A Literature Review on the Adherence to Screening Guidelines for Latent Tuberculosis Infection Among Persons Living With HIV

Rodson Allan Zorilla MD; Cecilia M. Shikuma MD

Abstract

Human immunodeficiency virus (HIV) infection increases the risk of reactivation of latent tuberculosis infection (LTBI). Although antiretroviral therapy decreases the progression of LTBI to tuberculosis disease (TBD), persons living with HIV (PLHIV) still have higher risk of TBD compared to the general population. LTBI screening is recommended for all newly diagnosed PLHIV to prevent TBD. However, several studies from low TBD incidence countries have reported sub-optimal implementation of these guidelines. This review aims to assess published studies on adherence to LTBI screening among PLHIV by identifying factors and determinants that affect the implementation of LTBI screening among PLHIV in low TBD incidence countries. Electronic databases were used to search for articles describing the adherence to LTBI screening guidelines. Fourteen studies were included in the final review. Ten studies assessed the frequency of PLHIV getting LTBI screening, and 4 studies assessed the compliance of health care providers in implementing the guidelines. PLHIV who were screened for LTBI ranged from 22.4% to 85%, of which 0.8% to 25.6% had positive results. Only 20% to 57.4% of surveyed physicians implemented the guidelines. Country of birth was an independent predictor of receiving LTBI screening. LTBI screening guidelines are inconsistently performed resulting in missed opportunities for TBD prevention. A comprehensive screening policy involving testing all PLHIV may be the best approach, rather than a targeted approach testing foreign-born individuals only. This will minimize missing domestic cases that can worsen disparity in HIV and tuberculosis infection among minority groups, including Asians, Native Hawaiians, and Pacific Islanders.

Keywords

Tuberculosis disease, tuberculosis infection, low TBD incidence countries, Human Immunodeficiency Virus (HIV) infection, Native Hawaiians, and Pacific Islanders

Abbreviations

AIDS = Acquired Immune-Deficiency Syndrome
ART = Antiretroviral therapy
BCG = Bacillus Calmette-Guerin
BHIVA = British HIV Association
CDC = Centers for Disease Control and Prevention
HIV = Human Immunodeficiency Virus
IDSA = Infectious Diseases Society of America
IGRA = Interferon-gamma release assay
LTBI = Latent tuberculosis infection
MSM = Men having sex with men
Mtb = Mycobacterium tuberculosis
NHPI = Native Hawaiians and Pacific Islanders
PLHIV = Persons living with HIV
TST = Tuberculin skin testing
TB = Tuberculosis
TBD = Tuberculosis disease
TBI = Tuberculosis infection
WHO = World Health Organization

Introduction

Tuberculosis disease (TBD), or active disease due to *Mycobacterium tuberculosis (Mtb)*, predominantly presents as an infection in the lungs and is a leading cause of mortality and morbidity among persons living with Human Immunodeficiency Virus (PLHIV).[1,2] Latent tuberculosis infection (LTBI), is a state of persistent immune response to *Mtb* with no evidence of active disease.[3] TB infection encompasses both LTBI and TBD. Compared with individuals without HIV, PLHIV have a 3-16% annual risk and 30% lifetime risk of LTBI progressing to TBD.[4,5] In 2019, an estimated 2 billion people worldwide had LTBI, and approximately 10 million were diagnosed with TBD. Of individuals with TBD, 8.2% were also living with HIV.[1] TBD is the most common opportunistic infection among PLHIV and often leads to death.[1]

In 2019, the US, a country with low TBD incidence, had 8 920 cases of TBD, and 13 million reported cases of LTBI. The prevalence of LTBI among PLHIV was 7.6%.[6,7] Seventy percent of TBD cases occurred among persons born outside the US, and the majority of cases were Asian immigrants with an incidence rate of 25.7 per 100 000 persons followed by Native Hawaiians and Pacific islanders (NHPI) with an incidence rate of 25.1 per 100 000 persons.[6] In the same year, there were 198 new cases of HIV-TBD coinfection in the country, including 2 cases in Hawai‘i.[6] In 2021, Hawai‘i reported 107 TBD cases with an incidence of 7.35 cases per 100 000 persons.[8] Although the incidence of TB infection in PLHIV overall is declining, new cases of foreign-born PLHIV and TBD have remained stable.[9]

TBD and HIV have disproportionately impacted NHPI in the US.[10] Among those who were born in the US, TBD were highest among NHPI population.[10] From 2010-2019, the annual incidence rates of TBD among NHPI born in the US and US Affiliated Pacific Islands (USAPI) were 6.5 cases and 150.7 cases per 100 000 persons, respectively, in comparison to the nationwide incidence rate of 2.2 cases per 100 000 persons.[11] The US populations consists of 0.4 percent of the NHPI race group, yet they are twice as likely to have TBD compared to the White population.[11,12] Moreover, NHPI are also 2.4 times more likely to have HIV compared to the White population.[11] Tuberculin skin test (TST) and interferon gamma release assay (IGRA) are 2 methods currently used to identify LTBI and TBD.[3] Both screening tools have a sensitivity greater than 90% when tested on the general population, but their sensitivities are decreased when used among PLHIV, particularly in subjects

with advanced immunosuppression.[13,14] Even with lower test sensitivities among PLHIV, use of the 2 screening methods is highly recommended by different LTBI screening guidelines.[15-18] LTBI treatment among PLHIV who have a positive TST reduces the risk of developing TBD by 62%.[19]

