A Molecular Epidemiological Approach to Studying the Transmission of Tuberculosis in Amsterdam

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We conducted a retrospective, population-based study with use of restriction fragment length polymorphism (RFLP) analysis to determine the incidence of and risk factors for clustering of *Mycobacterium tuberculosis* isolates, indicative of recently transmitted infection, among patients with culture-proven tuberculosis diagnosed between 1 July 1992 and 1 January 1995 in Amsterdam. We found that 214 (47%) of 459 patients were in 53 clusters, probably because of recent transmission of *M. tuberculosis* among 161 (35%) of these patients. Conventional contact tracing resulted in identification of 5.6% of the 161 patients. Clustering was more frequent among Dutch patients (59.3%) than among foreign ethnic patients (42.1%) ($P = .002$). The independent risk factor for clustering among Dutch patients was younger age; the independent risk factors among foreign ethnic patients were hard-drug use; alcohol abuse; and country of origin (Surinam or the Netherlands Antilles). These findings suggest the shortcomings of the usual tuberculosis control policies in Amsterdam. We identified several risk factors for clustering, which may guide adjustment of tuberculosis control and contact tracing strategies.

The incidence of tuberculosis has increased during recent years in several developed countries. This increase has been attributed to immigration from developing countries, the HIV epidemic, deteriorating social conditions, and a declining public health infrastructure [1–4]. A resurgence of tuberculosis has also been observed in the Netherlands, where the incidence increased from 9.7 cases per 100,000 population in 1984 to 11.8 cases per 100,000 population in 1994 [5]. In Amsterdam, this incidence increased from 24 cases per 100,000 population to 41 cases per 100,000 population during this period, which is the highest figure since 1966 [6]. In contrast, the incidence of tuberculosis was 33.4 cases per 100,000 population in 1995 in New York City [7].

It has long been assumed that the majority of tuberculosis cases among the indigenous and foreign-born populations in developed countries result from reactivation of latent, remote infections [8]. Typing of *Mycobacterium tuberculosis* strains by using restriction fragment length polymorphism (RFLP) analysis has improved the understanding of tuberculosis transmission. Patients infected with *M. tuberculosis* strains showing identical RFLP patterns are usually epidemiologically linked [9–12]. Such clustered cases of tuberculosis seem to be the result of recently transmitted infection, with rapid progression to clinical disease [11–15].

Recent studies using RFLP analysis have demonstrated that, in contrast with previous assumptions, a large proportion (28%–40%) of tuberculosis cases in urban areas in some industrialized countries occur in clusters and therefore are probably the result of recent transmission [13–15]. In one study, only a minority (10%) of these clustered cases were identified by conventional contact tracing [14].

Amsterdam is a medium-sized city (population, 724,096 in 1994); 41% of the population is of foreign ethnicity, and these persons predominantly originate from countries with a high prevalence of tuberculosis. Furthermore, the city has a relatively large concentration of homeless persons and hard-drug users, and ~50% of cumulatively reported AIDS cases in the Netherlands were diagnosed among residents of Amsterdam. These conditions are well-known risk factors for the development of tuberculosis [1, 2].

We conducted this population-based retrospective study to determine to what extent the relatively high incidence of tuberculosis in Amsterdam is the result of recently transmitted disease and to identify risk factors for recent transmission among patients in Amsterdam. To our knowledge, this is the first large, thoroughly population-based study conducted in an urban area outside the United States.

Methods

Study population and data collection. Nominative notification of tuberculosis cases is mandatory in the Netherlands. Cases among residents of Amsterdam are reported to the Tuberculosis Department of the Municipal Health Service. These

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patients are routinely interviewed about their social histories by a public health nurse who uses a standardized questionnaire. Mycobacterial cultures of specimens from these patients are performed at five microbiological laboratories in Amsterdam.

The population we studied included 608 patients who were residing in Amsterdam and were found to have tuberculosis between 1 July 1992 and 1 January 1995, as reported to the Municipal Health Service.

