Beijing/W genotype Mycobacterium tuberculosis and drug resistance: European Concerted Action on New Generation Genetic Markers and Techniques for the Epidemiology and Control of Tuberculosis * (1)

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Beijing/W genotype Mycobacterium tuberculosis is widespread, may be increasing, and may have a predilection for drug resistance. Individual-level data on >29,000 patients from 49 studies in 35 countries were combined to assess the Beijing genotype's prevalence worldwide, trends over time and with age, and associations with drug resistance. We found 4 patterns for Beijing/W genotype tuberculosis (TB): 1) endemic, not associated with drug resistance (high level in most of East Asia, lower level in parts of the United States); 2) epidemic, associated with drug resistance (high level in Cuba, the former Soviet Union, Vietnam, and South Africa, lower level in parts of Western Europe); 3) epidemic but drug sensitive (Malawi, Argentina); and 4) very low level or absent (parts of Europe, Africa). This study confirms that Beijing/VV genotype TB is an emerging pathogen in several areas and a predominant endemic strain in others; it is frequently associated with drug resistance.

The Mycobacterium tuberculosis genotype family known as "Beijing/W," "W-Beijing," or "Beijing" is widespread (1-3). Described in 1995 as the prevalent genotype in East Asia (4), >80% of strains from the Beijing area were of this type. The multidrug-resistant W strain is a member of the family. We use "Beijing" for the whole genotype family.

Researchers are concerned that the Beijing genotype may have a predilection for developing drug resistance (5) and may be spreading worldwide, perhaps as a result of increased virulence (6). A systematic review of the published literature in 2002 concluded that although Beijing genotype tuberculosis (TB) was widespread, associations with drug resistance varied, and little information on time trends was available (2).

The review highlighted the problems of relying on published literature: varying strain definitions; reporting bias; and limited information on selection criteria, population subgroups, age groups, or time trends. As part of the European Concerted Action on New Generation Genetic Markers and Techniques for the Epidemiology and Control of Tuberculosis, we have combined available datasets, using a common strain definition and individual-level data.

Methods

Studies for inclusion were identified from the systematic review and from contacting members of the European Concerted Action and authors of relevant articles published since the review. We aimed to include as many studies as possible in which the proportion of TB caused by the Beijing genotype could be

ascertained in an unbiased way. Studies could represent all or random samples of patients in an area, hospital, or laboratory. Studies limited to outbreaks, drug-resistant isolates, or of <30 patients were excluded. A study description and individual patient data that included at least the year the case was diagnosed and the genotype were required.

Strain Classification

Three methods identify Beijing genotype strains: spoligotyping (7), IS6110 restriction fragment length polymorphism (RFLP) (8), and region A RFLP (9). The typical Beijing spoligotype shows hybridization to spacers 35-43. Beijing-like patterns with <9 spacers (but not solely spacers 37-38, which represents M. microti), were included (10).

By using IS6110 RFLP, fingerprints are compared to 19 patterns representative of the Beijing genotype (https:// hypocrates.rivm.nl/bnwww/index.html). With standard techniques, allowing 1% position tolerance and classifying all matches >80% as Beijing, these patterns have 96%-100% sensitivity and 98%-100% specificity to detect Beijing strains, taking spoligotyping as the accepted standard (10). Sensitivity is increased by spoligotyping strains with RFLP patterns that match 75%-80% to the reference strains. The third technique uses a characteristic IS6110 insertion in region A. This method has 100% sensitivity and 98% specificity compared with spoligotyping (10).

Analysis

The proportion of Beijing genotype strains in each study was calculated overall and after excluding immigrants. The proportion of Beijing genotype in immigrants was examined by place of birth. Time trends were examined directly and by examining trends with age; an association with younger age groups would suggest that the proportion of TB attributable to the Beijing genotype was increasing. Associations with drug resistance were examined, after immigrants were excluded, with and without excluding patients with previous TB. For pooled analyses, heterogeneity in the associations between studies was examined, and the results presented are adjusted for study.

