

Tuberculosis in immigrants in Finland, 1995–2013

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SUMMARY

Increasing immigration from high tuberculosis (TB) incidence countries is a challenge for surveillance and control in Finland. Here, we describe the epidemiology of TB in immigrants by using national surveillance data. During 1995–2013, 7030 (84.7%) native and 1199 (14.4%) immigrant cases were identified. The proportion of immigrant cases increased from 5.8% in 1995 to 32.1% in 2013, consistent with increasing immigrant population (2.1–5.6%) and decreasing incidence of TB in the native population (from 12.1 to 3.5/100 000). TB cases in immigrants were significantly younger, more often female, and had extrapulmonary TB more often than native cases ($P < 0.01$ for all comparisons); multidrug resistance was also more common in immigrants than natives ($P < 0.01$). Immigrant cases were born in 82 different countries; most commonly in Somalia and the former Soviet Union/Russia. During 2008–2013, 433 *Mycobacterium tuberculosis* isolates from immigrants were submitted for spoligotyping; 10 different clades were identified. Clades were similar to those found in the case's country of birth. Screening immigrants from high-incidence countries and raising awareness of common characteristics and symptoms of TB is important to ensure early diagnosis and to prevent transmission.

Key words: Epidemiology, immigrants, molecular epidemiology, *Mycobacterium tuberculosis*, spoligotyping, tuberculosis (TB).

INTRODUCTION

According to the World Health Organization (WHO), tuberculosis (TB) remains one of the most important infectious diseases, with an estimated 8.6 million incident TB cases and about 1.3 million deaths reported globally in 2013 [1]. Finland is classified as a low

TB incidence country (<10/100 000 population) [2]. However, increasing immigration from high TB incidence countries constitutes a growing risk group for TB. The recent transition from an epidemiological situation where most reported cases have been reactivation of latent TB infection in older Finnish adults to highly infectious pulmonary TB cases in young immigrants has implications for national screening, diagnosis and treatment strategies for TB [3]. We evaluated national trends in the epidemiology of TB cases in immigrants during 1995–2013 and characterized

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Mycobacterium tuberculosis isolates by genotyping and antimicrobial susceptibility patterns during 2008–2013 by using population-based surveillance data.

METHODS

National surveillance of TB in Finland

Clinical microbiology laboratories notify new *M. tuberculosis* isolations directly to the National Infectious Disease Register (NIDR) and submit isolates to the Mycobacterial Reference Laboratory at National Institute for Health and Welfare (THL) for drug susceptibility testing and genotyping. In addition, physicians notify clinically suspected or confirmed TB cases; reporting is mandatory. From 1995 to 2006, the case definition for TB surveillance included all culture or sputum smear-positive cases or histologically confirmed cases. However, with the adoption of the standard European Union case definition for TB in 2007 [4] a new reporting category was added to NIDR: ‘physician’s decision to initiate full TB treatment on the basis of clinical suspicion of TB despite lack of laboratory confirmation’. Data collected with each notification include age, gender, country of birth, nationality, place of residence, date of diagnosis, and clinical syndrome of TB (pulmonary/extrapulmonary).

Laboratory methods

M. tuberculosis isolates from culture-positive TB cases reported during 2008–2013 were characterized by spoligotyping according to standard methods at the THL Mycobacterial Reference Laboratory [5]. The resulting spoligotype patterns were compared to the data in the international SITVITWEB database [6]. An isolate was assigned a shared type (SIT) if the same spoligotype was found in the database. Genotypic clades were obtained from the SITVITWEB database.

Definitions

Pulmonary and extrapulmonary TB were defined according to WHO guidelines [1]. In this study, a native was defined as a person born in Finland or, if the country of birth was not known, the most recent nationality was Finnish. An immigrant was defined as a person whose country of birth was not Finland or, when the country of birth was not known, the most recent nationality was other than Finnish.

Population data

The number of persons immigrating to Finland by year and country and the size of different immigrant populations in Finland was obtained from the Statistics Finland population database (National Population Information System) which contains data on all persons residing legally in Finland (http://www.stat.fi/index_en.html).

