TB cases were defined according to agreed case definitions published by the European Commission [14] and confirmed, probable and possible cases were included in the analysis. Surveillance data reported by 29 EU/EEA countries and covering the period from 2007 to 2013 were extracted from the database on 3 October 2014. Place of birth was used as a proxy indicator for the geographic origin of a TB case in most countries; except for Austria, Belgium, Greece, Poland, Hungary (from 2010 onwards) and for Malta (only in 2010) where citizenship was used. Place of birth outside EU/EEA borders was used as proxy for migrant TB in most countries. Non-EU/ EEA citizenship was used for Austria, Belgium, Greece, Poland, Hungary (from 2010 onwards) and for Malta (only in 2010).

The analysis was restricted to TB cases with known origin. The areas of origin were defined according to the World Health Organization (WHO) regions described in the *Global Tuberculosis Report*, 2013 [15].

FIGURE 2

Number of tuberculosis cases of non- European Union/ European Economic Area origin by year and World Health Organization Region, 2007–2013 (n=91,925)



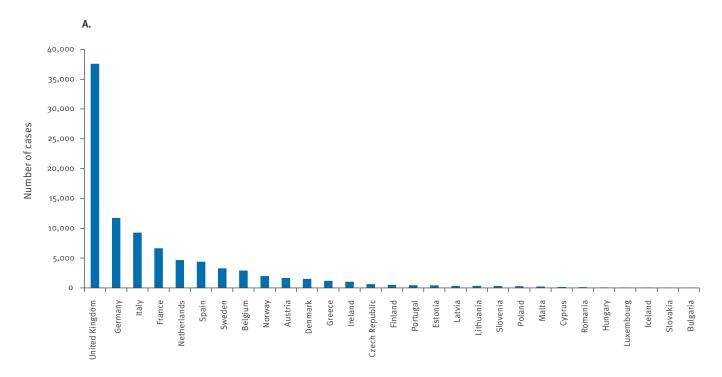
EEA: European Economic Area; EU: European Union.

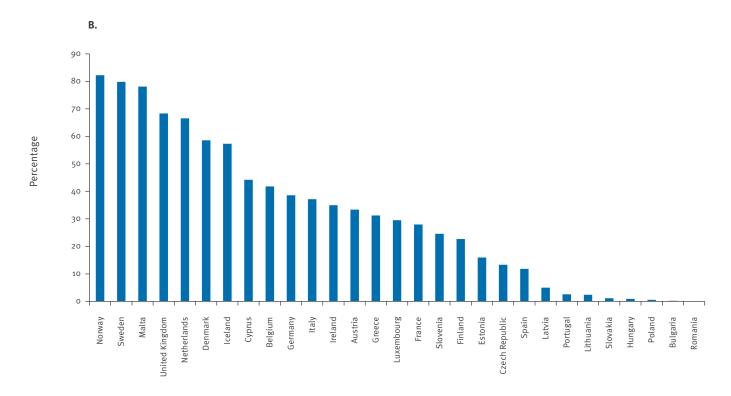
The European Region refers to the WHO European Region excluding the EU and EEA (Iceland, Liechtenstein and Norway) countries. To assign country of origin (based on place of birth), we used the ISO 3166-1 codes for countries, dependent territories, and special areas of geographical interest which are published by the International Organization for Standardization [16]. The origin of cases reported by or from populated Overseas Countries and Territories of EU countries was assigned according to their geographic location and such cases counted as cases in individuals of non-EU/EEA origin. Cases reported/coded in the system as originating (based on place of birth) either from 'Soviet Union' (Former Soviet Union (FSU) countries: Armenia, Azerbaijan, Belarus, Estonia (EU), Georgia, Kazakhstan, Kyrgyzstan, Latvia (EU), Lithuania (EU), Moldova, Russian Federation, Tajikistan, Turkmenistan, Ukraine and Uzbekistan) or 'Yugoslavia' (Bosnia and Herzegovina, Croatia (EU), Kosovo*, Montenegro, Serbia, Slovenia (EU) and the former Yugoslav Republic of Macedonia) were classified as cases of unspecified origin (n=114), because some parts of those two historical countries belong to the EU today as indicated in brackets.

Liechtenstein reported TB surveillance data to TESSy only for 2007 and was therefore excluded from the analysis. Croatia joined the EU in July 2013 and was considered a non-EU/EEA country in the analysis. France, Italy, and Spain are not reporting drug resistance data to TESSy and were excluded from the analysis of laboratory data and drug resistance. Treatment outcome data were not reported by France, Greece, and Italy in

FIGURE 3

Number of tuberculosis cases (A) and percentage of tuberculosis cases (B) of non- European Union/European Economic Area origin among tuberculosis cases with known country of origin (B), by reporting country, European Union/European Economic Area, 2007–2013 (n=91,925)



