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Mycobacterium tuberculosis transmission over an 11-year period in a low-incidence, urban setting

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SUMMARY

SETTING: Montreal, Canada, has a mean annual tuberculosis (TB) incidence of 9 per 100 000 population, 1996–2007.

OBJECTIVE: To characterise potential *Mycobacterium tuberculosis* transmission by patient subgroups defined by age, sex, birthplace, smear and human immunodeficiency virus status, and to estimate the proportion of cases that resulted from transmission between these patient subgroups.

DESIGN: Retrospective study using DNA fingerprinting techniques, with clinical and demographic information from the public health department. Among cases with matching fingerprints, a pulmonary index case was identified. The transmission index was defined as the average number of subsequent TB cases generated directly or indirectly from an index case, and was compared among subgroups, including Haitian immigrants.

RESULTS: Compared to non-Haitian foreign-born index cases, Canadian-born index cases were associated with 2.38 times as many (95%CI 1.24–4.58) subsequent cases, while Haitian-born index cases were associated with 3.58 times as many (95%CI 1.74–7.36). Smear-positive index cases were not independently associated with increased transmission. However, middle-aged Canadian-born index patients were associated with a disproportionate number of subsequent cases.

CONCLUSION: In Montreal, index patients from several high-risk groups are associated with subsequent transmission. This approach can be applied to other low-incidence settings to identify where targeted interventions could potentially further reduce transmission.

KEY WORDS: molecular epidemiology; foreign-born; Canada; transmission index

IN LOW-INCIDENCE COUNTRIES, tuberculosis (TB) has remained a significant public health issue, particularly in urban settings. In Canada, where the overall incidence rate was 4.8 per 100 000 population in 2008,[1] TB is increasingly concentrated in large cities, notably among the foreign-born.[2] In 2004, approximately two thirds of all reported TB cases occurred in the 11 largest metropolitan areas of Canada, reflecting the settlement patterns of recently arrived immigrants from high-incidence countries.[3] At an estimated 13.3/100 000 in 2008, overall TB incidence among the foreign-born remains substantially higher than among Canadian-born non-Aboriginals, whose overall incidence rate was 0.8/100 000.

In low-incidence countries, a key element of TB control is the identification and interruption of transmission. Mycobacterial genotyping has permitted the identification of specific transmission events above and beyond conventional epidemiological investigation.[4] Community-based genotyping studies in Canadian cities, as elsewhere, have highlighted social, demographic and clinical risk factors for membership in transmission chains, which have helped shape contact investigation practices.[5–8] These studies have compared the characteristics of individuals who were determined to be part of genetic 'clusters' with those who were not, as suggested by mycobacterial genotyping results.

The methodology used in these studies, however, does not distinguish potential transmitters from others who have become infected with *Mycobacterium tuberculosis*. An alternative approach is to attribute each cluster to an index case, and then examine the capacity for generating subsequent cases according to the characteristics of these potential sources.[9,10] The transmission index measures the average number of

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subsequent cases, produced directly or indirectly, by potential index cases with particular demographic or clinical characteristics. It can be used to compare transmission between population subgroups of interest.

The objective of this study was to evaluate subsequent *M. tuberculosis* transmission in Montreal, Canada, between January 1996 and May 2007. Specifically, we sought to evaluate and compare transmission according to demographic and clinical characteristics of potential source patients, using the transmission index. As previous genotyping studies from Montreal identified Haitian birth as a potential risk factor for cluster membership, this group was considered distinct among the foreign-born population. We examined its transmission characteristics separately, as we hypothesised that they would be different from the remainder of the foreign-born population.[7,11]

STUDY POPULATION AND METHODS

Study population

At the time of the last Canadian census in 2006, the Island of Montreal had a population of 1.8 million. Montreal is Canada's second largest city, and the second most frequent destination for new immigrants: 558 000 of its residents (30.1%) were born outside Canada, and 135 000 have arrived within the last 5 years.[12] A single public health department is responsible for TB reporting and control throughout the Island of Montreal. Any physician who diagnoses active TB in a patient or any microbiology laboratory that grows *M. tuberculosis* must report case details to the public health department. All such isolates are sent to the provincial reference laboratory for confirmation and drug susceptibility testing.

Demographic and clinical characteristics

We abstracted clinical, microbiological and demographic data for all cases reported to the Montreal Public Health Department with active TB disease from 1 January 1996 to 31 May 2007. Cases with no recorded country of birth were excluded from the study, and Haitian-born immigrants were considered separately from the rest of the foreign-born population.

