Tuberculosis control among immigrants

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Chapter 6

Coverage and yield of tuberculosis contact investigations in the Netherlands

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SUMMARY

Setting: An increasing proportion of tuberculosis patients in low-incidence countries are immigrants. It is unclear whether contact investigations among immigrant patients are adequate.

Objective: To determine whether ethnicity of pulmonary tuberculosis patients was associated with the coverage and yield of contact investigations in the Netherlands.

Design: Contact investigation results were extracted from the records of patients reported in the nationwide surveillance register in 2006 and 2007. Prevalence odds ratios with 95% confidence intervals were calculated to determine the association between patients' ethnicity and the coverage of contact investigations and the yield of individuals with *Mycobacterium tuberculosis* infection or tuberculosis.

Results: Out of the 1040 pulmonary tuberculosis patients reported, 642 (62%) were eligible for analysis. Compared to close contacts of Dutch patients, close contacts of immigrant patients were significantly less likely to be examined for tuberculosis (89% versus 93%, POR: 0.6; 95%CI: 0.5-0.7) and infection (50% versus 75%, POR: 0.3; 95%CI: 0.3-0.4), whereas the yield was significantly higher for disease (1.5% versus 0.4%, POR: 3.4; 95%CI: 1.8-6.4) and infection (13% versus 10%, POR: 1.2; 95%CI: 1.0-1.5).

Conclusion: The effectiveness of contact investigations in the Netherlands can be optimized by expanding the investigation of contacts of immigrant patients.

INTRODUCTION

Tuberculosis (TB) is a major cause of illness and death worldwide. The incidence of TB in the Netherlands has declined over the last decades, reaching 7.0 cases per 100,000 population in 2009. As in other industrialized countries (1-2), most TB cases occur among the immigrant population (73% in 2009) (3), and the decline in incidence is likely to level off with continuing migration (4). The TB control strategy in the Netherlands focuses on case finding and treatment, screening of high-risk groups, and contact investigation (5). The objective of contact investigation is to identify and examine the contacts of a pulmonary tuberculosis (PTB) patient and provide infected contacts with treatment to prevent further transmission. In low-incidence countries contact investigations are considered as an essential component of TB control (6-8).

As different strategies and different definitions are used internationally, it is difficult to compare the effectiveness of contact investigations (9). Case-studies of contacts for a single patient, and contact investigations for several patients from a local area over a certain time period have been reported (10-15). The yield of latent TB infection (LTBI) and TB in these studies ranged from 13% to 42% and from 0% to 2%, respectively. These wide ranges of outcomes may be attributed to the different characteristics of the patients and their contacts selected for these studies. Evaluating national data on contact investigation outcomes would give a more comprehensive insight in current practice and will help policy makers and health care workers in improving the effectiveness of contact investigations.

Previous research in the Netherlands has shown that, in contrast with Dutch patients, recent infection in the majority immigrant patients was attributable to sources with the same nationality (16). Furthermore, the proportion of Dutch patients with TB attributable to recent transmission with an immigrant patient increased from 29% in 1995 to 50% in 2005 (17). The increasing proportion of TB cases among immigrants underlines the fact that interventions aimed at early detection and prevention of disease were suboptimal for immigrant patients.

The objective of the present study was to assess whether patient ethnicity was associated with contact investigation outcomes in terms of coverage and yield for TB and LTBI.

STUDY POPULATION AND METHODS

Since 2006, data on numbers of identified and examined contacts, together with infection and disease status, have been collected routinely for TB patients notified in the

Netherlands Tuberculosis Register (NTR) by 35 of 37 Public Health Services (PHSs). We extracted the records of all cases registered in 2006 and 2007, including retreatment cases with a PTB component (denoted 'index cases'). Patients whose records were incomplete or inconsistent were excluded. No characteristics of the contacts were reported in the NTR, except for the level of exposure to the index case.

The main study outcomes were coverage and yield of TB and LTBI. We defined coverage as the number of contacts investigated divided by the total number of identified contacts. We defined yield as the total number of patients diagnosed among contacts divided by the total number of contacts investigated. LTBI was assessed using the tuberculin skin test (TST) or an interferon gamma release assay (IGRA), while TB was assessed using chest X-ray (CXR), sometimes in combination with TST and/or IGRA, and confirmed by a positive culture or by clinical response to treatment.