Statistical analysis

Statistics Finland data were used as denominators to calculate age- and gender-specific TB incidence rates. Statistical significance for categorical variables were analysed with the χ^2 test or Fisher’s exact test. Continuous variables were analysed using the Mann–Whitney *U* test. A Poisson regression model was used to assess the significances of the log-linear trend in annual incidence rates. IBM SPSS v. 22.0 (SPSS Inc., USA) and Microsoft Excel (Microsoft Corp., USA) were used to analyse the data.

RESULTS

From 1995 to 2013, a total of 8299 TB cases were reported to NIDR. Of these cases, 7030 were defined as native [6978 (84.1%) on the basis of country of birth and 52 (0.6%) on the basis of most recent nationality]; 1199 (14.4%) of reported cases were defined as immigrants, 1085 (90.5%) on the basis of country of birth and 114 (9.5%) on the basis of most recent nationality (Table 1). Overall, 74 (0.9%) had no information on country of birth or nationality.

The annual incidence of TB in Finland decreased from 12.8/100 000 population in 1995 to 5.0/100 000 in 2013. The number of TB cases decreased by 58.6% during this period (Table 1). TB cases in the native population decreased by 70.0% from 1995 to 2013. The Poisson regression model showed a decreasing log-linear trend in the TB rate both overall ($P < 0.001$) and for natives ($P < 0.001$), with mean annual rate decreases of 5.2% and 6.7%, respectively. During the same period, the number of TB cases in immigrants increased by 128.9%. However, as the number of immigrant population increased, the trend in TB rate was not significant ($P = 0.344$). The overall incidence of TB in immigrants ranged between 24.7 and 53.6/100 000 by year.

The proportion of reported TB cases who were immigrants increased from 5.8% in 1995 to 32.1% in

Table 1. Incidence of tuberculosis cases in all, native and immigrant populations in Finland, 1995–2013