Results

Data were received from 49 studies representing 29,259 TB patients in 35 countries, including 11 studies from the systematic review (2); other studies in the review had no individual patient data available, used nonstandard case definitions, or researchers declined to participate. Other studies were contributed by members or contacts of the Concerted Action or were identified from subsequently published studies. Details of all included studies are shown in online Appendix Table 1 (available from http://www. cdc.gov/ncidod/EID/vol12no05/05-0400_app.htm).

The proportion of tuberculosis due to the Beijing genotype in the included studies is shown in online Appendix Table 2 (available from http://www.cdc.gov/ncidod/EID/vol12no05/05-0400_app.htm#table2).

Overall, 9.9% had the Beijing genotype. In Western Europe and the Czech Republic, the proportion was low: <6% of cases among nonimmigrants. In sub-Saharan Africa, the proportion was low except in Cape Town, South Africa. In Latin America, data were only available from Argentina and Brazil; both studies found <1% of TB cases were caused by Beijing genotype. In North America and

the Caribbean, the proportion was higher (8%-14%). In the former Soviet Union the proportion was high: 45%-56% in Russia and 29% in Estonia. The proportion was low in India (1%), higher in Bangladesh (7%), and increased further east: >50% in many parts of Southeast and East Asia.

Analyses by region of birth showed similar patterns (Table 1). Beijing genotype strains were rare (0.5%) among immigrants from Eastern Europe other than the former Soviet Union; most came from the former Yugoslavia. The Beijing genotype was much less common among immigrants from the Indian subcontinent (3.4%) than among those from Southeast Asia (19%) or East Asia (58%). Beijing genotype strains were uncommon among immigrants from North Africa (3.0%), the Middle East (5.2%), and sub-Saharan Africa (2.2%, including 50 [2.1%] of 2,427 persons from Somalia). Among Middle Eastern immigrants, Beijing genotype was found in 6 (1%) of 620 persons from Turkey but in 8 (9.9%) of 81 from Afghanistan.

Time Trends

Time trends were analyzed among nonimmigrants within individual studies with [greater than or equal to] 3 years of data (Table 2). (Studies from France, Iran, Thailand, Vietnam, and Spain are excluded because of small numbers in some years or absence of Beijing genotype strains.)

All Western European sites except London showed a slight increase in Beijing strains over time, but this finding was only significant in the Netherlands. Combining data for Western Europe, the odds ratio (OR), adjusted for study, for having the Beijing genotype in the later period compared to the earlier period was 1.5 (95% confidence interval [CI] 1.2-1.9). This figure was unchanged after adjusting for age. The trend was similar after excluding the Netherlands (adjusted OR 1.7, 95% CI 0.96-3.1).

In St. Petersburg, Okayama, Buenos Aires, Sao Paulo, and San Francisco, no significant change occurred over time, but the studies only covered a few years. In Cape Town and Malawi, significant increases occurred over time and were unchanged after adjusting for age.

Trends with Age

Trends with age for studies with [greater than or equal to] 3 cases of Beijing genotype TB among nonimmigrants are summarized in Table 3. Most Western European studies found the highest proportion of Beijing

genotype TB in the youngest age groups. Overall, for Western Europe, compared to those age [greater than or equal to] 50 years, the OR, adjusted for study, of having the Beijing genotype was 1.2 (0.87-1.6) for those 30-49 years of age, and 2.4 (95% CI 1.8-3.3) for those <30 years of age, [P.sub.trend]<0.001. Excluding the Netherlands, the trend was stronger: adjusted OR 2.2 (95% CI 1.1-4.2) for those 30-49 years of age and 3.9 (95% CI 1.9-7.9) for those <30 years of age, [P.sub.trend]<0.001.