We have referred to the autochthonous population as Dutch, and first and second generation immigrants as the immigrant population.

The level of exposure of the contacts was defined by PHS staff based on national guidelines for contact investigation. Close contacts were individuals with intimate (talking distance), prolonged *and* frequent (cumulatively >48 hours) confirmed contact with the infectious index case (e.g., household contacts). Casual contacts were individuals with intimate *or* frequent confirmed contact with the infectious index case (e.g., workplace colleagues). Community contacts were individuals with less intimate and less frequent, often not confirmed, contact with the infectious index case (e.g., people who visit the same building regularly). Contacts were screened according to the stone-in-the-pond principle (18).

Exploratory variables were sex, age (0-14, 15-34, 35-64 and ≥65 years), smear positivity (Ziehl- Neelsen microscopy of sputum or bronchoalveolar lavage), case finding, risk group and region. Actively found index cases were identified by (periodic) screening. Index cases belonging to a risk group were: contacts, refugees, asylum seekers, illegal residents, homeless persons, prisoners, drug addicts, health care workers, relapse patients, travelers (>3 months in endemic area), sailors and others. Index cases were categorized as urban when they lived in one of the four largest cities of the Netherlands.

Because we used retrospective surveillance data without the possibility of linking patient records to patient personal data, ethical approval was not deemed necessary.

Statistical analysis

Coverage and yield estimates were stratified by the level of exposure of the contacts and were compared between Dutch and immigrant index cases by calculating the crude prevalence odds ratios (PORs). We assessed whether explanatory variables were an effect modifier for these crude PORs by applying the Breslow-Day test for homogeneity. Stratum-specific PORs for the explanatory variables were reported when tests for homogeneity indicated that reporting a pooled POR was not adequate ($P \leq 0.05$). In case of homogeneity, the Mantel-Haenszel pooled POR (POR_{MH}) with 95% confidence intervals (CI) was calculated and compared to the crude POR to check for confounding (19). We used the POR_{MH} instead of logistic regression analyses because in the NTR the results of contact investigations were reported aggregated per index case record.

We performed a sensitivity analysis through multiple imputations to estimate the number of eligible close contacts for the index cases without identified contacts (predictive mean matching). This is to rectify a possible overestimation of the coverage. All exploratory variables were used in the multiple imputation model. SPSS Version 17.0 (Chicago, IL, USA) was used to perform the analyses.

RESULTS

Study population

During 2006 and 2007, 1040 index cases were reported in the NTR by the participating PHSs (Figure), representing 84% of the nationwide notified number of index cases. Of these, 944 (91%) had data on contact investigations outcomes. We excluded 302 index cases for further analysis due to inconsistent data (n=103) or because no contact investigation was done or the results were unknown (n=199). Compared to the study population, excluded patients were significantly younger (mean age: 41.1 vs. 45.3 years, P<0.01), more often non-Dutch (17% Dutch vs. 35% Dutch, P<0.001), actively found (33% vs. 16%, P<0.001), considered from a risk group (59% vs. 36%, P<0.001), and smear negative or with unknown smear status (61% vs. 46%, P<0.001, Table 1). Close, casual, and community contacts were investigated for 227, 130 and 44 Dutch index cases and for 415, 185 and 40 immigrant index cases, respectively. The median number of identified contacts was 18 (interquartile range [IQR] 5-45) for Dutch index cases and 9 (IQR 4-26) for immigrant index cases.