To be included in this study, patients had to have had at least one positive culture for *M. tuberculosis*. In our analysis, patients were classified as having pulmonary TB if sputum, bronchoalveolar lavage or lung biopsy material grew *M. tuberculosis*. They were considered to have extra-pulmonary TB if *M. tuberculosis* was cultured from one or more other sites, but not from a pulmonary specimen. Those with positive cultures from both pulmonary and extra-pulmonary sites were considered to have pulmonary TB.

Genotyping of M. tuberculosis *isolates*

Genotyping of *M. tuberculosis* isolates from all cases with culture-positive disease used the standard insertion sequence (IS) *6110* restriction fragment length polymorphism (RFLP) methodology.[13] Resulting isolates were scanned and analysed using GelCompar II (Applied Maths NV, Sint-Martens-Latem, Belgium). Isolates with fewer than six IS*6110* bands were also spoligotyped (Isogen Bioscience, Maarssen, The Netherlands).[14] Clusters were defined by identical RFLP band numbers and positions; in addition, isolates with $\leqslant 5$ IS*6110* bands also required identical spoligotypes to be considered clustered. Clustered cases were assumed to be linked by one or more transmission events.

Data analysis and transmission index

The χ^2 test was used to compare demographic and clinical characteristics between patient subgroups. Denominators for incidence rate estimates were calculated using 2006 Canadian census data.[11] Odds ratios for predictors of being clustered were calculated using logistic regression.

For calculations of transmission indices, an index case was defined as a pulmonary case where the corresponding *M. tuberculosis* genotype was unique to the study population on the date of diagnosis.[9] Within every cluster, the pulmonary case with the earliest date of diagnosis was considered the index case, while subsequent cases were considered to result from transmission. The transmission index was then derived by dividing the number of subsequent TB cases by the total number of index cases (sum of clustered and non-clustered index cases). To explore the effect of a stricter temporal definition of potential transmission chains, we performed a sensitivity analysis where clusters were restricted to 3 years following the diagnosis of the putative index case. This is consistent with other studies that have used a 1- to 3-year window for matching isolates to define recent transmission.[15,16]

Unlike previous studies,[9,10] we included secondary extra-pulmonary cases, as these also involve relevant transmission events—notably to children and the immunosuppressed. Clusters with only extra-pulmonary cases were excluded. For these clusters, we assumed that the index cases occurred outside the temporal or geographic limits of the study or were unavailable for genotyping.

We calculated transmission indices for patient subgroups according to age, sex, country of birth, smear status, human immunodeficiency virus (HIV) status and time since immigration. We then estimated the ratios of the indices between patient subgroups of interest, with adjustment for other predictors, using negative binomial regression.[17] We also accounted for the time available for detection of subsequent transmission from each case using time at risk as an offset variable in the regression models, because potential index cases identified later in the study period had less time at risk for detection of subsequent cases as compared with potential index cases diagnosed earlier.

As HIV serological status and time since immigration were unavailable for some patients, we calculated the adjusted transmission index ratios for these characteristics separately, using only those patients for whom these data were available. Finally, we estimated the proportion of subsequent cases that resulted from transmission within and between subgroups by country of birth, and performed a subgroup analysis on clusters from Canadian-born index cases. Statistical analyses were performed using Stata IC v11.1 (Stata Corp., College Station, TX, USA).

The study was approved by the research ethics committees of the McGill University Faculty of Medicine and the Montreal Public Health Department.

RESULTS

Between January 1996 and May 2007, 1859 cases of TB were reported on the Island of Montreal (Table 1). Of these, 339 (18.3%) occurred among the Canadian-born, 264 (14.2%) among the Haitian-born, and 1247 cases (67.1%) involved other foreign-born individuals. Average annual incidence among the Haitian-born population was 64.2/100 000, while among Canadian-born it was 2.3/100 000. Nearly half of all Canadian-born patients were aged ⩾55 years, while in the foreign-born groups TB cases were more often reported in younger people. Extra-pulmonary disease was reported in 34% of Haitian and other foreign-born TB cases, compared to 18% in the Canadian-born ($P < 0.001$).

