Tuberculosis Caused by *Mycobacterium africanum*, United States, 2004–2013

Aditya Sharma, Emily Bloss, Charles M. Heilig, Eleanor S. Click

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Learning Objectives

Upon completion of this activity, participants will be able to:

- Distinguish the prevalence of *Mycobacterium africanum* tuberculosis in the United States
- Analyze the phylogenetics and epidemiology of *M. africanum* tuberculosis in the United States
- Compare the clinical characteristics of infection with *M. africanum* vs. *M. tuberculosis*
- Assess risk factors for *M. africanum* infection

CME Editor

Thomas J. Gryczan, MS, Technical Writer/Editor, *Emerging Infectious Diseases. Disclosure: Thomas J. Gryczan, MS, has disclosed no relevant financial relationships*.

CME Author

Charles P. Vega, MD, Clinical Professor of Family Medicine, University of California, Irvine. *Disclosure: Charles P. Vega, MD, has disclosed the following financial relationships: served as an advisor or consultant for Allergan, Inc.; McNeil Consumer Healthcare; Takeda Pharmaceuticals North America, Inc.; served as a speaker or a member of a speakers bureau for Shire Pharmaceuticals.*

Authors

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Mycobacterium africanum is endemic to West Africa and causes tuberculosis (TB). We reviewed reported cases of TB in the United States during 2004–2013 that had lineage assigned by genotype (spoligotype and mycobacterial interspersed repetitive unit variable number tandem repeats). *M. africanum* caused 315 (0.4%) of 73,290 TB cases with lineage assigned by genotype. TB caused by *M. africanum* was associated more with persons from West Africa (adjusted odds ratio [aOR] 253.8, 95% CI 59.9–1,076.1) and US-born black persons (aOR 5.7, 95% CI 1.2–25.9) than with US-born white persons. TB caused by *M. africanum* did not show differences in clinical characteristics when compared with TB caused by *M. tuberculosis*. Clustered cases defined as ≥2 cases in a county with identical 24-locus mycobacterial interspersed repetitive unit genotypes, were less likely for *M. africanum* (aOR 0.1, 95% CI 0.1–0.4), which suggests that *M. africanum* is not commonly transmitted in the United States.

Author affiliation: Centers for Disease Control and Prevention, Atlanta, Georgia, USA

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Tuberculosis (TB) is an infectious disease caused by a group of highly-related organisms comprising the *Mycobacterium tuberculosis* complex (MTBC), which includes *M. tuberculosis*, *M. africanum*, and *M. bovis*. Although all members of MTBC might cause disease in humans, *M. tuberculosis* and *M. africanum* are the primary cause of disease in humans globally, whereas *M. bovis* primarily causes disease in cattle (*1*,*2*). Like *M. tuberculosis, M. africanum* is spread by aerosol transmission (*3*).

Phylogenetic analysis has suggested there are 7 major lineages of MTBC, designated L1–L7 (*4*,*5*). *M africanum* was traditionally identified by using biochemical methods. However, molecular methods have shown that *M. africanum* is composed of 2 distinct lineages: L5 (also known in other nomenclature systems as *M. africanum* West African 1 [MAF1], West African lineage I), which is genetically part of *M. tuberculosis* sensu stricto, and L6 (also known as *M. africanum* West African 2 [MAF2], West African lineage II), which is genetically more similar to *M. bovis* (*4*–*9*).

Among lineages that primarily infect humans, *M. africanum* lineages are considered phylogenetically more ancient relative to the modern lineages of *M. tuberculosis* (Euro-American, East African Indian, East Asian). *M. africanum* has been described as endemic to equatorial Africa, with specimens isolated from countries such as Nigeria, Côte d'Ivoire, Benin, Senegal, Cameroon, Burkina Faso, The Gambia, Sierra Leone, and Uganda (*8*,*10*–*21*). *M. africanum* has also been isolated from patients with TB in countries in Europe (*22*–*25*), Brazil (*26*), and the United States (*27*). It is likely that TB caused by *M. africanum* in non-African countries is secondary to human migration from disease-endemic areas in equatorial Africa (*25*).

Several studies have explored whether there are clinical differences between TB caused by *M. africanum* and TB caused by *M. tuberculosis*. These studies demonstrated variable findings with regard to associations of *M. africanum* with HIV status and findings on chest radiography (*8*,*28*–*30*). Contacts of persons with TB caused by *M. africanum* appeared to have a lower rate of progression to active TB compared with contacts of persons with TB caused by *M. tuberculosis*, and a lower rate of genotype clustering has been described for *M. africanum* than for *M. tuberculosis* in relatively small studies from West Africa (*14,29*).

Although bacterial strains causing TB from all over the world can be found among cases of TB in the United States, analysis of routinely collected genotyping data for 2005–2009 showed that 179 (0.5%) of 36,458 TB cases reported nationally were caused by *M. africanum* (*31*). We sought to further expand knowledge of *M. africanum* in the United States by reviewing all cases of TB reported nationally during 2004–2013. The objectives of this study were to ascertain the proportion of TB cases caused by *M. africanum* in the United States; compare clinical and epidemiologic characteristics between *M. africanum* and *M. tuberculosis*; and determine the extent to which *M. africanum* strains in the United States might be related by transmission on the basis of genotype clustering.

Methods

Genotype data from the Centers for Disease Control and Prevention (CDC; Atlanta, GA, USA) National TB Genotyping Service for 2004 through 2013 were linked to routine demographic and clinical data from all culture-confirmed cases in the CDC National TB Surveillance System from all 50 US states and the District of Columbia (*32*). As described previously (*33*), phylogenetic lineage (*M. africanum* and *M. tuberculosis*) for TB cases was assigned on the basis of spoligotype by using a set of rules correlating spoligotype to lineages defined by large sequence polymorphisms; for cases that did not meet a full rule for assignment on the basis of spoligotype, 12-locus mycobacterial interspersed repetitive unit variable number tandem repeats (MIRU-VNTRs) was used in addition to spoligotype to assign lineage. Cases reported during 2004–2008 only had 12-locus MIRU-VNTR data available, and cases reported during 2009–2013 had 24-locus MIRU-VNTR data available. To identify cases that could be caused by ongoing transmission in the United States, clusters of cases were defined as $\geq$2 cases with the same spoligotype and 24-locus MIRU-VNTR pattern in a given county. Cases that were caused by organisms other than *M. africanum* or *M. tuberculosis* were excluded from analysis.

All analyses were conducted by using R statistical software version 3.0.1 (R Core Group, Vienna, Austria). Statistical test results were considered significant at $p<0.05$. We examined patient attributes, genotype clustering, clinical characteristics (e.g., disease site), and social risk factors (e.g., homelessness) associated with *M. africanum* and *M. tuberculosis*. Odd ratios (ORs) and 95% CIs were calculated. Differences in proportions of cases were detected by using Fisher exact and Pearson χ^2 tests.

Factors identified as statistically significant by bivariable analysis at $p<0.05$ were entered into a multivariable logistic regression model to assess whether these factors were independently associated with *M. africanum* and *M. tuberculosis*. Tolerance <0.10 was used to detect colinearity, and the likelihood ratio test was used to test for interaction. To address collinearity between race/ethnicity and origin of birth, variables for race/ethnicity, country of origin, and West African origin were combined into a single variable and included in selection of the multivariable regression model. West African origin was defined as having been born in any of the following countries in West Africa: Nigeria, Liberia, Sierra Leone, Guinea, The Gambia, Ghana, Mali, Senegal, Côte d'Ivoire, Togo, Cameroon, Mauritania, Niger, and Guinea-Bissau.

Ethics Statement

Data for this study were collected as part of routine TB surveillance by CDC. Thus, this study was not considered research involving human subjects, and institutional review board approval was not required.

Results

A total of 125,038 cases were reported to the National TB Surveillance System during 2004–2013 (Figure 1). Of these cases, 95,836 (76.6%) had a culture result positive for MTBC. Of cases with positive culture results, 73,290 (76.5%) had available lineage identification on the basis of genotype data. Of the cases for which lineage identification was available, the causative agent was determined to be *M. africanum* for 315 (0.4%) and *M. tuberculosis* for 71,727 (97.9%) cases: 1,248 (1.7%) cases had an isolated organism other than *M. africanum* or *M. tuberculosis* and were excluded from further analysis (Figure 1).