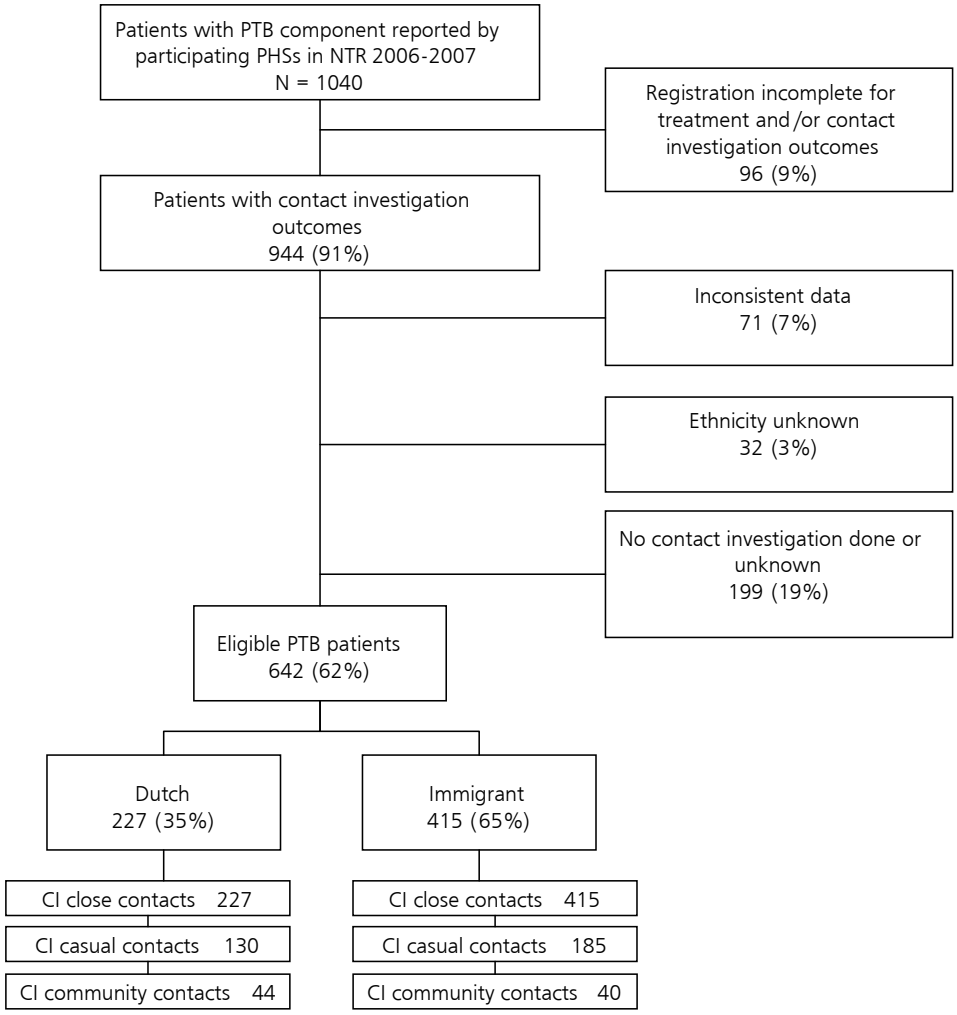

Figure. Flowchart of study population. Abbreviations: CI = contact investigation, PHSs = Public Health Services, NTR = Netherlands Tuberculosis Register, PTB = pulmonary tuberculosis

Close contacts

Close contacts of immigrant index cases were significantly less likely to be examined for TB compared to close contacts of Dutch index cases (89% versus 93%, POR: 0.6; 95%CI: 0.5-0.7, Table 2). As sex, smear positivity, risk group and region were effect modifiers for the association between ethnicity of the index case and coverage of TB, stratum-specific PORs were reported. The POR_{MH} for age and case finding showed not to confound the crude POR.

Table 1. Characteristics of individuals eligible and non-eligible for participation.

	Eligible n (%)	Non-eligible n (%)	P-value χ2 test
Total	642 (62)	398 (38)	
Sex			0.270
Male	373 (58)	245 (62)	
Female	269 (42)	153 (38)	
Age, years, mean (SD)	45.3 (21.1)	41.1 (20.5)	<0.01*
Ethnicity			<0.001
Dutch	227 (35)	67 (17)	
1st generation immigrant	378 (59)	215 (54)	
Morocco	53 (14)	32 (15)	
Turkey	33 (9)	7 (3)	
Indonesia	32 (8)	10 (5)	
Somalia	31 (8)	42 (20)	
Surinam	20 (5)	19 (9)	
Other	209 (55)	105 (49)	
2nd generation immigrant	37 (6)	77 (19)	
unknown	n.a.	39 (10)	
Region			0.540
Urban	174 (27)	101 (25)	
Rural	468 (73)	297 (75)	
Smear positive			<0.001
No/Unknown	294 (46)	244 (61)	
Yes	348 (54)	154 (39)	
Case finding			<0.001
Passive	518 (81)	236 (59)	
Active	102 (16)	133 (33)	
Unknown	22 (3)	29 (7)	
Risk group			<0.001†
No	413 (64)	159 (40)	
Yes	229 (36)	233 (59)	
Unknown	0 (0)	6 (2)	

