# Recent *Mycobacterium tuberculosis* Transmission, United States, 2018–2022

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**To the Editor:** A recent article published in June 2026 described the characteristics of plausible source cases responsible for recent *Mycobacterium tuberculosis* transmission in the United States by using national surveillance and whole-genome sequencing data (*1*). The authors expertly applied molecular epidemiology and machine-learning methods to identify factors associated with tuberculosis (TB) transmission and demonstrated the heterogeneity of transmission events.

The study relied on a plausible source–case algorithm incorporating spatial proximity, temporal linkage, and genomic similarity. Although that information is valuable for surveillance, recent evidence suggests that TB transmission networks are often more complex than can be captured by predefined genomic thresholds and hierarchical source assignment rules. Contemporary transmission-reconstruction approaches integrate genomic, epidemiologic, and spatial data to account for incomplete sampling, undetected intermediaries, and within-host evolution. Consequently, some transmission events might have been misclassified, potentially influencing estimates of source-case characteristics (*2*,*3*).

Although the adaptive boosting model demonstrated good discriminatory performance, its generalizability remains uncertain because validation was restricted to the study dataset. Predictive models frequently experience performance degradation when applied to populations with different demographic compositions, healthcare access patterns, and transmission dynamics. External validation across diverse settings is essential before such models are used to prioritize public health interventions (*4*).

Finally, several social and healthcare-system factors that influence TB transmission, including diagnostic delay, were not included. Untreated disease increases opportunities for transmission and might contribute to highly infectious disease phenotypes, including cavitary disease and sputum smear positivity. Because populations facing barriers to healthcare access often experience longer diagnostic delays, some associations between demographic characteristics, markers of infectiousness, and source-case attribution might reflect prolonged infectious periods rather than independent transmission-promoting effects. Diagnostic delay remains a critical but underrecognized target for tuberculosis control interventions (*5*).

Despite those considerations, the study provides evidence on persons contributing most to ongoing TB transmission. Future investigations incorporating transmission-reconstruction methods, diagnostic-delay metrics, and external validation of predictive models might strengthen TB prevention and control.

## References

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**In Response:** We thank Dr. Zubairi for raising the points in his letter (1). We view those methodological considerations as valid questions within the context of applying our results to tuberculosis (TB) prevention and control.

We agree that transmission networks can be more complex than are represented by our plausible source case algorithm and use of whole-genome single nucleotide polymorphism distances to assess genomic similarity. However, our integration of spatial and temporal proximity with genomic similarity represents our best estimates of recent transmission, which were validated with locally provided contact investigation data from multiple sites in the United States. In addition, we accept that those estimates can misclassify cases as false-positive or false-negative transmission events. Validation of the algorithm demonstrated an accuracy of 95.8% compared with on-the-ground epidemiologic data, with sensitivity of 79.1% and specificity of 97.7% (S. Kammerer, unpub. data)

Regarding external validation of the adaptive boosting machine learning model, our study examined the epidemiology of TB transmission in the United States. Generalization to other settings with different transmission dynamics, demographics, genomic diversity, healthcare utilization, and public health infrastructure, including settings that do not genotype nearly all isolates from culture-confirmed cases, would not be appropriate. Our findings are appropriate to consider for prioritizing interventions in the United States. The methodological approach could also be a starting place for a similar analysis in other settings with similar epidemiology and genotyping coverage.

We agree that diagnostic delay is a major driver of TB transmission; however, we did not have reliable data regarding symptom onset to assess in our study. Accurate data regarding symptom onset are challenging to obtain in clinical settings. However, we did consider objective clinical findings associated with diagnostic delay and advanced disease (e.g., sputum smear positivity), and those findings were associated with plausible source cases in our analysis.

## References

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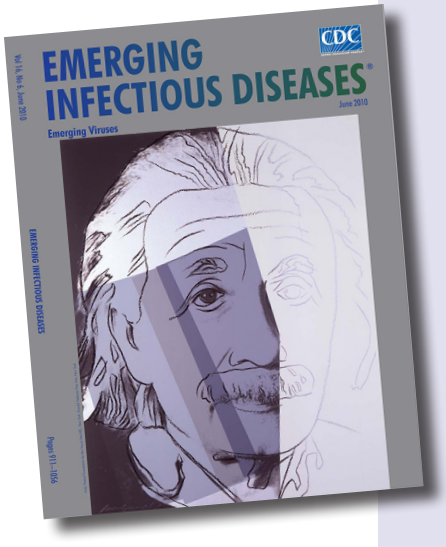
# etymologia revisited




## Lassa Virus

[lah sə] virus

This virus was named after the town of Lassa at the southern end of Lake Chad in northeastern Nigeria, where the first known patient, a nurse in a mission hospital, had lived and worked when she contracted this infection in 1969. The virus was discovered as part of a plan to identify unknown viruses from Africa by collecting serum specimens from patients with fevers of unknown origin. Lassa virus, transmitted by field rats, is endemic in West Africa, where it causes up to 300,000 infections and 5,000 deaths each year.

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