In Russia and Estonia, Beijing genotype strains were more common in younger patients, and the trend was significant in St. Petersburg ($p = 0.02$). Overall, compared to those [greater than or equal to] 50 years of age, the study-adjusted OR was 1.1 (95% CI 0.70-1.8) for those 30-49 years of age and 1.7 (95% CI 1.1-2.9) for those <30 years of age, [P.sub.trend] = 0.02.

The African studies that found any Beijing strains noted a higher proportion in younger persons than in older persons. This difference was not significant in individual studies but was when studies were combined: study-adjusted OR, 1.9 (95% CI 1.1-3.4) for those 30-49 years of age and 2.1 (95% CI 1.2-3.7) for those <30 years of age, compared to those [greater than or equal to] 50 years of age, [P.sub.trend] = 0.03.

Among nonimmigrants in US studies, no significant trend occurred with age, either individually or overall. In Cuba, Beijing genotypes were more common in younger persons than in older persons in the larger study and overall ([P.sub.trend] = 0.06). In Buenos Aires and Sao Paulo, all Beijing genotype--infected patients were <30 years of age (p = 0.002).

Most Asian studies showed no association with age, but trends were seen in Bangladesh, Vietnam, and Hong Kong. In Vietnam, Beijing genotype was more common in younger patients in all 4 studies: overall, compared to those [greater than or equal to] 50 years of age, the study-adjusted OR was 1.5 (95% CI 1.0-2.2) for those 30-49 years of age and 2.7 (95% CI 1.7-4.2) for those <30 years of age, [P.sub.trend]<0.001. In Hong Kong, Beijing genotypes were least common in patients <30 years of age.

Drug Resistance

Studies with drug resistance data for all or most patients and with [greater than or equal to] 3 Beijing genotype TB patients among non-immigrants are summarized in online Appendix Table 3 (available at http://www.cdc.gov/ncidod/EID/vol12no05/ 05-0400_app.htm#table3). In the Western European studies, with the exception of inner London, resistance was more common among Beijing genotype strains than among other strains. Beijing genotype was significantly associated with resistance in Denmark (rifampin and ethambutol), Finland (rifampin and streptomycin), and the Netherlands (streptomycin). Overall, the study-adjusted OR for the association of Beijing genotype and resistance among nonimmigrants in Western Europe was 1.8 (95% CI 1.2-2.7) for any drug, 1.7 (95% CI 0.95-2.9) for isoniazid, 4.0 (95% CI 1.4-11.9) for rifampin, 2.3 (95% CI 1.4-3.7) for streptomycin, 3.0 (95% CI 0.38-23.2) for ethambutol, and 4.2 (95% CI 1.2-14.7) for multidrug resistance (i.e., resistance to at least isoniazid and rifampin). Of the Western European studies, only those from Denmark, Hamburg, the Netherlands, and London had data on previous treatment. After patients who had previously received treatment were excluded, the associations in the Netherlands and Denmark persisted, and the adjusted combined ORs were similar to those overall but with wider CIs (e.g., 1.6, 95% CI 1.0-2.6 for any drug resistance).

In Russia and Estonia, Beijing genotype was strongly associated with resistance to all tested drugs. None of the patients in Estonia had been previously treated. In the Archangel Oblast, the association persisted after previously treated patients were excluded, but in St. Petersburg only the association with isoniazid resistance remained significant. In Cuba, Beijing genotype was associated with streptomycin resistance in both studies, and this association persisted after previously treated patients were excluded.

In Malawi and Zimbabwe, none of the Beijing genotype isolates was drug resistant. In Cape Town, 14 (35%) of the 40 Beijing isolates that were tested were drug resistant, but the resistance of most Beijing isolates and of the other isolates was unknown.

