# Latent Tuberculosis Infection

This is a PDF version of the following document:
Module 4: Co-Occurring Conditions
Lesson 1: Latent Tuberculosis Infection

You can always find the most up-to-date version of this document at https://www.hiv.uw.edu/go/co-occurring-conditions/latent-tuberculosis/core-concept/all.

---

## Background

*Mycobacterium tuberculosis* infection is an important cause of morbidity in persons with HIV. Although combination antiretroviral therapy has significantly decreased the rates of active tuberculosis in people with HIV, the risk of developing active tuberculosis remains enhanced among those with HIV compared to those without HIV.[1,2] The development of active tuberculosis disease can occur soon after an exposure to a person with active *M. tuberculosis* disease or from reactivation of latent tuberculosis infection (LTBI).[4] Individuals with HIV who have LTBI have a substantial risk of developing active tuberculosis disease.[5,6,7,8,9] Thus, identifying a recent exposure or LTBI in a person with HIV provides an opportunity to intervene and prevent active tuberculosis disease.[2] For primary care clinicians, the main goal related to tuberculosis should be to diagnose and treat latent tuberculosis infection. In contrast, the evaluation and treatment of active tuberculosis disease in people with HIV is highly complex and typically managed by a tuberculosis expert and/or an infectious diseases specialist. Thus, the diagnosis and treatment of active tuberculosis disease is not addressed in this curriculum. For a detailed discussion and recommendations for the diagnosis and treatment of active tuberculosis disease, see the Adult and Adolescent OI Guidelines topic *Mycobacterium tuberculosis* Infection and Disease.[2]

### Epidemiology of Tuberculosis in the United States

In 2025, there were 10,260 cases of tuberculosis reported in the United States.[10] The incidence of tuberculosis in the United States substantially declined from 1992 to 2020, but cases have increased from 2021-2024.[10,11] Among people born in the United States, the highest rates of tuberculosis have occurred in Native Hawaiian or Other Pacific Islander people and in American Indian or Alaska Native people.[10] In recent years, most tuberculosis cases in the United States were among persons who were non-United States-born (77% of all cases in 2025).[10] The following graphic shows the epidemiologic features of tuberculosis in the United States (Figure 1).[11]

### Epidemiology of Tuberculosis in Persons with HIV

In the United States, the number of tuberculosis cases among people with HIV declined from 2011-2021, but increased during 2022-2024 (Figure 2).[12] For the year 2024, the CDC reported 418 cases of tuberculosis in persons with HIV coinfection.[12] Among all persons diagnosed with tuberculosis in the United States in 2024 for whom HIV status was known, 4.6% had HIV coinfection.[12] Of the 418 reported cases of tuberculosis involving people with HIV in the United States, 104 (24.8%) occurred in persons who were born in the United States.[12]

# Rationale and Indications for LTBI Screening

## Rationale for LTBI Screening

Multiple factors underscore the rationale for routine LTBI screening in persons with HIV. Most notably, the risk of progression from LTBI to active disease is markedly increased in individuals with HIV: the risk is approximately 3 to 16% per year in persons with HIV compared with 5 to 10% lifetime risk in those without HIV.[2,13,14] Other factors that support routine screening and treatment of LTBI in persons with HIV include poor outcomes associated with active tuberculosis disease and the availability of multiple effective treatment options for LTBI. Among persons with LTBI who also have HIV, treatment of LTBI in conjunction with combination antiretroviral therapy markedly decreases the risk of developing active tuberculosis.[15,16,17,18]

## Indication and Timing of LTBI Screening

The Adult and Adolescent OI Guidelines recommend screening for LTBI at the time of initial HIV diagnosis or entry into medical care, regardless of the presence or absence of other epidemiologic tuberculosis risk factors.[2] In addition to LTBI screening at entry to care, recent contact with a person with known tuberculosis should prompt LTBI screening, as well as evaluation for active disease.

## Repeat LTBI Screening

Individuals with advanced HIV disease (CD4 count less than 200 cells/$mm^3$) with an initial negative LTBI screening test should have repeat testing after they initiate antiretroviral therapy and reach a CD4 count of at least 200 cells/$mm^3$, due to the possibility of false-negative results in the setting of advanced immunosuppression.[2] Yearly repeat testing for LTBI is recommended only in situations when individuals with HIV have enhanced risk for ongoing or repeat exposure to persons with tuberculosis.[2]

# Methods Used to Test for Latent Tuberculosis

There are two primary methods for detection of LTBI: tuberculin skin test (TST) and interferon gamma release assay (IGRA).[19,20] Both methods are indirect measures of T-cell-mediated immune responses to *M. tuberculosis*. Tuberculin skin testing is an *in vivo* skin test, whereas IGRA is an *in vitro* blood-based approach.[21] Routine dual testing with TST and IGRA is not recommended, though CDC guidelines recommend that repeat testing (with the other test) may be appropriate when the initial test was negative in persons at high risk for tuberculosis infection.[22] Importantly, a positive TST or IGRA does not distinguish between LTBI and active tuberculosis disease, nor does a negative LTBI test rule out active tuberculosis disease. Following initial infection with *M. tuberculosis*, the TST and IGRA tests typically have a gap of 2 to 10 weeks before they become positive. Neither TST nor IGRA tests can be used to monitor LTBI treatment responses, as both tests typically remain positive after treatment.

## Tuberculin Skin Test

The Mantoux TST method consists of giving an intradermal injection of 5 tuberculin units of purified protein derivative (PPD) that contains *M. tuberculosis* antigens; the transverse diameter of induration (not erythema) should be measured as the amount of induration (mm) at a follow-up visit 48 to 72 hours after placement of the PPD (Figure 3).[19] In persons with *M. tuberculosis* infection (past or current), intradermal injection of the PPD will stimulate a T-lymphocyte-mediated type IV delayed hypersensitivity response, leading to induration of the site of injection within 48 to 72 hours.[21]

### Criteria for Positive TST

For individuals with HIV, an induration of 5 mm or greater is considered a positive test.[23] Following exposure to *M. tuberculosis*, the TST conversion to positive typically occurs within 8 weeks.[24] The sensitivity of TST for the diagnosis of LTBI is estimated at 45 to 85% and specificity at approximately 85%.[22,25,26] Persons with prior treatment of tuberculosis (latent or active) typically have a persistently positive TST.

### False-Positive TST

Previous exposure to nontuberculous mycobacteria, as well as immunization with Bacille Calmette–Guérin (BCG), can cause a false-positive TST.[20] Receipt of BCG in infancy is thought to have a relatively minimal effect on TST, especially if at least 10 years have elapsed after administration.[27]

### False-Negative TST

False-negative TSTs can occur in the setting of advanced HIV disease, malnutrition, active tuberculosis, or early in the window period after recent *M. tuberculosis* infection.[20]

## Interferon Gamma Release Assay (IGRA)

For the diagnosis of LTBI, the two most commonly used FDA-approved IGRAs in the United States are the QuantiFERON-TB Gold Plus (QFT-Plus) assay and the T-SPOT.TB (T-SPOT) assay (Figure 4).[22] The QFT-Plus and T-SPOT are in vitro tests that measure the release of interferon gamma by T-lymphocytes after stimulation to a peptide antigen cocktail that simulates two *M. tuberculosis*-specific antigens: early secreted antigenic target 6 (ESAT-6) and culture filtrate protein 10 (CFP-10).[20,28,29] The ESAT-6 and CFP-10 mycobacterial antigens are absent from all mycobacterial strains used in BCG vaccines and from most nontuberculous mycobacteria, except for *M. marinum*, *M. kansasii*, and *M. szulgai*.[20] Hence, the IGRAs are less likely to show cross-reactivity in persons who have received BCG vaccination and/or had prior infection with non-tuberculous mycobacteria. Persons with active tuberculosis or prior treated LTBI usually have persistently positive IGRAs. Although IGRA testing requires a blood draw, unlike TST, it does not require a follow-up visit for test result reading.