Year	All cases			Native cases			Immigrant cases		
	Population in Finland*	No. of cases†	Incidence‡ (95% CI)	Native population in Finland (%)*	No. of cases (%)	Incidence‡ (95% CI)	Immigrant population in Finland (%)*	No. of cases (%)	Incidence‡ (95% CI)
1995	5 116 826	654	12.8 (11.8–13.8)	5 010 523 (97.9)	608 (93.0)	12.1 (11.2–13.1)	106 303 (2.1)	38 (5.8)	35.7 (26.0–49.1)
1996	5 132 320	632	12.3 (11.4–13.3)	5 021 189 (97.8)	584 (92.4)	11.6 (10.7–12.6)	111 131 (2.2)	41 (6.5)	36.9 (27.2–50.1)
1997	5 147 349	557	10.8 (10.0–11.8)	5 029 279 (97.7)	508 (91.2)	10.1 (9.3–11.0)	118 070 (2.3)	46 (8.3)	39.0 (29.2–52.0)
1998	5 159 646	610	11.8 (10.9–12.8)	5 034 596 (97.6)	549 (90.0)	10.9 (10.0–11.9)	125 050 (2.4)	58 (9.5)	46.4 (35.9–60.0)
1999	5 171 302	598	11.6 (10.7–12.5)	5 040 182 (97.5)	541 (90.5)	10.7 (9.9–11.7)	131 120 (2.5)	47 (7.9)	35.8 (26.9–47.7)
2000	5 181 115	545	10.5 (9.7–11.4)	5 044 912 (97.4)	49 (91.2)	9.9 (9.0–10.8)	136 203 (2.6)	47 (8.6)	34.5 (25.9–45.9)
2001	5 194 901	503	9.7 (8.9–10.6)	5 049 766 (97.2)	434 (86.3)	8.6 (7.8–9.4)	145 135 (2.8)	66 (13.1)	45.5 (35.7–57.9)
2002	5 206 295	477	9.2 (8.4–10.0)	5 054 238 (97.1)	428 (89.7)	8.5 (7.7–9.3)	152 057 (2.9)	49 (10.3)	32.2 (24.4–42.6)
2003	5 219 732	415	8.0 (7.2–8.8)	5 060 865 (97.0)	363 (87.5)	7.2 (6.5–7.9)	158 867 (3.0)	51 (12.3)	32.1 (24.4–42.2)
2004	5 236 611	335	6.4 (5.7–7.1)	5 070 250 (96.8)	290 (86.6)	5.7 (5.1–6.4)	166 361 (3.2)	42 (12.5)	25.2 (18.7–34.2)
2005	5 255 580	373	7.1 (6.4–7.9)	5 078 968 (96.6)	319 (85.5)	6.3 (5.6–7.0)	176 612 (3.4)	54 (14.5)	30.6 (23.4–39.9)
2006	5 276 955	295	5.6 (5.0–6.3)	5 089 045 (96.4)	239 (81.0)	4.7 (4.1–5.3)	187 910 (3.6)	53 (18.0)	28.2 (21.5–36.9)
2007	5 300 484	350	6.6 (5.9–7.3)	5 097 956 (96.2)	276 (78.9)	5.4 (4.8–6.1)	202 528 (3.8)	74 (21.1)	36.5 (29.1–45.9)
2008	5 326 314	343	6.4 (5.8–7.2)	5 107 688 (95.9)	288 (84.0)	5.6 (5.0–6.3)	218 626 (4.1)	54 (15.7)	24.7 (18.9–32.2)
2009	5 351 427	416	7.8 (7.1–8.6)	5 118 244 (95.6)	285 (68.5)	5.6 (5.0–6.3)	233 183 (4.4)	125 (30.0)	53.6 (45.0–63.9)
2010	5 375 276	323	6.0 (5.4–6.7)	5 127 141 (95.4)	213 (65.9)	4.2 (3.6–4.8)	248 135 (4.6)	106 (32.8)	42.7 (35.3–51.7)
2011	5 401 267	326	6.0 (5.4–6.7)	5 135 119 (95.1)	240 (73.6)	4.7 (4.1–5.3)	266 148 (4.9)	80 (24.5)	30.1 (24.1–37.4)
2012	5 426 674	276	5.1 (4.5–5.7)	5 141 203 (94.7)	182 (65.9)	3.5 (3.1–4.1)	285 471 (5.3)	81 (29.3)	28.4 (22.8–35.3)
2013	5 451 270	271	5.0 (4.4–5.6)	5 146 991 (94.4)	182 (67.2)	3.5 (3.1–4.1)	304 279 (5.6)	87 (32.1)	28.6 (23.2–35.3)
Total		8299			7026 (84.7)			1199 (14.4)	

CI, Confidence interval.

* Statistics Finland (www.stat.fi).

† Includes 74 cases without country of birth or nationality.

‡ Cases per 100 000 population.

Table 2. Characteristics of immigrant and native tuberculosis cases in Finland, 1995–2013

	Native (n = 7026)	Immigrant (n = 1199)	P value
Median age, years (min-max)	70 (0–105)	30 (1–93)	<0.01
Age group, years, n (%)			
0–14	34 (0.5)	55 (5)	
15–29	183 (3)	544 (45)	
30–44	522 (7)	396 (33)	
45–59	1417 (20)	111 (9)	
60–74	2268 (32)	53 (4)	
≥75	2602 (37)	40 (3)	
Male cases, n (%)	4027 (57)	609 (51)	<0.01
Pulmonary tuberculosis, n (%)	4870 (69)	726 (61)	<0.01
Smear positive, n (%)	2356 (48)	339 (47)	0.397
Multidrug resistance, n (%)	17 (0.2)	29 (2)	<0.01

2013 while the proportion of all immigrants in the Finnish population increased from 2.1% in 1995 to 5.6% in 2013. Over the period 1995–2013, TB cases in immigrants were significantly younger, more often female and had extrapulmonary TB more often than native cases (Table 2). Multidrug resistance was more common in immigrants than natives ($P < 0.01$). The median age of TB cases in immigrants remained stable at about 30 years (range 27–34 years). Minimum age was 1 year (range 1–16 years) and maximum age 93 years (range 70–93 years). Overall, 78.4% of the immigrant cases were aged 15–44 years.