In the Asian studies, only those in Bangladesh, Vietnam, and Taiwan found more drug resistance in Beijing genotype strains. In Bangladesh, 99% of the patients had previously received treatment for TB. In Vietnam, the results were little changed by excluding the few previously treated patients. In Taiwan, previous treatment was unknown. Two studies found that Beijing genotypes were less commonly drug resistant. In China, Beijing genotypes were less likely to exhibit ethambutol resistance; no information was available on previous treatment. In Malaysia, among patients without previous treatment, 1 (2%) of 48 isolates from patients with the Beijing genotype and 33 (13%) of 252 isolates from patients with other genotypes were resistant to any drugs ($p = 0.03$).

Other Associations

In most studies, the proportion of nonimmigrants with the Beijing genotype was similar for men and women. In Japan, the proportion was higher among men, and in Malawi, it was higher among women. Only 23 studies had data on HIV status in nonimmigrants, and of these, 13 found no Beijing genotype, no HIV-positive patients, or information was lacking on HIV status of the patients with Beijing genotype. In the 10 remaining studies (inner London, Lyon, the Netherlands, Tuscany, San Francisco, Cuba [both studies], Buenos Aires, Malawi, and Ho Chi Minh City), no association was found between HIV status and Beijing genotype.

No significant association was found between strain type and site of tuberculosis (pulmonary or extrapulmonary) in any of the 20 studies in which this information was available and both types of tuberculosis were included. In Cuba, outside Havana, and in the Archangel Oblast patients with recurrent TB were more likely than patients in their first episode of disease to have the Beijing genotype, but these associations were lost after adjusting for drug resistance. No associations with previous TB were found in any of the other 17 studies for which information was available, but the numbers of recurrent cases were often small.

Discussion

In this study, we have brought together published and unpublished data to document the spread of Beijing genotype tuberculosis worldwide. Little information was available from many countries including most of the Americas, Eastern Europe, North Africa, the Middle East, and Australasia. All eligible studies were requested, whether Beijing genotypes were found or not, and within the included studies, the proportion with Beijing genotype should be representative of those settings. The individual-level data allowed comparable analyses in all sites and pooled analysis within regions. This study complements the spoligotype database (3), which includes only studies that used spoligotyping and is more inclusive and less detailed epidemiologically. The database shows a similar global distribution of the Beijing genotype to that described here.

The proportion of TB attributable to the Beijing genotype is variable: high in Asia, apart from the Indian subcontinent, increasing further east; low in parts of Africa, Latin America, and Western Europe; intermediate in the United States and Cuba; low in Eastern Europe (other than the former Soviet Union); low in the Middle East (including <1% in a recent study from Tehran [11]). In Western Europe, Beijing genotype is more common among immigrant TB patients than among indigenous patients. The proportion of Beijing genotype TB among nonimmigrants may reflect the importance of immigrants to the total TB prevalence in these countries as well as the origin of these immigrants. Immigrants accounted for >50% of TB cases in London, the Netherlands, France, Denmark, Sweden, and

Hamburg, compared to 25% of cases in Italy, 24% in Austria, 8% in Finland, and 4% in Spain.

Using information from time and age group trends, we found that an increasing proportion of TB is due to Beijing genotype strains in Western Europe, southern Africa, and the former Soviet Union. We found little evidence of increase in Asia, except in Vietnam and Bangladesh.

Strong associations with drug resistance have been found in the former Soviet Union, Cuba, and Vietnam. The combined data for Western Europe suggest an association there. No association was found in a large study in Malawi or in most of the Asian studies.

When the data on trends and drug resistance presented here and from other studies are combined, the results suggest that the distribution of Beijing genotype TB has several patterns (Figure). The Beijing genotype probably originated in the Beijing region of China (1,4); it was found in 90% of stored biopsy specimens in the 1950s, and this proportion has not changed over time (12). Beijing strains appear to have spread and become established as the predominant M. tuberculosis genotype in much of East and Southeast Asia, so little evidence of increase was found. In these areas, the Beijing genotype appears to be endemic and not associated with drug resistance (pattern 1).