Clinical practice guidelines from the American Thoracic Society, the Infectious Diseases Society of America (IDSA), and Centers for Disease Control and Prevention (CDC) recommend screening populations who have increased risk of infection with *Mtb*, including PLHIV and immigrants from countries with high burden of TBD.[15] The US Preventive Services Task Force recommends LTBI testing of asymptomatic adults who were born in or previously lived-in countries with increased TBD prevalence or who live in or have lived in high-risk congregate settings, but no recommendations are given for PLHIV.[16] The Guidelines for Prevention and Treatment of Opportunistic Infections in HIV-infected Adults and Adolescents developed by the CDC, the National Institutes of Health (NIH), and the HIV Medicine Association (HIVMA) of the IDSA recommend that all PLHIV should be tested for LTBI at the time of HIV diagnosis regardless of the risk of TBD exposure; persons with negative diagnostic tests for LTBI, advanced HIV infection (CD4 count <200 cells/mm^3), and without indications for initiating empiric LTBI treatment should be retested for LTBI once they start antiretroviral therapy (ART) and attain a CD4 count ≥200 cells/mm^3.[17] In addition, annual testing for LTBI using TST is recommended for PLHIV who are at high risk of repeated or ongoing exposure to persons with TBD.[17]

LTBI screening guidelines are based on evidence-based medicine, but several studies from low TBD incidence countries, where there are fewer than 10 TBD cases per million population, reported sub-optimal implementation of these guidelines.[20-34] The objective of this article is to review published studies on adherence to LTBI screening on PLHIV and to identify factors and determinants that affect the implementation of LTBI screening in low TBD incidence countries.

Methods

The online databases used for this study were OneSearch, the search engine of John A. Burns School of Medicine Library, PubMed, and PubMed Central. The keywords used for all 3 search engines was "LTBI screening" AND "HIV." Hand searching of studies that were not indexed in the online databases was also done. Google search was performed for grey literature to extract data from CDC and World Health Organization (WHO) websites to compliment the literature. Peer-reviewed studies published in English between 1990 to 2021 were included in the study. Studies that assessed the adherence and implementation of LTBI screening among newly diagnosed PLHIV in low TBD incidence countries based on WHO's criteria (<10 TBD cases per million population) were included in the study.[20] Studies that merely reported on knowledge and perception of LTBI screening in HIV patients were not included. Studies that measured the predictive value, sensitivity, and specificity of LTBI screening tools used in PLHIV were also excluded from this study.

Titles and abstracts of all references were all screened by 1 reviewer. The title of the article was important for initial impressions of relevancy based on keywords and topic of interests. If the study seemed significant for the review, then the abstract was read to confirm the information within the article. Full text versions of potentially relevant articles were examined for eligibility. In order to prevent excluding relevant articles, results of the database searches were screened 3 times. The articles that were of interest for this study were organized using the Zotero version 6.0.20 (Corporation for Digital Scholarship, Vienna, VA).[35]

Results

A total of 471 articles were compiled through Zotero, of which 38 articles were duplicates. Three hundred seventy-six articles were excluded based on the relevance of their titles. Fifty-seven articles were then included for abstract and article review. Forty-five articles were excluded based on the exclusion criteria. Two articles cited by 1 study were hand-searched and included after reviewing the articles. A total of 14 articles were included in the final review (**Figure 1**). These studies were published from 1998 to 2019 and were conducted in low TBD incidence countries: USA, Switzerland, Canada, Belgium, the Netherlands, the United Kingdom (UK), New Zealand, and Italy.[21-34] These studies either focused mainly on implementation and adherence to LTBI screening among newly diagnosed PLHIV or included LTBI screening adherence as 1 of the objectives of the study. Ten studies assessed the implementation of LTBI screening among HIV patients through retrospective medical chart review (**Table 1**). They assessed the frequency of HIV patients getting LTBI screening, of which, 9 studies measured the positivity rate of HIV patients who were tested for LTBI. Nine studies reviewed protocol adherance to LTBI screening guidelines performed within the first 6 months or 12 months of HIV diagnosis. The LTBI screening method used by 6 studies was TST alone whereas 4 studies used IGRA and TST in their studies. Four studies assessed the compliance of physicians in implementing the LTBI screening guidelines through survey of medical practitioners (**Table 2**).

PLHIV who were screened for LTBI ranged from 22.4% to 85% of the screening population. It is important to note that while the study by Schulte et al in the US reported the highest adherence to LTBI screening with 85% adherence, the population used for the study was limited only to pregnant women.[23] On the other hand, the study by Kaplan et al reported an adherence percentage of 80%, but analyzed the general PLHIV population in Ryan White HIV/AIDS facilities.[22] Gow et al in New Zealand reported improvement of LTBI guideline adherence from 55% in 2011 to 93% in 2014.[29] TST and IGRA were both used as