- **QuantiFERON-TB Gold Plus (QFT-Plus)**: This test has replaced the previously used QuantiFERON-TB Gold test and has the advantage of measuring both CD4 and CD8 T-lymphocyte responses (Figure 5).[30,31,32] To perform the test, blood is drawn into 4 specialized collection tubes: (1) Nil (negative control), (2) mitogen (positive control), (3) TB1 (primarily detects CD4 T cell response), and (4) TB2 (optimized for detection of CD4 and CD8 T cell responses).[30,33,34,35] The interferon gamma response is quantified in international units (IU) per millimeter, and test results are reported as positive, negative, or indeterminate.[33] Reversion from a positive to negative test result can occur,[36,37,38] but this tends to occur when the initial test is close to the cutoff threshold.[20,30,34]
- **T-SPOT.*TB* (T-SPOT)**: The T-SPOT is an enzyme-linked immunosorbent spot (ELISPOT) assay that quantitates the response of mononuclear T-cells to *M*. *tuberculosis* antigens (Figure 6).[22] First, a blood sample is obtained, and peripheral blood mononuclear cells are separated from whole blood and counted. The peripheral blood mononuclear cells are then placed into microtiter wells pre-coated with high-affinity antibodies to interferon gamma; four different panels are set up by coincubating with either *M*. *tuberculosis* ESAT-6 antigens (Panel A), *M*. *tuberculosis* CFP10 antigens (Panel B), positive control that contains phytohemagglutinin (Panel C), or Nil negative control (Panel D).[39] The number of T-cells producing interferon gamma (spot-forming cells) are then counted. The test results are categorized as either positive, borderline, negative, or indeterminate.[22]

**Performance of IGRA Tests**

Similar to TST, the IGRA tests may be falsely negative early in the window period after a recent *M*. *tuberculosis* infection. The IGRA tests have greater specificity than the TST, and the IGRA tests are not impacted by prior receipt of BCG vaccine.[2] In addition, IGRA cutoffs are not stratified by risk group, including HIV status. The presence of immunosuppression decreases the sensitivity of IGRAs, but the impact is relatively less than on TST.[20] In a meta-analysis of IGRA studies in persons with HIV, the pooled sensitivity was higher for the T-SPOT than for QFT.[40] In a study that evaluated T-SPOT versus QFT versus TST in 1,510 individuals with HIV in the United States, the T-SPOT had the highest sensitivity, specificity, and positive predictive value.[41]

# Recommended LTBI Testing in Persons with HIV

## Choice of Test Method for LTBI Screening

Use of either TST or IGRA is appropriate for LTBI screening in persons with HIV.[2,19,22] The correlation between positive TST and IGRA in persons with HIV is poor to moderate.[5,40,42,43] In recent years, many clinics have predominantly used IGRAs because of several negative aspects of TST, including the requirement for a second visit to read the test, false-positive results in people immunized with BCG vaccine, and lower sensitivity in persons with advanced immunosuppression. From a practical standpoint, the decision regarding which test to use is often based on a combination of the availability of the test, trained staff, lab capability, and likelihood of patient follow-up for a second visit to read a TST.

## LTBI TESTING IN PERSONS WITH HIV

The Adult and Adolescent OI Guidelines recommendations regarding testing for LTBI in persons with HIV are summarized as follows:[2]

- All persons with HIV should undergo testing for LTBI at the time of HIV diagnosis, regardless of their epidemiological risk of TB exposure.
- The TST or IGRA can be used as the screening method for LTBI, and the decision for which one to use may be based on the likelihood of patient follow-up for reading a TST and access to laboratory testing for IGRAs.
- Annual testing for LTBI is recommended for persons with HIV who are at high risk for repeated or ongoing exposure to persons with active TB.
- Persons with HIV and advanced immunosuppression (CD4 count less than 200 cells/$mm^3$) who have a negative LTBI test result should undergo repeat testing for LTBI after they start on antiretroviral therapy and have an increase in CD4 count to 200 cells/$mm^3$ or greater.
- The use of both TST and IGRA to screen for LTBI is not routinely recommended, though some experts recommend dual testing to increase the sensitivity in individuals who have a high likelihood of having infection with *M. tuberculosis* and a high risk of progression to active disease.
- All persons with a positive TST or IGRA should be evaluated for the possibility of active TB disease.

## Evaluation After a Positive LTBI Screening Test

Any individual with HIV who has a new positive LTBI screening test should undergo tuberculosis symptom screening and chest radiography to exclude active tuberculosis disease.[44] A meta-analysis of individual participant data of more than 8,000 persons with HIV found that having at least one positive symptom in a 4-symptom tuberculosis screen (cough, fever, weight loss, or night sweats) has a sensitivity of 78.9%, a specificity of 49.6%, and negative predictive value of 97.7% (at a 5% prevalence) to identify those with culture-confirmed pulmonary tuberculosis.[45] A more recent systematic review and meta-analysis found this 4-symptom tuberculosis screen had a lower pooled sensitivity, but higher specificity, when comparing people with HIV on antiretroviral therapy versus those not on antiretroviral therapy.[46] Sputum examination, including acid-fast smear microscopy, nucleic acid amplification testing, and culture, is indicated for those individuals with either an abnormal chest radiograph or a positive symptom screen (even if their chest radiograph is negative). In a low-burden setting such as in the United States, routine use of sputum culture to screen for tuberculosis in asymptomatic individuals with a negative chest radiograph is not considered cost-effective.[2]

# Management of LTBI in Persons with HIV

## Indications for LTBI Treatment

A positive TST or IGRA is associated with a significantly increased risk of developing tuberculosis disease.[5,43] The risk of progression to active tuberculosis disease is even higher among recent LTBI test converters.[42,47,48] Some studies indicate a positive IGRA is a stronger predictor than a positive TST for the risk of developing tuberculosis disease.[49,50] Note that a history of BCG vaccination should not affect the decision about whether to treat LTBI in persons with HIV. The following summarizes the two main indications for initiating LTBI in persons with HIV.[2]

- A new positive screening test (TST or IGRA) for LTBI with no evidence of active tuberculosis disease, and no prior history of treatment for either active disease or LTBI.
- Close contact with a person who has infectious tuberculosis, irrespective of LTBI test result.

## Regimens for LTBI Treatment

The choice for the LTBI regimen should strongly consider the individual's antiretroviral regimen.[2,51] All regimens to treat LTBI are taken orally, and when isoniazid is given, concomitant pyridoxine (vitamin B6) is prescribed to prevent isoniazid-induced peripheral neuropathy.[2] The regimens for LTBI are commonly referred to as short name abbreviations:

- **3HP** = **3-**month duration with isoniazid (IN**H**) *plus* rifapentine (R**P**T)
- **3HR** = **3-**month duration with isoniazid (IN**H**) *plus* rifampin (**R**IF)
- **6H/9H** = (**6**-or **9**-month duration with IN**H**)
- **4R** = **4**-month duration with rifampin (**R**IF)
- **1HP** = **1**-month duration with isoniazid (IN**H**) *plus* rifapentine (R**P**T).

The following summarizes recommendations for the preferred and alternative regimens for the treatment of LTBI in adults with HIV (Table 1).[2,51] Note the LTBI regimens should only be used with the antiretroviral regimens that are outlined below in the table. In particular, note that the 6H and 9H regimens are the only recommended options in persons taking bictegravir-tenofovir alafenamide-emtricitabine.[2]

## Summary of Data for Regimens Used to Treat LTBI

- **3HP: Isoniazid plus Rifapentine Weekly for 3 Months**: The 3HP regimen has efficacy equal to standard isoniazid monotherapy, with the added likely benefit of improved adherence and completion rates due to a shorter duration.[52,53,54,55] Self-administered 3HP therapy is equivalent to directly observed therapy (DOT).[56]
- **3HR: Isoniazid plus Rifampin Daily for 3 Months**: In studies involving use of 3HR in individuals with HIV, there was no significant difference in rates of developing TB disease among those taking 3HR compared to those taking 6 months or longer of daily isoniazid.[57,58,59]
- **6H or 9H: Isoniazid for 6 or 9 Months**: These isoniazid monotherapy regimens are considered standard-length LTBI treatment for persons with HIV (6 or 9 months).[2,51] These regimens are referred to as 6H and 9H (6 or 9 months of INH). These regimens are generally well tolerated, but isoniazid has been associated with an increased risk of hepatotoxicity. Isoniazid does not cause problematic drug interactions with antiretroviral medications. These regimens, however, are no longer rated as preferred treatment for LTBI because completion rates are lower than with shorter-course LTBI regimens.[60,61]
- **4R: Rifampin for 4 Months (BI)**: In a recent large international open-label clinical trial that enrolled persons with and without HIV, investigators demonstrated 4 months of rifampin was noninferior to 9 months of isoniazid for the treatment of LTBI.[62] Furthermore, the rifampin regimen cohort had higher rates of treatment completion and fewer adverse effects.[62] Among all study participants,

only 4% had HIV.[62] This regimen is an alternative regimen because of minimal data in persons with HIV and potential drug interactions between rifampin and other medications commonly taken by people with HIV.

- **1HP: Isoniazid plus Rifapentine Daily for 1 month (BI)**: In the BRIEF-TB/A5279 trial, a short-course 1-month regimen of daily isoniazid plus rifapentine was noninferior to 9 months of isoniazid alone in preventing tuberculosis in persons with HIV who were taking efavirenz- or nevirapine-based antiretroviral therapy, with fewer adverse events, and higher completion rates.[63]

## Medication-Related Adverse Effects

Individuals on LTBI therapy should undergo clinical monitoring on a monthly basis. Isoniazid can cause peripheral neuropathy, but this can be prevented with concomitant use of pyridoxine (vitamin B6). In addition, isoniazid is associated with an increased risk of hepatotoxicity, particularly in patients of older age, with alcohol use, and if used during pregnancy.[65] Persons taking isoniazid should receive education on the signs and symptoms of hepatitis (jaundice, abdominal discomfort, nausea and vomiting) and be advised to promptly stop isoniazid and report their symptoms to their medical provider. Baseline hepatic aminotransferase levels should be obtained. Individuals at increased risk of hepatotoxicity, including those with abnormal baseline tests, pregnant women, persons with hepatitis B or C coinfection, or those receiving antiretroviral therapy, should have routine lab monitoring during treatment with isoniazid.[2] The Adult and Adolescent OI Guidelines recommend withholding isoniazid if the hepatic aminotransferase level exceeds three times the upper limit of normal (with associated symptoms) or five times the upper limit of normal (with or without associated symptoms).[2] A 2-month short course regimen of rifampin and pyrazinamide has been studied, but this regimen has an unacceptably high risk of causing severe liver injury and thus should never be used for treatment of latent TB.[2,66,67]

## Management with Missed Doses or Treatment Interruption

If interruptions were frequent or prolonged enough to preclude completion of treatment within the recommended time frame, therapy should be extended or restarted. When treatment has been interrupted for more than 2 months, the patient should be reevaluated for active tuberculosis.