In certain areas, including the former Soviet Union (13), Cuba, and Cape Town, epidemic spread was found, which was associated with drug resistance (pattern 2). Vietnam and Bangladesh follow this pattern, unlike most other Asian countries. Recent Indian studies suggest that India may also fit pattern 2 (14,15). In Taiwan, the association with drug resistance was not confirmed in a larger sample in 2003 (unpub. data), which suggests that it follows pattern 1. In parts of Western Europe, although the Beijing genotype remains uncommon, it appears to be increasing and is associated with drug resistance (pattern 2).

In the United States, the pattern is mixed. Nonimmigrant patients in San Francisco fit pattern 1: no association with drug resistance and no evidence of time trends. In this area, most Beijing isolates came from Asian immigrants, among whom no association was found between Beijing genotype and drug resistance. In the New Jersey study, no data on drug resistance were available, but a previous study in this area found that most Beijing isolates from nonimmigrants were pansusceptible (1,16). The age distribution does not suggest recent increase, which fits pattern 1. In contrast, the spread of the multidrug-resistant W strain in New York and beyond during the 1990s has been well documented (17-19). Other published studies from the United States confirm that the Beijing genotype is widespread but do not report drug resistance or trends (20-23).

In Malawi, an increase in the Beijing genotype over time was documented, but with drug sensitive strains (pattern 3). Argentina may fit this pattern, and spread of drug-sensitive Beijing genotype TB has been described in Gran Canaria (24). The final pattern (pattern 4) is of very low level or absent Beijing genotypes, as seen in parts of Africa and Europe.

The wide distribution of the Beijing genotype could be attributable to a founder effect or random drift, though these mechanisms would be unlikely to account for recent increases in multiple settings. The distribution could reflect particular stability of the genetic markers used to identify the genotype. High levels and epidemic spread may suggest that it transmits more easily or is more virulent

than other strains. In vitro and animal studies have suggested increased multiplication or virulence for some Beijing strains (6,25) but not others (26). In Vietnam, the Beijing genotype was associated with treatment failure and relapse (27), but we found no such association. In Indonesia, patients with the Beijing genotype had a similar clinical picture to other TB patients for almost all parameters studied (28). In the Netherlands, the appearance on chest radiograph was similar for patients infected with Beijing genotype and for other TB patients (29). In Malawi, the Beijing genotype was not associated with death or transmissibility (30).

External factors may select for Beijing strains. In the former Soviet Union and the United States, spread has been associated with prisons and with high rates of drug resistance (13,17,31,32). In Mongolia, data were also available from prisoners. They had a higher proportion of Beijing genotype than did other patients, 46 (82%) of 56 compared to 97 (58%) of 168, $p = 0.001$, and a higher prevalence of drug resistance. Population movements (33), for example, from the former Soviet Union into Western Europe and through Afghanistan, may account for spread, recent increases, and the association with drug resistance (34).

Beijing genotypes may have a particular propensity to acquire drug resistance. Mutations in putative mutator genes have been found in Beijing genotypes, which suggests adaptability (5), but no increase in the rate of acquisition of resistance to rifampicin was found in in vitro studies (35). Once established, resistance could encourage spread if it delays effective treatment. Although the fitness of resistant strains is slightly reduced, this may be less marked for Beijing strains (36).

Conclusion

This study has confirmed that Beijing genotype M. tuberculosis is an emerging infection in many parts of the world and is a highly endemic pathogen in other areas. Its association with drug resistance, sometimes at high levels, in a number of settings, underlines its importance. The reasons for its apparent success are not well understood but may depend on human population movements as well as on any intrinsic factors.

