JAMA | US Preventive Services Task Force | RECOMMENDATION STATEMENT

Screening for Latent Tuberculosis Infection in Adults
US Preventive Services Task Force Recommendation Statement

US Preventive Services Task Force

IMPORTANCE In the US, tuberculosis remains an important preventable disease, including active tuberculosis, which may be infectious, and latent tuberculosis infection (LTBI), which is asymptomatic and not infectious but can later progress to active disease. The precise prevalence rate of LTBI in the US is difficult to determine; however, estimated prevalence is about 5.0%, or up to 13 million persons. Incidence of tuberculosis varies by geography and living accommodations, suggesting an association with social determinants of health.

OBJECTIVE To update its 2016 recommendation, the US Preventive Services Task Force (USPSTF) commissioned a systematic review on LTBI screening and treatment in asymptomatic adults seen in primary care, as well as the accuracy of LTBI screening tests.

POPULATION Asymptomatic adults 18 years or older at increased risk for tuberculosis.

EVIDENCE ASSESSMENT The USPSTF concludes with moderate certainty that there is a moderate net benefit in preventing active tuberculosis disease by screening for LTBI in persons at increased risk for tuberculosis infection.

RECOMMENDATION The USPSTF recommends screening for LTBI in populations at increased risk. (B recommendation)

JAMA. 2023;329(17):1487-1494. doi:10.1001/jama.2023.4899

Editorial page 1457

Multimedia

Related article page 1495 and **JAMA Patient Page** page 1526

Supplemental content

Related article at jamanetworkopen.com

Author/Group Information: The US Preventive Services Task Force (USPSTF) members are listed at the end of this article.

Corresponding Author: Carol M. Mangione, MD, MSPH, David Geffen School of Medicine, University of California, Los Angeles, 10940 Wilshire Blvd, Ste 700, Los Angeles, CA 90024 (chair@uspstf.net).

Summary of Recommendation

Population	Recommendation	Grade
Asymptomatic adults at increased risk of latent tuberculosis infection (LTBI)	The USPSTF recommends screening for LTBI in populations at increased risk. See the Assessment of Risk section for additional information on adults at increased risk.	B

USPSTF indicates US Preventive Services Task Force.

See the Summary of Recommendation figure.

Pathway to Benefit

To achieve the benefit of screening, it is important that persons who screen positive for LTBI receive follow-up and treatment.

Preamble

The US Preventive Services Task Force (USPSTF) makes recommendations about the effectiveness of specific preventive care services for patients without obvious related signs or symptoms to improve the health of people nationwide.

It bases its recommendations on the evidence of both the benefits and harms of the service and an assessment of the balance. The USPSTF does not consider the costs of providing a service in this assessment.

The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decision-making to the specific patient or

Table. Summary of USPSTF Rationale

Rationale	Assessment
Detection	The USPSTF found adequate evidence that the tuberculin skin test and interferon-gamma release assay are accurate screening tests to detect LTBI.
Benefits of early detection and intervention and treatment	• The USPSTF found no studies that evaluated the direct benefits of screening for LTBI. • The USPSTF found adequate to convincing evidence that treatment of LTBI with regimens recommended by the CDC decreases progression to active tuberculosis, resulting in a substantial magnitude of benefit. • The USPSTF found adequate evidence to link screening for and treatment of LTBI to a substantial health benefit in preventing active tuberculosis.
Harms of early detection and intervention and treatment	• The USPSTF found no direct evidence on the harms of screening for LTBI. • The USPSTF found adequate evidence that the magnitude of harms of treatment of LTBI with CDC-recommended regimens is small. The primary harm of treatment is hepatotoxicity. • The USPSTF found convincing evidence to link screening for and treatment of LTBI to a small magnitude of harms, mainly hepatotoxicity.
USPSTF assessment	The USPSTF concludes with moderate certainty that there is moderate net benefit in preventing progression to active tuberculosis disease by screening for LTBI in persons at increased risk for tuberculosis infection.