The 1085 immigrant TB cases for whom data on the country of birth was available were born in 82 different countries (Table 3). The most common countries of origin were Somalia, the former Soviet Union/Russia and Vietnam. Of the 1085 immigrant TB cases, 947 (87.3%) were born in high-incidence countries (>50 cases/100 000 population) and 138 (12.7%) in middle- or low-incidence countries (<50 cases/100 000). Of the 947 cases born in high-incidence countries, 708 (74.8%) were born in very high-incidence countries (>150 cases/100 000).

Of the 1199 immigrant cases, 726 (60.6%) had pulmonary TB and 473 (39.4%) extrapulmonary TB. Of all pulmonary cases 410 (56.5%) were male, 339 (46.7%) were sputum smear positive (range 9–30 cases per year). Of the sputum smear-positive cases, 60 were born in Somalia, 40 in the former Soviet

Union/Russia, 26 in Vietnam and 16 in the former Socialist Federal Republic of Yugoslavia. The country of birth was unknown in 44 sputum smear-positive cases.

In 29 (2.4%) immigrant cases the *M. tuberculosis* isolate was resistant to at least isoniazid and rifampicin (MDR-TB) (Table 3). Of the 29 TB cases caused by a MDR-TB strain, eight were born in the former Soviet Union/Russia, eight in Somalia, three in Estonia and one each in The Netherlands, Pakistan, The Philippines, Lithuania and Thailand. The country of birth was unknown for five MDR-TB cases. During 1995–2004 and 2005–2013, there were 11 (range by year 0–4) and 18 (range by year 0–5) MDR-TB immigrant cases, respectively.

Genotyping

During 2008–2013, 533 cases of TB were reported in immigrants born in 57 countries. Of those, 433 (81.2%) *M. tuberculosis* isolates were submitted for genotyping. On the basis of the spoligotyping results, the isolates belonged in 10 different clades. The distribution of spoligotype clades in isolates obtained from immigrants is shown in Figure 1. The East-African-Indian (EAI) and T family were the most common clades in immigrants in Finland, 78 (18%) and 75 (17%) cases, respectively. Of TB cases born in Somalia both of these clades were common as there were 39 (28%) cases belonging to the EAI clade and 25 (18%) belonging to the T family. Altogether, nine different clades were identified in TB cases born in Somalia. There were 62 (14%) cases belonging to Beijing clade. Most of these cases were born in the former Soviet Union/Russian, Estonia, Vietnam or Thailand.

DISCUSSION

Our nationwide, population-based study showed that during the 19-year study period the number of TB cases in immigrants tripled as the immigrant population from high-incidence countries grew. The proportion of all TB cases who were immigrants increased more than fivefold reflecting both increased immigration and the decrease in the number of native TB cases in Finland. Reported TB cases were born in over 80 different countries, nearly 90% were born in high TB incidence countries and more than a third were born in Somalia. Patient characteristics in immigrant TB cases were different from native TB cases.

Table 3. Incidence of tuberculosis cases in immigrants by country of birth in Finland, 1995–2013

Country of birth*	Incidence of tuberculosis†	No. of cases (%)	Population at risk (person years)‡	Rate per 100 000/year (95% CI)	No. of multidrug-resistant cases	No. of pulmonary cases
Somalia	286	354 (33)	106 489	332 (299–368)	8	152
Ethiopia	247	36 (3)	19 408	185 (133–256)	0	26
Democratic Republic of the Congo	327	18 (2)	11 433	157 (99–249)	0	14
Afghanistan	189	36 (3)	26 935	134 (97–186)	0	25
Vietnam	147	76 (7)	66 661	114 (91–143)	0	54
Philippines	265	24 (2)	23 580	102 (68–152)	1	6
Thailand	119	60 (6)	73 593	82 (64–106)	1	29
India	176	35 (3)	43 912	80 (57–111)	0	11
Former Socialist Federal Republic of Yugoslavia	—	31 (3)	94 236	33 (23–47)	0	28
Iraq	45	26 (2)	87 668	30 (20–44)	0	19
Estonia	23	30 (3)	293 753	10 (7–14)	3	26
Former Soviet Union/Russia	91	83 (8)	834 489	10 (8–12)	8	68
Unknown	—	114 (10)	94 014	121 (101–145)	5	80
Other	—	276 (23)	1 732 031	16 (14–18)	3	188

CI, Confidence interval.