# Considerations in Special Populations

## LTBI in Pregnancy

### Screening for LTBI in Pregnancy

All pregnant women with HIV who have not had previous screening for LTBI (or who are at high risk of exposure to individuals with active tuberculosis) should undergo testing for LTBI during pregnancy.[2] Although data remain conflicting if the pregnancy stage affects both TST and IGRA testing,[68,69,70] either test is considered appropriate for screening in pregnancy.

### Treatment of LTBI in Pregnancy

Pregnant women with recent significant close contact with an active tuberculosis case or at high risk of developing active tuberculosis, or with a recent TST or IGRA conversion can be offered LTBI treatment. For pregnant women on effective ART with recent contact or TST or IGRA conversion, LTBI treatment may be deferred until the postpartum period.[2,71] Data from a randomized controlled trial involving women with HIV suggest that women who are pregnant or in the postpartum period may have a higher risk for isoniazid-associated hepatotoxicity.[71] In this trial, isoniazid given during pregnancy was associated with higher rates of adverse pregnancy outcomes compared to postpartum administered isoniazid.[71] In contrast, two recent observational studies from South Africa have demonstrated no hepatotoxicity and improved pregnancy outcomes in women with HIV on antiretroviral therapy who are given isoniazid for LTBI.[72,73] Rifampin is generally considered safe in pregnancy and some experts recommend its use in pregnancy due to a lower risk of hepatotoxicity, though drug interactions with antiretroviral therapy may limit its use. There are inadequate efficacy and safety data for the use of rifapentine in pregnancy.[74,75] Thus, if LTBI therapy is required during pregnancy, and there are problematic drug interactions with rifampin, the recommended regimen is isoniazid (given with pyridoxine), with monitoring for hepatotoxicity.[2] If there are no problematic drug interactions with rifampin, the two options are daily rifampin for 4 months (4R) or daily isoniazid (given with pyridoxine) *plus* rifampin, for 3 months (3HR). Regimens that use rifapentine are not recommended during pregnancy.[2]

## Treatment of LTBI in Persons with Liver Disease

Individuals with chronic liver disease are at increased risk of LTBI treatment-associated hepatitis. Active hepatitis and end-stage liver disease are relative contraindications for LTBI treatment. Isoniazid or rifampin have been used in this population in the setting of stable liver disease, but close clinical and laboratory monitoring is recommended.[2] In addition, management of LTBI in a patient with chronic liver disease should involve consultation with a tuberculosis expert.

## Summary Points

- Despite a declining incidence of tuberculosis in the United States, individuals with HIV remain at significant risk for tuberculosis, even when taking antiretroviral therapy.
- All individuals with HIV should undergo screening for LTBI at either the time of HIV diagnosis or entry into care. Severe immunosuppression can lead to false-negative LTBI tests; therefore, LTBI screening should be repeated once CD4 counts increase to at least 200 cells/$mm^3$ on antiretroviral treatment.
- Testing for LTBI should be performed with either a TST or IGRA. Limitations to TST, when compared with IGRA testing, include the requirement for a second visit to read the test, lower specificity, and potentially lower sensitivity with advanced immunosuppression.
- All individuals with HIV and a positive LTBI screening test should receive LTBI treatment after active tuberculosis disease has been ruled out. In addition, all individuals with HIV who have recent exposure to a person with active tuberculosis should receive LTBI treatment, irrespective of TST and/or IGRA results.
- Selection of an LTBI treatment regimen will depend on duration and frequency of the regimen, the likelihood of patient completion of the regimen, and drug interactions between the LTBI treatment medications and the antiretroviral regimen.
- There are two preferred regimens for LTBI treatment in persons with HIV: a 3-month course of weekly isoniazid plus rifapentine (3HP) or a 3-month course of daily isoniazid plus rifampin (3HR). Whenever isoniazid is given, pyridoxine is also given to prevent the development of isoniazid-induced peripheral neuropathy.
- There are three alternative LTBI regimens for persons with HIV: daily isoniazid for 6 or 9 months (6H or 9H), a 4-month course of daily rifampin (4R), or a 1-month course of daily isoniazid plus rifapentine (1HP).
- For pregnant women diagnosed with LTBI, delaying treatment of LTBI until after the pregnancy is typically recommended. For women requiring LTBI treatment during pregnancy, isoniazid monotherapy given daily for 6 or 9 months is the preferred regimen.

# Citations


1. Kufa T, Mabuto T, Muchiri E, et al. Incidence of HIV-associated tuberculosis among individuals taking combination antiretroviral therapy: a systematic review and meta-analysis. PLoS One. 2014;9:e111209.
[PubMed Abstract] -

2. Panel on Opportunistic Infections in Adults and Adolescents with HIV. Guidelines for the prevention and treatment of opportunistic infections in adults and adolescents with HIV: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. *Mycobacterium tuberculosis* infection and disease. Last update: May 2, 2024.
[HIV.gov] -

3. Drain PK, Bajema KL, Dowdy D, et al. Incipient and Subclinical Tuberculosis: a Clinical Review of Early Stages and Progression of Infection. Clin Microbiol Rev. 2018;31(4). pii: e00021-18.
[PubMed Abstract] -

4. Markowitz N, Hansen NI, Hopewell PC, et al. Incidence of tuberculosis in the United States among HIV-infected persons. The Pulmonary Complications of HIV Study Group. Ann Intern Med. 1997;126:123-32.
[PubMed Abstract] -

5. Kim YJ, Kim SI, Kim YR, Wie SH, Park YJ, Kang MW. Predictive value of interferon-γ ELISPOT assay in HIV 1-infected patients in an intermediate tuberculosis-endemic area. AIDS Res Hum Retroviruses. 2012;28:1038-43.
[PubMed Abstract] -

6. 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;44:94-102.
[PubMed Abstract] -

7. Aichelburg MC, Rieger A, Breitenecker F, et al. Detection and prediction of active tuberculosis disease by a whole-blood interferon-gamma release assay in HIV-1-infected individuals. Clin Infect Dis. 2009;48:954-62.
[PubMed Abstract] -

8. Ledesma JR, Ma J, Zheng P, Ross JM, Vos T, Kyu HH. Interferon-gamma release assay levels and risk of progression to active tuberculosis: a systematic review and dose-response meta-regression analysis. BMC Infect Dis. 2021;21:467.
[PubMed Abstract] -

9. Centers for Disease Control (CDC). Provisional 2025 Tuberculosis Data, United States. National Data. Atlanta, GA: U.S. Department of Health and Human Services, CDC. March 23, 2026
[CDC] -

10. Centers for Disease Control (CDC). Reported Tuberculosis in the United States, 2023. National Data. Atlanta, GA: U.S. Department of Health and Human Services, CDC.
[CDC] -

11. Centers for Disease Control (CDC). Tuberculosis in the United States, 2024. December 19, 2025
[CDC] -

12. Comstock GW, Livesay VT, Woolpert SF. The prognosis of a positive tuberculin reaction in childhood and adolescence. Am J Epidemiol. 1974;99:131-8.
[PubMed Abstract] -

13. Selwyn PA, Hartel D, Lewis VA, et al. A prospective study of the risk of tuberculosis among intravenous drug users with human immunodeficiency virus infection. N Engl J Med. 1989;320:545-50.
[PubMed Abstract] -

14. 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;21:1441-8.
[PubMed Abstract] -

15. Durovni B, Saraceni V, Moulton LH, et al. Effect of improved tuberculosis screening and isoniazid preventive therapy on incidence of tuberculosis and death in patients with HIV in clinics in Rio de Janeiro, Brazil: a stepped wedge, cluster-randomised trial. Lancet Infect Dis. 2013;13:852-8.
[PubMed Abstract] -

16. Akolo C, Adetifa I, Shepperd S, Volmink J. Treatment of latent tuberculosis infection in HIV infected persons. Cochrane Database Syst Rev. 2010;:CD000171.
[PubMed Abstract] -

17. Ross JM, Badje A, Rangaka MX, et al. Isoniazid preventive therapy plus antiretroviral therapy for the prevention of tuberculosis: a systematic review and meta-analysis of individual participant data. Lancet HIV. 2021;8:e8-e15.
[PubMed Abstract] -

18. 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:e1-e33.
[PubMed Abstract] -