M. africanum was assigned as the causative agent of TB for isolates with a genotype-assigned lineage of L5 or L6. All isolates designated as *M. africanum* met the conventional spoligotype rule of the absence of spacers 8, 9, and 39 or the absence of spacers 7–9 and 39 (*7*). *M. tuberculosis* was assigned as the causative agent of TB for isolates with a genotype-assigned lineage of L1, L2, L3, L4, or L7.

Of the 315 case-patients with TB caused by *M. africanum*, 155 (49.2%) had the L5 lineage and 160 (50.8%) had the L6 lineage. Case-patients with the L5 lineage were most commonly born in Nigeria (n = 76), Liberia (n = 12), and Ghana (n = 12), and case-patients with the L6 lineage were most commonly born in Liberia (n = 27), Sierra Leone (n = 22), Guinea (n = 17), and The Gambia (n = 16).

Among case-patients with *M. africanum* as the causative agent of TB, 276 (87.6%) had country of birth other than the United States (online Technical Appendix Table 1, http://wwwnc.cdc.gov/EID/article/22/3/15-1505-Techapp1.pdf). Of the 276 foreign-born persons with *M. africanum*, most (254, 92.0%) persons were born in countries in West Africa, such as Nigeria (79, 31.1%), Liberia (39, 15.4%), and Sierra Leone (24, 9.4%).

Among all US states, 35 reported ≥1 case of TB caused by *M. africanum* (Figure 2). States that reported more than >10 cases of *M. africanum* TB during the study were New York (n = 77), Maryland (n = 41), Texas (n = 26), Virginia (n = 19), Georgia (n = 15), and California (n = 14). Across the United States, many reported cases of *M. africanum* TB appeared to be near major metropolitan areas, such as Atlanta, Georgia; Chicago, Illinois; Detroit, Michigan; Houston, Texas; Los Angeles, California; New York, New York; and Washington, DC.

The annual number of reported TB cases identified with *M. africanum* in the United States during 2004–2013 ranged from 18 to 40 (median 34 annual cases) (Figure 3). During this period, the proportion of *Mycobacterium* spp. TB isolates from persons born in West Africa with culture-

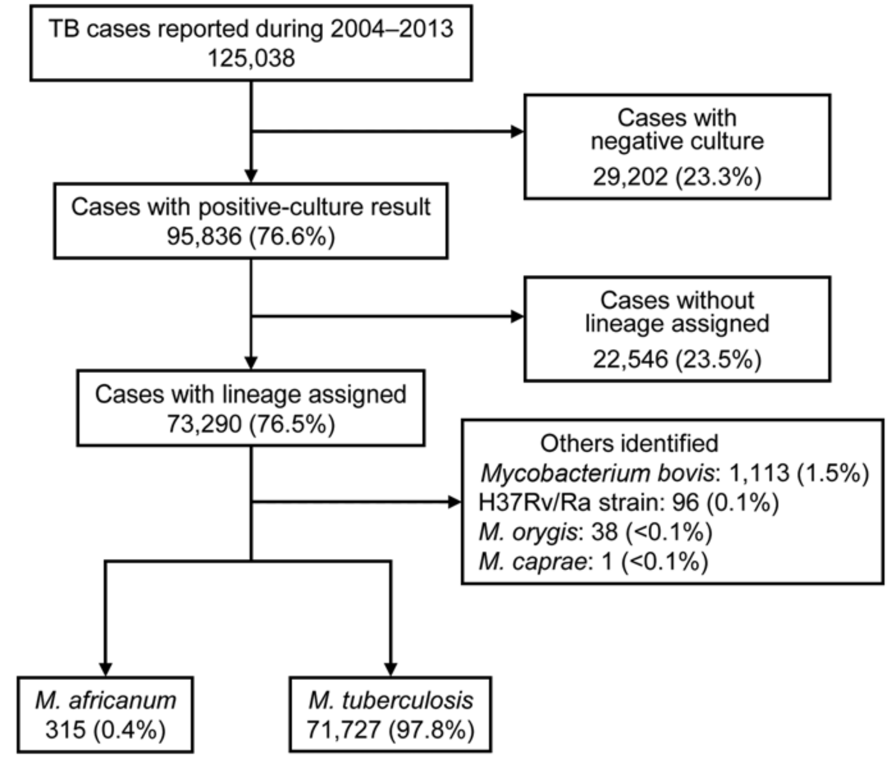

Figure 1. Selection of cases included in analysis of tuberculosis (TB) caused by *Mycobacterium africanum*, United States, 2004–2013.

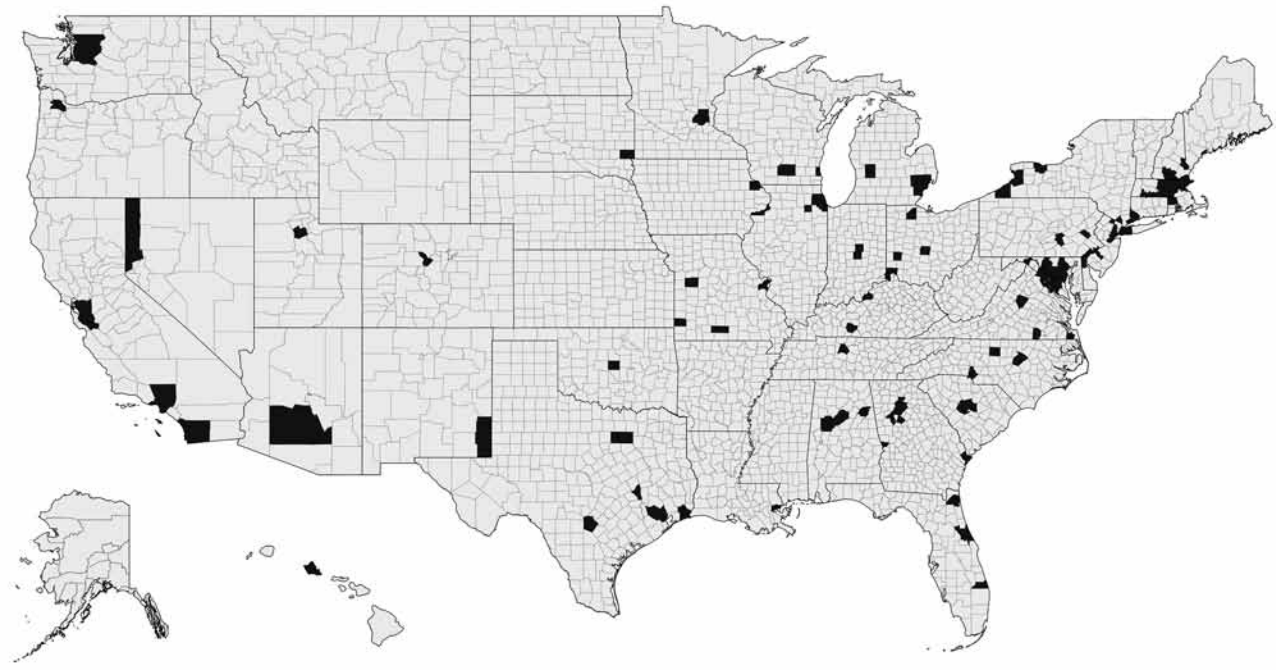

Figure 2. Counties in the United States with *Mycobacterium africanum* infections identified among tuberculosis (TB) cases (black) reported during 2004–2013.

confirmed TB that were genotyped ranged from 68.0% to 97.1%, which was comparable with the overall proportion of culture-confirmed TB cases that were genotyped nationally.

On the basis of the genotype cluster definition of ≥2 cases in the same county with identical spoligotype and 24-locus MIRU-VNTR patterns, only 1 cluster of *M. africanum* cases was identified during 2009–2013. The cluster consisted of 2 case-patients with the L5 lineage: 1 foreign-born person and 1 US-born person.

Among 315 cases of *M. africanum* TB, 183 distinct genotypes were identified (spoligotype and 12-locus MIRU-VNTR available for cases reported during 2004–2013; online Technical Appendix Table 2). Of these 183 genotypes, 139 (76.0%) were found in a single case only; the remaining 44 (24.0%) caused 176 cases. Among 141 *M. africanum* cases reported during 2009–2013 with spoligotype and 24-locus MIRU-VNTR data available, 123 distinct genotypes were identified (online Technical Appendix Table 3). Of these 123 genotypes, 113 (91.9%) were found in isolates from 1 case only, and 10 (8.1%) were found in >1 case.

