RESEARCH ARTICLE

The effect of migration within the European Union/ European Economic Area on the distribution of tuberculosis, 2007 to 2013

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Immigration from tuberculosis (TB) high-incidence countries is known to contribute notably to the TB burden in low-incidence countries. However, the effect of migration enabled by the free movement of persons within the European Union (EU)/European Economic Area (EEA) on TB notification has not been analysed. We analysed TB surveillance data from 29 EU/EEA countries submitted for the years 2007-2013 to The European Surveillance System. We used place of birth and nationality as proxy indicators for native, other EU/EEA and non-EU/EEA origin of the TB cases and analysed the characteristics of the subgroups by origin. From 2007-2013, a total of 527,467 TB cases were reported, of which 129,781 (24.6%) were of foreign origin including 12,566 (2.4%) originating from EU/EEA countries other than the reporting country. The countries reporting most TB cases originating from other EU/EEA countries were Germany and Italy, and the largest proportion of TB cases in individuals came from Poland (n=1,562) and Romania (n=6,285). At EU/ EEA level only a small proportion of foreign TB cases originated from other EU/EEA countries, however, the uneven distribution of this presumed importation may pose a challenge to TB programmes in some countries.

Introduction

The epidemiology of communicable diseases can be affected by migration; between 2007 and 2011, around 40% of HIV cases in the European Union (EU) and European Economic Area (EEA) were reported among migrants [1] [2] [3]. Migration from high-incidence countries (defined as incidence as ≥20 tuberculosis (TB) cases/100,000 inhabitants/year) is known to contribute notably to TB burden in low-incidence countries (<20 TB cases/100,000 inhabitants/year) using the thresholds previously proposed by the Wolfheze working group [4] and adopted in the EU monitoring framework [5] [6-14]. Persons with latent TB infection as well as patients with active TB and multidrug-resistant (MDR) TB can easily move from one country to another in the EU.

The free movement of persons within the EU is a fundamental right guaranteed to EU citizens by the Treaties [15]. Before 2010, the migration flows within the EU/ EEA were mainly from eastern European Member States to Member States in the south and west [16] [17]. Driven by the economic crisis, from 2007 onwards, an increase was seen in numbers of people migrating from the countries most heavily affected by the depression (Greece, Spain, Italy, Ireland and Portugal) to western and northern EU countries [16]. In 2013, 17.7 million EU citizens were living in an EU country other than their country of birth, corresponding to 3.5% of the total population [18]. The highest number of migrants from other EU countries resided in Germany (3,635,265; 4.4% of the total population) and the lowest in Estonia (13,238; 1.0% of the total population). Possible crossborder transmission of communicable diseases as a consequence of free movement of persons across the borders has raised concerns in some countries [19,20].

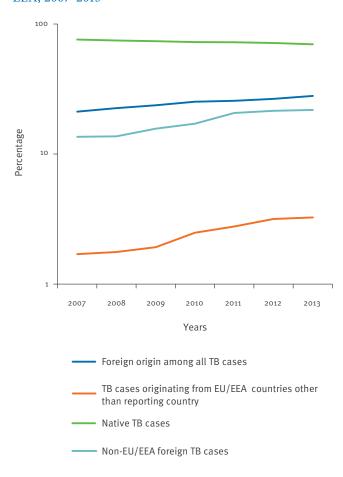
To our knowledge, the effect of migration within the EU/EEA on the epidemiology of TB has not been analysed previously. The objective of this study was therefore to estimate the extent of cross-border movement of TB cases within the EU/EEA. In addition, we aimed to characterise the 'foreign' TB cases originating from other EU/EEA countries, and to identify possible major patterns with respect to countries from which cases originate and which countries report such cases. Our quantitative descriptive analysis of the EU/EEA-wide TB surveillance data by geographical origin of cases may support decisions to implement targeted TB prevention and control measures where needed.

Methods

We carried out a descriptive analysis of all TB cases reported to The European Surveillance System (TESSy)

FIGURE 1

Proportions of tuberculosis cases by origin in the EU/ EEA, 2007–2013



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

by national surveillance institutes in 27 EU and two EEA countries from 2007 to 2013. Data collection methods and definitions are described elsewhere [21]. Liechtenstein reported TB surveillance data to TESSy only in 2007 and Croatia joined the EU in July 2013, so both countries were excluded from the analysis.