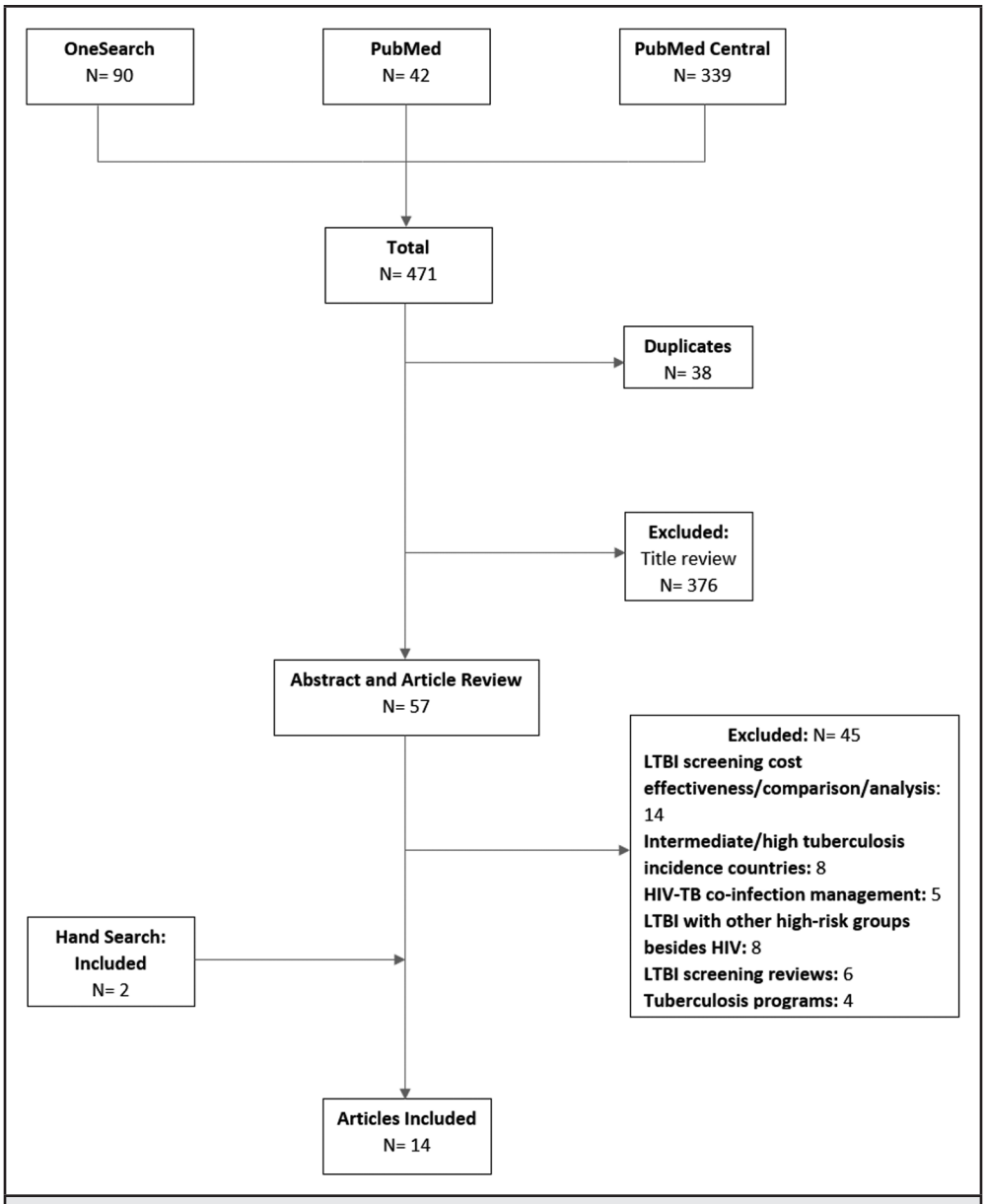

Figure 1. Flow Diagram of Study Selection for Review on Adherence to Latent Tuberculosis Infection (LTBI) Screening Guidelines Among People Living with HIV (PLHIV)

the screening tools in 2011, but the significant improvement in 2014 was noted when IGRA was used as the sole screening tool. Similar results were noted by Adams et al in the US, where an improvement from 28% to 37% was noted as the facility transitioned from TST to IGRA-based screening.[28]

Nine studies reported positive results ranging from 0.8% to 25.6% of PLHIV screened for LTBI.[21,23-30] The study by Schulte showed a 25.6% positive result in HIV-infected pregnant women, and the study by Brassard et al in Canada showed 14.1% positive results in all PLHIV.[23,25] LTBI treatment was initiated in 36.9% to 100% positive patients, but only 5 studies showed treatment completion that ranged between 22.6% to 74.3%.[21,25,26,29,30] Schulte reported that while LTBI treatment was initiated in all positive patients, completion and compliance among patients were not documented.[23] In the study by Elzi et al, among the 246 LTBI positive participants who did not receive preventive treatment, 16 (6.5%) developed TBD.[25] Missed opportunities to prevent TBD were also noted by Brassard et al in Canada where 4 (6%) subjects who tested positive but did not received treatment progressed to TBD.[26]

Seven studies assessed if CD4 count level was considered a factor in performing LTBI screening, and contrasting results