In 493 (81%) of 608 cases, the diagnosis was confirmed by a positive culture. The isolates were all stored at the five laboratories, along with isolates recovered from 21 Amsterdamers with tuberculosis that was diagnosed during the study period and had never been reported to the Municipal Health Service. These 21 patients were also included in the study. Four patients were excluded because culture results were thought to represent cross-contamination in the laboratory. These four patients, who had no clinical evidence of tuberculosis, each had a single positive culture that was processed on the same day as other patients' cultures and showed identical RFLP patterns.

Isolates from 51 of the remaining 510 patients were nonviable. These 51 patients did not differ significantly from the other 459 patients with regard to age, sex, ethnicity, or site of tuberculosis. Therefore, isolates from 459 Amsterdamers with culture-confirmed tuberculosis during the study period were typed by using RFLP analysis.

Sociodemographic and clinical data and the results of contact tracing and microbiological studies were collected retrospectively from hospital medical records, tuberculosis registries, and public health nursing files. Data for 21 patients whose cases were not reported to the Municipal Health Service were obtained through the microbiological laboratories. All data were entered anonymously on standardized records.

Collected data were assigned to three sets of variables. Set 1 (general characteristics) included age, sex, nationality, country of origin of patients' mothers (ethnicity), and duration of residency in the Netherlands. Country of origin of patients' mothers was selected as a variable because this information better reflects patients' ethnicities than does nationality or country of origin. Many immigrants and their children, who are often born in the Netherlands and have reached adulthood by now, have obtained the Dutch nationality.

Set 2 (behavioral characteristics, which applied to the period between 2 years and 2 months before the diagnosis of tuberculosis) included homelessness, alcohol abuse ($\geq$5 U/d), use of hard drugs, current smoking, sexual inclination, illegal residency, employment as a health care worker, and duration of stay ($>$2 months) in areas with a high prevalence of tuberculosis.

Set 3 (clinical characteristics) included date of diagnosis of tuberculosis, site of disease (pulmonary, extrapulmonary, or both), resistance to any antituberculous drug, the presence of HIV infection (confirmed seropositivity vs. confirmed seronegativity or unknown serostatus), reporting of the case to the Municipal Health Service, and identification of the case by contact tracing.

Collection of M. tuberculosis isolates and RFLP analysis. As of 1 January 1993, all *M. tuberculosis* isolates recovered in the Netherlands have routinely been typed by use of RFLP analysis at the National Institute of Public Health and the Environment in Bilthoven. *M. tuberculosis* isolates that were recovered from patients who were residing in Amsterdam and that were cultured between 1 July 1992 and 1 January 1995, when RFLP analysis was not yet being performed, were collected and typed at the five microbacteriological laboratories as well at the National Institute in Bilthoven.

All isolates available for RFLP analysis were subjected to standard IS*6110* DNA fingerprinting, as previously described [16]. Because strains with few IS*6110* copies are difficult to differentiate, all strains with fewer than five IS*6110* copies (n = 33) were subjected to additional DNA fingerprinting by using the polymorphic GC-rich sequence (PGRS) as a probe [17]. Strains were considered identical when no differences were found in both IS*6110* and PGRS banding patterns. Nine (27%) of these 33 strains, which showed identical IS*6110* patterns, yielded distinct patterns after analysis with use of PGRS.

Computer-assisted analysis of IS*6110* DNA fingerprints was done by using the software Gelcompar, version 3.1b for Windows (Applied Maths, Kortrijk, Belgium), as previously described [18, 19].

Statistical analysis. For the univariate analysis, we used the χ^2 test and χ^2 test for trend. P values of $<.05$ were considered significant. For the multivariate analysis, we used logistic regression to determine independent risk factors for clustering, to adjust for confounding, and to check for effect modification.

Variables showing univariate significance levels of $\leq.1$ were considered for entry in multivariate models. Independent risk factors per set of variables (see above) were defined, after which the remaining risk factors were combined. Forward and backward stepwise variable selection was used.

On analyzing risk factors for clustering, we found that there appeared to be a strong statistical interaction between ethnicity and several other variables. Because of this marked difference between risk factors among Dutch and foreign ethnic patients, analyses were performed for these two groups separately.