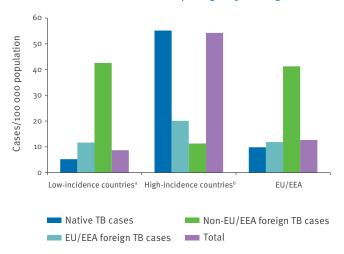
After submission to TESSy, data are subjected to automated checks for completeness and accuracy followed by expert-driven manual data validation. For the calculation of notification rates, country population denominators were obtained from Eurostat (www.epp. eurostat.ec.europa.eu) [18]. Notification rates for 'foreign TB cases' of EU/EEA origin and non-EU/EEA origin, and for the native population were calculated only for 2013 due to incomplete historical population data stratified by area of origin from Eurostat [18].

Definition of native and foreign tuberculosis cases

For Austria, Belgium, Greece, Hungary and Poland, we used citizenship to assign geographic origin, for the remaining 24 countries place of birth was used as a proxy indicator for the geographic origin of a TB case.

FIGURE 2

Tuberculosis notification rates in low^a- and high-incidence^b EU/EEA countries by subgroup of origin, 2013



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

Low-incidence countries are defined as having an incidence <20 TB cases per 100,000 inhabitants per year, and high-incidence countries as having an incidence ≥20 TB cases per 100,000 inhabitants per year, using the thresholds previously proposed by the Wolfheze working group [4] and adopted in the EU monitoring framework [5].

a Low TB incidence countries: Austria, Belgium, Cyprus, Czech Republic, Denmark, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Luxembourg, Malta, the Netherlands, Norway, Poland, Slovakia, Slovenia, Spain, Sweden and United Kingdom.

b High TB incidence countries: Bulgaria, Estonia, Latvia, Lithuania, Portugal and Romania.

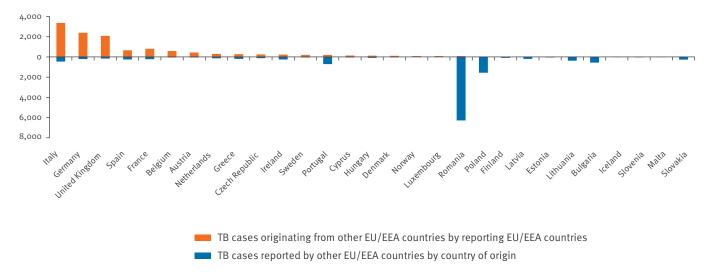
A 'native TB case' was defined as a TB case reported by the patient's country of birth or citizenship, and a 'foreign TB case' as a case reported by a country different from the patient's country of birth or citizenship. The foreign cases were further divided into cases originating from outside of the EU/EEA and cases from other EU/EEA countries. Cases defined as 'foreign' but with missing country of origin, were excluded from the analysis. Cases originating from countries that do not exist any longer i.e. 'Soviet Union', 'Yugoslavia', 'Czechoslovakia' were recoded as 'foreign, country not specified'. TB cases originating from Greenland and Faroe Islands were considered as native Danish cases, and the cases originating from Jersey and Gibraltar were classified as native cases of the United Kingdom (UK).

Data analysis

We analysed the data by age and sex, site of disease, previous treatment, laboratory confirmation, and drug susceptibility testing results for the two main first-line anti-TB drugs (isoniazid and rifampicin), HIV co-infection and treatment success 12 months after start of treatment. The distribution of these variables was stratified by origin, excluding the unknowns where

FIGURE 3

Tuberculosis cases originating from other EU/EEA countries by reporting EU/EEA country and tuberculosis cases reported by other EU/EEA countries by country of origin, 2007–2013



EEA: European Economic Area; EU: European Union.

applicable. In a sensitivity analysis, we excluded all native cases reported by Romania and Poland. Both countries accounted for large shares of native cases and foreign cases reported by other EU/EEA countries while hardly reporting any cases of other EU/EEA origin themselves. The exclusion of Romanian and Polish native cases was thus meant to identify and avoid any potential bias resulting from largely comparing foreign and native cases from these two countries.

To compare incidence levels, countries were grouped as high- and low-incidence TB countries based on the data reported for 2013. Thus, high-incidence countries were six countries: Bulgaria, Estonia, Latvia, Lithuania, Portugal and Romania, and low-incidence countries all other EU/EEA countries.

For data analysis, we used Stata 13 (StataCorp LP, College Station, Texas, US) and Microsoft Excel 2010. Chi-squared tests were used to analyse differences between percentages. A p value of less than 0.01 was considered as statistically significant.