Table 1. Characteristics of Studies on Adherence to Guidelines for Screening LTBI Among PLHIV Based on Medical Chart Review			
Source	**Year/ Country**	**Method of Screening and Adherence**	**Predictors of Having TST and/or IGRA Performed/Reasons of Low Adherence**
Sackoff, et al[21]	1998/USA	TST: 865/1342 (64%); Screened within 6 months of diagnosis; Positive: 48 (6%)	Numbers of visit, same sex behavior with men, >200 CD4 count
Kaplan, et al[22]	1999/Ryan White Title III facilities USA	TST: 1129/1411 (80%); Screened within 12 months of diagnosis	Male sex, injecting drug users, patients from urban area, more than 1 year at the facility, who had had > 1 CD4 count in the past year.
Schulte, et al[23]	2002/ Miami, FL USA	TST: 176/207 (85%); Positive: 45 (25.6%)	Foreign born, unknown HIV status at the first prenatal visit, history of drug use
Lee, et al[24]	2005/USA	TST: 436/841 (51.8%); Screened within 6 months of diagnosis; Positive: 27 (6.7%)	Additional risk factors for TB, history of HIV related preventive treatment, higher number of clinic visits, and attendance at facilities with a written policy to provide TST for all PLHIV
Elzi, et al[25]	2007/ Switzerland	TST: 4158/6018 (69%); Screened within 12 months of diagnosis; Positive: 390 (9.4%)	<200 CD4 count, patients not on HAART, female sex, country of birth
Brassard, et al[26]	2009/ Canada	TST: 476/2123 (22.4%); Screened within 6 months of diagnosis; Positive: 67 (14.1%)	Foreign born, having a first clinic visit during the HAART era, time between HIV diagnosis and first visit, and previous antiretroviral exposure.
Reaves, et al[27]	2017/USA	TST and IGRA: 1907/2772 (68.8%); Screened within 12 months of diagnosis; Positive: 131 (6.9%)	Foreign-born, Non-Hispanic Blacks or other race/ethnicities; lower educational attainment, household income at or below the federal poverty level; uninsured; currently prescribed ART; CD4 count<500 cells/mL; undetectable viral load
Adams, et al[28]	2017/Pennsylvania USA	TST: 61/158 (27.9%) IGRA: 57/96 (37.3%) Screened within 12 months of diagnosis; Positive: 1 (0.8%)	Male sex, transfer patient status, > 1 year of clinical attendance, >200 CD4 count
Gow, et al[29]	2017 New Zealand	TST and IGRA: Screened within 12 or more months of diagnosis 2011: 416/752 (55%); Positive: 74 (10%) 2014: 68/73 (93%); Positive: 2 (2%)	Reasons of low adherence: Perceived low probability of LTBI in PLHIV without a clear epidemiological risk.
Goletti, et al[30]	2019/Italy	TST and IGRA: Screened within 6 months of diagnosis 507/774 (65.5%); Positive: 32 (6.5%)	Foreign born, older population, and CD4 <100

Abbreviations: ART: antiretroviral therapy; HAART: highly active antiretroviral therapy; IGRA: interferon-gamma release assay; LTBI: latent tuberculosis infection; PLHIV: people living with HIV; TB: tuberculosis; TST: tuberculin skin testing.

Table 2. Characteristics of Studies on Adherence to Guidelines for Screening LTBI Among PLHIV Based on Health Care Provider Surveys			
Source	**Year/ Country**	**Adherence**	**Predictors of Having TST Performed/Reasons of Low Adherence**
DeRiemer et al[31]	1999/San Francisco, CA USA	139/350 (39.4%) physicians provide annual PPD testing	Reasons of low adherence: physicians were not aware of the standards of care for preventing tuberculosis among PLHIV even in a geographic area with a high prevalence of M. tuberculosis and HIV. Physicians with the least experience with PLHIV are the least familiar with current guidelines and standards of care for preventing tuberculosis.
Wyndham-Thomas, et al[32]	2015/ Belgium	7/34 (20%) AIDS physicians screened patients	Reasons of low adherence: lack of sensitivity of screening tools, risk associated with polypharmacy, toxicity of treatment.
Verbon, et al[33]	2016/ Netherland	12/51 (25%) physicians intended to screen patients as the guideline stipulate	Predictors of having TST/IGRA performed: foreign born (Liberians vs Dutch), alcohol intake, higher CD4 count Reasons of low adherence: perceived low a priori risk for LTBI in the Dutch population as the majority of PLHIV being Dutch gay men, the preventive effect of ART on the risk of TB, and the absence of actual TB diagnoses in their own practice in PLHIV who are under regular follow-up.
White, et al[34]	2017/UK	93/162 (57.4%) offered LTBI screening	Predictors of having TST/IGRA performed: CD4 count< 200 cells/mm3 and patients from high TB incidence countries Reasons of low adherence: cohort at low risk of LTBI, lack of confidence in the existing guidelines, unavailability and high cost of screening, and concern over chemoprophylaxis efficacy, toxicity/drug interactions, and conflicting local advice.

Abbreviations: ART: antiretroviral therapy; HAART: highly active antiretroviral therapy; IGRA: interferon-gamma release assay; LTBI: latent tuberculosis infection; PLHIV: people living with HIV; TB: tuberculosis; TST: tuberculin skin testing.

were noted. In Swiss and Italian studies, LTBI screening was performed more frequently among patients with CD4 <200 cells/mm^3 at registration.[25,30] In a study conducted by Sackoff et al in New York and by Adams et al in Philadelphia, CD4 level >200 cells/mm^3 was associated with likelihood of getting screened with TST.[21,28] In Canada, TST screening was done regardless of CD4 count level.[26]

Four survey studies among health care providers in the Netherlands, Belgium, USA, and UK were included in this review (**Table 2**).[31-34] These studies showed only 20% to 57.4% of health care providers and representatives adhere to and implement LTBI screening guidelines. The study by White et al in the UK showed that 57.4% of health care representatives from 162 UK geographical areas, consisting of English, Welsh, Irish, and Scottish HIV healthcare provider organizations, reported offering LTBI screening, but adherence to British HIV Association (BHIVA) and National Institute for Health Care Excellence guidelines was only 35.5% and 6.5%, respectively.[34] A study by Verbon et al in the Netherlands revealed that only 24% of physicians had the intention to screen PLHIV for LTBI; however, the Netherlands HIV-TB guidelines stipulate screening regardless of birth place, sex, and CD4 count.[33] Barriers noted for low implementation include lack of sensitivity of screening tools, lack of confidence in the existing guidelines, and belief of cohorts having low risk of LTBI.[31-34] Experience was a noted factor as physicians with the most encounters with HIV or TBD were more likely to adhere and implement the guideline.[31]

Thirteen studies assessed predictors of having TST and/or IGRA performed. Seven studies identified that PLHIV who were born from high TBD incidence countries were more likely to get screened for LTBI ranging from 40.4% to 82% compared to non-foreign-born patients, 15.3% to 68.9%.[23,25-27,30,33,34] Other noted factors for increased likelihood of being screened include male sex, men having sex with men (MSM), and multiple clinic visits. Determinants of having a positive LTBI screening included, foreign birth, higher than 100 cells/mm^3 CD 4 count baseline, and MSM.