Abbreviations: CDC, Centers for Disease Control and Prevention; LTBI, latent tuberculosis infection; USPSTF, US Preventive Services Task Force.

situation. Similarly, the USPSTF notes that policy and coverage decisions involve considerations in addition to the evidence of clinical benefits and harms.

The USPSTF is committed to mitigating the health inequities that prevent many people from fully benefiting from preventive services. Systemic or structural racism results in policies and practices, including health care delivery, that can lead to inequities in health. The USPSTF recognizes that race, ethnicity, and gender are all social rather than biological constructs. However, they are also often important predictors of health risk. The USPSTF is committed to helping reverse the negative impacts of systemic and structural racism, gender-based discrimination, bias, and other sources of health inequities, and their effects on health, throughout its work.

Importance

In the US, tuberculosis remains an important preventable disease, including active tuberculosis, which may be infectious, and latent tuberculosis infection (LTBI), which is asymptomatic and not infectious but can later progress to active disease. The precise prevalence rate of LTBI in the US is difficult to determine; however, estimated prevalence is about 5.0%,[1] or up to 13 million persons.[2] Tuberculosis is spread through respiratory transmission. Approximately 30% of persons exposed to *Mycobacterium tuberculosis* will develop LTBI[3,4] and, if left untreated, approximately 5% to 10% of healthy, immunocompetent persons will progress to having active tuberculosis disease.[5,6] Rates of progression may be higher in persons with certain risk factors or medical conditions.

Tuberculosis disproportionately affects certain populations in the US, including Asian, Black, Hispanic/Latino, Native American/Alaska Native, and Native Hawaiian/Pacific Islander persons.[7] Incidence of tuberculosis varies by geography[8] and living accommodations,[9] suggesting an association with social determinants of health.[10] An effective strategy for reducing the transmission, morbidity, and mortality of active tuberculosis disease is the identification and treatment of LTBI.

USPSTF Assessment of Magnitude of Net Benefit

The US Preventive Services Task Force (USPSTF) concludes with moderate certainty that there is a **moderate net benefit** in preventing active tuberculosis disease by screening for LTBI in persons at increased risk for tuberculosis infection.

See the **Table** for more information on the USPSTF recommendation rationale and assessment and the eFigure in the Supplement for information on the recommendation grade. See the **Figure** for a summary of the recommendation for clinicians. For more details on the methods the USPSTF uses to determine the net benefit, see the USPSTF Procedure Manual.[11]

Practice Considerations

Patient Population Under Consideration

This recommendation applies to asymptomatic adults 18 years or older at increased risk for tuberculosis (see the Assessment of Risk section for more information). It does not apply to adults with symptoms of tuberculosis or to children and adolescents.

Definitions

According to the Centers for Disease Control and Prevention (CDC),[12] *latent tuberculosis infection* or *LTBI* is an infection with *M tuberculosis* in which the bacteria are alive but contained by the immune system. Persons with LTBI have no apparent symptoms, do not feel sick, cannot spread tuberculosis to others, and usually have a positive tuberculosis skin test result or positive tuberculosis blood test reaction. Persons with LTBI may develop tuberculosis disease if they do not receive treatment for LTBI. *Active tuberculosis* or *tuberculosis disease* is an illness in which tuberculosis bacteria are multiplying and attacking a part of the body, usually the lungs. Tuberculosis disease may be symptomatic (including weakness, weight loss, fever, no appetite, chills, sweating at night, bad cough, pain in the chest, or coughing up blood). A person with tuberculosis disease may be infectious and spread tuberculosis bacteria to others.