Abbreviations: SD=Standard Deviation, n.a.=not applicable
*Tested by Independent Samples T-testing
†Fisher's exact test

The TB yield among close contacts of immigrant index cases was 1.5% compared to 0.4% among close contacts of Dutch index cases (POR: 3.4; 95%CI: 1.8-6.4, Table 2). Region was an effect modifier, with a higher POR in the association between ethnicity and TB yield for rural than for urban index cases. A weaker association between ethnicity and TB yield was found when we corrected for age (POR_{MH}: 1.9; 95%CI: 1.0-3.6). None of the other explanatory variables confounded this association.

Identified close contacts of immigrant index cases were significantly less likely to be examined for LTBI compared to close contacts of Dutch index cases (50% versus 75%,

Table 2. TB coverage and TB yield of close contacts of Dutch and immigrant index cases.

Characteristics	Dutch index cases				Immigrant index cases				Immigrant vs. Dutch§	
	IC n	Contacts n	TB coverage* n (%)	TB yield† n (%)	IC n	Contacts n	TB coverage* n (%)	TB yield† n (%)	Coverage POR (95% CI)‡¶	Yield POR (95% CI)‡¶
All	227	2648	2468 (93.2)	11 (0.4)	415	4334	3846 (88.7)	57 (1.5)	0.6 (0.5-0.7)	3.4 (1.8-6.4)
Sex										
Male	133	1474	1384 (93.9)	4 (0.3)	240	2773	2372 (85.5)	34 (1.4)	0.4 (0.3-0.5)	3.4 (1.8-6.4)¶
Female	94	1174	1084 (92.3)	7 (0.6)	175	1561	1474 (94.4)	23 (1.6)	1.4 (1.0-1.9)	
Age (yr)										
0-14	4	42	42 (100.0)	0 (0.0)	15	258	249 (96.5)	4 (1.6)	0.6 (0.5-0.7)¶	1.9 (1.0-3.6)¶
15-34	33	381	357 (93.7)	0 (0.0)	189	2186	1920 (87.8)	40 (2.1)		
35-64	90	1198	1105 (92.2)	11 (1.0)	160	1298	1165 (89.8)	12 (1.0)		
65+	100	1027	964 (93.9)	0 (0.0)	51	592	512 (86.5)	1 (0.2)		
Smear positive										
No/Unknown	110	713	653 (91.6)	1 (0.2)	184	1194	1083 (90.7)	11 (1.0)	0.9 (0.6-1.2)	3.4 (1.8-6.5)¶
Yes	117	1935	1815 (93.8)	10 (0.6)	231	3140	2763 (88.0)	46 (1.7)	0.5 (0.4-0.6)	
Case finding										
Passive	192	2495	2323 (93.1)	11 (0.5)	326	3663	3262 (89.1)	52 (1.6)	0.6 (0.5-0.7)¶	3.0 (1.6-5.5)¶
Active	25	106	99 (93.3)	0 (0.0)	77	623	542 (87.0)	5 (0.9)		
Unknown	10	47	46 (97.9)	0 (0.0)	12	48	42 (87.5)	0 (0.0)		
Risk group										
No	151	1964	1828 (93.1)	10 (0.5)	262	2854	2479 (86.9)	39 (1.6)	0.5 (0.4-0.6)	3.5 (1.8-6.8)¶
Yes	76	684	640 (93.6)	1 (0.2)	153	1480	1367 (92.4)	18 (1.3)	0.8 (0.6-1.2)	
Region										
Urban	43	318	259 (81.4)	3 (1.2)	131	872	735 (84.3)	8 (1.1)	1.2 (0.9-1.7)	0.9 (0.2-3.6)
Rural	184	2330	2209 (94.8)	8 (0.4)	284	3462	3111 (89.9)	49 (1.6)	0.5 (0.4-0.6)	4.4 (2.1-9.3)

Abbreviations: IC=index cases, TB=tuberculosis, POR=prevalence odds ratio

*Number of contacts investigated for TB (as a percent of the contacts identified)

†Number of contacts diagnosed with TB (as a percent of investigated contacts)

‡In case of empty cells, 0.5 was added to each cell in order to calculate stratum-specific POR's.