Discussion

LTBI screening guidelines for PLHIV are developed to identify patients who should be evaluated for LTBI to reduce the morbidity and mortality of subsequent TBD and to prevent TBD transmission. However, LTBI screening guidelines among PLHIV in low TBD incidence countries is often not adhered to. Testing by TST involves a multistep process that requires 2 clinical encounters for administration and interpretation of TST reaction after 48 to 72 hours.[3] This creates an opportunity for both the health care provider and the patient to fail to complete the screening process. Failure to follow-up and noncompliance of patients may result in missed opportunities in preventing TBD, hence, strategies should be considered to improve the compliance of these patients, such as requiring counseling and advising for those who refused to be screened and treated. Another strategy that could improve the adherence to LTBI screening is the implementation of LTBI screening policy in HIV care facilities. High adherence as a result of having a TST implementation policy in HIV care clinics is supported by studies from Schulte and Lee who reported that PLHIV were more likely to get screened for LTBI if they were seen in a facility with a written policy or TST programs to provide LTBI screening for all PLHIV.[23,24] This approach may help reduce disparities in HIV and TBD among NHPI who are less likely to be screened for sexually transmitted diseases and opportunistic infections, including HIV and LTBI screening.[36-38]

A barrier identified for poor physician adherence to LTBI screening is the lack of sensitivity of the 2 recommended screening tools when used in PLHIV.[39] Anergic reaction and bacillus Calmette-Guerin (BCG) vaccination may induce false-positive screening test results in PLHIV, which may discourage healthcare providers from adhering to the LTBI screening guideline. In addition, both screening tests are inadequate to predict the progression of LTBI to TBD.[39,40] IGRA and TST have sensitivity of more than 90% when tested in non-HIV infected individuals, but sensitivity decreases in PLHIV to 72% and 61% for IGRA (TSPOT and QFT-GIT tests, respectively) and 64.3% and 71.2% for TST (at cut-off value of 10 mm and 5 mm, respectively).[41,42] However, IGRA has higher specificity and less cross-reactivity with BCG vaccination than TST in low TBD prevalence settings.[43-46] Therefore, testing by IGRA should be recommended as the diagnostic test of choice for patients who were born from high TBD incidence countries and those who received the BCG vaccination.

PLHIV who are on ART have significantly reduced hazard ratio (HR) of incident TBD (HR=.44), but their risk still remains higher than in general population.[24,47] Hence, TBD preventive therapy should be offered for its beneficial effects in reducing the reactivation of LTBI in PLHIV on ART. However, poor initiation and completion of LTBI treatment was noted in this review. The treatment was initiated in 36.9% to 100% positive patients, but only 22.6% to 74.3% completed the treatment.[21,23-26,29-30] Some of the low treatment initiation results may be attributed to physician decision making. Despite evidence of low isoniazid toxicity and the efficacy of isoniazid preventive therapy for 6 to 12 months in reducing TBD, some physicians are hesitant to follow the treatment guidelines due to fear and concerns of isoniazid toxicity and risks of polypharmacy treatment.[32,34,48-50] Continued training in LTBI care in PLHIV is needed to implement evidence-based therapeutic guidelines. Other possible reasons for incomplete LTBI treatment were noncompliance of patients, refusal to be treated, loss to follow-up, and adverse reaction to treatment. One factor that results in noncompliance of patients is the length of preventive treatment of LTBI. A 1-month regimen of rifapentine and isoniazid therapeutic regimen for prevention of LTBI in PLHIV was recently proposed, and implementing this therapeutic regimen could result in

better patient compliance and higher completion rate of LTBI treatment.[51,52] Shorter duration of treatment could also result in fewer adverse reactions. NHPI and Asians are less adherent to medications compared to other races, and a shorter treatment regimen will be beneficial in reducing health disparities among this group.[53,54]

An observational prospective study by Capocci in the UK showed that it is not cost-effective to screen for LTBI in PLHIV with high ART usage from countries with medium and high TBD incidence settings.[55] In this review, 6 studies advocated targeted LTBI screening among PLHIV who are born outside of low TBD incidence countries. All the European studies suggested adopting the BHIVA guidelines which recommends targeted screening of PLHIV who have the highest risk of developing TBD based on the country of origin, CD4 level, and length of time on ART. The BHIVA guideline also recommends screening PLHIV from low TBD incidence countries if they have additional TBD risk factors, including recent travel to high TBD incidence countries or close exposure to a known TBD case.[56] Although a targeted LTBI screening guideline among PLHIV in the US may be cost-effective, this approach will likely result in missed opportunities to detect both LTBI and TBD cases among PLHIV who were born in the US. The Canadian study by Brassard et al found that 55.6% cases of TBD in individuals who were not TST screened were born in Canada.[26]

In 2021, Asians and NHPI constitute two-thirds of population in Hawai‘i and include groups who experience notable health disparities in TBD and HIV infection due to social and demographic risk factors contributing to poorer health outcomes.[57,58] Some Asian ethnic groups and NHPI are less likely to be screened and tested for HIV compared to other racial groups resulting to late HIV diagnosis and having opportunistic infection at the time of diagnosis.[36-38] A targeted screening program, as advocated by several European countries, may miss domestic cases and create racial stereotypes. Triaging NHPI and Asians by country of birth could worsen the disparity in health care access and the prevalence of HIV infection and LTBI.