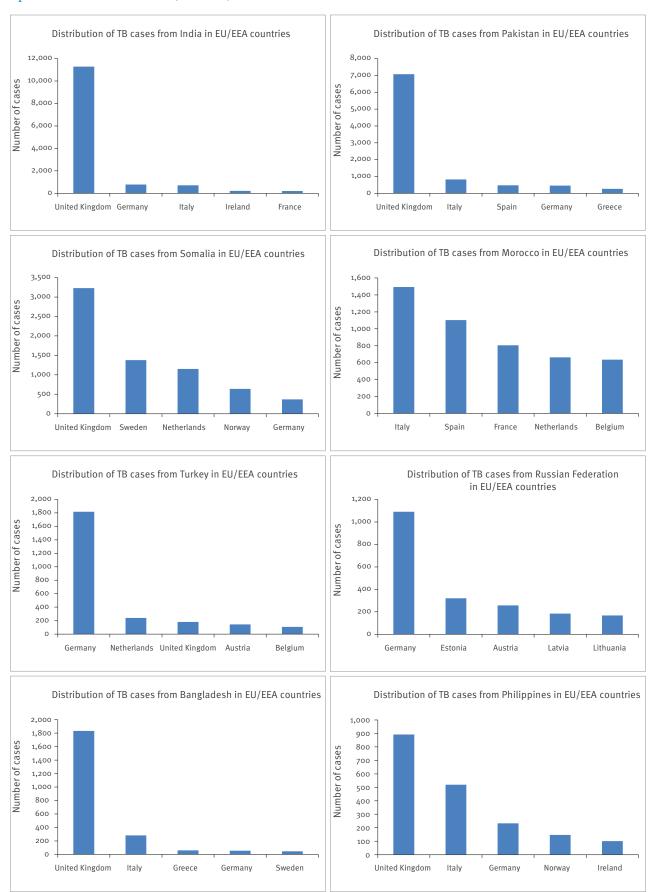


2007–2012, and by Spain in 2007–2009. Therefore, these countries were excluded from the treatment outcome analysis. TB treatment was considered successful if a case was cured or their treatment completed 12 months after start of treatment.

TB cases were described by year of reporting, origin and country of reporting. Native cases (EU/EEA origin) and cases from outside the EU/EEA were compared by sex, age, previous treatment history, TB site, laboratory confirmation status, drug resistance, HIV status and treatment outcome. Differences were considered statistically significant, if p<0.01 as determined by

FIGURE 4

Distribution of tuberculosis cases originating from India, Pakistan, Somalia, Morocco, Turkey, Russian Federation, Bangladesh and the Philippines across the five European Union/European Economic Area countries with the highest reported numbers, 2007–2013 (n=47,440)



EEA: European Economic Area; EU: European Union; TB: tuberculosis.

TABLE A

Characteristics of tuberculosis cases with reported country of origin by region of origin, European Union/European Economic Area, 2007-2013 (n=491,538)

	WHO Region																	
	EU/EEA		Total non-EU/EEA		Eastern Mediterranean		South-East Asian		African		European (excluding EU/ EEA)		Western Pacific		Americas		Total	
	N	%	N	%	N	%ª	N	% ^a	N	% ^a	N	% ^a	N	% ^a	N	% ª	N	%
Total	399,613	81.3	91,925	18.7	26,945	29.3	21,097	23.0	19,629	21.4	12,280	13.4	6,697	7.3	5,277	5.7	491,538	100
Sex							,								1			
Male	264,068	66.1	53,122	57.8	16,348	60.7	12,022	57.0	11,667	59.4	7,381	60.1	3,112	46.5	2,592	49.1	317,190	64.5
Female	135,220	33.8	38,580	42.0	10,545	39.1	9,016	42.7	7,918	40.3	4,868	39.6	3,561	53.2	2,672	50.6	173,800	35.4
Unknown	325	0.1	223	0.2	52	0.2	59	0.3	44	0.2	31	0.3	24	0.4	13	0.2	548	0.1
Age groups (1		l .		Γ				1					Г			l .	
0-14	18,034	4.5	2,601	2.8	1,052	3.9	276	1.3	612	3.1	368	3.0	138	2.1	155	2.9	20,635	4.2
15-24	39,266	9.8	14,741	16.0	5,538	20.6	3,007	14.3	3,338	17.0	1,071	8.7	1,049	15.7	738	14.0	54,007	11.0
25-44	122,780	30.7	48,683	53.0	13,012	48.3	12,439	59.0	11,584	59.0	4,910	40.0	3,740	55.8	2,998	56.8	171,463	34.9
45-64	135,147	33.8	17,611	19.2	4,786	17.8	3,499	16.6	3,210	16.4	3,680	30.0	1,379	20.6	1,057	20.0	152,758	31.1
65+ Unknown	83,946	0.1	8,157	8.9 0.1	2,504	9.3	1,864	0.1	856	0.1	2,236	18.2 0.1	379 12	5.7 0.2	318	0.2	92,103	0.1
Previous TB I	440	0.1	132	0.1	53	0.2	12	0.1	29	0.1	15	0.1	12	0.2	11	0.2	572	0.1
No	317,268	79.4	70,386	76.6	21,080	78.2	17,409	82.5	14,728	75.0	7,838	63.8	5,105	76.2	4,226	80.1	387,654	78.9
Yes	58,781	14.7	5,721	6.2	1,627	6.0	1,137	5.4	996	5.1	1,411	11.5	337	5.0	213	4.0	64,502	13.1
Unknown	23,564	5.9	15,818	17.2	4,238	15.7	2,551	12.1	3,905	19.9	3,031	24.7	1,255	18.7	838	15.9	39,382	8.0
Site of diseas		3.7	-5,		7,-3-	-5.7	-,,,,-		3,7-3	-5.5	3,-3-	-4.7	-,-,,	/	- 50	-5.7	37,3	
Pulmonary	333,989	83.6	53,111	57.8	13,737	51.0	9,215	43.7	11,961	60.9	10,168	82.8	4,287	64.0	3,743	70.9	387,100	78.8
Extra- pulmonary	64,968	16.3	38,463	41.8	13,109	48.7	11,818	56.0	7,592	38.7	2,032	16.5	2,384	35.6	1,528	29.0	103,431	21.0
Unknown	656	0.2	351	0.4	99	0.4	64	0.3	76	0.4	80	0.7	26	0.4	6	0.1	1,007	0.2
Laboratory co	onfirmation																	
Confirmed	214,612	53.7	47,925	52.1	13,920	51.7	12,278	58.2	9,202	46.9	7,748	63.1	3,577	53.4	1,200	22.7	262,537	53.4
Not confirmed	119,397	29.9	23,693	25.8	7,457	27.7	7,013	33.2	4,103	20.9	3,105	25.3	1,484	22.2	531	10.1	143,090	29.1
Laboratory data not reported	65,604	16.4	20,307	22.1	5,568	20.7	1,806	8.6	6,324	32.2	1,427	11.6	1,636	24.4	3,546	67.2	85,911	17.5
Drug resistar	ce among [ST don	e															
DST done among laboratory confirmed	147,090	68.5	46,499	97.0	13,580	97.6	12,030	98.0	8,945	97.2	7,322	94.5	3,443	96.3	1,179	98.3	193,589	73.7
Susceptible	126,945	86.3	40,538	87.2	12,044	88.7	10,794	89.7	8,046	89.9	5,679	77.6	2,912	84.6	1,063	90.2	167,483	86.5
Mono- resistant	8,664	5.9	3,492	7.5	1,069	7.9	813	6.8	614	6.9	552	7.5	358	10.4	86	7.3	12,156	6.3
Poly- resistant	2,821	1.9	1,107	2.4	270	2.0	199	1.7	145	1.6	387	5.3	92	2.7	14	1.2	3,928	2.0
MDR among DST done	8,660	5.9	1,362	2.9	197	1.5	224	1.9	140	1.6	704	9.6	81	2.4	16	1.4	10,022	5.2
XDR among MDR	691	8.0	80	5.9	6	3.0	2	0.9	2	1.4	68	9.7	2	2.5	0	0.0	771	7.7
HIV status																		
Tested for HIV	83,062	20.8	5,876	6.4	1,626	6.0	372	1.8	1,189	6.1	1,206	9.8	422	6.3	1,061	20.1	88,938	18.1
HIV-positive among tested	3,999	4.8	567	9.6	32	2.0	18	4.8	289	24.3	114	9.5	14	3.3	100	9.4	4,566	5.1

