Cascade of Care in the Management of Latent Tuberculosis Infection in the United States: A Lot to Improve and to Scale Up

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Tuberculosis (TB) remains the highest global cause of infection-driven (non-coronavirus disease [COVID-19]) mortality (1). An estimated 25% of the global population, including 14 million people in the United States, are infected with *Mycobacterium tuberculosis* and with an expected 5–10% lifetime risk of progressing to active disease (notably higher in patients with immunosuppressive conditions) (1–5). Both the World Health Organization and the Centers for Disease Control and Prevention highlight the importance of treating people with latent TB infection (LTBI), especially those at a higher risk of developing active TB, as an important component to TB elimination efforts (6, 7). The identification and successful management of patients with LTBI, however, entail a multistep process toward successful treatment completion. Often referred to as a "cascade of care" management plan and commonly modeled after patients with human immunodeficiency virus (HIV), the plan links efforts in appropriate testing, notification of results, access to longitudinal care, initiation of treatment, and medication compliance to optimize the likelihood of treatment completion (8, 9).

In this issue of *AnnalsATS*, Mancuso and colleagues (pp. 1669–1676) appropriately address different areas of patient engagement with LTBI testing and management within the United States while highlighting corresponding steps within the cascade at which patients are at a higher risk for incomplete care (3). They accessed population-based survey data from the 2011–2012 NHANES (National Health and Nutrition Examination Survey), which enabled the composing of a large U.S. patient cohort and the assessment of patient engagement with care prior to the start of LTBI treatment. Testing for TB infection using the tuberculin skin test (TST) and/or interferon-γ release assay (IGRA) were used. Consistent with prior reports, and remaining of high concern, is the dismal 10% rate of successful completion of treatment by millions of people living in the United States with LTBI.

Mancuso and colleagues reveal that a large percentage of patients with LTBI who test positive fail to appropriately enter the latter steps of LTBI cascade management, including receiving a formal diagnosis, initiating treatment, and confirming treatment completion. This drop midway into the cascade of care can also be seen with high-risk patients, including close contacts of active TB cases. A meta-analysis of patient retention and the LTBI cascade-of-care model also found higher losses of patient retention in the earlier steps of testing completion, recommendations for treatment, and treatment initiation (9).

A critical analysis is required to better understand the barriers to the successful completion of the LTBI cascade of care, especially for the highest-priority groups, including non–U.S.-born individuals, the incarcerated, the homeless, and patients with HIV infection and diabetes (10). Patients need to have timely notification of their test results and have mechanisms in place for medical evaluation referral and treatment. TB testing also often occurs in settings that are not equipped to medically evaluate or appropriately educate patients who test positive. Most TB testing programs must refer or recommend patients who test positive to medical providers for a formal evaluation (including a chest X-ray and examination) and appropriate management. A more culturally appropriate and comprehensive patient understanding of test results, TB infection diagnosis, and rationale for treatment do not commonly occur until a formal evaluation has been conducted.

Mancuso and colleagues show that improved strategies are needed to both optimally inform patients of test results and ensure appropriate engagement with medical care for TB infection. Whether the identified gaps are inadequate patient communication about test results or insufficient education regarding appropriate treatment may depend on both the indication for testing (e.g., screening vs. contact investigation) and the person or organization performing the testing. Moreover, it is unclear whether the mandatory notification of test results to patients or the facilitation of access to medical care is actually occurring. Patients may not have a primary physician, speak the local language, or know how best to access medical care. Many city and county health departments have relationships with medical providers and will preschedule patients with positive test results for an evaluation and LTBI management. However, testing centers for immigration and preemployment screenings often do not have such access to medical evaluations by providers and may rely on patients to find appropriate medical care themselves.

Importantly, it is possible that the LTBI cascade of care may have improved in the United States since the 2011–2012 NHANES

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survey. In 2016, the U.S. Preventive Services Task Force published its grade B recommendation to screen asymptomatic adults for TB risk, to test those who screen positive, and to treat those who test positive (11). Perhaps this recommendation has already spurred primary care providers to do so. In 2018, the technical instructions for civil surgeons were updated regarding people seeking changes in immigration status (12). New was the requirement that IGRAs be used instead of TSTs to test all applicants 2 years of age or older. High-risk non–U.S.-born individuals are more likely to trust IGRA than TST results, accept a diagnosis, and be engaged in completing treatment. Also new was the requirement that applicants with an LTBI diagnosis be reported to the local health departments. It is likely that these two requirements have already resulted in improvement in the cascade of care since the last NHANES survey. Despite this limitation, Mancuso and colleagues and others demonstrate comparatively lower rates of patient dropout during treatment compared with those encountered during earlier steps; however, successful patient compliance with prolonged LTBI treatments remains problematic. In recent years, increased patient compliance has been demonstrated with shorter treatment regimens for LTBI, which should be a consideration to enhance successful cascade-of-care completion (7, 12, 13). Clearly, we need additional studies to provide a more updated picture of the LTBI cascade of care and to show the impact of more recently implemented treatment strategies and policies.

Of note, improvement is ongoing in diagnostics to identify patients with *M. tuberculosis* infection who have the highest risk of progress or incipient TB, which will likely allow a more targeted management of asymptomatic individuals with TB infection testing reactivity (14–16). For now, and with the current diagnostic tools available, closing the gap within the LTBI management cascade shown by Mancuso and colleagues will require systematic improvements at each step of the cascade, reinforcing the "team-based" multidisciplinary approach involving public health, nursing, and physician engagement for optimal TB infection management toward TB elimination in the United States. ■

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