In conclusion, in a low-burden TBD country, such as the US, prevention among PLHIV is best accomplished through strict adherence to LTBI screening guidelines regardless of racial group and country of birth. Early detection and treatment of LTBI in high-risk populations can improve TBD control and decrease morbidity and mortality. As the US seeks to achieve the WHO TBD elimination goal, improving LTBI screening among PLHIV will be an important element of a comprehensive national strategy in TBD prevention.

Conflict of Interest

None of the authors identify a conflict of interest.

Authors' Affiliation:
- John A. Burns School of Medicine, University of Hawai'i at Mānoa, Honolulu, HI

Corresponding Author:
Cecilia M. Shikuma MD; Email: shikuma@hawaii.edu

References

1. Global tuberculosis report 2020. World Health Organization. Published October 15, 2020. Accessed February 22, 2022. https://www.who.int/publications/i/item/9789240013131
2. O'Garra A, Redford PS, McNab FW, et al. The immune response in tuberculosis. *Annu Rev Immunol*. 2013;31:475-527. doi:10.1146/annurev-immunol-032712-095939
3. Guidelines on the management of latent tuberculosis infection. World Health Organization. Published January 01, 2015. Accessed May 26, 2022. https://www.who.int/publications/i/item/9789241548908
4. Sonnenberg P, Glynn JR, Fielding K, et al. How soon after infection with HIV does the risk of tuberculosis start to increase? A retrospective cohort study in South African gold miners. *J Infect Dis*. 2005;191(2):150-158. doi:10.1086/426827
5. Latent tuberculosis infection. National HIV Curriculum. Updated April 22, 2023. Accessed June 9, 2023. https://www.hiv.uw.edu/go/co-occurring-conditions/latent-tuberculosis/core-concept/all
6. Schwartz NG, Price SF, Pratt RH, Langer AJ. Tuberculosis - United States, 2019. *MMWR Morb Mortal Wkly Rep*. 2020;69(11):286-289. Published March 20, 2020. doi:10.15585/mmwr.mm6911a3
7. Miramontes R, Hill AN, Yelk Woodruff RS, et al. Tuberculosis infection in the United States: prevalence estimates from the National Health and Nutrition Examination Survey, 2011-2012. García-GarcíaJ-M,ed. *PLoSONE*.2015;10(11):e0140881. doi:10.1371/journal.pone.0140881
8. Filardo TD, Feng PJ, Pratt RH, Price SF, Self JL. Tuberculosis - United States, 2021. *MMWR Morb Mortal Wkly Rep*. 2022;71(12):441-446. Published March 25, 2022. doi:10.15585/mmwr.mm7112a1
9. Mirzazadeh A, Kahn JG, Haddad MB, et al. State-level prevalence estimates of latent tuberculosis infection in the United States by medical risk factors, demographic characteristics and nativity. *PLoS One*. 2021;16(4):e0249012. Published April 1, 2021. doi:10.1371/journal.pone.0249012
10. Deutsch-Feldman M, Springer YP, Felix D, Tsang CA, Brostrom R, Haddad M. Tuberculosis among Native Hawaiian and Other Pacific Islander Persons: United States and U.S.-Affiliated Pacific Islands, 2010-2019. *Health Equity*. 2022;6(1):476-484. doi:10.1089/heq.2022.0065
11. HIV/AIDS and Native Hawaiians/Other Pacific Islanders. US Department of Health and Human Services- The Office of Minority Health. Accessed November 9, 2022. https://minorityhealth.hhs.gov/omh/browse.aspx?lvl=4&lvlid=81
12. Native Hawaiians and other Pacific Islanders. Centers for Disease Control and Prevention. Accessed February 18, 2023. https://www.cdc.gov/nchhstp/healthdisparities/hawaiians.html
13. Vincenti D, Carrara S, Butera O, et al. Response to region of difference 1 (RD1) epitopes in human immunodeficiency virus (HIV)-infected individuals enrolled with suspected active tuberculosis: a pilot study. *Clin Exp Immunol*. 2007;150(1):91-98. doi:10.1111/j.1365-2249.2007.03462.x
14. Kussen GMB, Dalla-Costa LM, Rossoni A, et al. Interferon-gamma release assay versus tuberculin skin test for latent tuberculosis infection among HIV patients in Brazil. *Braz J Infect Dis*. 2016;20(1):69-75. doi:10.1016/j.bjid.2015.10.007
15. Lewinsohn DM, Leonard MK, LoBue PA, et al. Official American Thoracic Society/Infectious Diseases Society of America/Centers for Disease Control and Prevention Clinical Practice Guidelines: Diagnosis of tuberculosis in adults and children. *Clin Infect Dis*. 2017;64(2):111-115. doi:10.1093/cid/ciw7781
16. Bibbins-Domingo K, Grossman DC, et al. Screening for latent tuberculosis infection in adults: US Preventive Services Task Force Recommendation Statement. *JAMA*. 2016;316(9):962. doi:10.1001/jama.2016.11046
17. Kaplan JE, Benson C, Holmes KK, et al. Guidelines for prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from CDC, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. *MMWR Recomm Rep*. 2009;58(RR-4):1-207.
18. Getahun H, Matteelli A, Abubakar I, et al. Management of latent Mycobacterium tuberculosis infection: WHO guidelines for low tuberculosis burden countries. *Eur Respir J*. 2015;46(6):1563-1576. doi:10.1183/13993003.01245-2015
19. Akolo C, Adetifa I, Shepperd S, Volmink J. Treatment of latent tuberculosis infection in HIV infected persons. *Cochrane Database Syst Rev*. 2010;2010(1):CD000171. doi: 10.1002/14651858.CD000171.pub3
20. Global tuberculosis report 2021. World Health Organization. Published October 14, 2021. Accessed November 9, 2022. https://www.who.int/publications/i/item/9789240037021
21. Sackoff JE, Torian LV, Frieden TR, et al. Purified protein derivative testing and tuberculosis preventive therapy for HIV-infected patients in New York City. *AIDS*. 1998;12(15):2017-2023. doi:10.1097/00002030-199815000-00013
22. Kaplan JE, Parham DL, Soto-Torres L, et al. Adherence to guidelines for antiretroviral therapy and for preventing opportunistic infections in HIV-infected adults and adolescents in Ryan White-funded facilities in the United States. *J Acquir Immune Defic Syndr*. 1999;21(3):228-235. doi:10.1097/00126334-199907010-00008
23. Schulte JM, Bryan P, Dodds S, et al. Tuberculosis skin testing among HIV-infected pregnant women in Miami, 1995 to 1996. *J Perinatol*. 2002;22(2):159-162. doi:10.1038/sj.jp.7210617
24. Lee LM, Lobato MN, Buskin SE, et al. Low adherence to guidelines for preventing TB among persons with newly diagnosed HIV infection, United States. *Int J Tuberc Lung Dis*. 2006;10(2):209-214.
25. Elzi L, Schlegel M, Weber R, et al. Reducing tuberculosis incidence by tuberculin skin testing, preventive treatment, and antiretroviral therapy in an area of low tuberculosis transmission. *Clin infect Dis*. 2007;44(1):94-102. doi:10.1086/510080