Results

During the period 2007 to 2013, a total of 527,467 TB cases (notification rate 14.9/ 100,000) were reported of which 11,788 cases (2.2%) were reported as 'origin unknown'. Of these cases with unknown origin, 11,595 (98.4%) were reported from countries defining origin by country of birth and 193 (1.6%) from countries defining origin by citizenship. Of the remaining 515,679 cases, 385,898 (74.8%) were reported as native and 129,781 (25.2%) as foreign. Among foreign cases, 121,994 (94.0%) were defined by country of birth and 7,787 (6.0%) by citizenship. Country of origin was reported for 104,491 (80.5%) of all foreign cases

whereas 25,290 (19.5%) foreign cases were reported without country of birth/citizenship. Country-specific proportions of foreign TB cases with country of origin reported ranged from 0.1% (213/147,843) in Romania to 85.7% (2,090/2,438) in Norway. The vast majority, 91,925 (88.0%) of foreign TB cases with known origin came from outside the EU/EEA. In total, 12,566 cases (2.4% of all TB cases and 9.7% of foreign TB cases) were reported to originate from another EU/EEA country. Country-specific proportions of foreign TB cases of EU/EEA origin varied between 0.05% (9/18,365) in Bulgaria and 36.6% (136/372) in Cyprus (Table 1). Most of the foreign TB cases of EU/EEA origin were diagnosed in Italy 3,368 (12.2% of all cases reported in Italy), Germany (2,388; 7.7%) and the UK (2,089; 3.5%). The proportion of TB cases originating from another EU/EEA country was reported to be below 1% in seven countries (Bulgaria, Latvia, Lithuania, Poland, Romania, Slovakia and Slovenia); 1 up to 10% in 18 countries (Austria, Belgium, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Malta, the Netherlands, Norway, Portugal, Spain, Sweden and UK) and more than 10% in Cyprus, Iceland, Italy and Luxembourg.

Even though the overall TB notification rate declined by 5% annually from 2007 to 2013, the number of foreign TB cases from other EU/EEA countries increased from 1,428 (1.7% of all TB cases) in 2007 to 2,093 (3.3%) in 2013 (p<0.01), while the overall number of foreign TB cases increased from 17,809 (21.2%) in 2007 to 18 011 (28.0%) in 2013 (Figure 1). In the same period, the number of cases with unknown origin decreased from 2,384 (2.8%) to 1,407 (2.2%).

TABLE 1

Total numbers and notification rates of tuberculosis cases per 100,000 population and percentage of cases of foreign origin and foreign EU/EEA origin, 2007–2013

Country	Total number of notified TB cases	TB notification rate per 100,000	Number of TB cases originating from outside the reporting country ^a	Percentage of foreign origin	Number of notified TB cases in persons originating from other EU/EEA countries ^a	Percentage of foreigners originating from other EU/EEA countries	Percentage of EU/EEA foreign cases among all cases
Austria	5,058	8.6	2,119	41.9	440	20.8	8.7
Belgium	7,065	9.3	3,595	50.9	581	16.2	8.2
Bulgaria	18,365	35.3	44	0.2	9	20.5	0.05
Cyprus	372	6.5	301	80.9	136	45.2	36.6
Czech Republic	4,771	6.5	884	18.5	242	27.4	5.1
Denmark	2,597	6.7	1,560	60.1 108		6.9	4.2
Estonia	2,592	27.7	441	17.0	27	6.1	1.0
Finland	2,289	6.1	574	25.1	33	5.7	1.4
France	36,632	8.1	17,547	47.9	799	4.6	2.2
Germany	31,197	5.4	14,360	46.0	2,388	16.6	7.7
Greece	3,966	5.1	1,601	40.4	269	16.8	6.8
Hungary	10,165	14.7	228	2.2	133	58.3	1.3
Iceland	82	3.7	55	67.1	9	16.4	11.0
Ireland	3,003	9.5	1,295	43.1	225	17.4	7.5
Italy	27,695	6.6	13,684	49.4	3,368	24.6	12.2
Latvia	7,019	47.3	385	5.5	33	8.6	0.5
Lithuania	14,067	64.5	360	2.6	24	6.7	0.2
Luxembourg	232	6.6	144	62.1	78	54.2	33.6
Malta	292	10.1	233	79.8	6	2.6	2.1
The Netherlands	7,048	6.1	5,005	71.0	295	5.9	4.2
Norway	2,438	7.2	2,090	85.7	85	4.1	3.5
Poland	55,709	20.8	345	0.6	36	10.4	0.1
Portugal	19,336	26.6	2,709	14	201	7.4	1.0
Romania	147,843	104.4	213	0.1	78	36.6	0.1
Slovakia	3,405	9.0	48	1.4	8	16.7	0.2
Slovenia	1,261	8.8	341	27	9	2.6	0.7
Spain	49,222	15.2	15,058	30.6	662	4.4	1.3
Sweden	4,163	6.4	3,518	84.5	195	5.5	4.7
UK	59,583	13.7	41,044	68.9	2,089	5.1	3.5
Total	527,467	14.9	129,781	24.6	12,566	9.7	2.4