Results

RFLP analysis and cluster characteristics. The main results of RFLP analysis of isolates from the 459 patients with culture-proven tuberculosis during the 2.5-year study period are shown in figure 1. By using IS*6110* and PGRS analysis, we identified 298 distinct RFLP patterns, 53 of which were found to be shared by two or more isolates from these patients.

Since the data from this study could be combined with the data from RFLP analysis of *M. tuberculosis* isolates from patients elsewhere in the Netherlands, 37 patterns, unique among the patients in Amsterdam, were each shown to be identical with the RFLP fingerprints of isolates from at least one patient outside Amsterdam. Since clinical and demographic data were

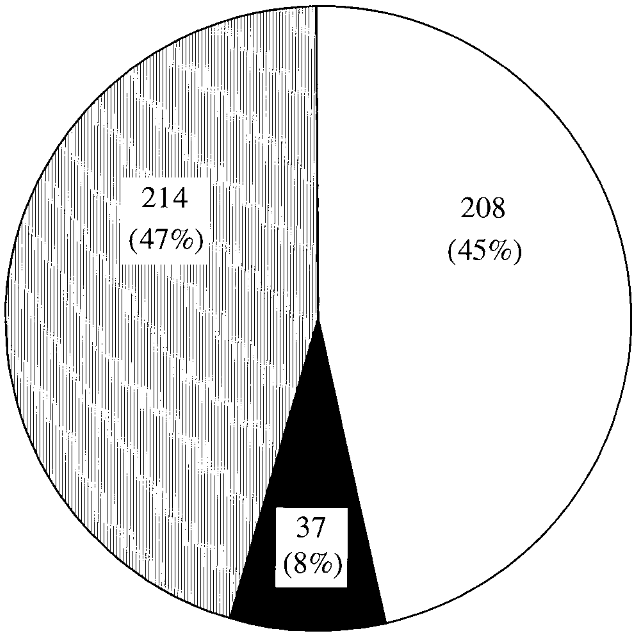

Figure 1. Results of restriction fragment length polymorphism (RFLP) analysis of *Mycobacterium tuberculosis* isolates from 459 patients with tuberculosis in Amsterdam; ▥ = patient isolates with 53 RFLP patterns shared in Amsterdam; ■ = patient isolates with 37 RFLP patterns that were unique in Amsterdam and identical with pattern(s) of isolates from one or more patients outside Amsterdam; □ = patient isolates with unique RFLP patterns.

not available for patients outside Amsterdam, we considered, for risk factor analysis, these 37 patients' isolates to have unique RFLP patterns. Considering the isolates to be clustered did not substantially change our results.

During the study period, 47% of the patients were in 53 clusters in Amsterdam, whereas 55% were clustered with patients in or outside Amsterdam.

Assuming that in each Amsterdam cluster one patient acted as an index patient for the other patient(s), the number of tuberculosis cases—probably acquired by infection transmitted during the 2.5-year study period—was 161 (214 − 53), accounting for 35% of 459 culture-proven cases in Amsterdam.

Figure 2 shows the sizes and frequencies of the Amsterdam clusters. Of 214 clustered patients, 34% were in small clusters (two patients), 28% were in medium-sized clusters (three to nine patients), and 38% were in large clusters (⩾10 patients). When patients in large clusters were compared with those in other clusters, the patients in large clusters were more likely to be >30 years of age, to be of Dutch, Surinam, or Netherlands Antilles ethnicity, to be hard-drug users, and to have resided >10 years in Amsterdam ($P < .05$, data not shown).

More-detailed information concerning the composition of the three largest clusters is shown in table 1. Cluster A ($n = 29$) contained a relatively large number of hard-drug users and homeless persons; cluster C ($n = 14$) contained more HIV-