26. Brassard P, Hottes TS, Lalonde RG, Klein MB. Tuberculosis screening and active tuberculosis among HIV-infected persons in a Canadian tertiary care centre. *Can J Infect Dis Med Microbiol*. 2009;20(2):51-57. doi:10.1155/2009/658382
27. Reaves EJ, Shah NS, France AM, et al. Latent tuberculous infection testing among HIV-infected persons in clinical care, United States, 2010-2012. *Int J Tuberc Lung Dis*. 2017;21(10):1118-1126. doi:10.5588/ijtld.17.0041
28. Adams JW, Howe CJ, Andrews AC, et al. Tuberculosis screening among HIV-infected patients: tuberculin skin test vs. interferon-gamma release assay. *AIDS Care*. 2017;29(12):1504-1509. doi:10.1080/09540121.2017.1325438
29. Gow N, Briggs S, Nisbet M. Screening for latent tuberculous infection in people living with HIV infection in Auckland, New Zealand. *Int J Tuberc Lung Dis*. 2017;21(9):1008-1012. doi:10.5588/jtld.17.0103
30. Goletti D, Navarra A, Petruccioli E, et al. Latent tuberculosis infection screening in persons newly-diagnosed with HIV infection in Italy: A multicentre study promoted by the Italian Society of Infectious and Tropical Diseases. *Int J Infect Dis*. 2020;92:62-68. doi:10.1016/j.ijid.2019.12.031
31. DeRiemer K, Daley CL, Reingold AL. Preventing tuberculosis among HIV-Infected Persons: A survey of physicians' knowledge and practices. *Prev Med*. 1999;28(4):437-444. doi:10.1006/pmed.1998.0452
32. Wyndham-Thomas C, Schepers K, Dirix V, Mascart F, et al. Implementation of latent tuberculosis screening in HIV care centres: evaluation in a low tuberculosis incidence setting. *Epidemiol Infect*. 2016;144(4):703-711. doi:10.1017/S0950268815001594
33. Evenblij K, Verbon A, van Leth F. Intention of physicians to implement guidelines for screening and treatment of latent tuberculosis infection in HIV-infected patients in The Netherlands: a mixed-method design. *BMC Public Health*. 2016;16(1). doi:10.1186/s12889-016-3539-2
34. White HA, Miller RF, Pozniak AL, et al. Latent tuberculosis infection screening and treatment in HIV: insights from evaluation of UK practice. *Thorax*. 2017;72(2):180-182. doi:10.1136/thoraxjnl-2016-209063
35. *Zotero* [Computer Software]. Version 6.0.20. Fairfax, VA: Corporation for Digital Scholarship; 2023.
36. Wong FY, Campsmith ML, Nakamura GV, et al. HIV testing and awareness of care-related services among a group of HIV-positive Asian Americans and Pacific Islanders in the United States: findings from a supplemental HIV/AIDS surveillance project. *AIDS Educ Prev*. 2004;16(5):440-447. doi:10.1521/aeap.16.5.440.48736
37. Li F, Juan BK, Wozniak M, et al. Trends and racial disparities of late-stage HIV Diagnosis: Hawaii, 2010-2016. *Am J Public Health*. 2018;108(S4):S292-S298. doi:10.2105/AJPH.2018.304506
38. Adih WK, Campsmith M, Williams CL, et al. Epidemiology of HIV among Asians and Pacific Islanders in the United States, 2001-2008. *J Int Assoc Physicians AIDS Care (Chic)*. 2011;10(3):150-159. doi:10.1177/1545109711399805
39. Petruccioli E, Scriba TJ, Petrone L, et al. Correlates of tuberculosis risk: predictive biomarkers for progression to active tuberculosis. *Eur Respir J*. 2016;48(6):1751-1763. doi:10.1183/13993003.01012-2016
40. Sester M, van Leth F, Bruchfeld J, et al. Risk assessment of tuberculosis in immunocompromised patients. A TBNET study. *Am J Respir Crit Care Med*. 2014;190(10):1168-1176. doi:10.1164/rccm.201405-0967OC
41. Cattamanchi A, Smith R, Steingart KR, et al. Interferon-gamma release assays for the diagnosis of latent tuberculosis infection in HIV-infected individuals: a systematic review and meta-analysis. *J Acquir Immune Defic Syndr*. 2011;56(3):230-238. doi:10.1097/QAI.0b013e31820b07ab