EEA: European Economic Area; EU: European Union; TB: tuberculosis; UK: United Kingdom.

Compared with native TB cases, cases from other EU/EEA countries were more frequently female, 15 to 44 years old and affected by pulmonary TB. Their previous treatment, culture result and treatment outcome were less commonly known, and they were less frequently successfully treated. In contrast, they were more frequently tested for susceptibility to TB drugs than native cases, but found to have 38% less MDR TB. Finally, compared with native TB cases, cases from other EU/EEA countries were 60% less frequently tested for HIV co-infection; those tested, however, were not significantly more often HIV-positive than native cases (Table 2).

A statistically significant difference (p<0.01) between the native cases and TB cases originating from other EU/EEA countries was seen for all the clinical and microbiological characteristics except for the proportions of cases with unknown site of disease and the proportions of HIV-positive cases.

Excluding Romanian and Polish native cases from this analysis made no difference to these findings.

^aData on country of origin not reported from years 2007 to 2010 by France, and from 2008 and 2009 by Portugal.

Notification rates by geographical origin of tuberculosis cases

Of the 64,327 TB cases notified in 2013, 44,909 (69.8%) were native TB cases, providing a notification rate of 9.8 per 100,000 for the native population. Of the total number of foreign cases, 14,050 (21.8%) were reported among foreigners originating from outside of the EU/EEA (notification rate 41.3/100,000 population), and 2,093 (3.3%) among foreigners originating from the EU/EEA outside of the reporting country (notification rate 11.9/100,000 population).

The vast majority, 2,015 (96.3% of all foreign cases from EU/EEA countries), of foreign TB cases originating from the EU/EEA, were reported in low-incidence countries and only 78 (3.7%) were registered in high-incidence EU countries in 2013. As illustrated in Figure 2, in 2013 the notification rate per 100,000 migrant population with EU/EEA origin was 20.1 for high-incidence countries, which is about one third of the notification rate among the native population (55.2), and almost two times higher than the notification rate among foreigners coming from outside the EU/EEA (11.3). The notification rate of 11.7 per 100,000 population observed in low-incidence countries among foreigners originating from the EU/EEA is twice as high as among the national population (5.2), and less than one third of the notification rate of TB cases coming from outside of EU/EEA (42.6) (Figure 2).

Country of origin of tuberculosis cases with foreign EU/EEA origin

TB cases originating from other EU/EEA countries, originated from 29 different countries: 6,285 cases (50.0%) from Romania, 1,562 (12.4%) from Poland, 704 (5.6%) from Portugal, 563 (4.5%) from Bulgaria, and 458 (3.6%) from Italy (Figure 3).

At the EU/EEA level, the seven-year average proportion of cases originating from other EU/EEA countries was 2.4%, but in some countries the share was much higher, reaching up to 36.6% of all TB cases reported in Cyprus during 2007 to2013, 33.6% in Luxembourg, 11.0% in Iceland and 12.2% in Italy (Table 1). A vast majority (92.5%) of TB cases from other EU/EEA countries reported by Italy originated from Romania, the country with the highest burden of TB in the EU/EEA.

Discussion

Our results show that only 3.3% (2,093/64,327) of TB cases notified in the EU/EEA in 2013 originated from other EU/EEA countries. This roughly matches the 3.5% of all persons residing in the EU that originated from other EU countries in 2013 [18]. Therefore, free movement between countries within the EU/EEA does not seem overall to cause disproportionate challenges for TB prevention and control in the EU/EEA.