DST: drug susceptibility testing; MDR: multidrug resistant; EEA: European Economic Area; EU: European Union; N: number; WHO: World Health Organization; XDR: extensively drug resistant.

 $^{^{\}rm a}$ Percentage among TB cases in individuals of non-EU/EEA origin.

TABLE B

Characteristics of tuberculosis cases with reported country of origin by region of origin, European Union/European Economic Area, 2007–2013 (n=491,538)

	WHO Region																	
	EU/EEA		Total non-EU/EEA		Eastern Mediterranean		South-East Asian		African		European (excluding EU/ EEA)		Western Pacific		Americas		Total	
	N	%	N	%	N	%ª	N	% a	N	% ª	N	% a	N	% ^a	N	% ª	N	%
Treatment outcome ^b																		
Number of reported cases 2007-2012	352,428		77,875		22,687		17,975		16,452		10,574		5,632		4,555		430,303	
Treatment outcome reported	305,945	86.8	63,600	81.7	18,841	83.0	16,492	91.7	11,994	72.9	9,148	86.5	4,443	78.9	2,656	58.3	369,545	85.9
Success	228,351	74.6	49,256	77-4	15,141	80.4	12,839	77.8	9,328	77.8	6,444	70.4	3,349	75.4	2,155	81.1	277,607	75.1
Failed	6,900	2.3	109	0.2	29	0.2	9	0.1	10	0.1	48	0.5	10	0.2	3	0.1	7,009	1.9
Defaulted	20,176	6.6	3,436	5.4	848	4.5	1,083	6.6	615	5.1	538	5.9	271	6.1	81	3.0	23,612	6.4
Died	25,123	8.2	2,052	3.2	503	2.7	475	2.9	303	2.5	595	6.5	101	2.3	75	2.8	27,175	7.4
Still on treatment	9,427	3.1	4,312	6.8	1,202	6.4	1,309	7.9	829	6.9	606	6.6	275	6.2	91	3.4	13,739	3.7
Not evaluated	15,968	5.2	4,435	7.0	1,118	5.9	777	4.7	909	7.6	917	10.0	437	9.8	251	9.5	20,403	5.5

DST: drug susceptibility testing; MDR: multidrug resistant; EEA: European Economic Area; EU: European Union; N: number; WHO: World Health Organization; XDR: extensively drug resistant.

chi-squared test. Statistical analysis was performed using Stata 13 software (StataCorp, Texas, US).

Results

6

Of 527,467 TB cases notified in the EU/EEA from 2007 to 2013, 399,613 (75.8%) were reported as originating from EU/EEA countries, 92,039 (17.4%) as originating from non-EU/EEA countries, and for 35,815 (6.8%), country of origin was not reported. Among 491,652 TB cases with reported country of origin, 122,627 (24.9%) originated from outside the reporting country. Of these, 91,925 (75%) originated from outside the EU/ EEA, 30,588 (24.9%) were of EU/EEA origin, and 114 (0.1%) originated from 'Soviet Union' or 'Yugoslavia'. The proportion of TB cases with reported non-EU/EEA origin increased from 13.6% (n=11,403) in 2007 to 21.8% (n=14,050) in 2013, the proportion of TB cases with reported EU/EEA origin decreased from 77.8% (n = 65,390) in 2007 to 73.4% (n = 47,185) in 2013, while the proportion of TB cases with unknown or unspecified origin decreased from 8.6% (n=7,221) to 4.8%(n=3,092) in the same period (p<0.001) (Figure 1).