19. Pai M, Denkinger CM, Kik SV, et al. Gamma interferon release assays for detection of *Mycobacterium tuberculosis* infection. Clin Microbiol Rev. 2014;27:3-20.
[PubMed Abstract] -

20. Andersen P, Munk ME, Pollock JM, Doherty TM. Specific immune-based diagnosis of tuberculosis. Lancet. 2000;356:1099-104.
[PubMed Abstract] -

21. Mazurek GH, Jereb J, Vernon A, LoBue P, Goldberg S, Castro K. Updated guidelines for using Interferon Gamma Release Assays to detect *Mycobacterium tuberculosis* infection - United States, 2010. MMWR Recomm Rep. 2010;59:1-25.
[PubMed Abstract] -

22. Targeted tuberculin testing and treatment of latent tuberculosis infection. This official statement of the American Thoracic Society was adopted by the ATS Board of Directors, July 1999. This is a Joint Statement of the American Thoracic Society (ATS) and the Centers for Disease Control and Prevention (CDC). This statement was endorsed by the Council of the Infectious Diseases Society of America. (IDSA), September 1999, and the sections of this statement. Am J Respir Crit Care Med. 2000;161:S221-47.
[PubMed Abstract] -

23. National Tuberculosis Controllers Association; Centers for Disease Control and Prevention (CDC). Guidelines for the investigation of contacts of persons with infectious tuberculosis. Recommendations from the National Tuberculosis Controllers Association and CDC. MMWR Recomm Rep. 2005;54:1-47. [Pub Med Abstract] -

24. Metcalfe JZ, Everett CK, Steingart KR, et al. Interferon-γ release assays for active pulmonary tuberculosis diagnosis in adults in low- and middle-income countries: systematic review and meta-analysis. J Infect Dis. 2011;204 Suppl 4:S1120-9. [PubMed Abstract] -

25. Santin M, Muñoz L, Rigau D. Interferon-γ release assays for the diagnosis of tuberculosis and tuberculosis infection in HIV-infected adults: a systematic review and meta-analysis. PLoS One. 2012;7:e32482. [PubMed Abstract] -

26. Farhat M, Greenaway C, Pai M, Menzies D. False-positive tuberculin skin tests: what is the absolute effect of BCG and non-tuberculous mycobacteria? Int J Tuberc Lung Dis. 2006;10:1192-204. [PubMed Abstract] -

27. Teixeira HC, Abramo C, Munk ME. Immunological diagnosis of tuberculosis: problems and strategies for success. J Bras Pneumol. 2007;33:323-34. [PubMed Abstract] -

28. Metcalfe JZ, Cattamanchi A, McCulloch CE, Lew JD, Ha NP, Graviss EA. Test variability of the QuantiFERON-TB gold in-tube assay in clinical practice. Am J Respir Crit Care Med. 2013;187:206-11. [PubMed Abstract] -

29. Moon HW, Gaur RL, Tien SS, Spangler M, Pai M, Banaei N. Evaluation of QuantiFERON-TB Gold-Plus in Health Care Workers in a Low-Incidence Setting. J Clin Microbiol. 2017;55:1650-1657. [PubMed Abstract] -

30. Day CL, Abrahams DA, Lerumo L, et al. Functional capacity of *Mycobacterium tuberculosis*-specific T cell responses in humans is associated with mycobacterial load. J Immunol. 2011;187:2222-32. [PubMed Abstract] -

31. Rozot V, Vigano S, Mazza-Stalder J, et al. *Mycobacterium tuberculosis*-specific CD8+ T cells are functionally and phenotypically different between latent infection and active disease. Eur J Immunol. 2013;43:1568-77. [PubMed Abstract] -

32. Qiagen. QuantiFERON®-TB Gold Plus (QFT®-Plus). Package Insert. July 2018 [Qiagen] -

33. Hoffmann H, Avsar K, Göres R, Mavi SC, Hofmann-Thiel S. Equal sensitivity of the new generation QuantiFERON-TB Gold plus in direct comparison with the previous test version QuantiFERON-TB Gold IT. Clin Microbiol Infect. 2016;22:701-3. [PubMed Abstract] -

34. Petruccioli E, Vanini V, Chiacchio T, et al. Analytical evaluation of QuantiFERON- Plus and QuantiFERON- Gold In-tube assays in subjects with or without tuberculosis. Tuberculosis (Edinb). 2017;106:38-43. [PubMed Abstract] -

35. Aichelburg MC, Reiberger T, Breitenecker F, Mandorfer M, Makristathis A, Rieger A. Reversion and

conversion of interferon-γ release assay results in HIV-1-infected individuals. J Infect Dis. 2014;209:729-33.
[PubMed Abstract] -

36. Gray J, Reves R, Johnson S, Belknap R. Identification of false-positive QuantiFERON-TB Gold In-Tube assays by repeat testing in HIV-infected patients at low risk for tuberculosis. Clin Infect Dis. 2012;54:e20-3.
[PubMed Abstract] -

37. Pullar ND, Steinum H, Bruun JN, Dyrhol-Riise AM. HIV patients with latent tuberculosis living in a low-endemic country do not develop active disease during a 2 year follow-up; a Norwegian prospective multicenter study. BMC Infect Dis. 2014;14:667.
[PubMed Abstract] -

38. Oxford Immunotec. T-SPOT.*TB*
[Oxford Immunotec] -

39. 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;56:230-8.
[PubMed Abstract] -

40. Pettit AC, Stout JE, Belknap R, et al. Optimal Testing Choice and Diagnostic Strategies for Latent Tuberculosis Infection Among US-Born People Living with Human Immunodeficiency Virus (HIV). Clin Infect Dis. 2021;73:e2278-e2284.
[PubMed Abstract] -

41. Watkins RE, Brennan R, Plant AJ. Tuberculin reactivity and the risk of tuberculosis: a review. Int J Tuberc Lung Dis. 2000;4:895-903.
[PubMed Abstract] -

42. Hill PC, Brookes RH, Fox A, et al. Longitudinal assessment of an ELISPOT test for *Mycobacterium tuberculosis* infection. PLoS Med. 2007;4:e192.
[PubMed Abstract] -

43. Backus LI, Boothroyd DB, Phillips BR, et al. National quality forum performance measures for HIV/AIDS care: the Department of Veterans Affairs experience. Arch Intern Med. 2010;170:1239-46.
[PubMed Abstract] -

44. Getahun H, Kittikraisak W, Heilig CM, et al. Development of a standardized screening rule for tuberculosis in people living with HIV in resource-constrained settings: individual participant data meta-analysis of observational studies. PLoS Med. 2011;8:e1000391.
[PubMed Abstract] -

45. Hamada Y, Lujan J, Schenkel K, Ford N, Getahun H. Sensitivity and specificity of WHO's recommended four-symptom screening rule for tuberculosis in people living with HIV: a systematic review and meta-analysis. Lancet HIV. 2018;5:e515-e523.
[PubMed Abstract] -

46. Machingaidze S, Verver S, Mulenga H, et al. Predictive value of recent QuantiFERON conversion for tuberculosis disease in adolescents. Am J Respir Crit Care Med. 2012;186:1051-6.
[PubMed Abstract] -

47. Diel R, Loddenkemper R, Meywald-Walter K, Niemann S, Nienhaus A. Predictive value of a whole blood

IFN-gamma assay for the development of active tuberculosis disease after recent infection with *Mycobacterium tuberculosis*. Am J Respir Crit Care Med. 2008;177:1164-70.
[PubMed Abstract] -

48. Diel R, Loddenkemper R, Niemann S, Meywald-Walter K, Nienhaus A. Negative and positive predictive value of a whole-blood interferon-γ release assay for developing active tuberculosis: an update. Am J Respir Crit Care Med. 2011;183:88-95.
[PubMed Abstract] -

49. Leung CC, Yam WC, Ho PL, et al. T-Spot.TB outperforms tuberculin skin test in predicting development of active tuberculosis among household contacts. Respirology. 2015;20:496-503.
[PubMed Abstract] -

50. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in adults and adolescents with HIV. Department of Health and Human Services. Considerations for antiretroviral use in patients with coinfections: Tuberculosis/HIV coinfection. September 12, 2024.
[HIV.gov] -

51. Sterling TR, Villarino ME, Borisov AS, et al. Three months of rifapentine and isoniazid for latent tuberculosis infection. N Engl J Med. 2011;365:2155-66.
[PubMed Abstract] -

52. Borisov AS, Bamrah Morris S, Njie GJ, et al. Update of Recommendations for Use of Once-Weekly Isoniazid-Rifapentine Regimen to Treat Latent *Mycobacterium tuberculosis* Infection. MMWR Morb Mortal Wkly Rep. 2018;67:723-6.
[PubMed Abstract] -

53. Sterling TR, Scott NA, Miro JM, et al. Three months of weekly rifapentine and isoniazid for treatment of Mycobacterium tuberculosis infection in HIV-coinfected persons. AIDS. 2016;30:1607-15.
[PubMed Abstract] -

54. Churchyard G, Cárdenas V, Chihota V, et al. Annual tuberculosis preventive therapy for persons with HIV infection: a randomized trial. Ann Intern Med. 2021;174:1367-76.
[PubMed Abstract] -