Bivariable analysis showed that *M. africanum* and *M. tuberculosis* TB cases had major differences for several characteristics (online Technical Appendix Table 1). When compared with *M. tuberculosis* TB cases, *M. africanum* TB cases had higher odds of being in foreign-born persons (odds ratio [OR] 4.8, 95% CI 3.4–6.7), being in non-Hispanic black or multiracial non-Hispanic persons (OR 27.0, 95% CI 17.1–42.5), originating from countries in West Africa (OR 318.4, 95% CI 239.0–424.2), being in persons positive for HIV (OR 2.8, 95% CI 2.0–3.7), and being in persons with only extrapulmonary disease (OR 1.8, 95% CI 1.4–2.4) or in persons with pulmonary and extrapulmonary disease (OR 1.6, 95% CI 1.1–2.2).

M. africanum TB cases had lower odds than *M. tuberculosis* TB cases of being in a cluster (defined by spoligotype and 24-locus MIRU) of cases (OR 0.1, 95% CI 0.1–0.2), being in persons ≥65 years of age (OR 0.2, 95% CI 0.1–0.5), being in persons with an abnormal chest radiographic result and cavitation (OR 0.6, 95% CI 0.5–0.9) and in persons without cavitation (OR 0.5, 95% CI 0.4–0.7), being in a resident of a correctional facility (OR 0.2, 95% CI 0.0–0.6), being in a homeless person (OR 0.4, 95% CI 0.2–0.8), being in persons reporting excessive drug (OR 0.2, 95% CI 0.1–0.5) or alcohol use (OR 0.2, 95% CI 0.1–0.4), and being in persons who died during treatment (OR 0.3, 95% CI 0.2–0.7). Among foreign-born persons, *M. africanum* TB cases had lower odds than *M. tuberculosis* TB cases of being in persons who had been in the United States for >5 years before reporting TB (OR 0.3, 95% CI 0.3–0.5).

Multivariable analysis restricted to cases reported during 2009–2013 that had 24-locus MIRU-VNTR data available showed that foreign-born West African origin (OR 253.8, 95% CI 59.9–1076.1) and US-born non-Hispanic black race (OR 5.7, 95% CI 1.2–25.9) were independently associated with TB caused by *M. africanum* but not with TB caused by *M. tuberculosis* (Table). Clustered cases (OR 0.1, 95% CI 0.1–0.4) had lower adjusted odds of TB caused

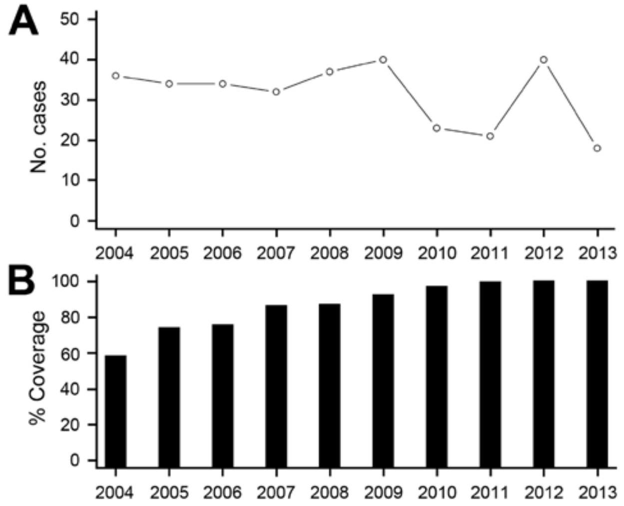

Figure 3. A) Annual number of reported *Mycobacterium africanum* tuberculosis cases and B) corresponding percentage of national genotype surveillance coverage, United States, 2004–2013.

by *M. africanum* than TB caused by *M. tuberculosis*. Other risk factors were not independently associated with *M. africanum* versus *M. tuberculosis*. No significant interaction terms were identified.

To control for possible host differences in larger analysis, we conducted a subanalysis of cases among foreign-born persons from West Africa. In this subanalysis, clustering was the only significant variable at the bivariable level, and *M. africanum* TB cases had lower odds of being in a cluster of cases than *M. tuberculosis* TB cases (OR 0.1, 95% CI 0.1–0.9). Among foreign-born persons with West African origin, we found no significant differences in clinical characteristics (e.g., HIV status, cavitary disease, sputum smear results) between TB cases caused by *M. africanum* versus those caused by *M. tuberculosis*. *M. africanum* TB cases with L5 and L6 lineages had similar proportions of HIV positivity (18.1% vs. 17.5%; p = 0.9) and cavitary disease by chest radiography (25.4% vs. 42.5%; p = 0.051). We found no significant differences in clinical characteristics or social risk factors for TB caused by L5 or L6 lineages.

Discussion

This study used nationally reported data on TB cases linked to genotype data to describe the epidemiology of *M. africanum* in the United States. The findings from this analysis indicate that *M. africanum* is a rare cause of TB in the United States and represents 315 (0.4%) of 73,290 cases with available genotype data reported during 2004–2013. Most cases were identified in large metropolitan areas throughout the United States. Although *M. africanum* is an infrequent cause of TB, most states reported ≥1 case of TB caused by *M. africanum* during the study period, which suggested that *M. africanum* is broadly distributed.

In this study, TB caused by *M. africanum* was more likely to occur in foreign-born West Africans and US-born non-Hispanic blacks and less likely in foreign-born persons originating from countries not in West Africa. These associations suggest that the epidemiology of *M. africanum* in the United States is driven primarily by migration of persons from West Africa. We also identified cases of *M. africanum* in US-born persons, primarily in non-Hispanic blacks. This finding suggests that transmission of *M. africanum* might

Table. Multivariable analysis of risk factors associated with tuberculosis caused by *Mycobacterium africanum* and *M. tuberculosis*, United States, 2009–2013

Risk factor	Adjusted OR (Wald 95% CI)
Combined race/ethnicity and origin	
Foreign born, non–West African	0.4 (0.1–1.9)
Foreign born, West African	253.8 (59.9–1076.1)
US born, non-Hispanic black	5.7 (1.2–25.9)
US born, Hispanic or other non-Hispanic race	1.1 (0.2–8.0)
US born, non-Hispanic white	Referent
Clustered case	
Yes	0.1 (0.1–0.4)
No	Referent
Age, y	
0–14	Referent
15–24	1.0 (0.3–3.5)
25–44	0.8 (0.2–2.5)
45–64	0.6 (0.2–2.0)
≥65	0.3 (0.1–1.3)
Sex	
F	0.9 (0.6–1.4)
M	Referent
Reported HIV status	
Negative	Referent
Positive	0.9 (0.5–1.4)
Unknown/not determined	1.7 (0.9–3.3)
Primary disease site	
Pulmonary	Referent
Extrapulmonary	1.9 (1.0–3.6)
Pulmonary and extrapulmonary	1.1 (0.6–2.3)
Chest radiography finding	
Abnormal, cavitary	2.1 (1.0–4.5)
Abnormal, noncavitary	0.9 (0.5–1.7)
Normal	Referent
Homeless in year before diagnosis	
Yes	1.0 (0.3–3.0)
No	Referent
Resident of correctional facility in year before diagnosis	
Yes	0.6 (0.1–4.8)
No	Referent
Any drug use	
Yes	0.4 (0.1–1.9)
No	Referent
Excessive alcohol use	
Yes	0.8 (0.3–2.4)
No	Referent
Reason therapy stopped	
Completed treatment	Referent
Died during treatment	0.2 (0.1–1.6)
Other reason	1.3 (0.5–3.2)

occur in the United States, but the possibility of acquisition of TB during travel (e.g., to West Africa) cannot be excluded because travel history was not available in national surveillance data. In an initial report of 5 *M. africanum* cases in the United States, several case-patients did not report a history of travel to West Africa (*34*).

The low proportion of TB cases attributed to *M. africanum* suggests decreased transmissibility in the United States. Reasons for decreased transmission of *M. africanum* are unknown but could include decreased infectiousness or decreased progression to disease compared with *M. tuberculosis*, as was previously reported (*8*).