Of the 1859 reported TB cases, 1583 (85.2%) were culture-positive; 1549 (97.9%) of these isolates were successfully genotyped (Figure 1). There were 96 clusters involving 282 patients, of whom 81 were Canadian-born, 74 were Haitian-born and 127 were born in other foreign countries. Canadian birth (odds ratio [OR] 2.97, 95% confidence interval [CI] 2.11–4.19) and Haitian birth (OR 3.10, 95%CI 2.21–4.36) were significantly associated with cluster

Table 1 Characteristics of TB cases by country of birth, Montreal, 1996–2007

Characteristic	Canadian-born *n* (%)	Haitian-born *n* (%)	Other foreign-born *n* (%)	Total*	*P* value†
Cases	339 (18.3)	264 (14.3)	1247 (67.4)	1850	
Incidence per 100 000	2.29	64.24	23.41	9.07	
Age, years					<0.001
<15	37 (10.9)	10 (3.8)	14 (1.1)	61 (3.3)	
15–24	32 (9.5)	39 (14.8)	186 (14.9)	257 (13.9)	
25–34	25 (7.4)	72 (27.2)	339 (27.2)	436 (23.6)	
35–44	34 (10.1)	63 (23.9)	248 (19.9)	345 (18.6)	
45–54	42 (12.4)	39 (14.8)	123 (9.8)	204 (11.0)	
55–64	32 (9.5)	21 (7.9)	104 (8.3)	157 (8.5)	
⩾65	137 (40.2)	20 (7.6)	233 (18.8)	390 (21.1)	
Sex‡					0.003
Male	184 (54.3)	118 (44.9)	697 (56.1)	999 (54.2)	
Female	154 (45.7)	145 (55.1)	546 (43.9)	845 (45.8)	
HIV status§					<0.001
Positive§	29 (21.5)	53 (26.6)	61 (10.1)	143 (15.3)	
Tested§	135	199	603	937	
Disease site					<0.001
Pulmonary	278 (82.0)	161 (61.0)	836 (67.1)	1275 (68.9)	
Extra-pulmonary	61 (18.0)	103 (39.0)	411 (32.9)	575 (31.1)	
Pulmonary TB smear status					<0.001
Smear-positive	154 (55.6)	101 (62.7)	374 (44.7)	629 (49.3)	
Smear-negative	124 (44.4)	60 (37.3)	462 (55.3)	646 (50.7)	
Culture status					0.215
Culture-positive	285 (84.0)	234 (88.6)	1056 (84.7)	1575 (85.1)	
Culture-negative	54 (16.0)	30 (11.4)	191 (15.3)	275 (14.9)	
Drug resistance¶					0.122
None	249 (87.3)	193 (82.5)	914 (86.6)	1356 (86.1)	
INH but not MDR-TB	14 (4.9)	19 (8.1)	80 (7.6)	113 (7.2)	
MDR-TB	0	2 (0.9)	13 (1.2)	15 (1.0)	
Other	10 (3.5)	4 (1.7)	18 (1.7)	32 (2.0)	
Unknown	12 (4.2)	16 (6.8)	31 (2.9)	59 (3.7)	

*Nine cases excluded because country of birth was unknown.
†χ^2 test used to compare characteristics of patients according to countries of birth.
‡Sex unknown for one Canadian-born case, one Haitian-born case and two other foreign-born cases.
§HIV-positive expressed as percentage of persons HIV-tested; HIV-tested expressed as proportion of all persons in the group. 204 Canadian-born, 65 Haitian-born, and 644 other foreign-born were not tested for HIV.
¶INH resistance was defined as resistance to at least INH, but not MDR-TB. MDR-TB was defined as resistance to at least INH and RMP.
TB = tuberculosis; HIV = human immunodeficiency virus; INH = isoniazid; MDR-TB = multidrug-resistant TB; RMP = rifampicin.