55. Belknap R, Holland D, Feng PJ, et al. Self-administered Versus Directly Observed Once-Weekly Isoniazid and Rifapentine Treatment of Latent Tuberculosis Infection: A Randomized Trial. Ann Intern Med. 2017;167:689-97.
[PubMed Abstract] -

56. Fitzgerald DW, Severe P, Joseph P, et al. No effect of isoniazid prophylaxis for purified protein derivative-negative HIV-infected adults living in a country with endemic tuberculosis: results of a randomized trial. J Acquir Immune Defic Syndr. 2001;28:305-7.
[PubMed Abstract] -

57. Johnson JL, Okwera A, Hom DL, et al. Duration of efficacy of treatment of latent tuberculosis infection in HIV-infected adults. AIDS. 2001;15:2137-47.
[PubMed Abstract] -

58. Whalen CC, Johnson JL, Okwera A, et al. A trial of three regimens to prevent tuberculosis in Ugandan adults infected with the human immunodeficiency virus. Uganda-Case Western Reserve University Research Collaboration. N Engl J Med. 1997;337:801-8.
[PubMed Abstract] -

59. Gordin F, Chaisson RE, Matts JP, et al. Rifampin and pyrazinamide vs isoniazid for prevention of tuberculosis in HIV-infected persons: an international randomized trial. Terry Beirn Community Programs for Clinical Research on AIDS, the Adult AIDS Clinical Trials Group, the Pan American Health Organization, and the Centers for Disease Control and Prevention Study Group. JAMA. 2000;283:1445-50.
[PubMed Abstract] -

60. Horsburgh CR Jr, Goldberg S, Bethel J, et al. Latent TB infection treatment acceptance and completion in the United States and Canada. Chest. 2010;137:401-9.
[PubMed Abstract] -

61. Menzies D, Adjobimey M, Ruslami R, et al. Four Months of Rifampin or Nine Months of Isoniazid for Latent Tuberculosis in Adults. N Engl J Med. 2018;379:440-53.
[PubMed Abstract] -

62. Swindells S, Ramchandani R, Gupta A, et al. One Month of Rifapentine plus Isoniazid to Prevent HIV-Related Tuberculosis. N Engl J Med. 2019;380:1001-11.
[PubMed Abstract] -

63. Saukkonen JJ, Cohn DL, Jasmer RM, et al. An official ATS statement: hepatotoxicity of antituberculosis therapy. Am J Respir Crit Care Med. 2006;174:935-52.
[PubMed Abstract] -

64. Centers for Disease Control and Prevention (CDC). Update: Fatal and severe liver injuries associated with rifampin and pyrazinamide treatment for latent tuberculosis infection. MMWR Morb Mortal Wkly Rep. 2002;51:998-9.
[PubMed Abstract] -

65. Centers for Disease Control and Prevention (CDC); American Thoracic Society. Update: adverse event data and revised American Thoracic Society/CDC recommendations against the use of rifampin and pyrazinamide for treatment of latent tuberculosis infection--United States, 2003. MMWR Morb Mortal Wkly Rep. 2003;52:735-9.
[PubMed Abstract] -

66. LaCourse SM, Cranmer LM, Matemo D, et al. Effect of Pregnancy on Interferon Gamma Release Assay and Tuberculin Skin Test Detection of Latent TB Infection Among HIV-Infected Women in a High Burden Setting. J Acquir Immune Defic Syndr. 2017;75:128-136.
[PubMed Abstract] -

67. Mathad JS, Bhosale R, Sangar V, et al. Pregnancy differentially impacts performance of latent tuberculosis diagnostics in a high-burden setting. PLoS One. 2014;9:e92308.
[PubMed Abstract] -

68. Covelli HD, Wilson RT. Immunologic and medical considerations in tuberculin-sensitized pregnant patients. Am J Obstet Gynecol. 1978;132:256-9.
[PubMed Abstract] -

69. Gupta A, Montepiedra G, Aaron L, et al. Isoniazid Preventive Therapy in HIV-Infected Pregnant and Postpartum Women. N Engl J Med. 2019;381:1333-1346.
[PubMed Abstract] -

70. Salazar-Austin N, Cohn S, Lala S, et al. Isoniazid Preventive Therapy and Pregnancy Outcomes in Women Living With Human Immunodeficiency Virus in the Tshepiso Cohort. Clin Infect Dis. 2020;71:1419-26.

[PubMed Abstract] -

71. Kalk E, Heekes A, Mehta U, et al. Safety and Effectiveness of Isoniazid Preventive Therapy in Pregnant Women Living with Human Immunodeficiency Virus on Antiretroviral Therapy: An Observational Study Using Linked Population Data. Clin Infect Dis. 2020;71:e351-e358.
[PubMed Abstract] -

72. Centers for Disease Control and Prevention (CDC). Recommendations for use of an isoniazid-rifapentine regimen with direct observation to treat latent *Mycobacterium tuberculosis* infection. MMWR Morb Mortal Wkly Rep. 2011;60:1650-3.
[PubMed Abstract] -

73. Mathad JS, Savic R, Britto P, et al. Pharmacokinetics and Safety of 3 Months of Weekly Rifapentine and Isoniazid for Tuberculosis Prevention in Pregnant Women. Clin Infect Dis. 2022;74:1604-13.
[PubMed Abstract] -

## References

- Centers for Disease Control and Prevention (CDC). Severe isoniazid-associated liver injuries among persons being treated for latent tuberculosis infection - United States, 2004-2008. MMWR Morb Mortal Wkly Rep. 2010;59:224-9.
[MMWR] -

- Dooley KE, Savic R, Gupte A, et al. Once-weekly rifapentine and isoniazid for tuberculosis prevention in patients with HIV taking dolutegravir-based antiretroviral therapy: a phase 1/2 trial. Lancet HIV. 2020;7:e401-e409.
[PubMed Abstract] -

- Ena J, Valls V. Short-course therapy with rifampin plus isoniazid, compared with standard therapy with isoniazid, for latent tuberculosis infection: a meta-analysis. Clin Infect Dis. 2005;40:670-6.
[PubMed Abstract] -

- Franks AL, Binkin NJ, Snider DE Jr, Rokaw WM, Becker S. Isoniazid hepatitis among pregnant and postpartum Hispanic patients. Public Health Rep. 1989;104:151-5.
[PubMed Abstract] -

- Geijo MP, Herranz CR, Vaño D, García AJ, García M, Dimas JF. [Short-course isoniazid and rifampin compared with isoniazid for latent tuberculosis infection: a randomized clinical trial]. Enferm Infecc Microbiol Clin. 2007;25:300-4.
[PubMed Abstract] -

- Ghassemieh BJ, Attia EF, Koelle DM, Mancuso JD, Narita M, Horne DJ. Latent Tuberculosis Infection Test Agreement in the National Health and Nutrition Examination Survey. Am J Respir Crit Care Med. 2016;194:493-500.
[PubMed Abstract] -

- Haddad MB, Raz KM, Lash TL, et al. Simple Estimates for Local Prevalence of Latent Tuberculosis Infection, United States, 2011-2015. Emerg Infect Dis. 2018;24:1930-3.
[PubMed Abstract] -

- Horsburgh CR Jr, Rubin EJ. Clinical practice. Latent tuberculosis infection in the United States. N Engl J Med. 2011;364:1441-8.
[PubMed Abstract] -

- Jonnalagadda S, Lohman Payne B, Brown E, et al. Latent tuberculosis detection by interferon γ release assay during pregnancy predicts active tuberculosis and mortality in human immunodeficiency virus type 1-infected women and their children. J Infect Dis. 2010;202:1826-35.
[PubMed Abstract] -

- Kahwati LC, Feltner C, Halpern M, et al. Primary Care Screening and Treatment for Latent Tuberculosis Infection in Adults: Evidence Report and Systematic Review for the US Preventive Services Task Force. JAMA. 2016;316:970-83.
[PubMed Abstract] -

- Martinson NA, Barnes GL, Moulton LH, et al. New regimens to prevent tuberculosis in adults with HIV infection. N Engl J Med. 2011;365:11-20.
[PubMed Abstract] -

- Metcalfe JZ, Porco TC, Westenhouse J, et al. Tuberculosis and HIV co-infection, California, USA, 1993–2008. Emerg Infect Dis. 2013;19:400-6.
[PubMed Abstract] -

- Pascopella L, Franks J, Marks SM, et al. Opportunities for tuberculosis diagnosis and prevention among persons living with HIV: a cross-sectional study of policies and practices at four large Ryan White Program-Funded HIV clinics. PLoS One. 2014;9:e101313.
[PubMed Abstract] -

- Podany AT, Cramer Y, Imperial M, et al. Twice-Daily Dolutegravir Based Antiretroviral Therapy with One Month of Daily Rifapentine and Isoniazid (1HP) for TB Prevention. Clin Infect Dis. 2024 Apr 3. Online ahead of print.
[PubMed Abstract] -