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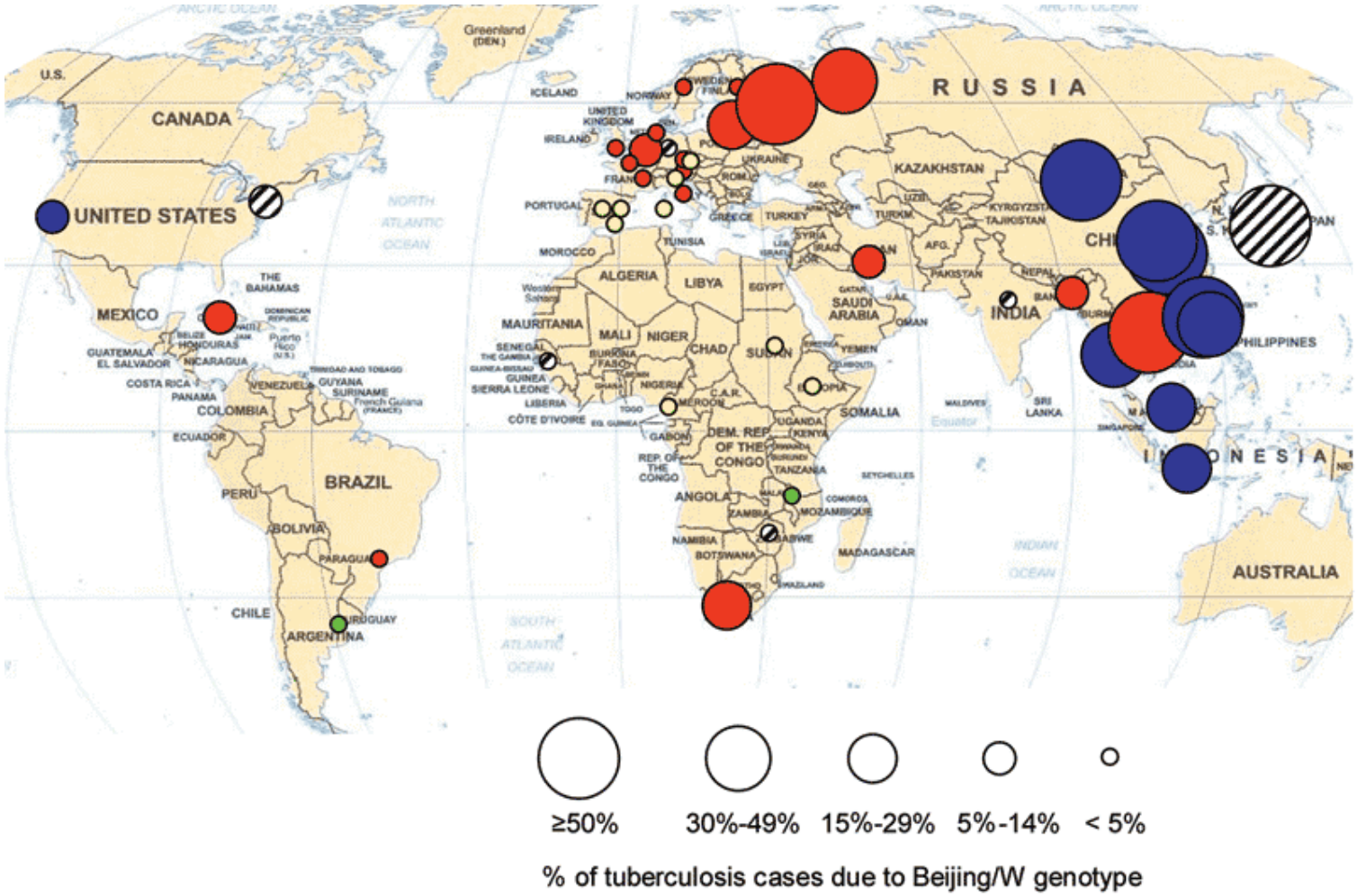

Figure.
Distribution of Beijing genotype tuberculosis (TB). Size of circle indicates percentage of TB cases due to Beijing genotype; color in circle indicates drug sensitivity and distribution trend. Blue, pattern 1 (stable, no association with drug resistance); red, pattern 2 (increasing, associated with drug resistance); green, pattern 3 (increasing, drug sensitive); yellow, pattern 4 (absent); striped, trend or association with drug resistance not known.