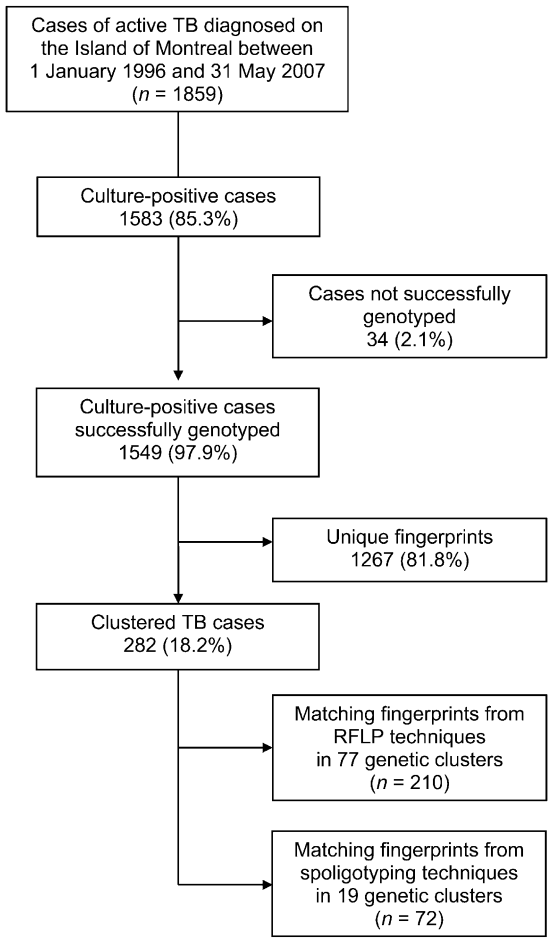

Figure 1 Flow chart for TB cases in Montreal, Canada, 1996–2007. TB = tuberculosis; RFLP = restriction fragment length polymorphism.

Table 2 Adjusted odds ratios for *M. tuberculosis* genotype-defined clustering, based on patient characteristics using multivariate logistic regression, Montreal, Canada, 1996–2007

Risk factor	Adjusted odds ratio*	95%CI
Age, years		
<15	1.74	0.77–3.95
15–24	1.00	
25–34	0.64	0.41–1.01
35–44	0.96	0.62–1.50
45–54	0.99	0.60–1.62
55–64	0.86	0.49–1.51
⩾65	0.49	0.30–0.79
Country of birth		
Canada	2.97	2.11–4.19
Haiti	3.10	2.21–4.36
Other	1.00	
Sex		
Male	1.00	
Female	1.00	0.76–1.31
Smear status†		
Positive	1.11	0.84–1.45
Negative	1.00	
HIV status‡		
Positive	1.63	1.03–2.57
Negative	1.00	
Duration of residence in Canada, years‡		
<5	1.00	
⩾5	1.26	0.87–1.82

*Adjusted for all other covariates using multivariate logistic regression.
†Restricted to pulmonary tuberculosis cases only.
‡Restricted to cases where HIV status and duration of residence prior to diagnosis were known. Duration of residence restricted to foreign-born only.
CI = confidence interval; HIV = human immunodeficiency virus.

membership as compared with birth in all other countries (Table 2). Patients aged ⩾65 years were significantly less likely to be cluster members relative to those aged between 15 and 24. Patients co-infected with HIV were also significantly more likely to be part of a cluster (OR 1.63, 95%CI 1.03–2.57).

Seven clusters included extra-pulmonary cases only (total 14 cases), and were excluded from the calculation of the transmission index. In seven other clusters, a pulmonary case was diagnosed after one or more extra-pulmonary cases, but without any subsequent cases. For the purposes of the index, these seven pulmonary cases were considered to have generated no subsequent cases. The final analysis included 82 pulmonary index cases that together generated 158 subsequent cases. The remaining 877 pulmonary TB cases generated no subsequent cases. Most clusters were small: 53 involved 2 cases, 14 had 3 cases, 6 had 4 cases, 4 had 6 cases, 2 had 10 cases, and 1 each had 6, 8 and 14 cases, respectively. The median time between the first two infectious TB cases within any cluster was 616 days (interquartile range [IQR] 225–964). The maximum time between an index case and the latest subsequent case in a cluster was 3899 days (IQR 403–1899).

Over the study period, the overall transmission index was 0.16 (Table 3). Canadian-born patients generated more than twice as many subsequent cases as all other foreign-born patients (adjusted transmission index 2.38, 95%CI 1.24–4.58). Similarly, Haitian-born patients generated more than three times as many subsequent cases (adjusted index 3.58, 95%CI 1.74–7.36) relative to the same reference group.

Transmission indices also varied with age, peaking in the 35–44 year age group overall (Table 3) and in the same age group for Canadian and Haitian-born patients (Figure 2). The index remained high for Canadian-born patients aged 45–54 years, and was five times higher than among Haitian and other foreign-born patients of the same age.