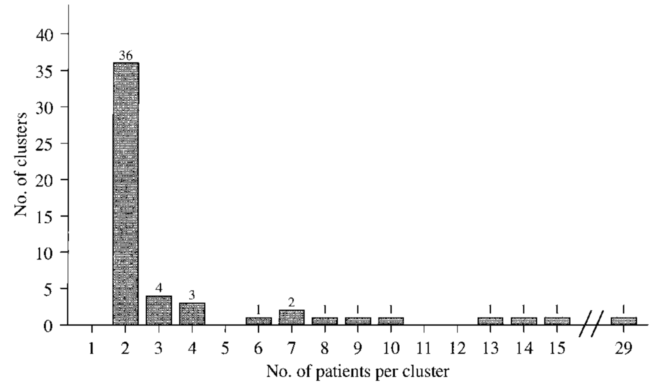

Figure 2. Sizes and frequencies of 53 clusters consisting of 214 patients with tuberculosis in Amsterdam.

infected patients and male homosexuals. Patients in cluster B ($n = 15$) were younger and more often female and of Moroccan, Surinam, or Netherlands Antilles ethnicity. Pulmonary involvement was less common in cluster B, and no patients in this cluster were recorded as being hard-drug users or HIV-infected.

Only nine (5.6%) of 161 patients in the Amsterdam clusters, where tuberculosis was probably the result of recent transmission, had already been identified by conventional contact tracing. Recent transmission was unsuspected in the other 152 patients.

Risk factors for clustering. The ethnicity of 11 Amsterdamers whose *M. tuberculosis* strains were available for RFLP

Table 1. Characteristics of patients with tuberculosis who were in the three largest clusters in Amsterdam.

	No. (%) of patients in indicated cluster		
Variable	A ($n = 29$)	B ($n = 15$)	C ($n = 14$)
Mean age in y	38.8	30.3	37.6
Male sex	25 (86)	10 (67)	12 (86)
Hard-drug use*	17 (59)	0	4 (29)
Homelessness*	12 (41)	1 (7)	0
HIV infection	8 (28)	0	6 (43)
Male homosexuality	2 (7)	0	6 (43)
Site of tuberculosis			
Pulmonary	19 (66)	7 (47)	9 (64)
Extrapulmonary	3 (10)	6 (40)	1 (7)
Both	7 (24)	2 (13)	4 (29)
Ethnicity			
Netherlands	11 (38)	1 (7)	6 (43)
Turkey	1 (3)	0	2 (14)
Morocco	2 (7)	7 (47)	0
Surinam or Netherlands Antilles	5 (17)	6 (40)	2 (14)
Other African countries	2 (7)	0	0
Other	8 (28)	1 (7)	4 (29)

* Applies to the period between 2 years and 2 months before the diagnosis of tuberculosis.

analysis was unknown; these patients were excluded from the analysis of risk factors for clustering. Among the remaining 448 patients, 108 were Dutch, and 340 were of foreign ethnicity; 59.3% of the Dutch patients and 42.1% of the foreign patients were clustered (χ^2 test; $P = .002$).

Table 2 shows the variables that were, by univariate analysis, significantly associated with clustering, either among Dutch or among foreign ethnic patients. We adjusted for age only among the Dutch patients, as this adjustment among foreign ethnic patients hardly changed the odds ratios.

Dutch tuberculosis patients in Amsterdam were more likely to be in a cluster if they were younger (mean age, 38 years vs. 52.8 years for patients not in clusters; $P < .001$), were current smokers, were hard-drug users, were homeless, or were HIV infected. These patients were less likely to be part of a cluster if they were health care workers or had recently stayed in an area with a high prevalence of tuberculosis. After adjustment for age, only hard-drug use remained a significant risk factor for clustering, whereas health care work and a recent stay in high-prevalence areas remained negative predictors of clustering.

For patients of foreign ethnicity, the risk of being clustered increased significantly as the duration of residency in the Netherlands increased. Other risk factors were alcohol abuse, current smoking, and hard-drug use. Patients whose countries of origin were Surinam or the Netherlands Antilles were more likely to be clustered. Indian or Pakistani ethnic origin significantly decreased the risk of being part of a cluster, as did a diagnosis of extrapulmonary tuberculosis, with or without pulmonary tuberculosis.

Multivariate analysis (table 3) revealed that among Dutch patients, older age, recent stay in a high-prevalence area, and health care work were associated with a decreased risk of being clustered.