Our findings support the observation that *M. africanum* is highly restricted to West Africa, where it has been estimated to cause up to 50% of all TB cases, although the reason for this restriction remains unclear (*8*). A recent study from Ghana reported an association between *M. africanum* and patient ethnicity, which suggests specificity of host–pathogen interaction could be 1 factor in limiting the spread of *M. africanum* to West Africa (*35*).

Most *M. africanum* TB cases were not part of genotype clusters, which suggested that transmission of *M. africanum* in the United States is not common. *M. africanum* TB cases were less likely to be associated with genotype clustering than *M. tuberculosis* TB cases by analyses of all cases reported in the United States and in a subanalysis of persons born in West Africa. This lower association of clustering is consistent with investigations from Ghana and The Gambia, which found *M. africanum* less likely to be in spoligotype-defined clusters (*30*,*36*).

After controlling for other factors, we found that TB cases in the United States caused by *M. africanum* and *M. tuberculosis* were similar regarding clinical presentation, social risk factors, and treatment outcomes. These findings are consistent with those of studies that compared treatment outcomes among cases of *M. africanum* and *M. tuberculosis* TB in West Africa, but contrast with studies describing differential associations with HIV and chest radiography findings (*8*,*14*,*28*,*29*). Unlike several reported studies, we could not compare specific chest radiographic findings for *M. africanum* versus *M. tuberculosis* because detailed radiographic information is not available in US surveillance data (*8*). Our study demonstrated similar clinical characteristics of TB caused by L5 and L6 lineages of *M. africanum*, which is consistent with that of a previous report (*29*).

Our results should be interpreted in light of the incomplete availability of genotype data. Nationwide coverage of genotyping has increased over time (*37*), but genotype data were not available for all culture confirmed cases. Although it is possible that our study underestimates the true burden of *M. africanum*, we expect that changes in system coverage do not substantially affect the main findings of the study. In addition, *M. africanum* and *M. tuberculosis* were identified by spoligotype and MIRU-VNTR, rather than by more phylogenetically robust methods, such as large-sequence polymorphism analysis. Therefore, some misclassification might have occurred, but there is no reason to assume any bias was introduced. Finally, our definition of clustered cases was based solely on identical spoligotype and 24-locus MIRU-VNTR in the same county during 2009–2013 and therefore probably overestimates the extent of transmission that might be occurring at the county level. More robust methods for identifying clustered cases rely on a narrower time interval between cases and evidence of epidemiologic links between cases (*38*). Even with the direction of bias toward overestimation of clustering, we found only 1 cluster.

Although the annual number of reported TB cases in the United States has decreased in the past decade, the proportion of TB contributed by foreign-born persons has increased to >60% in recent years (*39*). Similar to this trend, TB caused by *M. africanum* is highest among foreign-born persons, which is consistent with the understanding that spread of *M. africanum* in countries outside Africa is driven by human migration from West Africa. Given the low burden of TB caused by *M. africanum* in the United States, the similarity in clinical features of TB caused by *M. africanum* and *M. tuberculosis*, and the lower odds of clustered cases of *M. africanum* than those of *M. tuberculosis*, routine reporting of TB caused by *M. africanum* above standard reporting for general TB does not appear warranted at this time.

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Dr. Sharma is an Epidemic Intelligence Service Officer at the National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention, Atlanta, Georgia. His primary interests are the epidemiology and control of infectious diseases, including TB, and drug-resistant bacteria.

References

1. Thorel MF. Isolation of *Mycobacterium africanum* from monkeys. Tubercle. 1980;61:101–4. http://dx.doi.org/10.1016/0041-3879(80)90018-5
2. Alfredsen S, Saxegaard F. An outbreak of tuberculosis in pigs and cattle caused by *Mycobacterium africanum*. Vet Rec. 1992; 131:51–3. http://dx.doi.org/10.1136/vr.131.3.51
3. de Jong BC, Hill PC, Brookes RH, Gagneux S, Jeffries DJ, Otu JK, et al. *Mycobacterium africanum* elicits an attenuated T cell response to early secreted antigenic target, 6 kDa, in patients

with tuberculosis and their household contacts. J Infect Dis. 2006;193:1279–86. http://dx.doi.org/10.1086/502977