Of 92,039 cases with non-EU/EEA origin, the country of origin was reported for 91,925 (99.9%) cases, with the majority coming from the Eastern Mediterranean Region (29.3%, n=26,945), the South-East Asian Region (23.0 %, n=21.097) and the African Region (21.4%, n=19,629) (Table).

Compared with native TB cases, TB cases in individuals of non-EU/EEA origin were more frequently female (42.0% vs 33.8%, p<0.001) and under 45 years of age (71.8% vs 45.1%, p<0.001) (Table). Cases of non-EU/

EEA origin had a previous TB history less frequently (6.2% vs 14.7%, p<0.001), but a proportion of cases with unknown previous history three times higher than native cases. Extrapulmonary TB was much more commonly diagnosed in cases of non-EU/EEA origin (41.8% vs 16.3%, p<0.001). Very similar proportions, just over 50% of cases were laboratory-confirmed in both native and migrant cases, but the latter were much more extensively tested for drug susceptibility (97.0% vs 68.5%, p<0.001), and were found to be mono-resistant and poly-resistant slightly more frequently, but not multidrug-resistant (9.9% vs 2.9%, p<0.001). The majority of multidrug-resistant (MDR) TB and extensively drug-resistant (XDR) TB cases in individuals of non-EU/EEA origin were from the European Region, where the highest percentage of MDR-TB cases among the cases with available drug susceptibility testing (DST) results (9.6%, n=704) was observed, as well as the highest percentage of XDR-TB cases among MDR-TB (9.7%, n=68). Of 704 MDR-TB cases originating from the European Region, 678 (96.3%) were notified in cases coming from 13 non-EU/EEA 'Soviet Union' countries (data not shown). The highest percentage of mono-resistance to a first-line anti-TB drug was observed in cases originating from the Western Pacific Region (10.4%, n = 358). Most cases with monoresistance originated from the Philippines, Vietnam and China (145, 117 and 48 respectively). Among the mono-resistant TB cases from the Philippines, 83.4% (n=121) were resistant to isoniazid, while in cases originating from Vietnam and China, 55.6% (n=65) and 60.4% (n = 29) were resistant to isoniazid (data not shown). In the period 2007–2013 the trend in MDR-TB prevalence among cases of non-EU/EEA origin did

^a Percentage among TB cases in individuals of non-EU/EEA origin.

^b Treatment outcome 12 months after starting treatment for cases notified in 2007–2012.

not change significantly (p = 0.94, data not shown). Cases of non-EU/EEA origin were tested for HIV much less frequently than native cases (6.4% vs 20.8%, p<0.001), but tested HIV-positive twice as often (9.6% vs 4.8%, p<0.001). Among cases of non-EU/EEA origin, the majority and highest prevalence of HIV co-infection was found in cases originating from the African Region. A higher proportion of treatment success was reported in migrant cases (77.4% vs 74.6%, p<0.001), while the proportion that died during treatment was lower (3.2% vs 8.2%, p<0.001). The percentage of TB cases where the treatment outcome was 'lost to followup' was lower in the cases of non-EU/EEA origin (5.4% vs 6.6%), but the percentage of non-evaluated cases was higher (7.0% vs 5.2%). The lowest treatment success rate, 70.4%, was observed among cases from the European Region.

From 2007 to 2011, the number of notified TB cases in individuals of non-EU/EEA origin increased for all WHO Regions except for the European region (Figure 2). Thereafter, the number remained the same or decreased slightly. In the same period, the number of TB cases with unknown country of origin decreased from 8.6% in 2007 to 4.8% in 2013. The mean annual increase in the period 2007-2011 was highest for cases originating from Americas (13.5%; standard deviation (SD): 18.4), followed by the African Region (10.9%; SD: 20.4), the South-East Asian Region (8.9%; SD: 8.1), the Eastern Mediterranean Region (8.9%; SD: 5.3) and the Western Pacific Region (2.8%; SD: 4.2), while for cases originating from the European Region a mean annual decrease of 1.3% (SD: 3.7) was observed. The mean increase in the number of notified cases was the highest for cases originating from the Eastern Mediterranean Region (n = 309; SD: 183.1), followed by the African Region (n = 256; SD: 411.3), the South-East Asian Region (n = 248; SD: 238.2), the Americas (n = 75; SD: 145.1) and the Western Pacific Region (n = 25; SD: 52.7). The notification of cases originating from the European Region showed the mean decrease of 26 cases annually (SD: 63.2).

Of all TB cases in individuals of non-EU/EEA origin, 40.9% (n=37,573) were reported by the United Kingdom (UK), 12.8% (n=11,728) by Germany and 10.1% (n=9,264) by Italy (Figure 3A. The highest contribution of TB cases in individuals of non-EU/EEA origin to the national TB burden was observed in Norway with 82.4% (n = 1,997), Sweden with 79.9% (n = 3,274) and Malta with 78.1% (n = 228) (Figure 3B).