For foreign ethnic patients, hard-drug use, alcohol abuse, or being from Surinam or the Netherlands Antilles was an independent risk factor for clustering. The presence of extrapulmonary tuberculosis, with or without pulmonary tuberculosis, was an independent negative predictor of clustering.

None of the interaction terms between variables in the two models was significant.

Discussion

Active transmission of tuberculosis appears to contribute greatly to the relatively high incidence of tuberculosis in Amsterdam, since 214 (47%) of 459 patients with culture-confirmed tuberculosis were in 53 clusters, 161 (35%) of which were probably the result of recently transmitted infection. Comparable studies in other industrialized countries have also demonstrated a high rate of clustering and recent transmission [13–15].

Our analysis probably underestimates the extent of recent transmission in Amsterdam because the patients who were considered to be the index patient in each cluster in many cases would have acquired tuberculosis through recent transmission in the time preceding our study period.

Furthermore, transmission of tuberculosis is not confined by city borders. We found that 37 (8%) of 459 patients' isolates had RFLP patterns that were unique in Amsterdam but identical to the pattern of the isolate from one or more patient(s) in the rest of the Netherlands. Since RFLP analysis was not performed systematically on all *M. tuberculosis* isolates in the Netherlands during our study period and we were not informed about the results of RFLP analysis in other countries, the true extent of clustering among Amsterdam patients with patients elsewhere in the Netherlands or abroad is probably greater.

On the other hand, clustering of tuberculosis cases might not necessarily always be the result of recently transmitted infection because genetically related *M. tuberculosis* strains could have been transmitted via different pathways to epidemiologically unrelated patients whose isolates showed identical RFLP patterns.

Furthermore, *M. tuberculosis* strains in countries with a high prevalence of tuberculosis show less genetic heterogeneity than do strains in countries such as the Netherlands [19, 20]. The presence of identical RFLP fingerprints of isolates from patients of the same foreign ethnicity could be the result of reactivation of latent infections independently acquired from the homogeneous population of *M. tuberculosis* in the country of origin.

In such a case, more clustering among foreign ethnic patients would be expected, as would the finding that the majority of clustered cases among these patients occur shortly after arrival in the Netherlands. However, we found that clustering was more frequent among Dutch patients than among foreign ethnic patients, for whom the risk of being clustered increased significantly with duration of residency in the Netherlands.

We therefore believe that the vast majority of clustered tuberculosis cases in Amsterdam are part of an active chain of transmission. This belief is supported by our findings regarding the three largest Amsterdam clusters: the composition of each cluster was entirely different from the others, and striking similarities between the patients within these clusters were discernable, indicative of an epidemiological relationship. Nevertheless, none of these clusters was completely homogeneous with regard to the characteristics of the patients, a finding that indicates mutual transmission between different demographic groups.

In the Netherlands, tuberculosis contact tracing is performed following the so-called ring-principle [20]. Contacts are examined in groups, located in concentric circles around the source case, until the observed prevalence of tuberculous infection corresponds with the expected prevalence. The effectiveness of this procedure is largely dependent on the willingness and capability of the index patient to cooperate by providing a careful social history.

This approach seems insufficient for following the pathways of transmission in a multicultural urban area like Amsterdam, as only 5.6% of the cases that were probably recently transmitted were identified by conventional contact tracing.

Table 2. Risk factors for clustering among 108 Dutch and 340 foreign ethnic patients with tuberculosis in Amsterdam.