In the sensitivity analysis, when clusters were restricted to a 3-year span, adjusted relative transmission indices were similar to those estimated without the time restriction. However, these adjusted indices became less precise (wider CIs), reflecting smaller cluster sizes (see Appendix Table A).*

*The Appendix is available in the online version of this article at http://www.ingentaconnect.com/content/iuatld/ijtld/2012/00000016/00000003/art00006

Table 3 Transmission indices for TB in Montreal, Canada, 1996–2007

	Non-clustered pulmonary cases *n*	Index cases *n*	Subsequent cases generated *n*	Transmission index			
				Crude	Relative crude	Relative adjusted*	Relative adjusted 95%CI
Total	877	82	158	0.16			
Age, years							
<15	12	2	11	0.79	9.30	3.15	0.51–19.4
15–24	131	11	12	0.08	1.00†	1.00†	
25–34	213	22	42	0.18	2.11	1.39	0.56–3.48
35–44	151	20	49	0.29	3.39	2.12	0.83–5.41
45–54	90	11	16	0.16	1.87	1.29	0.43–3.91
55–64	64	4	4	0.06	0.70	0.54	0.12–2.38
≥65	216	12	24	0.11	1.25	0.99	0.37–2.62
Country of birth							
Canada	169	16	42	0.23	2.45	2.38	1.24–4.58
Haiti	94	20	55	0.48	5.21	3.58	1.74–7.36
Other	613	46	61	0.09	1.00†	1.00†	
Sex							
Male	515	50	97	0.17	1.00†	1.00†	
Female	359	32	61	0.16	0.91	0.75	0.44–1.28
Smear status							
Positive	473	54	103	0.20	1.54	1.37	0.80–2.35
Negative	404	28	55	0.13	1.00†	1.00†	
HIV status‡							
Positive	62	15	25	0.32	1.99	1.79	0.75–4.30
Negative	397	38	71	0.16	1.00†	1.00†	
Time since immigration at date of diagnosis, years§							
<5	348	35	69	0.18	1.00†	1.00†	
≥5	309	29	42	0.12	0.69	0.66	0.36–1.20

* Adjusted for age, country of birth, sex, bacillary status and person-time at risk using negative binomial regression.
† Reference category.
‡ Adjusted for age, country of birth, sex, smear status and person-time at risk using negative binomial regression. Restricted to 512 cases whose HIV status was known.
§ Adjusted for age, country of birth, sex, smear status and person-time at risk using negative binomial regression. Restricted to 721 foreign-born cases with known length of stay prior to diagnosis.
CI = confidence interval; HIV = human immunodeficiency virus.

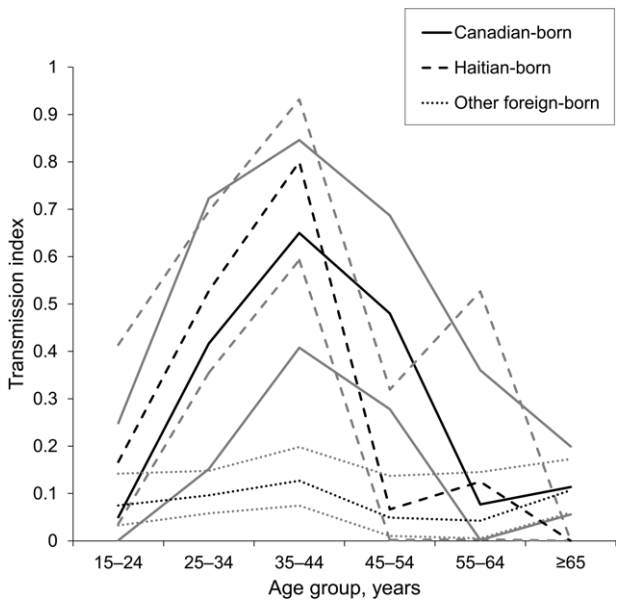

Figure 2 Crude transmission indices of tuberculosis and 95%CIs (in grey) by age group (years) stratified by country of origin, Montreal, Canada, 1996–2007. CI = confidence interval.

There was evidence of transmission linking Canadian and foreign-born patients (Table 4). Among Canadian-born non-index cases within clusters, 55% (31/56) were associated with foreign-born index cases, while 17% of foreign-born non-index cases (17/102) in clusters were linked to Canadian-born index cases. Among the Haitian-born, 21% (9/43) were linked to index cases born in Canada or other countries.

Of the 16 clusters with a Canadian-born index case, eight contained only Canadian-born subsequent cases. Four of these clusters had a HIV-positive index and at least one subsequent case who was also

Table 4 Index and subsequent tuberculosis cases in clusters by country of birth, Montreal, Canada, 1996–2007

	Subsequent cases *n*	Origin of index cases		
		Canadian-born *n* (%)	Haitian-born *n* (%)	Other foreign-born *n* (%)
Canadian-born	56	25 (44.6)	13 (23.2)	18 (32.1)
Haitian-born	43	5 (11.6)	34 (79.1)	4 (9.3)
Other foreign-born	59	12 (20.3)	8 (13.6)	39 (66.1)

HIV-positive. In total, 17/23 (74%) patients in exclusively Canadian-born clusters were HIV-positive, and 20/23 (87%) were smear-positive.