The reported non-EU/EEA TB cases originated from 186 countries, dependent territories, and special areas of geographical interest with 51.6% coming from India (15.3%), Pakistan (10.9%), Somalia (8.5%), Morocco (5.7%), Turkey (3.0%), Russian Federation (2.9%), Bangladesh (2.7%), and the Philippines (2.6%). Their distribution mirrors the typical migration flows and destination country preferences (Figure 4). Between 2007 and 2013, increasing numbers of TB cases from

India, Pakistan and Morocco were notified (p<0.001, data not shown).

Most cases from India (80.3%, n=11,293) were reported by the UK (Figure 4). The UK also reported a large percentage of the cases originating from Pakistan (70.5%, n=7,073), from Somalia (41.2%, n=3,228), from Bangladesh (74.7%, n=1,833), and from Philippines (36.7%, n=892). Germany reported 66.8% (n=1,818) of all reported cases from Turkey and 40.6% (n=1,091) of all reported cases from Russian Federation. While, Italy reported the largest percentage of cases from Morocco (28.7%, n=1,493).

Discussion

Almost one in five TB cases notified in the EU/EEA between 2007 and 2013 originated from a country outside the EU/EEA, but this varied from<1% to>80% between the 29 countries included in this study. The percentage of migrant TB cases increased from 13.6% to 21.8% between 2007 and 2013, while the overall number of cases of non-EU/EEA origin increased from 11,403 in 2007 to 14,975 in 2011 and slightly decreased thereafter to 14,050 in 2013. The increasing percentage of migrant TB among all notified TB cases is largely attributable to the decreasing numbers of native TB cases and cases with unknown origin. The highest mean annual increase in notifications was observed in TB cases originating from the Eastern Mediterranean and African Regions. The only decreasing trend was seen in cases originating from the European Region. Increasing trends in notified TB cases in migrants have also been observed in other high-income countries such as Australia, Canada, and the United States (US) [17-19].

TB cases originating from eight countries accounted for 51.6% of all TB cases in individuals of non-EU/ EEA origin. This can be explained by the burden of TB in these countries [15] and the relatively high number of migrants from these countries to the EU/EEA [5,6]. Data from Australia, Canada and the US showed that the TB notification rate among migrants is strongly associated with the TB burden in the country of origin [18]. Among foreign-born and US-born cases in the US, the level of education, living conditions, low income and unemployment were associated with higher TB rates; this association was stronger in the foreign-born cases. According to the authors, these results support the hypothesis that the TB rates among foreign-born cases are more strongly influenced by experiences in their country of origin than by the environments in the host country [19]. Similarly to the situation in the EU/ EEA, the 25 to 44 years-old age group was most represented in the US among foreign-born TB cases [20]. In the EU/EEA, the high proportions of males seen among cases originating from the Eastern Mediterranean and European Regions suggest that the majority of TB cases from these regions are migrant workers. This is supported by Eurostat data according to which, on average

29% of residence permits were issued in 2008–2012 due to employment and 28% due to family reasons [5].

Exposure to TB before immigration to the EU/EEA and when travelling back to the country of origin for family visits may result in relatively high latent TB infection rates in migrant populations [21-23]. Several studies suggest that the majority of cases among migrants occur due to TB infection or reinfection when travelling to their home country [20,24,25] or due to reactivation of latent TB [20,26,27]. However, TB in migrants might also be due to recent infection or reinfection in the host country after local exposure [27-30].

According to the Eurostat data, there are remarkable differences in the number of migrants received by different EU/EEA countries. The UK, Italy, Germany, France, the Netherlands and Spain received the highest number of non-EU/EEA migrants during the period 2007-2012 [4]. In most EU/EEA Member States, this migration peaked in 2010, which was probably largely attributable to the global financial crisis [4,31]. Both the geographical distribution of reported TB cases in individuals of non-EU/EEA origin and their overall trend over time appears to follow the general migration patterns described [5,20]. As the biggest reporting country of TB cases in individuals of non-EU/EEA origin, the UK saw the majority of these cases originating from India, Pakistan and Bangladesh. The same three countries were also among the top five countries contributing to the TB burden in the US [20].

The highest prevalence of MDR-TB and XDR-TB was observed among cases of non-EU/EEA European origin. In the US in 2007–2009, 1.5% of foreign-born cases with available DST results were reported with MDR-TB, and the highest percentage (9.3%) was also observed among cases of European origin [32]. Equally, in Canada, the highest percentage of MDR-TB cases (2.9%) among foreign-born TB cases originated from the European Region [33]. This reflects the high prevalence of drug resistance among TB cases in the non-EU/EEA European Region [15].

Extrapulmonary TB was more frequently reported in TB cases in individuals of non-EU/EEA origin. Since extrapulmonary TB (excluding laryngeal TB) is rarely infectious, these cases will not contribute to transmission in the host country but do have an impact on health service costs. Further, extrapulmonary TB can result in significant suffering [34] and the diagnosis is often challenging [35]. Therefore, healthcare workers need to have a relatively high level of suspicion when persons of non-EU/EEA origin present with unexplained signs and symptoms that might be caused by extrapulmonary TB.

As expected, given the global HIV situation [36], most HIV co-infections were observed among cases of African and Western Pacific origin.