§Dutch index cases are considered as the reference category.

¶ Mantel-Haenszel pooled PORs are reported unless tests for homogeneity indicated heterogeneous PORs (in that case stratum-specific PORs are reported)

Table 3. LTBI coverage and LTBI yield among close contacts of Dutch and immigrant index cases.

Characteristics	Dutch index cases				Immigrant index cases				Immigrant vs Dutch§	
	IC n	Contacts n	LTBI coverage* n (%)	LTBI yield† n (%)	IC n	Contacts n	LTBI coverage* n (%)	LTBI yield† n (%)	Coverage POR (95% CI)‡¶	Yield POR (95% CI)‡¶
All	227	2648	1973 (74.5)	206 (10.4)	415	4334	2146 (49.5)	270 (12.6)	0.3 (0.3-0.4)	1.2 (1.0-1.5)
Sex										
Male	133	1474	1099 (74.6)	103 (9.4)	240	2773	1390 (50.1)	195 (14.0)	0.3 (0.3-0.4)¶	1.6 (1.2-2.0)
Female	94	1174	874 (74.4)	103 (11.8)	175	1561	756 (48.4)	75 (9.9)		0.8 (0.6-1.1)
Age (yr)										
0-14	4	42	41 (97.6)	15 (36.6)	15	258	142 (55.0)	7 (4.9)	0.0 (0.0-0.2)	0.1 (0.0-0.2)
15-34	33	381	323 (84.8)	56 (17.3)	189	2186	1103 (50.5)	181 (16.4)	0.2 (0.1-0.2)	0.9 (0.7-1.3)
35-64	90	1198	893 (74.5)	98 (11.0)	160	1298	658 (50.7)	61 (9.3)	0.4 (0.3-0.4)	0.8 (0.6-1.2)
65+	100	1027	716 (69.7)	37 (5.2)	51	592	243 (41.0)	21 (8.6)	0.3 (0.2-0.4)	1.7 (1.0-3.0)
Smear positive										
No/Unknown	110	713	506 (71.0)	31 (6.1)	184	1194	463 (38.8)	24 (5.2)	0.3 (0.2-0.3)	1.2 (1.0-1.5)¶
Yes	117	1935	1467 (75.8)	175 (11.9)	231	3140	1683 (53.6)	246 (14.6)	0.4 (0.3-0.4)	
Case finding										
Passive	192	2495	1853 (74.3)	193 (10.4)	326	3663	1870 (51.1)	254 (13.6)	0.4 (0.3-0.4)	1.4 (1.1-1.7)
Active	25	106	79 (74.5)	11 (13.9)	77	623	253 (40.6)	16 (6.3)	0.2 (0.1-0.4)	0.4 (0.2-0.9)
Unknown	10	47	41 (87.2)	2 (4.9)	12	48	23 (47.9)	0 (0.0)	0.1 (0.0-0.4)	0.6 (0.1-5.6)
Risk group										
No	151	1964	1495 (76.1)	167 (11.2)	262	2854	1402 (49.1)	180 (12.8)	0.3 (0.3-0.3)	1.3 (1.0-1.5)¶
Yes	76	684	478 (69.9)	39 (8.2)	153	1480	744 (50.3)	90 (12.1)	0.4 (0.4-0.5)	
Region										
Urban	43	318	204 (64.2)	13 (6.4)	131	872	292 (33.5)	27 (9.2)	0.4 (0.3-0.4)¶	1.3 (1.0-1.5)¶
Rural	184	2330	1769 (75.9)	193 (10.9)	284	3462	1854 (53.6)	243 (13.1)		

Abbreviations: IC=index cases, LTBI=latent tuberculosis infection, POR=prevalence odds ratio
*Number of contacts investigated for LTBI (as a percent of the contacts identified)
†Number of contacts diagnosed with LTBI (as a percent of investigated contacts)
‡In case of empty cells, 0.5 was added to each cell in order to calculate stratum-specific POR's.
§Dutch index cases are considered as the reference category.
¶ Mantel-Haenszel pooled PORs are reported unless tests for homogeneity indicated heterogeneous PORs (in that case stratum-specific PORs are reported)

Table 4. TB coverage and TB yield of casual contacts of Dutch and immigrant index cases.