- Sterling TR, Njie G, Zenner D, et al. Guidelines for the Treatment of Latent Tuberculosis Infection: Recommendations from the National Tuberculosis Controllers Association and CDC, 2020. MMWR Recomm Rep. 2020;69:1-11.
[PubMed Abstract] -

- Sutherland JS, Young JM, Peterson KL, et al. Polyfunctional CD4(+) and CD8(+) T cell responses to tuberculosis antigens in HIV-1-infected patients before and after anti-retroviral treatment. J Immunol. 2010;184:6537-44.
[PubMed Abstract] -

- TEMPRANO ANRS 12136 Study Group, Danel C, Moh R, et al. A Trial of Early Antiretrovirals and Isoniazid Preventive Therapy in Africa. N Engl J Med. 2015;373:808-22.
[PubMed Abstract] -

- World Health Organization (WHO). Global Tuberculosis Report. 2023
[WHO] -

# Figures

**Figure 1 Tuberculosis Epidemiology in the United States**

Source: Centers for Disease Control (CDC). Provisional 2025 Tuberculosis Data, United States. National Data. Atlanta, GA: U.S. Department of Health and Human Services, CDC. March 23, 2026

**This is a dynamic visualization.** Please visit our website to experience this dynamic content.

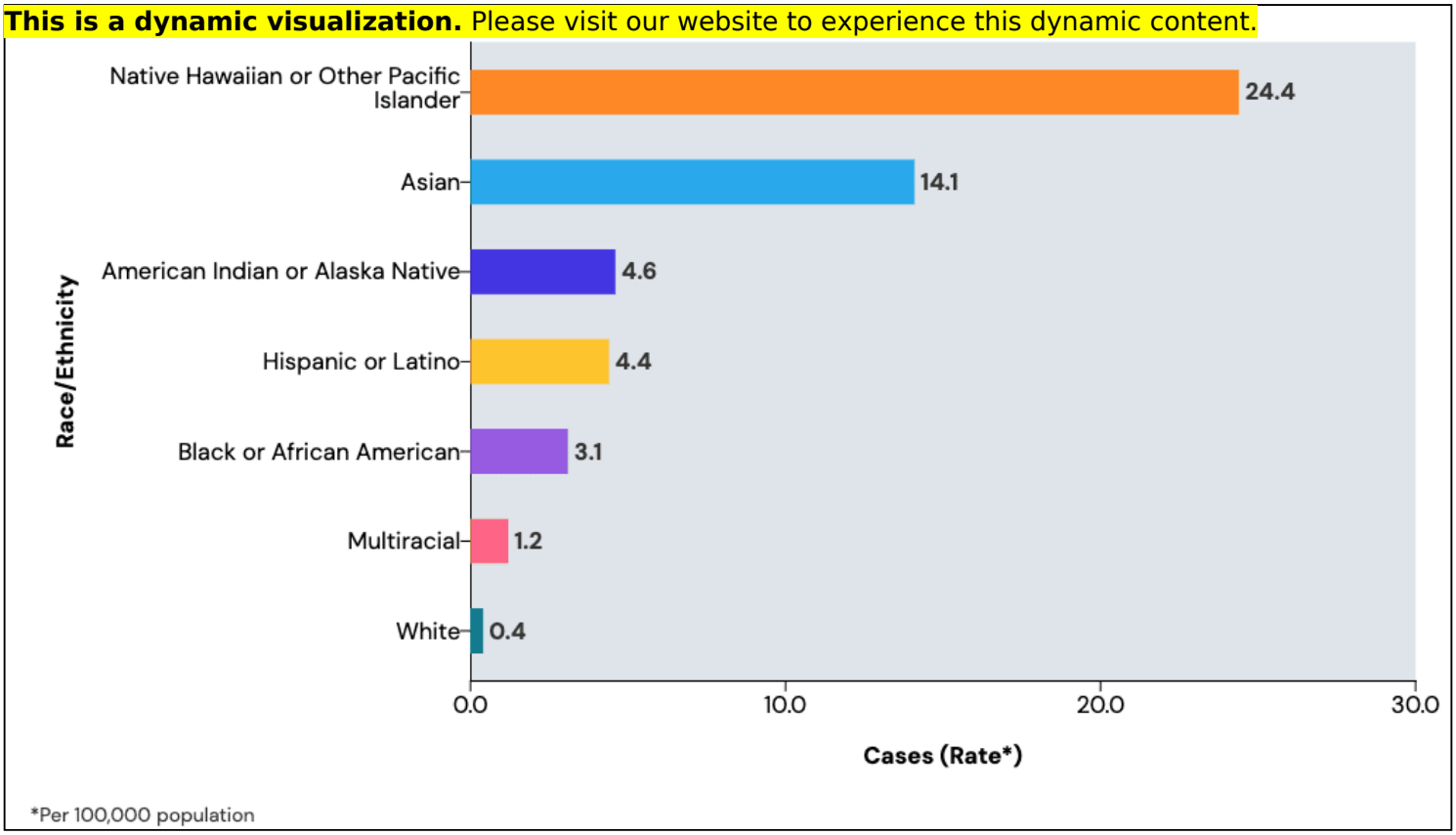

**Figure 2 Tuberculosis Cases among Persons with HIV—United States, 2011-2024**

This graphic shows the number of persons diagnosed with tuberculosis among persons with a positive HIV test result.

Source: Centers for Disease Control (CDC). Tuberculosis in the United States, 2024. December 19, 2025

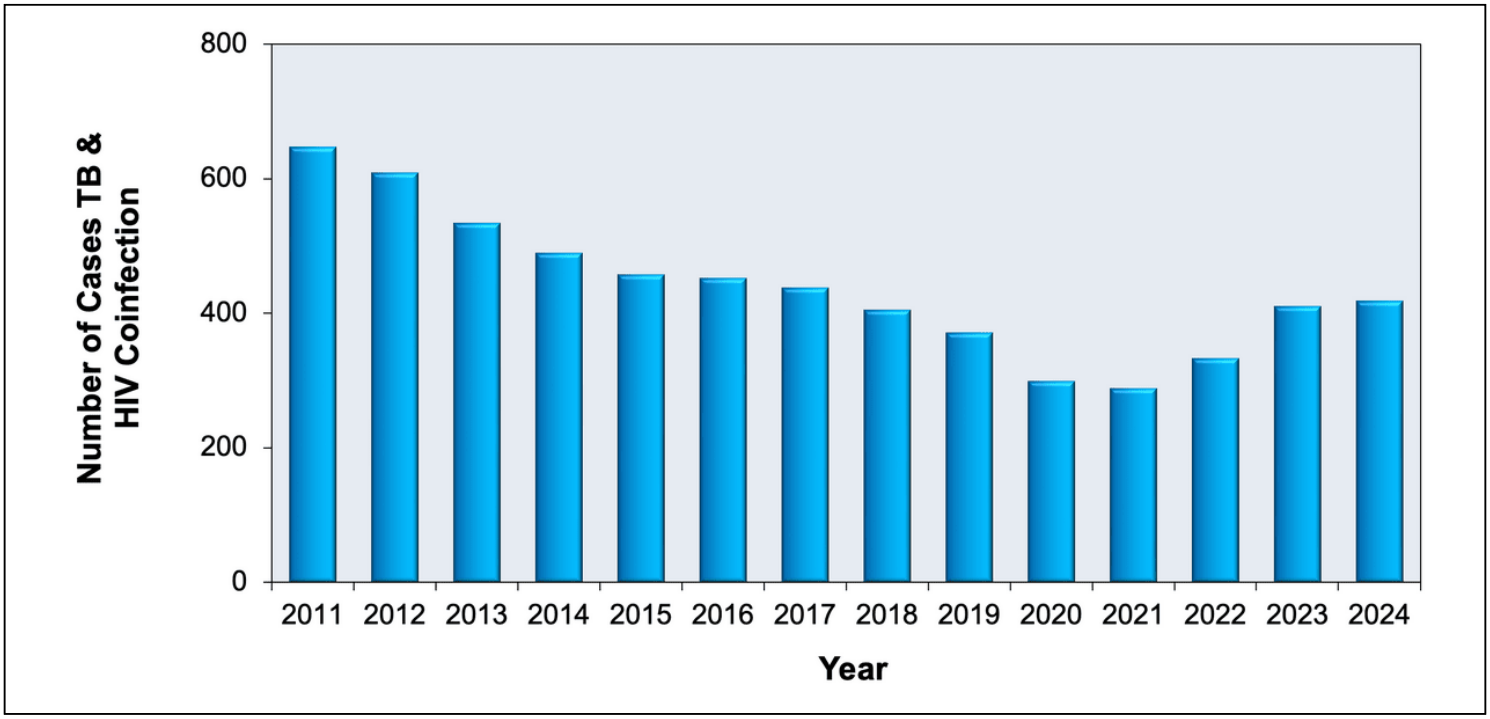

**Figure 3 Mantoux Tuberculin Skin Test**

A. The standard Mantoux tuberculin skin test is performed by injecting 0.1 mL of 5 tuberculin purified protein derivative (PPD) units intradermally on the volar surface of the forearm.
B. The transverse diameter of cutaneous induration (not erythema) should be measured 48 to 72 hours after placement of the PPD.