4. Comas I, Chakravartti J, Small PM, Galagan J, Niemann S, Kremer K, et al. Human T cell epitopes of *Mycobacterium tuberculosis* are evolutionarily hyperconserved. Nat Genet. 2010; 42:498–503. http://dx.doi.org/10.1038/ng.590
5. Firdessa R, Berg S, Hailu E, Schelling E, Gumi B, Erenso G, et al. Mycobacterial lineages causing pulmonary and extrapulmonary tuberculosis, Ethiopia. Emerg Infect Dis. 2013;19:460–3. http://dx.doi.org/10.3201/eid1903.120256
6. Hershberg R, Lipatov M, Small PM, Sheffer H, Niemann S, Homolka S, et al. High functional diversity in *Mycobacterium tuberculosis* driven by genetic drift and human demography. PLoS Biol. 2008;6:e311. http://dx.doi.org/10.1371/journal.pbio.0060311
7. Vasconcellos SE, Huard RC, Niemann S, Kremer K, Santos AR, Suffys PN, et al. Distinct genotypic profiles of the two major clades of *Mycobacterium africanum*. BMC Infect Dis. 2010;10:80. http://dx.doi.org/10.1186/1471-2334-10-80
8. de Jong BC, Antonio M, Gagneux S. *Mycobacterium africanum*: review of an important cause of human tuberculosis in West Africa. PLoS Negl Trop Dis. 2010;4:e744. http://dx.doi.org/10.1371/journal.pntd.0000744
9. Gagneux S, Small PM. Global phylogeography of *Mycobacterium tuberculosis* and implications for tuberculosis product development. Lancet Infect Dis. 2007;7:328–37. http://dx.doi.org/10.1016/S1473-3099(07)70108-1
10. Frothingham R, Strickland PL, Bretzel G, Ramaswamy S, Musser JM, Williams DL. Phenotypic and genotypic characterization of *Mycobacterium africanum* isolates from West Africa. J Clin Microbiol. 1999;37:1921–6.
11. Niemann S, Rusch-Gerdes S, Joloba ML, Whalen CC, Guwatudde D, Ellner JJ, et al. *Mycobacterium africanum* subtype II is associated with two distinct genotypes and is a major cause of human tuberculosis in Kampala, Uganda. J Clin Microbiol. 2002;40:3398–405. http://dx.doi.org/10.1128/JCM.40.9.3398-3405.2002
12. Sola C, Rastogi N, Gutierrez MC, Vincent V, Brosch R, Parsons L. Is *Mycobacterium africanum* subtype II (Uganda I and Uganda II) a genetically well-defined subspecies of the *Mycobacterium tuberculosis* complex? J Clin Microbiol. 2003;41:1345–6, author reply 6–8. http://dx.doi.org/10.1128/JCM.41.3.1345-1348.2003
13. Cadmus S, Palmer S, Okker M, Dale J, Gover K, Smith N, et al. Molecular analysis of human and bovine tubercle bacilli from a local setting in Nigeria. J Clin Microbiol. 2006;44:29–34. http://dx.doi.org/10.1128/JCM.44.1.29-34.2006
14. de Jong BC, Hill PC, Aiken A, Awine T, Antonio M, Adetifa IM, et al. Progression to active tuberculosis, but not transmission, varies by *Mycobacterium tuberculosis* lineage in The Gambia. J Infect Dis. 2008;198:1037–43. http://dx.doi.org/10.1086/591504
15. Cadmus SI, Yakubu MK, Magaji AA, Jenkins AO, van Soolingen D. *Mycobacterium bovis*, but also *M. africanum* present in raw milk of pastoral cattle in north-central Nigeria. Trop Anim Health Prod. 2010;42:1047–8. http://dx.doi.org/10.1007/s11250-010-9533-2
16. Gomgnimbou MK, Refregier G, Diagbouga SP, Adama S, Kabore A, Ouiminga A, et al. Spoligotyping of *Mycobacterium africanum*, Burkina Faso. Emerg Infect Dis. 2012;18:117–9. http://dx.doi.org/10.3201/eid1801.110275
17. Lawson L, Zhang J, Gomgnimbou MK, Abdurrahman ST, Le Moullec S, Mohamed F, et al. A molecular epidemiological and genetic diversity study of tuberculosis in Ibadan, Nnewi and Abuja, Nigeria. PLoS ONE. 2012;7:e38409. http://dx.doi.org/10.1371/journal.pone.0038409
18. Aliyu G, El-Kamary SS, Abimiku A, Brown C, Tracy K, Hungerford L, et al. Prevalence of non-tuberculous mycobacterial infections among tuberculosis suspects in Nigeria. PLoS ONE. 2013;8:e63170. http://dx.doi.org/10.1371/journal.pone.0063170
19. Gehre F, Antonio M, Faihun F, Odoun M, Uwizeye C, de Rijk P, et al. The first phylogeographic population structure and analysis of transmission dynamics of *M. africanum* West African 1—combining molecular data from Benin, Nigeria and Sierra Leone. PLoS ONE. 2013;8:e77000. http://dx.doi.org/10.1371/journal.pone.0077000
20. Gehre F, Antonio M, Otu JK, Sallah N, Secka O, Faal T, et al. Immunogenic *Mycobacterium africanum s*trains associated with ongoing transmission in The Gambia. Emerg Infect Dis. 2013;19:1598–604. http://dx.doi.org/10.3201/eid1910.121023
21. Kuaban C, Um Boock A, Noeske J, Bekang F, Eyangoh S. *Mycobacterium tuberculosis* complex strains and drug susceptibility in a cattle-rearing region of Cameroon. Int J Tuberc Lung Dis. 2014;18:34–8. http://dx.doi.org/10.5588/ijtld.13.0333
22. Lari N, Rindi L, Bonanni D, Rastogi N, Sola C, Tortoli E, et al. Three-year longitudinal study of genotypes of *Mycobacterium tuberculosis* isolates in Tuscany, Italy. J Clin Microbiol. 2007; 45:1851–7. http://dx.doi.org/10.1128/JCM.00170-07
23. Grange JM, Yates MD. Incidence and nature of human tuberculosis due to *Mycobacterium africanum* in South-East England: 1977–87. Epidemiol Infect. 1989;103:127–32. http://dx.doi.org/10.1017/S0950268800030429
24. Jungbluth H, Fink H, Reusch F. Tuberculous infection caused by Myco. africanum in black africans resident in the German Federal Republic (author's transl) [in German]. Prax Klin Pneumol. 1978; 32:306–9.
25. Isea-Peña MC, Brezmes-Valdivieso MF, Gonzalez-Velasco MC, Lezcano-Carrera MA, Lopez-Urrutia-Lorente L, Martin-Casabona N, et al. *Mycobacterium africanum*, an emerging disease in high-income countries? Int J Tuberc Lung Dis. 2012;16:1400–4. http://dx.doi.org/10.5588/ijtld.12.0142
26. Gomes HM, Elias AR, Oelemann MA, Pereira MA, Montes FF, Marsico AG, et al. Spoligotypes of *Mycobacterium tuberculosis* complex isolates from patients residents of 11 states of Brazil. Infect Genet Evol. 2012;12:649–56.
27. Desmond E, Ahmed AT, Probert WS, Ely J, Jang Y, Sanders CA, et al. *Mycobacterium africanum* cases, California. Emerg Infect Dis. 2004;10:921–3. http://dx.doi.org/10.3201/eid1005.030016
28. de Jong BC, Adetifa I, Walther B, Hill PC, Antonio M, Ota M, et al. Differences between TB cases infected with *M. africanum*, West-African type 2, relative to Euro-American *M. tuberculosis*: an update. FEMS Immunol Med Microbiol. 2010;58:102–5. http://dx.doi.org/10.1111/j.1574-695X.2009.00628.x
29. Meyer CG, Scarisbrick G, Niemann S, Browne EN, Chinbuah MA, Gyapong J, et al. Pulmonary tuberculosis: virulence of *Mycobacterium africanum* and relevance in HIV co-infection. Tuberculosis (Edinb). 2008;88:482–9. http://dx.doi.org/10.1016/j.tube.2008.05.004
30. de Jong BC, Hill PC, Aiken A, Jeffries DJ, Onipede A, Small PM, et al. Clinical presentation and outcome of tuberculosis patients infected by *M. africanum* versus *M. tuberculosis*. Int J Tuberc Lung Dis. 2007;11:450–6.
31. Moonan PK, Ghosh S, Oeltmann JE, Kammerer JS, Cowan LS, Navin TR. Using genotyping and geospatial scanning to estimate recent *Mycobacterium tuberculosis* transmission, United States. Emerg Infect Dis. 2012;18:458–65. http://dx.doi.org/10.3201/eid1803.111107
32. Centers for Disease Control and Prevention. Reported tuberculosis in the United States, 2012. Atlanta: The Centers; 2013.
33. Click ES, Moonan PK, Winston CA, Cowan LS, Oeltmann JE. Relationship between *Mycobacterium tuberculosis* phylogenetic lineage and clinical site of tuberculosis. Clin Infect Dis. 2012;54:211–9. http://dx.doi.org/10.1093/cid/cir788

34. Desmond E, Ahmed AT, Probert WS, Ely J, Jang Y, Sanders CA, et al. *Mycobacterium africanum* cases, California. Emerg Infect Dis. 2004;10:921–3. http://dx.doi.org/10.3201/eid1005.030016
35. Asante-Poku A, Yeboah-Manu D, Otchere ID, Aboagye SY, Stucki D, Hattendorf J, et al. *Mycobacterium africanum* is associated with patient ethnicity in Ghana. PLoS Negl Trop Dis. 2015;9:e3370. http://dx.doi.org/10.1371/journal.pntd.0003370
36. Yeboah-Manu D, Asante-Poku A, Bodmer T, Stucki D, Koram K, Bonsu F, et al. Genotypic diversity and drug susceptibility patterns among *M. tuberculosis* complex isolates from southwestern Ghana. PLoS ONE. 2011;6:e21906. http://dx.doi.org/10.1371/journal.pone.0021906
37. Centers for Disease Control and Prevention. Tuberculosis genotyping—United States, 2004–2010. MMWR Morb Mortal Wkly Rep. 2012;61:723–5.
38. Moonan PK, Ghosh S, Oeltmann JE, Kammerer JS, Cowan LS, Navin TR. Using genotyping and geospatial scanning to estimate recent *Mycobacterium tuberculosis* transmission, United States. Emerg Infect Dis. 2012;18:458–65. http://dx.doi.org/10.3201/eid1803.111107
39. Centers for Disease Control and Prevention. Reported tuberculosis in the United States, 2013: Atlanta: The Centers.

Address for correspondence: Aditya Sharma, Centers for Disease Control and Prevention, 1600 Clifton Rd NE, Mailstop E10, Atlanta, GA 30329-4027, USA; email: asharma4@cdc.gov

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Tuberculosis Caused by *Mycobacterium africanum*, United States, 2004–2013

Technical Appendix

Technical Appendix Table 1. Characteristics of patients with tuberculosis caused by *Mycobacterium africanum* and *M. tuberculosis*, United States, 2004–2013*