* By rate (high to low).

† Cases per 100 000 population (WHO, 2013 [1]).

‡ Statistics Finland (www.stat.fi).

In other low-incidence countries such as Sweden, Norway, Denmark and The Netherlands [7–13], TB cases in the immigrant population dominate the epidemiology of TB. In these countries, the proportion of immigrant cases varies between 50% and 85% of all cases. In Finland, the majority of TB cases are still reported in the native population and represent reactivation of an infection acquired decades ago when TB transmission was common. The number of native cases will probably decrease as the population of older adults with latent TB contracted decades ago decreases. Finland currently has fewer immigrants than other Nordic countries. However, as more foreign-born persons move to Finland, TB cases in the immigrant population are likely to change the epidemiological picture to become similar to other Nordic countries in the future.

Nearly 90% of the immigrant TB cases in Finland were born in countries where the incidence of TB is $\geq 50/100\,000$ population (e.g. Somalia, Russia, Vietnam and Thailand). Similar proportions have been reported from Sweden [8], Norway [9] and The Netherlands [14], where most immigrant cases are from Asia or Africa, mostly from Somalia. This

finding supports the strategy of focusing screening efforts on immigrants from high-incidence countries to ensure timely detection and treatment of pulmonary TB cases and interrupting the transmission. However, we did not have information on the immigrant cases' time of arrival in Finland and whether their TB was diagnosed immediately after arrival through screening or by clinical symptoms years after arrival. Our results are in line with the new Finnish Ministry of Health guidelines in which all immigrants arriving from high-incidence countries who intend to stay in Finland for more than 3 months should be screened for active TB on arrival with chest X-ray and health check-up. In previous guidelines, only refugees and asylum seekers were screened [15].

A recent systematic review and meta-analysis [16] found that refugees were four times more likely to be diagnosed with active pulmonary TB than other immigrants. Refugees usually have left their country of origin against their will and might have stayed in overcrowded camps before moving to the host country. Immigrants who are not refugees may be difficult to reach because they do not come to the country via a single entry point, as they might relocate for work, to