Source: Centers for Disease Control and Prevention (CDC)

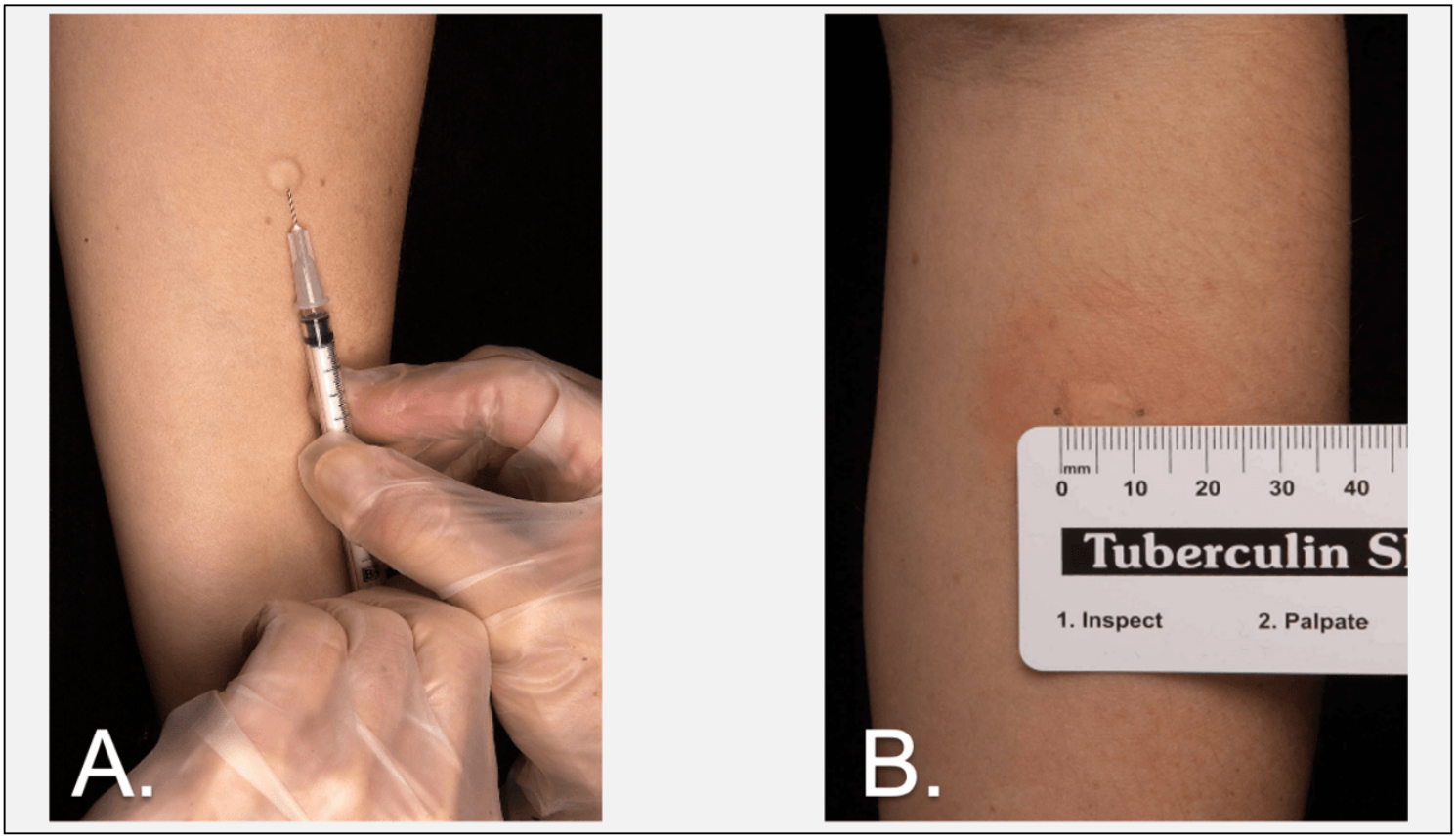

**Figure 4 Interferon-Gamma Release Assays (IGRAs)**

Source: Mazurek GH, Jereb J, Vernon A, LoBue P, Goldberg S, Castro K. Updated guidelines for using Interferon Gamma Release Assays to detect *Mycobacterium tuberculosis* infection - United States, 2010. MMWR Recomm Rep. 2010;59:1-25.

**Interferon-Gamma Release Assays (IGRAs)**

| Feature | Quantiferon-TB Gold Plus | T-SPOT.TB |
|---|---|---|
| Format | Process whole blood within 16 hours | Process peripheral blood mononuclear cells (PBMCs) within 8 hours |
| *M. tuberculosis* Antigen | Single mixture of synthetic peptides representing ESAT-6 and CFP-10 | Separate mixtures of synthetic peptides representing ESAT-6 and CFP-10 |
| Measurement | IFN-gamma concentration | Number of IFN-gamma producing cells (spots) |
| Possible Results | Positive, negative, indeterminate | Positive, negative, indeterminate, borderline |

Abbreviations: CFP-10 = culture filtrate protein 10; ESAT-6 = early secretory antigenic target-6: IFN = interferon

**Figure 5 (Image Series) - QuantiFERON-TB Gold Plus (Image Series) - Figure 5 (Image Series) - QuantiFERON-TB Gold Plus**
**Image 5A: QuantiFERON-TB Gold Plus Blood Draw Tubes**

The QuantiFERON-TB Gold utilizes four tubes and 1 mL of blood is required for each tube: (1) the gray top Nil tube that serves as a negative control to adjust for background interferon gamma production; (2) the green top TB1 tube that primarily detects CD4 T-lymphocytes responses to mycobacterial antigens; (3) the yellow top TB2 tube that is optimized for detection of CD4 and CD8 T-lymphocyte responses to mycobacterial antigens; and (4) the purple top Mitogen tube that functions as a positive control to confirm baseline immune status; a low response may indicate inability to generate interferon gamma.

Source: Qiagen

**Figure 5 (Image Series) - QuantiFERON-TB Gold Plus**
**Image 5B: Interpretation Criteria for QuantiFERON-TB Gold Plus (QFT-Plus)**

Source: Qiagen

**Interpretation Criteria for QuantiFERON-TB Gold Plus (QFT-Plus)**

| Result | Nil | TB Response | Interpretation |
|---|---|---|---|
| Positive | ≤8.0 | • TB1 and/or TB2 minus Nil ≥0.35 and ≥25% of Nil | *M. tuberculosis* infection is likely |
| Negative | ≤8.0 | • Mitogen minus Nil ≥0.5; and<br>• TB1 and TB2 minus Nil <0.35 or ≥0.35 and <25% of Nil | *M. tuberculosis* infection is NOT likely |
| Indeterminate | >8.0 | • Any | Likelihood of *M. tuberculosis* infection cannot be determined |
| | ≤8.0 | • TB1 and TB2 <0.35 or ≥0.35 and <25% of Nil and Mitogen minus Nil <0.5 | |

* All values are IU/mL interferon gamma

**Figure 6 (Image Series) - T-SPOT (Image Series) - Figure 6 (Image Series) - T-SPOT**
**Image 6A: Interpretation of T-SPOT Results**

Results are interpreted by subtracting the spot count in the negative (Nil) control from the spot count in Panels A and B. The test is considered positive if Panel A minus Nil and/or Panel B minus Nil is 8 or more spots. The test is considered negative if both Panel A minus Nil and Panel B minus Nil is less than or equal to 4 spots. The test is considered borderline (equivocal) if the highest of the Panel A or Panel B spot count is such that the (Panel minus Nil) spot count is 5, 6, or 7 spots.

Source: Oxford Immunotec. T-SPOT.TB. Prescribing Information.