In Japan, 63.4% foreign-born smear-positive TB cases had a successful treatment outcome in the period 2007-2010 [37]. The situation in the EU/EEA is much better with 77.4% of TB cases in individuals of non-EU/ EEA origin having a successful treatment outcome 12 months after starting treatment. Among TB cases in individuals of non-EU/EEA origin notified in EU/EEA, 17.9% percent did not have treatment outcome data reported, while in Japan, treatment outcome was not available for 16.6% of foreign-born smear-positive cases [37]. In the EU/EEA, the lowest treatment success rate (70.4%) was observed in cases from the European Region. This is probably attributable to the high percentage of MDR TB and XDR TB cases which require more than 12 months of treatment and would therefore be reported as 'still on treatment' 12 months after starting treatment. Another reason may be the high percentage of non-evaluated cases (10.0%) which might mask the real number of cases lost to follow-up. The non-uniform use of treatment outcome categories such as 'lost to follow-up', 'transferred out', 'still on treatment' and 'unknown' across the EU/EEA Member States might contribute to the high number of cases with non-evaluated treatment outcome [38]. In contrast to an earlier publication from the year 2000 that covers the period 1993-1997, where origin from 'Eastern Europe' and 'Yugoslavia' were identified as risk factors for loss to follow-up [39], the percentage of this treatment outcome in our study was smaller in TB cases in individuals of non-EU/EEA origin than in cases of EU/ EEA origin. The percentage was especially low in cases originating from the European Region outside the EU/ EEA. The treatment success rate in TB cases in individuals of non-EU/EEA origin was higher compared with native TB cases (77.4% vs 74.6%), and the fatality rate was lower (3.2% vs 8.2%). The percentage of TB cases over 64 years of age was lower in migrants compared with native TB cases (8.9% vs 21.0%) which explains the treatment outcome results.

Limitations

This study is based on TB surveillance data submitted to ECDC by the EU/EEA countries. In the EU/EEA TB surveillance system, only a limited number of variables are collected. Also, not all reported information is complete, and data quality is primarily the responsibility of the individual country. The origin of 6.8% of TB cases notified between 2007 and 2013 was not reported. In addition, three countries did not report case-based drug resistance data, and four countries did not report case-based treatment outcome data for the whole period. Due to this missing information, our results might not provide the complete picture of TB epidemiology among cases of non-EU/EEA origin. Furthermore, TB rates among immigrants could not be calculated due to the unavailability of migrant population data.

The differences in reporting of country of origin (country of birth vs nationality) might affect the comparability of data between some countries. The burden of non-EU/EEA migrant TB cases might be underestimated

in countries reporting nationality, as the migrants might have obtained the citizenship of the host country before TB was diagnosed.

Italy, France and Spain are not reporting TB drug resistance data to TESSy. The exclusion of TB cases reported by these countries compromises the representativeness of laboratory results in this study as these three countries received a relatively high number of non-EU/EEA immigrants.

The laboratory confirmation rate has been shown to be below 50% in some major reporting countries EU/ EEA MSs [1] which might lead to the underestimation of resistant TB cases.

The HIV testing coverage among TB cases is suboptimal and does therefore not allow for an in-depth analysis of the data. The low testing coverage might lead to under- or over estimation of TB/HIV co-infection in EU/FFA.

Conclusions

Migration from outside the EU/EEA contributes markedly to the TB burden in the EU/EEA. Targeted prevention and control efforts (e.g. access to healthcare for all migrants including undocumented migrants, avoiding interruption of treatment) and implementation of active case finding approaches (e.g. screening at entry point, screening for latent TB infection) focussed on non-EU/EEA migrants may be needed in order to diagnose cases early, provide adequate treatment and support and reduce the burden of TB among migrants.

*This designation is without prejudice to positions on status, and is in line with United Nations Security Council resolution 1244/99 and the International Court of Justice Opinion on the Kosovo declaration of independence.

Acknowledgements

The authors acknowledge the nominated national operational contact points for tuberculosis (in alphabetical order): Peter Henrik Andersen, Delphine Antoine, Trude Margrete Arnesen, Thorsteinn Blondal, Domnica Ioana Chiotan, Edita Davidavičienė, Irene Demuth, Raquel Duarte, Sabine Erne, Walter Haas, Alexander Indra, Jerker Jonsson, Ourania Kalkouni, Maria Koliou, Maria Korzeniewska – Kosela, Gábor Kovács, Joan O'Donnell, Analita Pace Asciak, Maria Grazia Pompa, Elena Rodríguez Valín, Alexandar Simuniovic, Erika Slump, Hanna Soini, Ivan Solovič, Petra Svetina, Lucy Thomas, Tonka Varleva, Piret Viiklepp, Kate Vulāne, Jiří Wallenfels and Maryse Wanlin, who provided the surveillance data used in this analysis.

No specific sources of funding were used for this study. The authors performed the study as part of their job at ECDC.

Conflict of interest

None declared.

Authors' contributions

CK contributed to the study design, performed the data analysis, and wrote the first draft of the manuscript, PZ contributed to the study design, and contributed to further versions of the manuscript and approved the final version before submission, MvdW contributed to the study design and data analysis, and contributed to further versions of the manuscript and approved the final version before submission.