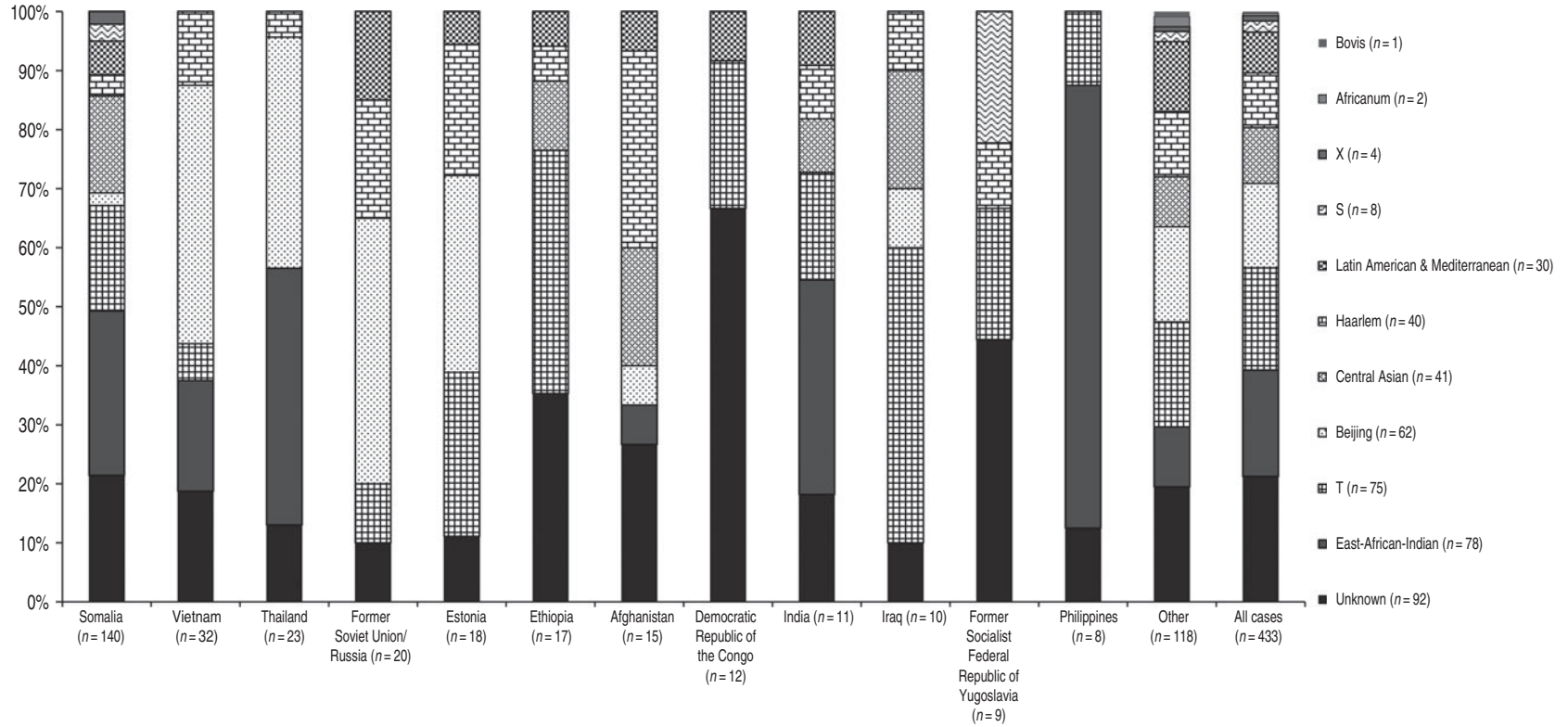


Fig. 1. Distribution of spoligotype clades by country of birth in Finland, 2008–2013.

join a family member or to study. As refugees are under surveillance at arrival they are easy to reach and screen but other immigrants are not comprehensively covered by any surveillance system in Finland even if they are from high-incidence TB countries. A Canadian study suggested that screening of all immigrants is not an easy task [17]. However, proactive screening, significantly reduces morbidity, prevents secondary infection of contacts, and is cost-effective. As immigrants might develop a disease years after relocating and may often be mobile, raising awareness about TB and its symptoms is important in addition to comprehensive screening [17].

When comparing the incidence rates in the cases' country of birth with the respective group's incidence rate in Finland, we found that Somalis had a higher risk of being diagnosed with TB in Finland than in Somalia. For most of the countries the reported rate was similar or somewhat smaller in Finland compared to the country of origin. Exceptions were persons born in the Philippines, Estonia and the former Soviet Union/Russia in whom the TB rate in Finland was considerably lower compared to the reported rate in their country of origin. Comparing the TB incidence rates reported in the cases' country of birth, and their likelihood of being diagnosed with TB after immigration to Finland, is difficult because of differences in surveillance and healthcare systems and population characteristics. As expected, observed rates were generally lower in Finland than in the country of birth. For example, the reported TB rate in Russia is nine times higher than the reported rate in Finland in persons born in the Soviet Union/Russia. This reflects the characteristics of the Russian immigrant population in Finland and the disease epidemiology in Russia where TB transmission occurs mainly in prisoners, homeless people and drug addicts. It was only in the Somali population that the likelihood of being diagnosed with TB in Finland appeared higher than reported from their country of birth. This could be due to the fact that in Somalia TB is very common, many people have latent TB infection and TB is not restricted to any specific population or group in Somalia. Moreover, as most Somalis who come to Finland are asylum seekers they are screened immediately after arrival in Finland, allowing for an early detection of TB.