42. Cobelens FG, Egwaga SM, van Ginkel T, Muwinge H, et al. Tuberculin skin testing in patients with HIV infection: limited benefit of reduced cutoff values. *Clin Infect Dis*. 2006;43(5):634-639. doi:10.1086/506432
43. Pai M, Denkinger CM, Kik SV, et al. Gamma interferon release assays for detection of Mycobacterium tuberculosis infection. *Clin Microbiol Rev*. 2014;27(1):3-20. doi:10.1128/CMR.00034-13
44. Menzies D, Pai M, Comstock G. Meta-analysis: new tests for the diagnosis of latent tuberculosis infection: areas of uncertainty and recommendations for research. *Ann Intern Med*. 2007;146(5):340-354. doi:10.7326/0003-4819-146-5-200703060-00006
45. Pai M, Riley LW, Colford JM Jr. Interferon-gamma assays in the immunodiagnosis of tuberculosis: a systematic review. *Lancet Infect Dis*. 2004;4(12):761-776. doi:10.1016/S1473-3099(04)01206-X
46. Pai M, Zwerling A, Menzies D. Systematic review: T-cell-based assays for the diagnosis of latent tuberculosis infection: an update. *Ann Intern Med*. 2008;149(3):177-184. doi:10.7326/0003-4819-149-3-200808050-00241
47. Corbett EL, Marston B, Churchyard GJ, De Cock KM. Tuberculosis in sub-Saharan Africa: opportunities, challenges, and change in the era of antiretroviral treatment. *Lancet*. 2006;367(9514):926-937. doi:10.1016/S0140-6736(06)68383-9
48. Churchyard GJ, Scano F, Grant AD, Chaisson RE. Tuberculosis preventive therapy in the era of HIV infection: overview and research priorities. *J Infect Dis*. 2007;196 Suppl 1:S52-S62. doi:10.1086/518662
49. Golub JE, Saraceni V, Cavalcante SC, et al. The impact of antiretroviral therapy and isoniazid preventive therapy on tuberculosis incidence in HIV-infected patients in Rio de Janeiro, Brazil. *AIDS*. 2007;21(11):1441-1448. doi:10.1097/QAD.0b013e328216f441
50. Saraceni V, Pacheco AG, Golub JE, et al. Physician adherence to guidelines for tuberculosis and HIV care in Rio de Janeiro, Brazil. *Braz J Infect Dis*. 2011;15(3):249-252. doi:10.1016/s1413-8670(11)70184-2
51. Latent tuberculosis infection: Updated and consolidated guidelines for programmatic management- Background document on the 2019 revision. World Health Organization. Accessed October 7, 2021. https://apps.who.int/iris/handle/10665/260233
52. Swindells S., Ramchandani R., Gupta A., et al. One month of rifapentine plus isoniazid to prevent HIV-related tuberculosis. *N Engl J Med*. 2019;380(11):1001-1011. doi:10.1056/NEJMoa1806808
53. Hu D, Taira D, Yeboah M, Castillo T. Issues affecting medication use among Asian Americans, Native Hawaiians, and Pacific Islanders: A qualitative study. *Calif J Health Promot*. 2016;14(2):45-55. doi:10.32398/cjhp.v14i2.1874
54. Taira DA, Seto BK, Davis JW, et al. Examining factors associated with nonadherence and identifying providers caring for nonadherent subgroups. *J Pharm Health Serv Res*. 2017;8(4):247-253. doi:10.1111/jphs.12193
55. Capocci SJ, Sewell J, Smith C, et al. Cost effectiveness of testing HIV infected individuals for TB in a low TB/HIV setting. *J Infect*. 2020;81(2):289-296. doi:10.1016/j.jinf.2020.05.055
56. BHIVA guidelines for the management of tuberculosis in adults living with HIV 2018 (2021 interim update). British HIV Association. Accessed June 29, 2021. https://www.bhiva.org/TB-guidelines
57. Esperat MC, Inouye J, Gonzalez EW, Owen DC, Feng D. Health disparities among Asian Americans and Pacific Islanders. *Annu Rev Nurs Res*. 2004;22:135-159.
58. Census-latest population estimate data. Department of Business, Economic Development and Tourism, State of Hawaii. Accessed October 14, 2022. https://census.hawaii.gov/home/population-estimate