	No. (%)			
Variable	*M. africanum*, n = 315	*M. tuberculosis*, n = 71,727	OR (95% CI)	p-value†
Country of birth				
United States	39 (12.4)	28,955 (40.4)	Referent	<0.001
Other	276 (87.6)	42,633 (59.6)	4.8 (3.4–6.7)	
Country of origin				
In West Africa‡	254 (80.6)	926 (1.3)	318.4 (239.0–424.2)	<0.001
Not in West Africa	61 (19.4)	70,801 (98.7)	Referent	
Time in the United States, y§				
0–2	102 (39.5)	8,998 (23.4)	Referent	<0.001
2–5	64 (24.8)	6,106 (15.9)	0.9 (0.7–1.3)	
≥5	92 (35.7)	23,282 (60.7)	0.3 (0.3–0.5)	
Clustered case¶				
Yes	2 (1.4)	9,655 (29.0)	0.1 (0.1–0.2)	<0.001
No	139 (98.6)	26,762 (71.0)	Referent	
Race/ethnicity				
Non−Hispanic White, Asian, or other race	20 (6.4)	34,047 (47.6)	Referent	<0.001
Non−Hispanic Black, or multiracial	286 (91.7)	18,052 (25.2)	27.0 (17.1–42.5)	
Hispanic	6 (1.9)	19,443 (27.2)	0.5 (0.2–1.3)	
Age, y				
0–14	7 (2.2)	1,349 (1.9)	Referent	<0.001
15–24	55 (17.5)	8,283 (11.5)	1.3 (0.6–2.8)	
25–44	167 (53.0)	24,122 (33.6)	1.3 (0.6–2.8)	
45–64	68 (21.6)	22,297 (31.1)	0.6 (0.3–1.3)	
≥65	18 (5.7)		0.2 (0.1–0.5)	
Sex				
F	118 (37.5)	26,755 (37.3)	1.0 (0.8–1.3)	0.957
M	197 (62.5)	44,947 (62.7)	Referent	
Reported HIV status				
Negative	207 (65.7)	46,920 (65.4)	Referent	<0.001
Positive	56 (17.8)	4,610 (6.4)	2.8 (2.0–3.7)	
Unknown/not determined	52 (16.5)	20,197 (28.2)	0.6 (0.4–0.8)	
Previous diagnosis of TB				
Yes	8 (2.7)	3,266 (4.6)	0.6 (0.3–1.1)	0.107
No	292 (97.3)	67,361 (95.4)	Referent	
Primary disease site				
Pulmonary	198 (62.9)	53,350 (74.4)	Referent	<0.001
Extrapulmonary	76 (24.1)	11,227 (15.7)	1.8 (1.4–2.4)	
Pulmonary and extrapulmonary	41 (13.0)	7,117 (9.9)	1.6 (1.1–2.2)	
Primary extrapulmonary site#				
Bone	13 (17.1)	1,482 (13.2)	Referent	0.095**
Genitourinary	3 (3.9)	637 (5.7)	0.5 (0.2–1.9)	
Cervical lymph node	17 (22.4)	3,075 (27.4)	0.6 (0.3–1.3)	
Other lymph node	14 (18.4)	1,659 (14.8)	1.0 (0.5–2.1)	
Meningeal	3 (3.9)	411 (3.7)	0.8 (0.2–2.9)	
Peritoneal	6 (7.9)	661 (5.9)	1.0 (0.4–2.7)	
Pleural	5 (7.9)	1,863 (16.6)	0.3 (0.1–0.9)	
Other	15 (19.7)	1,439 (12.8)	1.2 (0.6–2.5)	
Chest radiography finding				
Abnormal, cavitary	83 (26.3)	19,249 (26.8)	0.6 (0.5–0.9)	<0.001
Abnormal, non-cavitary	158 (50.0)	41,794 (58.3)	0.5 (0.4–0.7)	
Normal	74 (23.7)	10,684 (14.9)	Referent	
Sputum smear result				
Positive	137 (50.7)	35,063 (56.4)	0.8 (0.6–1.0)	0.061
Negative	133 (49.3)	27,101 (43.6)	Referent	

	No. (%)			
Variable	*M. africanum*, n = 315	*M. tuberculosis*, n = 71,727	OR (95% CI)	p-value†
Tuberculin skin test result				
Positive	163 (80.3)	36,640 (79.8)	1.0 (0.7–1.5)	0.853
Negative	40 (19.7)	9,292 (20.2)	Referent	
Homeless in year before diagnosis				
Yes	8 (2.6)	4,561 (6.4)	0.4 (0.2–0.8)	0.006
No	304 (97.4)	66,677 (93.6)	Referent	
Resident of correction institution in year before diagnosis				
Yes	2 (0.6)	2,718 (3.8)	0.2 (0.0–0.6)	0.003**
No	313 (99.4)	68,796 (96.2)	Referent	
Resident of long-term care facility in year before diagnosis				
Yes	8 (2.5)	1,600 (2.2)	1.1 (0.6–2.3)	0.716
No	307 (97.5)	69,968 (97.8)	Referent	
Drug use				
Yes	6 (1.9)	6,193 (8.8)	0.2 (0.1–0.5)	<0.001
No	303 (98.1)	64,181 (91.2)	Referent	
Excessive alcohol use				
Yes	11 (3.5)	10,135 (14.4)	0.2 (0.1–0.4)	<0.001
No	300 (96.5)	60,383 (85.6)	Referent	
Multidrug resistance††				
Yes	2 (0.6)	1,006 (1.4)	0.5 (0.1–1.8)	0.337**
No	307 (99.4)	69,847 (98.6)	Referent	
Reason therapy stopped				
Completed treatment	271 (91.2)	57,230 (86.7)	Referent	0.005
Died during treatment	8 (2.7)	5,082 (7.7)	0.3 (0.2–0.7)	
Other reason	18 (6.1)	3,668 (5.6)	1.0 (0.6–1.7)	
Reported resistance to isoniazid††				
Resistant	25 (8.1)	6,269 (8.8)	0.9 (0.6–1.4)	0.644
Susceptible	284 (91.9)	64,658 (91.2)	Referent	
Reported resistance to rifampin††				
Resistant	2 (0.6)	1,235 (1.7)	0.4 (0.1–1.5)	0.187**
Susceptible	308 (99.4)	69,688 (98.3)	Referent	

*Sums of counts for a variable might be less than the total counts in column headings because of missing data. OR, odds ratio.

†Determined by Pearson χ^2 test unless otherwise specified.

‡Includes Nigeria, Liberia, Sierra Leone, Guinea, The Gambia, Ghana, Mali, Senegal, Côte d'Ivoire, Togo, Cameroon, Mauritania, Niger, and Guinea-Bissau.

§Restricted to cases in foreign-born persons.

¶Restricted to cases reported after 2009, for which complete 24-locus MIRU-VNTR data were available.

#Restricted to cases with only extrapulmonary disease.

**Determined by Fisher exact test.

††Reported resistance is based on results from conventional drug susceptibility testing of the initial specimen on which drug susceptibility testing was performed.

Technical Appendix Table 2. Unique spoligotype and 12-locus MIRU-VNTR combinations with corresponding number of cases of TB caused by *Mycobacterium africanum*, United States, 2004–2013*

Spoligotype	MIRU-VNTR†	No.
1111110001111111111111111111111101111101111	236214333522	13
1111110001111111111111111111111111111101111	226224243521	13
1111110001111111111111111111111111111101111	236224233422	13
1111110001111111111100011111111111111101111	225424243522	9
1111110000000000111100001111111111110001111	224424243221	8
1111111000001111111100001111111111110001111	224424244221	8
1111110001111111111100011111111111111101111	224424243522	7
1011111000001111111100001111111111110001111	224424243221	6
1111111000001111111100001111111111110001111	224424243221	6
1111110001111111111111111111111111111101111	227224243521	5
1111111000001111111100000000000000000000111	224424244221	5
1111111000001111111100001101111101110001111	224424244221	5
1111110000000000111100001100111111110001111	224424243221	4
1111110001111111111111111111111111111101111	225424243522	4
1111111000001111111111111111111111110001111	224424244221	4
1001110001111111111111111111111101111101111	236214233522	3
1111110001111111111100011111111111111100111	225124241522	3
1111110001111111111111111111011101111101111	236214333522	3
1111110001111111111111111111111101111100011	236214323522	3
1111111000000000000011111111111111110001111	124424244221	3
1111111000001111110000011111111111110001111	224424234221	3
1111111000001111111100001111111000000001111	224424243221	3
1111111000001111111100001111111111110001111	224324244221	3
1001111000001111111100001111111111110001111	222424243221	2