In our study the male/female sex ratio in immigrant TB cases was equal, even though several international surveys have shown that TB occurs more often in males than in females [13, 18]. These analyses,

however, have generally included only pulmonary TB cases. Our study shows a similar trend as international surveys in which males have more pulmonary TB and females extrapulmonary TB.

MDR-TB is increasing in immigrant TB cases in Finland. In a previous study of MDR-TB in Finland by Vasankari *et al.* [19] 14 immigrant MDR-TB cases were notified during 1994–2005. Towards the end of our study period the number of MDR-TB cases increased, as 18 MDR-TB immigrant cases out of the total 29 cases were detected during the last 9 years of the study (2005–2013). The increase in MDR-TB cases in Finland may be associated with the increase in MDR-TB in countries with high incidence of TB such as Somalia and Russia [1].

The most common spoligotype clades of TB strains in immigrants in Finland were found to be the EAI clade and T family clade, which are also common in Sweden [8]. When comparing the clades in TB cases' country of birth, we observed that in most cases the EAI and T clades were common also in the country of birth. A total of 10 different clades were identified in immigrant patients in Finland in general, and nine of the clades were found in cases born in Somalia, suggesting that a wide variety of *M. tuberculosis* isolates circulate in that country. A detailed analysis of molecular epidemiology of TB in Finland [20, 21] recently found that T and Haarlem strains were the most common in Finnish isolates. By combining spoligotyping and MIRU-VNTR, only 10 out of 100 clusters were found to contain both Finnish and foreign-born cases. In addition, clustering was less common in immigrants than natives, suggesting that TB in immigrants is more often caused by a reactivation of TB obtained in their country of birth, than recent transmission of TB in Finland.

There are several limitations in our study. First, the sensitivity of TB surveillance increased in the middle of our study period as the case definition for TB was changed in 2007. This change is likely to affect the number of immigrant and native cases similarly. Furthermore, the change may have affected the sensitivity for detecting pulmonary TB more than extrapulmonary TB. However, pulmonary TB was not more common in immigrants.

Second, we defined an immigrant as a person born outside Finland. If data on the country of birth was missing, and immigrant was defined as a person whose recent nationality was not Finnish. This definition was based on the available administrative classification and chosen because a person can only have one

country of birth. However, it is possible that a Finn who was born abroad would therefore be defined as an immigrant, but this was rare. Further, second-generation immigrants are defined as natives by this definition. Beside nationality, the parents' country of birth or ethnic background has sometimes been used [8, 11, 22] and would probably be more accurate in defining the immigrant/native status, as it would cover second-generation immigrants. However, this information was not available in our surveillance data.

Third, we did not have information on the immigrant cases' time of arrival in Finland and whether their TB was diagnosed immediately after arrival through screening or by clinical symptoms years after arrival. We also did not have information available about the coverage and timeliness of the screening of refugees and asylum seekers in Finland. Moreover, we did not have data available on the visa status of the immigrants to determine whether the immigrants came to Finland as refugees or with a working visa.

Fourth, the study period of genotyping data was shorter compared to the epidemiology data as genotyping information has only been available since 2008.

A strength of our analysis is the ability to link the NIDR data to a laboratory database and analyse isolates by spoligotyping and characterize them to obtain a national view of our genotypes. Only spoligotyping data was used in this study, in order to obtain a general picture of the population structure of *M. tuberculosis* isolates. Previous studies have shown that a better resolution of *M. tuberculosis* isolates is obtained by combination of spoligotyping and MIRU-VNTR typing data [7, 14, 20]. A more detailed comparison of the immigrant and native *M. tuberculosis* isolates will provide specific information about transmission of TB in Finland.

As TB becomes less common in native Finns over time, increasing TB cases in the immigrant population will probably change the epidemiology in the future as has occurred in other northern European countries. Screening of immigrants from high-incidence countries and raising awareness of typical TB signs and symptoms, both in patients and clinicians, is important to ensure early diagnosis and to prevent transmission of TB in Finland.

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DECLARATION OF INTEREST

None.

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