Characteristics	Dutch index cases				Immigrant index cases				Immigrant vs Dutch§	
	IC n	Contacts n	TB coverage* n (%)	TB yield† n (%)	IC n	Contacts n	TB coverage* n (%)	TB yield† n (%)	Coverage POR (95% CI)‡¶	Yield POR (95% CI)‡¶
All	130	4470	3978 (89.0)	9 (0.2)	185	5672	4910 (86.6)	14 (0.3)	0.8 (0.7-0.9)	1.3 (0.5-2.9)
Sex										
Male	72	2776	2442 (88.0)	6 (0.2)	117	3275	2712 (82.8)	12 (0.4)	0.7 (0.6-0.8)	1.3 (0.6-3.0)¶
Female	58	1694	1536 (90.7)	3 (0.2)	68	2397	2198 (91.7)	2 (0.1)	1.1 (0.9-1.4)	
Age (yr)										
0-14	3	73	73 (100)	0 (0.0)	6	293	269 (91.8)	0 (0.0)	0.1 (0.0-1.1)	0.7 (0.3-1.5)¶
15-34	21	483	433 (89.6)	4 (0.9)	93	3228	2742 (84.9)	10 (0.4)	0.7 (0.5-0.9)	
35-64	54	2799	2467 (88.1)	5 (0.2)	60	1480	1291 (87.2)	3 (0.2)	0.9 (0.8-1.1)	
65+	52	1115	1005 (90.1)	0 (0.0)	26	671	608 (90.6)	1 (0.2)	1.1 (0.8-1.5)	
Smear positive										
No/Unknown	44	657	578 (88.0)	1 (0.2)	49	914	812 (88.8)	1 (0.1)	1.1 (0.8-1.5)	1.3 (0.5-2.9)¶
Yes	86	3813	3400 (89.2)	8 (0.2)	136	4758	4098 (86.1)	13 (0.3)	0.8 (0.7-0.9)	
Case finding										
Passive	112	4154	3704 (89.2)	7 (0.2)	158	4576	3996 (87.3)	13 (0.3)	0.8 (0.7-1.0)	1.1 (0.5-2.5)¶
Active	12	234	192 (82.1)	1 (0.5)	24	816	687 (84.2)	1 (0.1)	1.2 (0.8-1.7)	
Unknown	6	82	82 (100)	1 (1.2)	3	280	227 (81.1)	0 (0.0)	0.1 (0.0-0.4)	
Risk group										
No	90	3179	2838 (89.3)	8 (0.3)	123	3976	3490 (87.8)	9 (0.3)	0.9 (0.8-1.0)¶	1.3 (0.5-2.9)¶
Yes	40	1291	1140 (88.3)	1 (0.1)	62	1696	1420 (83.7)	5 (0.4)		
Region										
Urban	28	610	536 (87.9)	2 (0.4)	73	1107	932 (84.2)	5 (0.5)	0.8 (0.7-0.9)¶	1.2 (0.5-2.8)¶
Rural	102	3860	3442 (89.2)	7 (0.2)	112	4565	3978 (87.1)	9 (0.2)		

Abbreviations: IC=index cases, TB=tuberculosis, POR=prevalence odds ratio

*Number of contacts investigated for TB (as a percent of the contacts identified)

†Number of contacts diagnosed with TB (as a percent of investigated contacts)

‡In case of empty cells, 0.5 was added to each cell in order to calculate stratum-specific POR's.

§Dutch index cases are considered as the reference category.

¶ Mantel-Haenszel PORs are reported unless tests for homogeneity indicated heterogeneous PORs (in that case stratum-specific PORs are reported)

Table 5. LTBI coverage and LTBI yield of casual contacts of Dutch and immigrant index cases.