DISCUSSION

Over an 11-year period, active TB was infrequently the result of transmission in Montreal, with only 18% of genotyped cases found to be clustered. Nonetheless, we identified varying probabilities of forward transmission, according to the demographic and clinical characteristics of the index patients. Canadian and Haitian-born patients generated significantly more subsequent cases than other groups. In the case of the Canadian-born, this likely reflected urban risk factors such as HIV co-infection, substance abuse and homelessness—as documented in other low-incidence settings such as San Francisco and Alberta.[10,18,19] We found that Canadian-born patients aged 35–54 years were at higher risk of transmitting TB. This finding contrasted with results from the Netherlands, where clusters with source cases who were aged <35 years and foreign-born generated larger cluster episodes.[20] This group, which included both men and women, was well represented in clusters that included only Canadian-born patients. In four of those eight clusters, the source and at least one secondary case were HIV-positive. These findings underline the need for careful investigation of contacts of middle-aged Canadian-born patients.

The reasons for the disproportionate transmission involving Haitian-born patients are not entirely clear. Possibilities include extended social networks, with important contacts outside the home and workplace, and delays in obtaining suitable diagnosis and treatment—possibly due to continued stigma attached to active TB.[7,21] The finding that most clustered cases in the Haitian-born population are linked to potential sources within the same group supports the importance of social networks. Further examination of social networks in this population could provide important insights in this respect.

The crude transmission index of 0.48 among Haitian-born cases was somewhat higher than observed in various foreign-born subgroups in the Netherlands, where the transmission index ranged from 0.07 to 0.37, although the latter reflected a 2-year window.[15] The same authors estimated a transmission index of 0.27 for the Dutch-born,[15] which is very similar to our estimate of 0.23 for Canadian-born TB cases in Montreal. Transmission patterns for other foreign-born TB patients in Montreal were similar to those in other low-incidence settings: transmission was distinctly uncommon, and most cases likely reflected reactivation of infection acquired abroad.[18,22,23]

Smear-positive index cases, which are more infectious in any given contact episode, were not associated with significantly more subsequent TB cases, compared to smear-negative sources. This could reflect more intensive contact investigation, hospitalisation and isolation practices for smear-positive patients.[24,25] As expected, in Montreal, smear-positive TB patients were more likely than smear-negative cases to have non-household contacts investigated.[26] As a result, public health authorities may not have detected or treated latent TB infection in some contacts infected outside the household.

It has been suggested that HIV-infected TB patients may be less infectious than those without concomitant HIV infection.[27] Our results do not support this view, which has not been a universal finding. For example, a study from San Francisco used a time window similar to ours: HIV-positive patients with reactivation TB were more likely to produce secondary active TB cases than HIV-negative patients with reactivation disease.[28] Specifically, in San Francisco, 17% of such HIV-infected TB patients were cluster sources, compared to 8% without HIV. In part, this could reflect over-representation of HIV-infected contacts among HIV-infected TB patients. However, the HIV-infected sources were each associated with a mean of 2.3 HIV-negative secondary cases vs. 1.6 HIV-negative secondary cases per HIV-negative source. Unfortunately, it is not possible to calculate a transmission index using published data from the San Francisco study.[28]

Strengths of our study included its time span, exceeding 11 years, and the inclusion of nearly 98% of all culture-positive cases in a well-defined jurisdiction. In addition, we accounted for the variable duration of time during which each potential source case could generate secondary cases detectable during our study period. This was absent in earlier transmission studies.

Our analysis was constrained by three key assumptions. First, we assumed that the first reported pulmonary case in each cluster was the source. This would lead to misclassification if there were substantial delays in diagnosis, or when the true source was diagnosed after contact investigation surrounding a less infectious case. However, clusters were generally small, and the median time between the first two infectious cases in a cluster exceeded 20 months. This suggests that misclassification of the source case was uncommon.

Second, to distinguish transmitters from those infected, our model assumed that the index case was responsible for all subsequent cases within each cluster. Clearly, this assumption becomes less valid in large clusters with complex chains of transmission or in clusters spread over long periods. In our study, we found clusters that extended as long as 10 years. However, in a sensitivity analysis where we used a 3-year time window for clustering, adjusted transmission index ratios were similar, highlighting the same risk factors for transmission.

Finally, the high proportion of genotyped cases led us to assume that we had identified all index and subsequent cases. However, we would have missed a small number of linked cases diagnosed outside the spatial and temporal limits of our study, as evidenced by the presence of seven clusters that contained only extra-pulmonary cases.