Spoligotype	MIRU-VNTR†	No.
1011111000001111111100001111111111110001111	224414243221	2
1110000000000000000000000000000000000001111	223424243221	2
1111000000001111111111111111111111111101111	225424243522	2
1111110000000000011100000000000000000110001111	224424243221	2
1111110000001111111100000100000000000001111	222324243221	2
1111110001111111111101000111111111111101111	224424243522	2
1111110001111111111110001111111111111101111	224324243522	2
1111110001111111111111111111111111111101111	226224253521	2
1111110001111111111111111111111111111101111	227224243421	2
1111110001111111111111111111111111111101111	235224233422	2
1111111000000000111111111111111111010001111	224424242221	2
1111111000000011110000001111111111110001111	224424234221	2
1111111000001011111100001111111111110001111	224324243221	2
1111111000001111011000000111111000010001111	224224244221	2
1111111000001111110000001111111111110001111	224424244221	2
1111111000001111111100000000000000000001111	224424244221	2
1111111000001111111100000100000000000000111	224424244221	2
1111111000001111111100001111111111110000111	224424254221	2
1111111000001111111100001111111111110001101	224424244221	2
1111111000001111111100001111111111110001111	222424244221	2
0111111000001111111100001111111111110000011	224424244221	1
0111111000001111111100001111111111110000111	224324244221	1
0111111000001111111100001111111111110000111	224424–24221	1
1010111000001111111100001111111111110001111	224424243221	1
1011011000001001111100001111111011110001101	224424244221	1
1011110000000000111100001111111111110001111	224424243221	1
1011111000001111111100001111111111110000111	2244–4243221	1
1011111000001111111100001111111111110001111	224424143221	1
1011111000001111111111111111111111110001111	224425244221	1
1101111000000111111111111111111111110000111	224424244221	1
1101111000001111111110011111111111110001111	234424224221	1
1110000000000000000011111111111111101101111	237224243511	1
1110000000001111011111111111000000001101111	224325253324	1
1110000000001111111111111111111111111101111	126224243521	1
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1110000000111111110001111111111111111101111	236224233422	1
1110010001111111111111111111111111111101111	226224243521	1
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1111110000000000010110000111111111110001111	224424243221	1
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1111110000000000011100000000000000000110001111	224524243221	1
1111110000000000011110000111111111110000001	234424243221	1
1111110000001111111100000000000000000001111	222324243221	1
1111110000001111111100000000000000000001111	222424243221	1
1111110000111001111111111111111101111101101	227224243521	1
1111110001001111111111111111111111111101111	227224243321	1
1111110001100111111111111111111101111101111	226214333522	1
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1111110001110111111110001111111111111101111	224424243522	1
1111110001110111111111111111111111111101111	225424243522	1
1111110001110111111111111111111111111101111	226224233422	1
1111110001110111111111111111111111111101111	227224243521	1
1111110001111000000000110111111111111001111	227224243521	1
1111110001111111000000111111111111111101111	227224243521	1
1111110001111111110000001000011111110101111	214324231522	1
1111110001111111110001111111111111111101111	226224233521	1
1111110001111111111011111111111111111101111	226224243521	1
1111110001111111111110000111111011111101111	225424–33522	1
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1111110001111111111110001111111110110101111	225424243522	1
1111110001111111111110001111111111111100111	225424243522	1
1111110001111111111110001111111111111101011	224424243522	1
1111110001111111111110001111111111111101100	225424243522	1
1111110001111111111110001111111111111101111	213424273522	1
1111110001111111111110001111111111111101111	215424243522	1
1111110001111111111110001111111111111101111	224424243722	1

Spoligotype	MIRU-VNTR†	No.
1111110001111111111110001111111111111101111	224624243522	1
1111110001111111111110001111111111111101111	225324243422	1
1111110001111111111110001111111111111101111	225324243522	1
1111110001111111111110001111111111111101111	225424233522	1
1111110001111111111110001111111111111101111	225424243622	1
1111110001111111111110001111111111111101111	225425243522	1
1111110001111111111111111111111000001101111	226224243521	1
1111110001111111111111111111111000011101111	236214233422	1
1111110001111111111111111111111101111100011	226214333522	1
1111110001111111111111111111111101111100011	236214323422	1
1111110001111111111111111111111101111100011	236214333522	1
1111110001111111111111111111111101111101111	235214233523	1
1111110001111111111111111111111101111101111	236212333522	1
1111110001111111111111111111111101111101111	236214233521	1
1111110001111111111111111111111101111101111	236214333523	1
1111110001111111111111111111111111111100111	222224243521	1
1111110001111111111111111111111111111100111	226224243521	1
1111110001111111111111111111111111111100111	227224243521	1
1111110001111111111111111111111111111100111	236224233422	1
1111110001111111111111111111111111111101101	226224243521	1
1111110001111111111111111111111111111101101	236224233422	1
1111110001111111111111111111111111111101110	215224233522	1
1111110001111111111111111111111111111101110	236224233422	1
1111110001111111111111111111111111111101111	127224243321	1
1111110001111111111111111111111111111101111	2–5424243522	1
1111110001111111111111111111111111111101111	223224243521	1
1111110001111111111111111111111111111101111	225224243521	1
1111110001111111111111111111111111111101111	226224233521	1
1111110001111111111111111111111111111101111	226224243–21	1
1111110001111111111111111111111111111101111	226224243511	1
1111110001111111111111111111111111111101111	226224243721	1
1111110001111111111111111111111111111101111	227224213521	1
1111110001111111111111111111111111111101111	227224242321	1
1111110001111111111111111111111111111101111	227224243321	1
1111110001111111111111111111111111111101111	227224263521	1
1111110001111111111111111111111111111101111	23–224233422	1
1111110001111111111111111111111111111101111	2352–4232422	1
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1111111000001111111100001111111111110000111	224324244221	1
1111111000001111111100001111111111110000111	224414–44221	1
1111111000001111111100001111111111110000111	224414244221	1
1111111000001111111100001111111111110001001	223424234221	1
1111111000001111111100001111111111110001111	214424243221	1
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1111111000001111111100001111111111110001111	224324213221	1
1111111000001111111100001111111111110001111	224324243221	1
1111111000001111111100001111111111110001111	224325244221	1
1111111000001111111100001111111111110001111	224414243221	1
1111111000001111111100001111111111110001111	224424143221	1

Spoligotype	MIRU-VNTR†	No.
1111111000001111111100001111111111110001111	224424211221	1
1111111000001111111100001111111111110001111	225424243221	1
1111111000001111111110110000000000010001111	224624244221	1
1111111000001111111111110000000001010001111	234424244221	1
1111111000001111111111101000000000010001111	224614244221	1
1111111000001111111111111111111111010001111	224424242221	1
1111111000001111111111111111111111110001111	223424244221	1
1111111000001111111111111111111111110001111	224224244221	1
1111111000001111111111111111111111110001111	224324244221	1
1111111000001111111111111111111111110001111	224424234221	1
1111111000001111111111111111111111110001111	224424242221	1
1111111000001111111111111111111111110001111	224424245221	1
1111111000001111111111111111111111110001111	224524244221	1

*MIRU-VNTR, mycobacterial interspersed repetitive unit variable number tandem repeat.

†Digits refer to number of repeats detected at the respective 12 MIRU-VNTR locus in the following order: 2, 4 (ETR D), 10, 16, 20, 23, 24, 26, 27 (QUB-5), 31 (ETR E), 39, 40.

Technical Appendix Table 3. Unique spoligotype and 24-locus MIRU-VNTR combinations with corresponding number of cases of tuberculosis caused by *Mycobacterium africanum*, United States, 2009–2013*