Characteristics	Dutch index cases				Immigrant index cases				Immigrant vs Dutch	
	IC n	Contacts n	LTBI coverage* n (%)	LTBI yield† n (%)	IC n	Contacts n	LTBI coverage* n (%)	LTBI yield† n (%)	Coverage POR (95% CI)‡¶	Yield POR (95% CI)‡¶
All	130	4470	2976 (66.6)	210 (7.1)	185	5672	3296 (58.1)	155 (4.7)	0.7 (0.6-0.8)	0.7 (0.5-0.8)
Sex										
Male	72	2776	1844 (66.4)	113 (6.1)	117	3275	1775 (54.2)	114 (6.4)	0.6 (0.5-0.7)	1.1 (0.8-1.4)
Female	58	1694	1132 (66.8)	97 (8.6)	68	2397	1521 (63.5)	41 (2.7)	0.9 (0.8-1.0)	0.3 (0.2-0.4)
Age (yr)										
0-14	3	73	53 (72.6)	2 (3.8)	6	293	253 (86.3)	3 (1.2)	2.4 (1.3-4.4)	0.7 (0.5-0.9)¶
15-34	21	483	362 (74.9)	21 (5.8)	93	3228	1756 (54.4)	89 (5.1)	0.4 (0.3-0.5)	
35-64	54	2799	1845 (65.9)	145 (7.9)	60	1480	872 (58.9)	39 (4.5)	0.7 (0.7-0.8)	
65+	52	1115	716 (64.2)	42 (5.9)	26	671	415 (61.8)	24 (5.8)	0.9 (0.7-1.1)	
Smear positive										
No/Unknown	44	657	411 (62.6)	13 (3.2)	49	914	524 (57.3)	17 (3.2)	0.7 (0.6-0.8)¶	0.7 (0.5-0.8)¶
Yes	86	3813	2565 (67.3)	197 (7.7)	136	4758	2772 (58.3)	138 (5.0)		
Case finding										
Passive	112	4154	2774 (66.8)	201 (7.3)	158	4576	2694 (58.9)	135 (5.0)	0.7 (0.7-0.8)¶	0.7 (0.5-0.8)¶
Active	12	234	138 (59.0)	5 (3.6)	24	816	439 (53.8)	14 (3.2)		
Unknown	6	82	64 (78.0)	4 (6.3)	3	280	163 (58.2)	6 (3.7)		
Risk group										
No	90	3179	2205 (69.3)	172 (7.8)	123	3976	2337 (58.8)	103 (4.4)	0.6 (0.6-0.7)	0.5 (0.4-0.7)
Yes	40	1291	771 (59.7)	38 (4.9)	62	1696	959 (56.5)	52 (5.4)	0.9 (0.8-1.0)	1.1 (0.7-1.7)
Region										
Urban	28	610	411 (67.4)	22 (5.4)	73	1107	506 (45.7)	28 (5.5)	0.4 (0.3-0.5)	0.7 (0.5-0.8)¶
Rural	102	3860	2565 (66.5)	188 (7.3)	112	4565	2790 (61.1)	127 (4.6)	0.8 (0.7-0.9)	

Abbreviations: IC=index cases, LTBI=latent tuberculosis infection, POR=prevalence odds ratio

*Number of contacts investigated for LTBI (as a percent of the contacts identified)

†Number of contacts diagnosed with LTBI (as a percent of investigated contacts)

‡In case of empty cells, 0.5 was added to each cell in order to calculate stratum-specific POR's.

§Dutch index cases are considered as the reference category.

¶ Mantel-Haenszel PORs are reported unless tests for homogeneity indicated heterogeneous PORs (in that case stratum-specific PORs are reported)

POR: 0.3; 95%CI: 0.3-0.4, Table 3). Age, smear positivity, case finding and risk group were effect modifiers. Sex and region were shown not to confound the association between ethnicity and LTBI coverage.

Among the close contacts of immigrant index cases examined, 13% had LTBI compared to 10% of close contacts of Dutch index cases (POR: 1.2; 95%CI: 1.0-1.5, P = 0.032, Table 3). Sex, age and case finding were effect modifiers. The relation between the ethnicity of the index case and LTBI yield was not confounded by any of the other explanatory variables.

Casual contacts

Casual contacts of immigrant index cases were marginally less likely to be examined for TB compared to casual contacts of Dutch index cases (87% versus 89%, POR: 0.8; 95%CI: 0.7-0.9, Table 4). No significant differences were found in the probability of having TB among casual contacts between immigrant and Dutch index cases (POR: 1.3; 95%CI: 0.5-2.9, Table 4).

Identified casual contacts of immigrant index cases were significantly less likely to be examined for LTBI compared to casual contacts of Dutch index cases (58% versus 67%, POR: 0.7; 95%CI: 0.6-0.8, Table 5). Overall, 5% of the examined casual contacts of immigrant index cases had LTBI compared to 7% of the examined casual contacts of Dutch index cases (POR: 0.7; 95%CI: 0.5-0.8, Table 5).