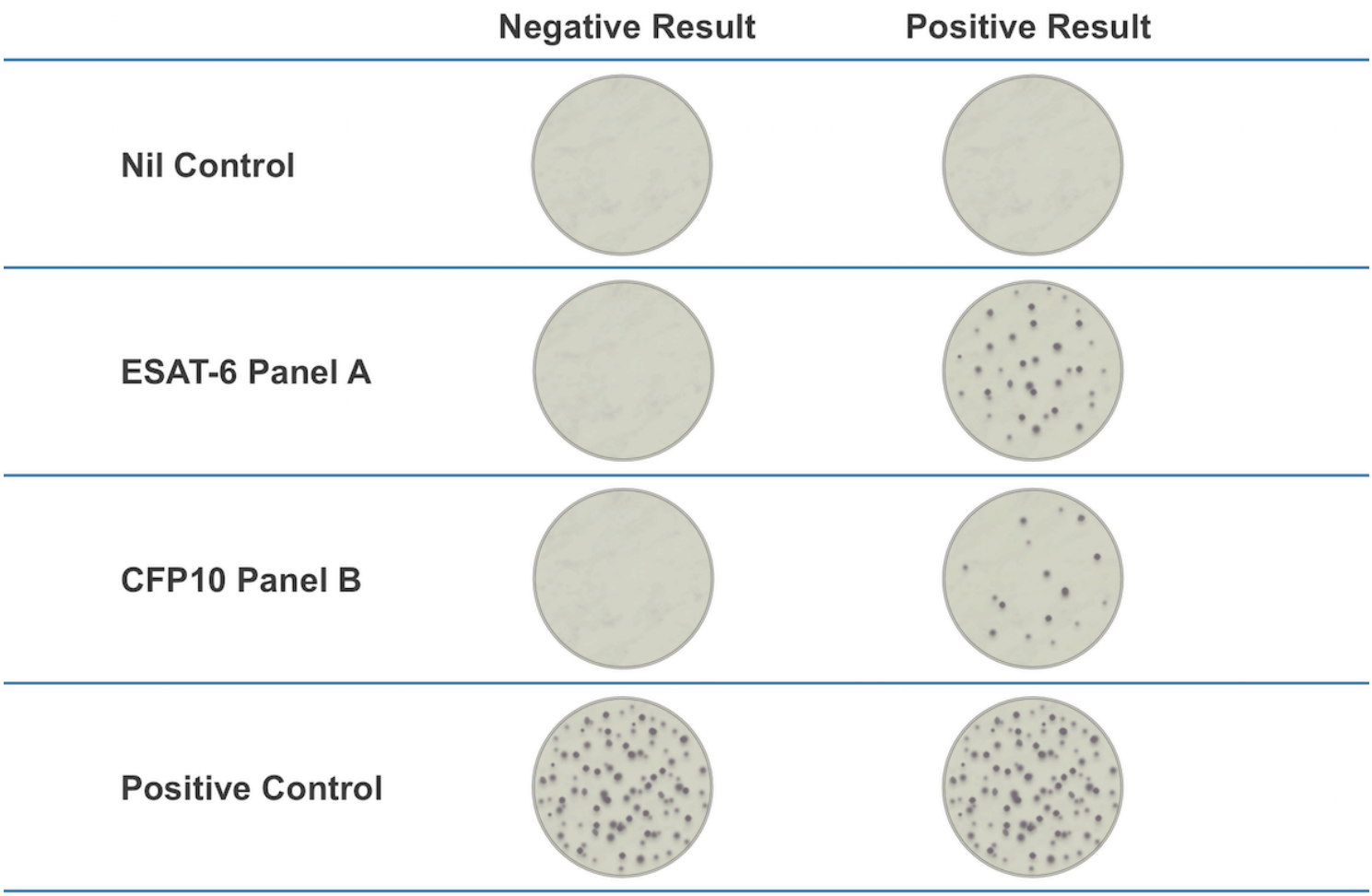

**Figure 6 (Image Series) - T-SPOT**
**Image 6B: Interpretation Criteria for the T-SPOT.TB Test (T-Spot)**

Source: Mazurek GH, Jereb J, Vernon A, LoBue P, Goldberg S, Castro K. Updated guidelines for using Interferon Gamma Release Assays to detect *Mycobacterium tuberculosis* infection - United States, 2010. MMWR Recomm Rep. 2010;59:1-25.

**Interpretation Criteria for T-SPOT.TB Test (T-Spot)**

| Interpretation | Nil* | TB Response† | Mitogen§ (Positive Control) |
|---|---|---|---|
| Positive¶ | ≤10 spots | ≥8 spots | Any number of spots |
| Borderline** | ≤10 spots | 5, 6, or 7 spots | Any number of spots |
| Negative†† | ≤10 spots | ≤4 spots | ≥ 20 spots |
| Indeterminate** | >10 spots | Any | Any number of spots |
| | ≤10 spots | <5 spots | < 20 spots |

* The number of spots resulting from incubation of PBMCs in culture media without antigens.

† The greater number of spots resulting from stimulation of peripheral blood mononuclear cells (PBMCs) with two separate cocktails of peptides representing Panel A (early secretory antigenic target-6 [ESAT-6]) minus Nil or Panel B (culture filtrate protein-10 [CFP-10]) minus Nil.

§ The number of spots resulting from stimulation of PBMCs with mitogen without adjustment for the number of spots resulting from incubation of PBMCs without antigens. Represents positive control and typically ≥ 20 spots.

¶ Result positive if (Panel A-Nil) and/or (Panel B-Nil) ≥8 spots. Interpretation indicating likely *M. tuberculosis* infection.

†† Result is negative if both (Panel A-Nil) and (Panel B-Nil) ≤4 spots and mitogen ≥ 20 spots; this includes value less than 0. Interpretation indicating that *M. tuberculosis* infection is not likely.

** Result is indeterminate if highest of Panel A or Panel B spot count is such that the (Panel-Nil) spot count is 5, 6, or 7. Interpretation indicating an uncertain likelihood of *M. tuberculosis* infection and retesting recommended.

Table 1. Treating Latent Tuberculosis Infection in Adults with HIV: Opportunistic Infections Guidelines

| Indications, Preferred Therapy, and Alternative Therapy | |
|---|---|
| | **Indications**<br><br>• Positive screening test for latent tuberculosis infecti<br>test ≥5 mm induration at 48-72 hours *or* positive int<br>◦ No evidence of active TB disease, *and*<br>◦ No prior history of treatment for active disea<br><br>• Close contact with a person with infectious tuberculo<br>such as in a household or close congregate setting, v<br>according to the Centers for Disease Control and Pre<br>Contacts of Persons with Infectious Tuberculosis) reg<br>(AII). |
| | **Preferred Therapy**<br><br>• **3HP: Weekly Isoniazid plus Rifapentine for 12 W**<br>◦ Isoniazid: 15 mg/kg PO once weekly (900 mg<br>weekly for 12 weeks.<br>*plus*<br>◦ Rifapentine PO once weekly (weight based ar<br>▪ *Weighing 25.1-32.0 kg:* 600 mg<br>▪ *Weighing 32.1-49.9 kg:* 750 mg<br>▪ *Weighing ≥50.0 kg:* 900 mg<br><br>Note: The 3HP regimen is recommended only for virally-supp<br>raltegravir-, or once-daily dolutegravir-based regimen (AII). I<br>alafenamide; if tenofovir alafenamide is used, monitor for vi<br><br>• **3HR: Daily Isoniazid plus Rifampin for 3 Months**<br>◦ Isoniazid: 300 mg PO daily *plus* pyridoxine 25<br>*plus*<br>◦ Rifampin: 600 mg PO daily for 3 months.<br><br>Note: when using rifampin for LTBI treatment, either dose ad<br>medications may be needed. See Drug Interaction Tables in<br>list of antiretroviral medications not recommended for use w<br>bictegravir) and those which require dosage adjustment (e.g<br>[50 mg twice daily], or maraviroc [600 mg twice daily unless |
| | **Alternative Therapy**<br><br>• **6H/9H: Daily Isoniazid for 6 to 9 Months** (AII)<br>◦ Isoniazid: 300 mg PO daily *plus* pyridoxine 25<br>• **4R: Daily Rifampin for 4 Months** (BI)<br>◦ Rifampin: 600 mg PO daily for 4 months.<br>▪ Consult the Tuberculosis/HIV Coinfect<br>Antiretroviral Guidelines for the list of<br>with rifampin (e.g., protease inhibitor<br>adjustment (e.g., raltegravir [800 mg<br>maraviroc [600 mg twice daily unless<br>• **1HP: Daily Isoniazid plus Rifapentine for 1 Mon** |

| | |
|---|---|
| | ◦ Isoniazid 300 mg PO daily *plus* pyridoxine 25<br>plus<br>◦ Rifapentine (weight-based) PO daily for 4 we<br>are:<br>▪ *Weighing <35 kg:* 300 mg<br>▪ *Weighing 35–45 kg:* 450 mg<br>▪ *Weighing >45 kg*: 600 mg<br><br>Note: The 1HP regimen is recommended only for patients re<br>(without dose adjustment of efavirenz) or a dolutegravir 50<br>should be increased to 50 mg twice daily throughout the co<br>days after 1HP completion—before switching back to 50 mg<br>concentrations of tenofovir alafenamide; if tenofovir alafena |
| | **Suspected Drug-Resistant TB**<br><br>For people exposed to drug-resistant tuberculosis, select dr<br>consultation with experts and with public health authorities |
| | Abbreviations: TB = tuberculosis; IGRA = interferon gamma<br>Regimen Short Names: **3HP** = **3-**month duration with isonia<br>duration using isoniazid (IN**H**) and rifampin (**R**IF); **6H and 9**<br>= **4**-month duration with rifampin (**R**IF); **1HP** = **1**-month du<br><br><u>Rating System for Prevention and Treatment Recommendat</u><br><br>• Strength of Recommendation: A = Strong; B = Mode<br>• Quality of Evidence for the Recommendation: I = On<br>outcomes and/or validated laboratory endpoints; II =<br>trials or observational cohort studies with long-term |

Source:

- Panel on Opportunistic Infections in Adults and Adolescents with HIV. Guidelines for the prevention and treatment of opportunistic infections in adults and adolescents with HIV: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. *Mycobacterium tuberculosis* infection and disease. Last update: May 2, 2024. [HIV.gov]