Spoligotype	MIRU-VNTR†	No.
1111110001111111111111111111111111111101111	236224233422 253463443434	7
1011111000001111111100001111111111110001111	224424243221 142–43423332	3
1111110000000000111100001111111111110001111	224424243221 142–43423332	3
1111111000001111111100001111111111110001111	224424244221 342–43423232	3
1110000000000000000000000000000000000001111	223424243221 142–43223332	2
1111110001111111111110001111111111111101111	225424243522 354563443316	2
1111111000001111111100001101111101110001111	224424244221 142–43423332	2
1111111000001111111100001111111111110001111	222424244221 343–43423332	2
1111111000001111111100001111111111110001111	224324244221 142–43423332	2
1111111000001111111100001111111111110001111	224424243221 142–43423332	2
0111111000001111111100001111111111110000011	224424244221 342–43433333	1
0111111000001111111100001111111111110000111	224324244221 342–43423333	1
1001110001111111111111111111111110111101111	236214233522 153473443436	1
1001110001111111111111111111111110111101111	236214233522 253573443436	1
1010111000001111111100001111111111110001111	224424243221 122–43423332	1
1011011000001001111100001111111011110001101	224424244221 342–43423212	1
1011111000001111111100001111111111110000111	2244–4243221 142643423432	1
1011111000001111111100001111111111110001111	224414243221 142–43423332	1
1011111000001111111111111111111111110001111	224425244221 442–43424333	1
1101111000000011111111111111111111110000111	224424244221 342–33423433	1
1110000000000000000111111111111111101101111	237224243511 253463432636	1
1110000000111111100011111111111111111101111	236224233422 253463443434	1
1110010001111111111111111111111111111101111	226224243521 254443453436	1
1110011000001111111111101000000000110001111	224424244221 342–33423333	1
1110111000001111111111111111111111110001111	224324244221 342–43523333	1
1111011000001111111100000000000000010001111	224424244221 342–43423233	1
1111110000000000111000000000000000110001110	223424243221 142–43423332	1
1111110000000000111100001100111111110001111	224424243221 122–43423232	1
1111110000000000111100001100111111110001111	224424243221 122243423232	1
1111110000000000111100001100111111110001111	224424243221 142–43423331	1
1111110000000000111100001100111111110001111	224424243221 142–43423332	1
1111110000000000111100001111111111110000001	234424243221 142–33423332	1
1111110000000000111100001111111111110001111	224424243221 142–43423432	1
1111110000000000111100001111111111110001111	224424243221 142233423332	1
1111110001001111111111111111111111111101111	227224243321 264473443–36	1
1111110001110111111000000100001111111101111	213424243522 354463443436	1
1111110001110111111110001111111111111101111	224424243522 254563453436	1
1111110001110111111111111111111111111101111	226224233422 253463443434	1
1111110001111111000000111111111111111101111	227224243521 254483443436	1
1111110001111111111011111111111111111101111	226224243521 254473433436	1
1111110001111111111110001111111110110101111	225424243522 354563443236	1
1111110001111111111110001111111111111100111	225424243522 354563442436	1
1111110001111111111110001111111111111101100	225424243522 354563443436	1
1111110001111111111110001111111111111101111	215424243522 356363443436	1
1111110001111111111110001111111111111101111	224324243522 354363443433	1
1111110001111111111110001111111111111101111	224424243522 3545–3443436	1
1111110001111111111110001111111111111101111	224424243522 354563443436	1
1111110001111111111110001111111111111101111	225324243522 354563443436	1
1111110001111111111110001111111111111101111	225424243522 354563433436	1
1111110001111111111110001111111111111101111	225424243522 366563443436	1

Spoligotype	MIRU-VNTR†	No.
1111110001111111111110001111111111111101111	225424243622 354563433436	1
1111110001111111111111111111011101111101111	236214333522 253443443436	1
1111110001111111111111111111111101111100011	236214323422 253473443436	1
1111110001111111111111111111111101111100011	236214323522 253473443433	1
1111110001111111111111111111111101111100011	236214323522 253473443436	1
1111110001111111111111111111111101111100011	236214333522 253473443436	1
1111110001111111111111111111111101111101111	235214233523 253473443436	1
1111110001111111111111111111111101111101111	236212333522 253473443436	1
1111110001111111111111111111111101111101111	236214333522 253–43443436	1
1111110001111111111111111111111101111101111	236214333522 253–73443436	1
1111110001111111111111111111111101111101111	236214333522 253363443436	1
1111110001111111111111111111111101111101111	236214333522 253363444435	1
1111110001111111111111111111111101111101111	236214333522 253443443436	1
1111110001111111111111111111111101111101111	236214333522 253473443%36	1
1111110001111111111111111111111101111101111	236214333522 254443443436	1
1111110001111111111111111111111111111100111	222224243521 254373453436	1
1111110001111111111111111111111111111100111	236224233422 252463443434	1
1111110001111111111111111111111111111101111	127224243321 254473443436	1
1111110001111111111111111111111111111101111	223224243521 254473453436	1
1111110001111111111111111111111111111101111	225224243521 354473453426	1
1111110001111111111111111111111111111101111	226224233521 253533443436	1
1111110001111111111111111111111111111101111	226224243–21 254473453436	1
1111110001111111111111111111111111111101111	226224243511 254473453226	1
1111110001111111111111111111111111111101111	226224243521 254373453436	1
1111110001111111111111111111111111111101111	226224243521 254443443436	1
1111110001111111111111111111111111111101111	226224243521 254473343436	1
1111110001111111111111111111111111111101111	226224243521 254473453434	1
1111110001111111111111111111111111111101111	226224243521 254473453634	1
1111110001111111111111111111111111111101111	226224243521 264373453436	1
1111110001111111111111111111111111111101111	227224213521 254473443634	1
1111110001111111111111111111111111111101111	227224243321 254373443436	1
1111110001111111111111111111111111111101111	227224243421 254473453436	1
1111110001111111111111111111111111111101111	227224243521 254473443434	1
1111110001111111111111111111111111111101111	227224243521 254473443534	1
1111110001111111111111111111111111111101111	2352–4232422 2–34–3443434	1
1111110001111111111111111111111111111101111	235224233422 253463443434	1
1111110001111111111111111111111111111101111	237224233422 253463443434	1
1111111000000000000000000000000000010001111	224524244221 342–43413333	1
1111111000000000000001111111111111110001111	124424244221 142–43423333	1
1111111000000011111100001111111111110001111	224624243221 142–43423332	1
1111111000000011111111111111111111110000111	224424244221 342–33423433	1
1111111000001011111100001111111111110001111	224324243221 342–43423332	1
1111111000001011111100001111111111110001111	224324243221 442–43223333	1
1111111000001100001111110000000001100001111	224424244221 342–43423332	1
1111111000001110110000000111111000010001111	224224244221 342–43423332	1
1111111000001111110000001111111111110001111	224424244221 242–43423313	1
1111111000001111111100000000000000000000111	224424244221%42–43423533	1
1111111000001111111100000000000000000000111	224424244221 242–43423533	1
1111111000001111111100000000000000000001111	224424244221 342423423332	1
1111111000001111111100001111101111110001111	224424234221 242–43423332	1
1111111000001111111100001111111000000001111	224324243221 142–43423332	1
1111111000001111111100001111111000000001111	224424243221 142–43423632	1
1111111000001111111100001111111100010000111	224414244221 342–43423333	1
1111111000001111111100001111111111100001111	224424243221 142243423332	1
1111111000001111111100001111111111110000111	224424254221 242243423333	1
1111111000001111111100001111111111110001101	224424244221 3—43423332	1
1111111000001111111100001111111111110001111	223424354221 342–43423232	1
1111111000001111111100001111111111110001111	224324244221 342–43423232	1
1111111000001111111100001111111111110001111	224325244221 342–23422432	1
1111111000001111111100001111111111110001111	224414243221 152–43423332	1
1111111000001111111100001111111111110001111	224424143221 142–43433332	1
1111111000001111111100001111111111110001111	224424243221 142–33423332	1
1111111000001111111100001111111111110001111	224424243221 142–43422332	1
1111111000001111111100001111111111110001111	224424243221 142–43423232	1
1111111000001111111100001111111111110001111	224424244221 242–43423232	1
1111111000001111111100001111111111110001111	224424244221 343–43423332	1
1111111000001111111111110000000001010001111	234424244221 342–43223333	1
1111111000001111111111110100000000010001111	224614244221 342–43421433	1
1111111000001111111111111111111111010001111	224424242221 342–43423533	1
1111111000001111111111111111111111110001111	223424244221 342–43423333	1
1111111000001111111111111111111111110001111	224424244221 3—-3423333	1
1111111000001111111111111111111111110001111	224424244221 342–43423333	1
1111111000001111111111111111111111110001111	224424244221 342233423333	1

Spoligotype	MIRU-VNTR†	No.

*MIRU-VNTR, mycobacterial interspersed repetitive unit variable number tandem repeat.

†Digits refer to number of repeats detected at the respective 24 MIRU-VNTR locus in the following order: 2, 4 (ETR D), 10, 16, 20, 23, 24, 26, 27 (QUB-5), 31 (ETR E), 39, 40, 424 (Mtub04), 577 (ETR C), 1955 (Mtub21), 2163b (QUB-11b), 2165 (ETR A), 2347 (Mtub 29), 2401 (Mtub 3), 2461 (ETR B), 3171 (Mtub 24), 3690 (Mtub 39), 4156 (QUB-4156), 4052 (QUB-26).