References

- European Centre for Disease prevention and Control (ECDC)/ WHO Regional Office for Europe. Tuberculosis surveillance and monitoring in Europe, 2015. Stockholm: ECDC; 2015. Available from: http://ecdc.europa.eu/en/publications/Publications/ tuberculosis-surveillance-monitoring-Europe-2015.pdf
- Abarca Tomás B, Pell C, Bueno Cavanillas A, Guillén Solvas J, Pool R, Roura M. Tuberculosis in migrant populations. A systematic review of the qualitative literature.PLoS One. 2013;8(12):e82440. DOI: 10.1371/journal.pone.0082440 PMID: 24349284
- 3. Millet JP, Moreno A, Fina L, del Baño L, Orcau A, de Olalla PG, et al. Factors that influence current tuberculosis epidemiology. Eur Spine J. 2013;22(S4) Suppl 4;539-48. DOI: 10.1007/s00586-012-2334-8 PMID: 22565801
- Eurostat. Databases. [Accessed 25 July 2014] Available from: http://ec.europa.eu/eurostat/en/data/database
- 5. Eurostat. European social statistics. 2013; [Accessed 15 August 2014]. Available from: http://ec.europa.eu/eurostat/documents/3930297/5968986/KS-FP-13-001-EN. PDF/6952d836-7125-4ff5-a153-6ab1778bd4da
- Klinkenberg E, Manissero D, Semenza JC, Verver S. Migrant tuberculosis screening in the EU/EEA: yield, coverage and limitations. Eur Respir J. 2009;34(5):1180-9. DOI: 10.1183/09031936.00038009 PMID: 19880618
- Kruijshaar ME, Abubakar I, Stagg HR, Pedrazzoli D, Lipman M. Migration and tuberculosis in the UK: targeting screening for latent infection to those at greatest risk of disease. Thorax. 2013;68(12):1172-4. DOI: 10.1136/thoraxjnl-2013-203254 PMID: 23828120
- 8. Tafuri S, Martinelli D, Melpignano L, de Palma M, Quarto M, Prato R, et al. Tuberculosis screening in migrant reception centers: results of a 2009 Italian survey. Am J Infect Control. 2011;39(6):495-9. DOI: 10.1016/j.ajic.2010.10.013 PMID: 21570737
- Alvarez GG, Clark M, Altpeter E, Douglas P, Jones J, Paty MC, et al. Pediatric tuberculosis immigration screening in highimmigration, low-incidence countries. Int J Tuberc Lung Dis. 2010;14(12):1530-7.PMID: 21144237
- 10. Kik SV, Mensen M, Beltman M, Gijsberts M, van Ameijden EJ, Cobelens FG, et al. Risk of travelling to the country of origin for tuberculosis among immigrants living in a low-incidence country. Int J Tuberc Lung Dis. 2011;15(1):38-43.PMID: 21276294
- Pace-Asciak A, Mamo J, Calleja N. Tuberculosis among undocumented boat migrants to Malta: implications for a migrant tuberculosis policy. Int J Tuberc Lung Dis. 2013;17(8):1065-70. DOI: 10.5588/ijtld.12.0622 PMID: 23827031
- 12. Wolfheze Transborder Migration Task Force, Dara M, de Colombani P, Petrova-Benedict R, Centis R, Zellweger JP, Sandgren A, et al. . Minimum package for cross-border TB control and care in the WHO European region: a Wolfheze consensus statement. Eur Respir J. 2012;40(5):1081-90. DOI: 10.1183/09031936.00053012 PMID: 22653772
- 13. World Health Organization (WHO). Framework towards tuberculosis elimination in low-incidence countries. Geneva: WHO; 2014. Available from: http://www.who.int/tb/publications/elimination_framework/en/
- 14. European Commission. Commission Decision of 28 April 2008 amending Decision 2002/253/EC laying down case definitions for reporting communicable diseases to the Community network under Decision No 2119/98/EC of the European Parliament and of the Council. Brussels: European Commission. 28 Apr 2008. Available from: http://ec.europa.eu/health/ph_threats/com/docs/1589_2008_en.pdf
- World Health Organization (WHO). Global Tuberculosis Report 2014. Geneva: WHO; 2014. Available from: http://apps.who. int/iris/bitstream/10665/137094/1/9789241564809_eng.pdf
- 16. International Organization for Standardization. Codes for the representation of names of countries and their subdivisions --Part 2: Country subdivision code. 15 Nov 2013. Available from: http://www.iso.org/iso/home/store/catalogue_tc/catalogue_ detail.htm?csnumber=63546