	Dutch patients			Foreign ethnic patients	
Variable	No. of patients with characteristic (% of patients in cluster)	Crude OR (95% CI)	OR adjusted for age (95% CI)	No. of patients with characteristic (% of patients in cluster)	Crude OR (95% CI)
Sex					
Male	75 (65.3)	1	1	235 (45.1)	1
Female	33 (45.5)	0.44 (0.19–1.02)	0.67 (0.25–1.78)	105 (35.2)	0.66 (0.41–1.07)
Age					
⩽30 y	28 (60.7)	1	NA	169 (43.8)	1
31–60 y	57 (75.4)	1.99 (0.75–5.24)	NA	158 (41.8)	0.92 (0.59–1.43)
⩾61 y	23 (17.4)	0.14 (0.04–0.51)	NA	13 (23.1)	0.39 (0.10–1.45)
Alcohol abuse[†]					
No	72 (55.6)	1	1	289 (40.1)	1
Yes	20[‡] (70.0)	1.87 (0.64–5.41)	1.27 (0.39–4.13)	18[‡] (72.2)	3.88 (1.35–11.17)
Smoking[†]					
No	40 (45.0)	1	1	126 (36.0)	1
Yes	49[‡] (71.4)	3.06 (1.27–7.36)	1.79 (0.66–4.85)	173[‡] (52.0)	1.97 (1.23–3.14)
Hard-drug use[†]					
No	85 (51.8)	1	1	301 (38.9)	1
Yes	22[‡] (90.9)	9.32 (2.05–42.37)	5.13 (1.06–24.81)	37[‡] (70.3)	3.72 (1.77–7.81)
Homeless[†]					
No	92 (54.3)	1	1	310 (41.9)	1
Yes	16 (87.5)	5.88 (1.26–27.36)	3.18 (0.66–15.41)	30 (43.3)	1.06 (0.50–2.26)
Health care work[†]					
No	96 (62.5)	1	1	329 (41.9)	1
Yes	8[‡] (25)	0.20 (0.04–1.04)	0.16 (0.03–0.88)	9[‡] (44.4)	1.11 (0.29–4.20)
Recent stay (>2 mo) in high-prevalence areas[†]					
No	94 (66.0)	1	1	148 (39.2)	1
Yes	11[‡] (9.1)	0.05 (0.01–0.42)	0.03 (0.003–0.23)	78[‡] (39.7)	1.02 (0.58–1.79)
Site of tuberculosis					
Pulmonary	69 (52.2)	1	1	188 (48.9)	1
Extrapulmonary	20 (70.0)	2.14 (0.74–6.22)	2.24 (0.67–7.42)	104 (34.6)	0.55 (0.34–0.91)
Both	19 (73.3)	2.57 (0.83–7.91)	2.24 (0.62–8.07)	48 (31.1)	0.47 (0.24–0.93)
HIV infection					
No or unknown	81 (50.6)	1	1	304 (42.4)	1
Yes	27 (85.2)	5.61 (1.78–17.68)	2.95 (0.88–9.87)	36 (38.9)	0.86 (0.43–1.75)
Ethnicity					
Other	NA	NA	NA	86 (34.9)	1
Turkey	NA	NA	NA	53 (43.4)	1.43 (0.71–2.89)
Morocco	NA	NA	NA	84 (42.9)	1.40 (0.75–2.60)
Surinam or Netherlands Antilles	NA	NA	NA	54 (70.4)	4.43 (2.13–9.23)
India or Pakistan	NA	NA	NA	29 (13.8)	0.30 (0.10–0.94)
Other African countries	NA	NA	NA	34 (35.3)	1.02 (0.44–2.34)
Duration of residency[§]	NA	NA	NA	325[‡] (18.8–49.5)	1.21 (1.05–1.40)*

NOTE. NA = not applicable.
* The odds ratio reflects the likelihood of being in a cluster for every category, as compared with the previous category.
[†] Applies to the period between 2 years and 2 months before the diagnosis of tuberculosis.
[‡] Numbers do not add up to total because of missing data.
[§] Duration of residency in the Netherlands was classified as follows: <2 months, 2 months–1 year, 1–2 years, 2–5 years, 5–10 years, and >10 years, and was analyzed as a continuous variable; 105 of the 108 Dutch patients had resided in the Netherlands for >10 years.

The inadequacy of contact tracing is reflected in our finding that the risk of being part of a cluster was not increased among patients who were not notified at the Municipal Health Service (4% of culture-confirmed cases). Since contact tracing is precluded in this situation, more cases of tuberculosis due to isolates with RFLP patterns identical to the patterns of isolates from unnotified patients would be expected. However, 10 (4.7%) of 214 clustered patients were not reported, whereas

Table 3. Results of a multivariate analysis of risk factors for clustering of cases, after adjustment for study variables, among 108 Dutch patients and 340 foreign ethnic patients with tuberculosis in Amsterdam.