Table 1. Proportion of tuberculosis patients due to the Beijing genotype by region of birth

Region	All patients, Beijing/total (%)	Immigrants only, Beijing/total (%)
Western Europe	272/9,496 (2.9)	10/353 (2.8)
Central and Eastern Europe	4/780 (0.5)	3/562 (0.5)
Former Soviet Union	244/590 (41.4)	25/106 (23.6)
Middle East	62/1,165 (5.3)	56/1,084 (5.2)
North Africa	30/991 (3.0)	30/991 (3.0)
Sub-Saharan Africa	275/6,816 (4.0)	86/3,881 (2.2)
Indian subcontinent	46/1,291 (3.6)	38/1,111 (3.4)
Southeast Asia	711/2,192 (32.5)	154/811 (19.0)
East Asia	1,032/1,712 (60.3)	213/370 (57.6)
Latin America	29/1,421 (2.0)	21/457 (4.6)
Caribbean	31/320 (9.7)	5/109 (4.6)
North America	28/275 (10.2)	1/15 (6.7)
Australasia	1/4 (25.0)	1/4 (25.0)

Table 2. Trends in proportion of tuberculosis cases due to the Beijing genotype over time among nonimmigrant populations*

Study	Period	Earlier period,† Beijing/total (%)	Later period,† Beijing/total (%)	OR (95% CI) for change/y	p for linear trend by y
Western Austria	1993–2004	2/363 (0.6)	5/310 (1.6)	1.2 (0.9–1.5)	0.2
Denmark	1992–2001	7/885 (0.8)	10/774 (1.3)	1.1 (0.9–1.3)	0.4
Finland	2000–2002	2/414 (0.5)	11/705 (1.6)	1.7 (0.9–3.5)	0.1
The Netherlands	1993–2002	91/1,862 (4.9)	111/1,607 (6.9)	1.1 (1.0–1.1)	0.004
Western Sweden	1999–2002	0/34 (0.0)	3/43 (7.0)	3.1 (0.6–15)	0.2
London, UK	1995–1997	9/200 (4.5)	1/73 (1.4)	0.7 (0.3–1.8)	0.4
St. Petersburg, Russia	1999–2001	66/120 (55.0)	67/116 (57.8)	1.0 (0.7–1.3)	0.9
Cape Town, South Africa	1992–1998	60/473 (12.7)	80/374 (21.4)	1.2 (1.1–1.3)	<0.001
Karonga, Malawi‡	1996–2003	12/460 (2.6)	32/570 (5.6)	1.2 (1.0–1.4)	0.03
San Francisco, USA	1998–2000	6/50 (12.0)	6/59 (10.2)	1.0 (0.5–2.1)	1.0
Buenos Aires, Argentina	1998–2001	1/188 (0.53)	4/424 (0.94)	1.0 (0.4–2.3)	1.0
São Paulo, Brazil	2000–2002	2/268 (0.75)	1/114 (0.88)	1.0 (0.2–4.3)	1.0
Okayama, Japan	2000–2002	42/56 (75.0)	61/86 (70.9)	0.8 (0.5–1.3)	0.4

*OR, odds ratio; CI, confidence interval.
†For each study, the period was split into 2 parts, earlier and later.
‡Includes immigrants from neighboring countries.