By using the transmission index, and assigning subsequent cases to an index case, we estimated the extent of *M. tuberculosis* transmission according to patients' demographic and clinical characteristics. As we attempted to separate potential transmitters from those infected by others, we were able to gain additional insights. We linked potential transmission events to middle-aged patients, a finding missed by the traditional 'clustered vs. non-clustered' molecular epidemiological analysis. This approach can be extended to other low-incidence settings, where public health officials can identify high-risk groups to further reduce *M. tuberculosis* transmission and enhance TB control.

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APPENDIX

Sensitivity analysis

It may be difficult to attribute subsequent clustered tuberculosis (TB) cases to a single index case that was diagnosed many years earlier. We therefore performed a sensitivity analysis, with recalculation of the transmission index and associated ratios, allowing a 3-year window during which subsequent cases could be attributed to each index case, based on shared *Mycobacterium tuberculosis* genotypes. This reduces misclassification of third- or fourth-generation transmission events.

The 3-year cut-off reflected the cumulative probability that any given patient was followed by another with a matching *M. tuberculosis* genotype (Figure A), as described by Jasmer et al.[1] Over the entire study period in Montreal, 13.7% of cases were followed by another with a matching fingerprint. At 3 years, this probability was 9.1%. Two thirds of matching cases were thus reported within 3 years of each other.

For this sensitivity analysis, an index case was defined as a pulmonary TB case where the corresponding *M. tuberculosis* genotype was unique to the study population during the previous 3 years. Within a cluster, the pulmonary case with the earliest date of diagnosis was considered the index case, while cases with matching genotypes diagnosed within 3 years of the index case were considered subsequent cases.

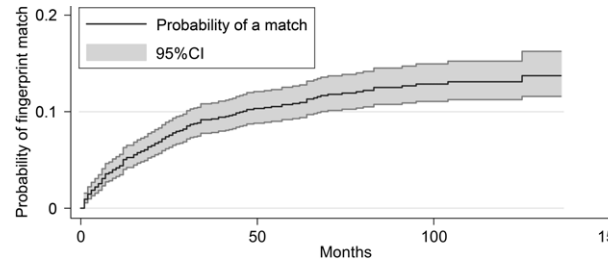

Figure A Kaplan-Meier analysis of *M. tuberculosis* fingerprinting.

Results

Compared to 'other' foreign-born TB patients, Canadian-born index cases generated 2.3 times as many subsequent cases (95% confidence interval [CI] 1.12–4.99) and Haitian-born index cases 3.08 times as many subsequent cases (95%CI 1.38–6.87). Other transmission index ratios were also similar to those from the primary analysis (Table A).

Reference

1 Jasmer R M, Hahn J A, Small P M, et al. A molecular epidemiologic analysis of tuberculosis trends in San Francisco, 1991–1997. Ann Intern Med 1999; 130: 971–978.

Table A Rolling 3-year transmission index, Montreal, Canada, 1996–2007

	Non-clustered pulmonary cases *n*	Index cases *n*	Subsequent cases generated *n*	Transmission index			
				Crude	Relative crude	Relative adjusted*	Relative adjusted 95%CI
Total	915	70	119	0.12			
Age							
<15	13	2	9	0.60	5.15	2.49	0.37–16.6
15–24	135	11	17	0.12	1.00†	1.00†	
25–34	224	15	22	0.09	0.79	0.68	0.26–1.77
35–44	157	19	35	0.20	1.71	1.61	0.63–4.16
45–54	94	10	13	0.13	1.07	0.82	0.26–2.59
55–64	67	3	3	0.04	0.37	0.42	0.09–2.04
⩾65	225	10	20	0.09	0.73	0.72	0.26–1.94
Country of birth							
Canada	178	15	32	0.17	2.23	2.36	1.12–4.99
Haiti	103	15	37	0.31	4.22	3.08	1.38–6.87
Other	633	40	50	0.07	1.00†	1.00†	
Sex							
Male	535	42	75	0.13	1.00†	1.00†	
Female	377	28	44	0.11	0.84	0.77	0.43–1.39
Smear status							
Positive	494	50	80	0.15	1.66	1.72	0.93–3.18
Negative	421	20	39	0.09	1.00†	1.00†	
HIV status‡							
Positive	69	12	20	0.25	1.76	1.86	0.71–4.89
Negative	412	36	63	0.14	1.00†	1.00†	
Time since immigration at date of diagnosis, years§							
<5	362	28	47	0.12	1.00†	1.00†	
⩾5	322	25	36	0.10	0.86	0.84	0.43–1.65

* Adjusted for age, country of birth, sex, bacillary status and person-time at risk using negative binomial regression.
† Reference category.
‡ Adjusted for age, country of birth, sex, smear status and person-time at risk using negative binomial regression. Restricted to 529 cases with known HIV serological status.
§ Adjusted for age, country of birth, sex, smear status and person-time at risk using negative binomial regression. Restricted to 737 foreign-born cases with known length of stay prior to diagnosis.
CI = confidence interval; HIV = human immunodeficiency virus.