Throughout the study period, the proportion of foreign TB cases originating from other EU/EEA countries slowly increased from 1.7 to 3.3% of all TB cases, while the percentage of native TB cases declined from 76.0% to 69.8%. There were notable differences between the numbers of TB cases originating from the respective countries and 'foreign TB cases' from EU/EEA reported by them. The migration flow of TB cases was mainly from TB high-incidence countries to low-incidence countries. This is expected since the TB burden is divided unevenly across the EU [22]. In 2007 to 2013, Germany, Italy and the UK reported most foreign TB cases from other EU/EEA countries and Bulgaria, Poland and Romania were the countries from which most TB cases from EU/EEA countries reported by other EU/EEA countries originated. In 2013, the EU countries with the largest population of EU immigrants were France, Germany and the UK [18] and the EU countries with the highest numbers of emigrants were Poland, Romania and Spain [23]. We do not see a clear pattern in the size of the migrant population from other EU/EEA countries and the number of foreign TB cases from other EU/EEA countries. This is expected as TB in migrants does not only depend on the size of the migrant population but also on the TB incidence in the country of origin and other factors such as living conditions of migrant populations and mixing patterns [14]. In general, the level of TB transmission is not high between groups of different ethnic origin in the EU/EEA [24], however, it is not known whether this applies to the migrants originating from the other EU/EEA countries.

Our study design entails some limitations. In the absence of data indicating in which country the infection was contracted, we used the country of birth and citizenship as proxy indicators for origin of the TB cases. This might have led to under- or overestimation of the case numbers in the subgroups by geographical origin, for example if native cases actually got infected abroad, or if foreign cases were infected in their current country of residence. In addition, the comparability of data between countries is compromised by three factors: not all countries have reported all data for the whole period 2007 to 2013; the method of reporting differs between countries; and some reporting practices applied by individual countries, e.g. relating to origin, previous treatment, drug susceptibility testing and treatment outcome are not consistent over time. For the descriptive analysis presented here, possible interactions between parameters like sex ratio and age distribution of migrants have not been taken into account. Finally, under-reporting of TB may have led to an underestimation of TB burden. Recent studies from England [25], Greece [26] and regions within Italy [27], the Netherlands [28], Romania [29] and Spain [30] have estimated under-reporting to range between 15% and 80%. One of these studies, however, found that underreporting applied less to migrants than the native population (18% vs 68%) [27].

Our results show that drug susceptibility testing results were available more frequently for foreign TB cases of EU/EEA origin than native cases. This is supported by the fact that the main countries reporting TB cases in

TABLE 2

Comparison of native and foreign tuberculosis cases originating from within or outside of the EU/EEA, 2007-2013a

	Nativa		p-value ^b		Fc	reign cases	
	Native	cases	EU/EEA origin		non-EU/EEA origin		
	N	%		N	%	N	%
Total	385,898	73.2	⟨0.01	12,566	2.4	91 925	17.4
Sex							
Female	130,124	33.7	⟨0.01	4.638	36.9	38,580	42.0
Male	255,523	66.2	⟨0.01	7,891	62.8	53,122	57.8
Unknown	251	0.1	⟨0.01	37	0.3	223	0.2
Age groups							
0-14	17,499	4.5	⟨0.01	506	4.0	2,601	2.8
15-24	37,285	9.7	⟨0.01	1 880	15.0	14,741	16.0
25-44	116,386	30.2	⟨0.01	6 040	48.1	48,683	53.0
45-64	132,046	34.2	⟨0.01	2 748	21.9	17,611	19.2
≥65	82,331	21.3	⟨0.01	1 349	10.7	8,157	8.9
Unknown	351	0.1	⟨0.01	43	0.3	132	0.1
Site of disease							
Pulmonary	322 277	83.5	⟨0.01	10 850	86.3	53 111	57.8
Extrapulmonary	63 025	16.3	⟨0.01	1 686	13.4	38 463	41.8
Unknown	596	0.2°	p=0.02	30	0.2 ^c	351	0.4
Previous treatment ^d							
No	308,126	79.8	⟨0.01	8,371	66.6	70,386	76.6
Yes	57,822	15.0	⟨0.01	891	7.1	5,721	6.2
Unknown	19,950	5.2	⟨0.01	3,304	26.3	15,818	17.2
HIV infection ^e							
HIV tested	81,518	21.1	⟨0.01	1,060	8.4	5,876	6.4
HIV infected ^f	3,634	4.5	p=0.03	62	5.8	567	9.6
Culture result							
Positive	238,373	61.8	⟨0.01	8,099	64.5	56,766	61.8
Negative	80,066	20.7	⟨0.01	1,261	10.0	8,321	9.1
Unknown	67,459	17.5	⟨0.01	3,206	25.5	26,838	29.2
DST result total	325,278	NA	NA	7,737	NA	71,386	NA
Test performed ^g	141,097	43.4	⟨0.01	5,419	70	46,393	65.0
MDR-TB	8,450	6.0	⟨0.01	200	3.7	1,356	2.9
Cohort 2007–2012 total	340,989	NA	NA	10,417	NA	77,845	NA
Treatment outcome reported	298,464	87.5	⟨0.01	6,618	63.5	63,600	81.7
Treatment success ^h	223,323	74.8	⟨0.01	4,449	67.2	49,256	77-4