- 17. Watkins RE, Plant AJ. Predicting tuberculosis among migrant groups. Epidemiol Infect. 2002;129(3):623-8. DOI: 10.1017/S0950268802007604 PMID: 12558347
- 18. Watkins RE, Plant AJ, Gushulak BD. Tuberculosis rates among migrants in Australia and Canada.Int J Tuberc Lung Dis. 2002;6(7):641-4.PMID: 12102305
- Olson NA, Davidow AL, Winston CA, Chen MP, Gazmararian JA, Katz DJ. A national study of socioeconomic status and tuberculosis rates by country of birth, United States, 1996-2005.BMC Public Health. 2012;12(1):365. DOI: 10.1186/1471-2458-12-365 PMID: 22607324
- 20. Ricks PM, Cain KP, Oeltmann JE, Kammerer JS, Moonan PK. Estimating the burden of tuberculosis among foreign-born persons acquired prior to entering the U.S., 2005-2009.PLoS One. 2011;6(11):e27405. DOI: 10.1371/journal.pone.0027405 PMID: 22140439
- 21. Pareek M, Abubakar I, White PJ, Garnett GP, Lalvani A. U.K. immigrant screening is inversely related to regional tuberculosis burden.Thorax. 2011;66(11):1010. DOI: 10.1136/thx.2010.152280 PMID: 21325664
- Pareek M, Abubakar I, White PJ, Garnett GP, Lalvani A. Tuberculosis screening of migrants to low-burden nations: insights from evaluation of UK practice. Eur Respir J. 2011;37(5):1175-82. DOI: 10.1183/09031936.00105810 PMID: 21071474
- 23. Pareek M, Watson JP, Ormerod LP, Kon OM, Woltmann G, White PJ, et al. Screening of immigrants in the UK for imported latent tuberculosis: a multicentre cohort study and cost-effectiveness analysis. Lancet Infect Dis. 2011;11(6):435-44. DOI: 10.1016/S1473-3099(11)70069-X PMID: 21514236
- 24. Lobato MN, Hopewell PC. Mycobacterium tuberculosis infection after travel to or contact with visitors from countries with a high prevalence of tuberculosis.Am J Respir Crit Care Med. 1998;158(6):1871-5. DOI: 10.1164/ajrccm.158.6.9804106 PMID: 9847280
- 25. Ormerod LP, Green RM, Gray S. Are there still effects on Indian Subcontinent ethnic tuberculosis of return visits?: a longitudinal study 1978-97. J Infect. 2001;43(2):132-4. DOI: 10.1053/jinf.2001.0872 PMID: 11676520
- 26. Codecasa LR, Porretta AD, Gori A, Franzetti F, Degli Esposti A, Lizioli A, et al. Tuberculosis among immigrants from developing countries in the province of Milan, 1993-1996. Int J Tuberc Lung Dis. 1999;3(7):589-95.PMID: 10423221
- 27. Lillebaek T, Andersen AB, Bauer J, Dirksen A, Glismann S, de Haas P, et al. Risk of Mycobacterium tuberculosis transmission in a low-incidence country due to immigration from high-incidence areas. J Clin Microbiol. 2001;39(3):855-61. DOI: 10.1128/JCM.39.3.855-861.2001 PMID: 11230395
- 28. Dahle UR, Sandven P, Heldal E, Caugant DA. Continued low rates of transmission of Mycobacterium tuberculosis in Norway. J Clin Microbiol. 2003;41(7):2968-73. DOI: 10.1128/JCM.41.7.2968-2973.2003 PMID: 12843028
- 29. Diel R, Rüsch-Gerdes S, Niemann S. Molecular epidemiology of tuberculosis among immigrants in Hamburg, Germany. J Clin Microbiol. 2004;42(7):2952-60. DOI: 10.1128/JCM.42.7.2952-2960.2004 PMID: 15243044
- Kamper-Jørgensen Z, Andersen AB, Kok-Jensen A, Kamper-Jørgensen M, Bygbjerg IC, Andersen PH, et al. Migrant tuberculosis: the extent of transmission in a low burden country. BMC Infect Dis. 2012;12(1):60. DOI: 10.1186/1471-2334-12-60 PMID: 22423983
- Eurostat. Migration and migrant population statistics 2014. [Accessed 25 August 2014]. Available from: http://ec.europa.eu/eurostat/statistics-explained/index.php/ Migration_and_migrant_population_statistics
- 32. Taylor AB, Kurbatova EV, Cegielski JP. Prevalence of antituberculosis drug resistance in foreign-born tuberculosis cases in the U.S. and in their countries of origin.PLoS One. 2012;7(11):e49355. DOI: 10.1371/journal.pone.0049355 PMID: 23145161
- 33. Minion J, Gallant V, Wolfe J, Jamieson F, Long R. Multidrug and extensively drug-resistant tuberculosis in Canada 1997-2008: demographic and disease characteristics.PLoS One. 2013;8(1):e53466. DOI: 10.1371/journal.pone.0053466 PMID: 23326436
- 34. N A, Ahmad F, Huda N. Osteoarticular tuberculosis-a three years' retrospective study. J Clin Diagn Res. 2013;7(10):2189-92. PMID: 24298472
- 35. Solovic I, Jonsson J, Korzeniewska-Koseła M, Chiotan DI, Pace-Asciak A, Slump E, et al. Challenges in diagnosing extrapulmonary tuberculosis in the European Union, 2011. Euro Surveill. 2013;18(12):20432.PMID: 23557946
- 36. World Health Organization (WHO). The global health sector strategy on HIV/AIDS 2011-2015: an interim review of progress: abridged report. Geneva: WHO; 2014. Available from: http://

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- apps.who.int/iris/bitstream/10665/112790/1/9789241507295_eng.pdf?ua=1
- 37. Uchimura K, Ngamvithayapong-Yanai J, Kawatsu L, Ohkado A, Yoshiyama T, Shimouchi A, et al. Characteristics and treatment outcomes of tuberculosis cases by risk groups, Japan, 2007-2010. Western Pac Surveill Response J. 2013;4(1):11-8. DOI: 10.5365/wpsar.2012.3.4.016 PMID: 23908950
- 38. Falzon D, Scholten J, Infuso A. Tuberculosis outcome monitoring--is it time to update European recommendations? Euro Surveill. 2006;11(3):20-5. PMID: 16567878
- 39. Borgdorff MW, Veen J, Kalisvaart NA, Broekmans JF, Nagelkerke NJ. Defaulting from tuberculosis treatment in The Netherlands: rates, risk factors and trend in the period 1993-1997.Eur Respir J. 2000;16(2):209-13. DOI: 10.1034/j.1399-3003.2000.16bo5.x PMID: 10968493

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