RÉSUMÉ

CONTEXTE : Montréal, Canada, où l'incidence annuelle moyenne de la tuberculose (TB) est de 9/100 000 de 1996 à 2007.

OBJECTIF : Caractériser la potentialité de transmission de *Mycobacterium tuberculosis* dans des sous-groupes de patients déterminés par l'âge, le sexe, le lieu de naissance, le statut du frottis et du virus de l'immunodéficience humaine (VIH), et estimer la proportion de cas résultant de la transmission dans ces sous-groupes de patients.

SCHÉMA : Etude rétrospective utilisant les techniques d'empreintes digitales de l'ADN accompagnées d'une information clinique et démographique provenant du département de la santé publique. Parmi les cas où les empreintes digitales correspondent, on a identifié un cas-index pulmonaire. L'index de transmission a été défini comme le nombre moyen de cas ultérieurs de TB produits directement ou indirectement à partir d'un cas-index. Nous l'avons comparé à l'intérieur des sous-groupes, y compris les immigrants d'origine haïtienne.

RÉSULTATS : Par comparaison avec les cas-index nés à l'étranger et non-Haïtiens, les cas-index nés au Canada sont en association avec un nombre de 2,38 fois supérieur (IC95% 1,24–4,58) de cas ultérieurs alors que les cas-index nés en Haïti sont en association avec une nombre de 3,58 fois supérieur (IC95% 1,74–7,36). Les cas-index à bacilloscopie positive sont en association non-indépendante avec l'augmentation de transmission. Toutefois, les patients nés au Canada et d'âge moyen sont en association avec un nombre disproportionné de cas ultérieurs.

CONCLUSION : A Montréal, des patients-index provenant de plusieurs groupes à haut risque sont en association avec une transmission ultérieure. Cette approche peut être appliquée à d'autres contextes à faible incidence afin d'identifier les interventions ciblées qui pourraient ensuite être susceptibles de réduire la transmission.

RESUMEN

MARCO DE REFERENCIA: En Montreal, Canadá, la incidencia anual promedio de tuberculosis (TB) entre 1996 y el 2007 fue 9 por 100 000 habitantes.

OBJETIVO: Caracterizar la posible transmisión de *Mycobacterium tuberculosis* por subgrupos de pacientes definidos en función de la edad, el sexo, el lugar de nacimiento, la baciloscopia y el estado frente al virus de la inmunodeficiencia humana (VIH) y calcular la proporción de casos que aparecieron a partir de una transmisión en estos subgrupos de pacientes.

MÉTODO: Se llevó a cabo un estudio retrospectivo con base en técnicas de huella genética y se obtuvo información clínica y demográfica del departamento de salud pública. En los casos con huellas genéticas idénticas se detectó el caso inicial de TB pulmonar. El índice de transmisión se definió como el número promedio de casos, que surgieron directa o indirectamente a partir de un caso inicial y se comparó este índice entre los subgrupos, incluidos los inmigrantes haitianos.

RESULTADOS: Comparados con los casos iniciales de personas nacidas en el extranjero (no haitianas), los casos iniciales de personas nacidas en el Canadá se asociaron con 2,38 veces más de casos secundarios (IC95% 1,24–4,58) y los casos iniciales de personas nacidas en Haití se asociaron con 3,58 veces más (IC95% 1,74–7,36). Los casos iniciales con baciloscopia positiva no se asociaron en forma significativa con una mayor transmisión. Sin embargo, los casos iniciales de las personas nacidas en Canadá, de mediana edad, se asociaron con un número desproporcionado de casos secundarios.

CONCLUSIÓN: En Montreal, los casos iniciales de TB en varios grupos con alto riesgo se asocian con transmisión secundaria. La presente estrategia se puede aplicar en otros entornos de baja incidencia, con el fin de detectar las poblaciones en las cuales las intervenciones dirigidas pueden disminuir aun más la transmisión.