Risk factor	OR (95% CI)
Dutch patients	
Age in y	
≤30	1
31–60	2.47 (0.76–8.06)
≥61	0.10 (0.02–0.42)
Recent stay (>2 mo) in a high-prevalence area*	
No	1
Yes	0.02 (0.002–0.20)
Health care work*	
No	1
Yes	0.11 (0.02–0.71)
Foreign ethnic patients	
Hard-drug use*	
No	1
Yes	2.84 (1.19–6.77)
Alcohol abuse*	
No	1
Yes	3.69 (1.15–11.84)
Site of tuberculosis	
Pulmonary	1
Extrapulmonary	0.49 (0.27–0.90)
Both	0.43 (0.20–0.93)
Ethnicity	
Other	1
Turkey	1.89 (0.83–4.33)
Morocco	1.97 (0.96–4.04)
Surinam or Netherlands Antilles	8.28 (3.47–19.77)
India or Pakistan	0.52 (0.15–1.74)
Other African countries	1.50 (0.59–3.86)

* Applies to the period between 2 years and 2 months before the diagnosis of tuberculosis.

8 (3.3%) of 245 unclustered patients were not reported ($P = .44$).

In our analysis several risk factors for clustering became apparent; these risk factors may have important implications for tuberculosis control and practicing physicians.

The univariate analysis revealed that for Dutch patients with tuberculosis, younger age, use of hard drugs (91% of these patients were part of a cluster), homelessness, and HIV seropositivity were associated with an increased risk of being clustered. There appeared to be substantial overlap of these risk factors according to age: after adjustment for this variable, only hard-drug use remained a significant risk factor for clustering among Dutch patients.

For foreign ethnic patients, alcohol abuse and origination from Surinam or the Netherlands Antilles, after smoking and hard-drug use, increased the risk of being clustered. This risk also increased with duration of residency in the Netherlands.

The multivariate analysis revealed that younger age was the only independent risk factor for clustering among Dutch patients. For foreign ethnic patients, hard-drug use, alcohol abuse, and origination from Surinam or the Netherlands Antilles were independently associated with clustering. Foreign ethnic drug users and alcohol abusers in Amsterdam are generally younger and lead more active social lives than do Dutch persons from the same groups; these findings probably make foreign ethnic drug users and alcohol abusers with tuberculosis more likely to be clustered.

Patients from Surinam or Netherlands Antilles easily feel stigmatized if they have tuberculosis and are therefore reluctant to mention names of contacts. This finding may explain why such ethnicity is an independent risk factor for clustering.

For Dutch patients, recent stay in an area with a high prevalence of tuberculosis, where, under certain conditions, tuberculosis infections can be acquired easily, and health care work were independently associated with a reduced risk of being clustered. We do not have a sufficient explanation for the latter finding, which contrasts with the findings of other studies (e.g., the study conducted in New York City [21]). However, health care work had a small impact as a factor because only a small number of patients in this group were included in our study population.

We found that the presence of extrapulmonary tuberculosis (with or without pulmonary tuberculosis) made foreign ethnic patients less likely to be part of a cluster. Extrapulmonary infection is common in HIV-infected patients with tuberculosis [22]. This finding may be explained by the higher frequency of HIV infection among Dutch patients (25%) than among foreign ethnic patients (11%), and it was associated with clustering in the univariate analysis only for the former group.

The results of our study necessitate a change in tuberculosis control strategies in Amsterdam. The contribution of recently transmitted tuberculosis is much greater than previously thought. It is apparent that the yield is strikingly low when conventional contact tracing is used to identify persons with recently transmitted tuberculosis and that there is an increased risk of tuberculosis transmission among several populations.

Education on tuberculosis and contact tracing strategies need to be adapted to the characteristics of distinct population groups. Expansion of screening programs should be considered for groups with increased risk of transmission, particularly if it appears that effective contact tracing is not feasible.

A prospective study of transmission routes for tuberculosis in Amsterdam and the surrounding areas is necessary to better identify the conditions for an increased risk of transmission, thereby facilitating interventional measures and improving contact tracing.

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