Sensitivity analysis

In the sensitivity analysis, TB coverage in Dutch index cases fell from 93% (base-case) to 82% and LTBI coverage from 75% to 66%. Among immigrant index cases, TB coverage decreased from 89% to 67% and the LTBI coverage from 50% to 37%.

DISCUSSION

This study shows that in 2006 and 2007, close contacts of immigrant index cases (pulmonary TB) in the Netherlands were significantly less likely to be examined for TB or LTBI than close contacts of Dutch index cases, whereas the yield of TB and LTBI was significantly higher in this group.

The reasons why contacts of immigrant index cases were examined less often for TB are speculative. We assume that most contacts of immigrant index cases were likely from the same age category as the index cases (20) and were immigrants themselves. A possible explanation therefore could be that a number of these contacts were already screened

for TB at entry in the Netherlands. In daily practice, recently screened persons and/or persons still in a screening program, are often not invited for a new TB examination. Other possibilities might be communication difficulties, fear of stigmatization or the inability of PHSs to trace contacts. In any case, the lower TB coverage among contacts of immigrant index cases suggests possible inequalities in access to care, leading to sustained higher TB incidence among immigrants.

The higher yield of TB in close contacts of immigrant index cases might be a result of acquired TB from an unknown source in their country of origin, rather than a result of recent exposure. For TB, it would be possible to prove actual transmission between index cases and contacts through DNA typing (21-22). This information was not available in our database. Nevertheless, even without having clinical evidence for transmission, our data show that it is essential to examine close contacts of immigrant index cases for TB.

The lower LTBI coverage amongst contacts of immigrant index cases could be explained by the fact that assessing recently acquired LTBI was deemed not feasible in bacille Calmette-Guérin (BCG) vaccinated individuals and in populations with a high risk of (previous) exposure, such as immigrants from endemic countries. The availability of IGRAs makes this group of contacts nowadays more suitable for LTBI screening.

The higher LTBI yield in close contacts of immigrant index cases can be explained by the fact that most contacts will be from high TB prevalence countries. Neither TST nor IGRA can distinguish well between remote and recent infections (23). However, an epidemiological link between contacts and index cases was established, indicating that contacts were expected to be recently exposed. Recent transmission, and the provision of prophylactic treatment, should therefore also be considered in BCG-vaccinated immigrant close contacts (24).

We did not observe large differences in LTBI and TB coverage and yield between casual contacts of Dutch and immigrant index cases. We assume that the casual contact group was more heterogeneous in terms of ethnicity and age and therefore more similar for both Dutch and immigrant index cases.

The most conservative estimates for TB and LTBI coverage among close contacts were obtained using sensitivity analysis showed. Actual coverage will be between these estimates and the initial figures presented, as some index cases may not have any identifiable contacts.

The main reason for the exclusion of some index cases was the absence of contact investigation or unknown results. We have shown that not performing contact

investigation was associated with a number of characteristics of the index case, including immigrant status, type of case finding, and smear status (25). These characteristics were all related (e.g., case finding is more often active in immigrant index cases due to screening policies). In the light of differences between included and excluded index cases, reported estimates of yield and coverage may therefore be overestimations. However, it is unlikely that there were marked differences in the overestimations between the Dutch and the immigrant populations, leading to a severely biased estimate of the differences between these groups.

To increase the TB and LTBI coverage among close contacts to 90%, as stipulated during a recent European consensus meeting (8), the PHSs should explore new strategies, especially for LTBI testing amongst contacts of immigrant index cases. IGRAs might play a role in this, although studies about the positive predictive value for the progression to active TB have been inconclusive in populations with a high risk of (previous) exposure (26-27).

The main limitation of this study is the absence of information on contact characteristics other than the level of exposure to the index case. We could not therefore determine which contact characteristics were predictive in acquiring infection or disease.

CONCLUSIONS

Our study findings suggest that performing contact investigations in the Netherlands is challenging in immigrant patients. Qualitative studies should explore the barriers to investigate contacts in immigrant populations. Further research is also needed on innovative diagnostics that can discriminate between recent and remote infections, especially among immigrants. This will help to provide updated, comprehensive national guidelines on how to effectively investigate contacts of immigrant TB cases.

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