Table 3. Proportion of tuberculosis cases caused by the Beijing genotype by age group of patient*

Study	Age <30 y, Beijing/total (%)	Age 30–49 y, Beijing/total (%)	Age ≥50 y, Beijing/total (%)	p for trend
Western Europe				
Western Austria	2/89 (2.3)	45/214 (1.9)	1/370 (0.3)	0.05
Denmark	4/210 (1.9)	6/623 (1.0)	7/826 (0.9)	0.3
Finland	2/35 (5.7)	5/128 (3.9)	6/931 (0.6)	0.002
The Netherlands	70/703 (10.0)	47/993 (4.7)	85/1773 (4.8)	<0.001
Western Sweden	1/5 (20.0)	1/7 (14.3)	1/65 (1.5)	0.05
United Kingdom				
Inner London	1/41 (2.4)	2/67 (3.0)	2/55 (3.6)	0.7
London	6/86 (7.0)	1/104 (1.0)	3/83 (3.7)	0.2
Eastern Europe				
Estonia	14/43 (32.6)	25/96 (26.0)	15/52 (28.9)	0.7
Russia				
St. Petersburg	74/112 (66.1)	61/111 (55.0)	19/45 (42.2)	0.02
Archangel†	13/25 (52.0)	32/77 (41.6)	8/16 (50.0)	0.8
Middle East				
Iran	2/20 (10.0)	2/25 (8.0)	1/26 (3.9)	0.4
Sub-Saharan Africa				
Malawi‡	19/341 (5.6)	21/522 (4.0)	4/167 (2.4)	0.08
South Africa: Cape Town	51/299 (17.1)	77/434 (17.7)	11/111 (9.9)	0.2
Zimbabwe: Harare	3/94 (3.2)	1/102 (1.0)	0/16 (0.0)	0.2
North America				
United States				
New Jersey	1/18 (5.6)	11/62 (17.7)	3/71 (4.2)	0.2
San Francisco	1/21 (4.8)	7/58 (12.1)	4/30 (13.3)	0.4
Caribbean				
Cuba				
Not Havana	10/48 (20.8)	6/42 (14.3)	6/70 (8.6)	0.06
Havana	1/11 (9.1)	2/21 (9.5)	1/19 (5.3)	0.7
Latin America				
Argentina: Buenos Aires	5/255 (2.0)	0/224 (0.0)	0/103 (0.0)	0.05
Brazil: São Paulo	3/144 (2.1)	0/187 (0.0)	0/51 (0.0)	0.1
Indian subcontinent				
Bangladesh†	3/20 (15.0)	4/42 (9.5)	0/35 (0.0)	0.03
Southeast Asia				
Indonesia: Jakarta	13/45 (28.9)	14/33 (42.4)	5/12 (41.7)	0.2
Malaysia	17/93 (18.3)	20/129 (15.5)	25/162 (15.4)	0.6
Thailand: Bangkok	33/64 (51.6)	41/88 (46.6)	24/52 (46.2)	0.5
Vietnam				
Hanoi†	11/15 (73.3)	17/26 (65.4)	9/23 (39.1)	0.03
Ho Chi Minh City†	94/147 (64.0)	134/265 (50.6)	35/87 (40.2)	<0.001
Ho Chi Minh City	13/21 (61.9)	17/40 (42.5)	4/14 (28.6)	0.04
Tien Giang	4/7 (57.1)	11/27 (40.7)	13/26 (50.0)	1.0
East Asia				
China				
Shanghai and other areas†	5/5 (100.0)	10/14 (71.4)	16/24 (66.7)	0.2
Henan	10/19 (52.6)	7/9 (77.8)	16/21 (76.2)	0.2
Hong Kong†	95/151 (62.9)	149/197 (75.6)	112/152 (73.7)	0.04
Japan: Okayama	9/12 (75.0)	19/25 (76.0)	75/105 (71.4)	0.7
Mongolia	50/95 (52.6)	42/63 (66.7)	5/10 (50.0)	0.3
Taiwan†	25/47 (53.2)	36/83 (43.4)	126/291 (43.3)	0.3

*Studies with ≥3 cases of Beijing genotype tuberculosis in nonimmigrants included.
†Immigration status not known.
‡Immigrants from neighboring countries included.