DST: drug susceptibility testing; EEA: European Economic Area; EU: European Union; HIV: human immunodeficiency virus, MDR: multidrugresistant; NA: not applicable; TB: tuberculosis; UK: United Kingdom.

^a Origin (native/foreign) was not reported for 11,788 (2.2% from all reported) cases and country of origin was not specified for 25,290 (4.8% from all reported) cases.

^b Comparing EU/EEA foreigners and native TB cases.

^c Real percentage of unknown site information for foreign cases of EU/EEA origin is 0.24 and for native cases 0.15.

^d Equals previous treatment history (reported as 'previous diagnosis' by Belgium, Denmark, Ireland, Norway, Sweden (2007) and the UK).

 $^{^{\}mathrm{e}}$ TB cases reported by countries that reported only HIV-positive cases are excluded from the nominator.

f Percentages based on HIV-tested cases.

g Percentage of cases tested for drug susceptibility to isoniazid and rifampicin among all culture-positive cases, excluding countries who did not report case-based DST data.

^h Calculated outcome after 12 months of treatment for all cases reported 2007 to 2012. France, Greece and Italy did not report treatment outcome results and are excluded from the treatment outcome analysis.

migrants of EU/EEA origin report higher proportions of drug susceptibility testing than the main countries reporting native cases, Romania and Poland. In 2007 to 2013, the proportion of MDR-TB was lower among foreign cases originating from other EU/EEA countries than in native cases. Also, of all MDR-TB cases reported by low-incidence countries of the EU/EEA, less than 10% originated from other EU/EEA countries. This implies that migration within the EU/EEA is not the main driver of MDR-TB incidence in low-incidence EU/EEA countries.

The mean age of foreign TB cases of EU/EEA origin was lower than among the native TB cases. It is not surprising that most of the foreign TB cases of EU/EEA origin occur within the population at working age considering that the most frequent factor influencing the decision to migrate in the EU is employment [16], followed by family reunion, study and retirement. The proportion of culture-positive and of pulmonary cases was higher among migrants from EU/EEA countries than among natives. This could possibly be explained by migrants having a higher threshold for seeking healthcare in a foreign country and the challenge of accessing healthcare in a foreign country, leading to a delayed diagnosis and more advanced disease.

We noted that the completeness of data on TB treatment history was exceptionally low and the treatment outcome 12 months after start of treatment was less frequently reported for foreign cases originating from other EU/EEA countries compared with native cases and cases from non-EU/EEA countries. Persons diagnosed with TB in another EU/EEA country may decide to return to their country of origin for treatment. In this case the treatment outcome may not be made available to the country that diagnosed the case. The issues in cross-border exchange of TB case information have been identified before [31,32], and the need for facilitated referral and exchange of information between EU/EEA countries is evident.

In conclusion, the uneven distribution of TB diagnosed in persons originating from other EU/EEA countries within the EU/EEA may pose an incentive for coordinated EU action to improve TB programmes in individual countries. Awareness of the number of cases deriving from specific EU high-incidence countries can facilitate targeted TB prevention and control efforts in receiving countries, optimally in collaboration with the TB cases' countries of origin. In all EU/EEA countries, however, the number of TB cases from non-EU/EEA countries was higher than the number of foreign TB cases originating from other EU/EEA countries [33], implying that TB control efforts addressing migrant populations should primarily focus on migrants coming from TB-endemic regions outside of the EU/EEA.

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Conflict of interest

None declared.

Authors' contributions

Vahur Hollo coordinated the data analysis, wrote the manuscript and contributed to the study design. Saara Magdalena Kotila drafted parts of the manuscript, contributed to the revision of the manuscript and data analysis. Csaba Ködmön contributed to the data analysis and study design. Phillip Zucs contributed to the study design, data analysis and the manuscript writing. Marieke Johanna van der Werf contributed to the design of the study, interpreted the results and revised the manuscript.

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