Assessment of Risk

Populations at increased risk for LTBI based on increased prevalence of active disease and increased risk of exposure include persons who were born in, or are former residents of, countries with high tuberculosis prevalence and persons who live in, or have lived in, high-risk congregate settings (eg, homeless shelters or correctional facilities). Clinicians can consult their local or state health departments for more information about populations at increased

Figure. Clinician Summary: Screening for Latent Tuberculosis Infection in Adults

What does the USPSTF recommend?	**For asymptomatic adults at increased risk of latent tuberculosis infection (LTBI):** Screen for LTBI in populations at increased risk. Grade: B See "How to implement this recommendation" for additional information on adults at increased risk.
To whom does this recommendation apply?	This recommendation applies to asymptomatic adults 18 years or older at increased risk for tuberculosis (TB). It does not apply to adults with symptoms of TB or to children and adolescents.
What's new?	• This recommendation replaces and is consistent with the 2016 USPSTF recommendation on LTBI screening. • In 2016, the USPSTF recommended screening for LTBI in populations at increased risk (B recommendation).
How to implement this recommendation?	• **Populations at increased risk for LTBI,** based on increased prevalence of active disease and increased risk of exposure, include persons who were born in, or are former residents of, countries with high TB prevalence and persons who live in, or have lived in, high-risk congregate settings (eg, homeless shelters or correctional facilities). • Clinicians can consult their local or state health departments for more information about populations at increased risk in their community, since local demographic patterns may vary across the US. • Two types of screening tests for LTBI are currently available in the US: the tuberculin skin test (TST) and the interferon-gamma release assay (IGRA). ° The TST requires trained personnel to administer intradermal purified protein derivative and interpret the response 48 to 72 hours later. ° The IGRA requires a single venous blood sample that measures the CD4 T-cell response to specific *Mycobacterium tuberculosis* antigens and laboratory processing within 8 to 30 hours after collection. ° Testing with IGRA may have advantages over TST for persons who have received a BCG vaccination, as IGRA does not cross-react with the vaccine, and for persons who may be unlikely to return for TST interpretation. • The USPSTF found no evidence on the optimal frequency of screening for LTBI. • In the absence of evidence, a reasonable approach is to repeat screening based on specific risk factors; screening frequency could range from 1-time-only screening among persons at low risk for future TB exposure to annual screening among those who are at continued risk of exposure. • Additional examinations, diagnostics, and tests (ie, medical history, physical examination, chest radiograph, and other laboratory tests) are essential to completing a diagnosis of LTBI. • Current recommendations for the treatment of LTBI are available from the Centers for Disease Control and Prevention (CDC).
What additional information should clinicians know about this recommendation?	• TB disproportionately affects Asian, Black, Hispanic/Latino, Native American/Alaska Native, and Native Hawaiian/Pacific Islander persons. Incidence of TB varies by geography and living accommodations, suggesting an association with social determinants of health. • LTBI is an infection with *M tuberculosis* in which the bacteria are alive but contained by the immune system. Persons with LTBI have no apparent symptoms, do not feel sick, cannot spread TB to others, and usually have a positive TB skin test result or positive TB blood test reaction. • Active TB or TB disease is an illness in which TB bacteria are multiplying and attacking a part of the body, usually the lungs. TB disease may be symptomatic (including weakness, weight loss, fever, no appetite, chills, sweating at night, bad cough, pain in the chest, or coughing up blood). A person with TB disease may be infectious and spread TB bacteria to others.
Why is this recommendation and topic important?	Approximately 30% of persons exposed to *M tuberculosis* will develop LTBI and, if left untreated, approximately 5% to 10% of healthy, immunocompetent persons will progress to having active TB disease.
What are additional tools and resources?	• The CDC offers expert medical consultation to US clinicians with questions about patients being evaluated for TB or LTBI (https://www.cdc.gov/tb/education/tb_coe/default.htm). • In addition, the CDC maintains several resources and continuing education activities on LTBI for clinicians (https://www.cdc.gov/tb/education/provider_edmaterials.htm), a guide for primary health care clinicians (https://www.cdc.gov/tb/publications/ltbi/pdf/LTBIbooklet508.pdf), and an online resource hub for information about LTBI (https://www.cdc.gov/tb/publications/ltbi/ltbiresources.htm). • Also, the CDC's "Think.Test.Treat TB" campaign offers community and clinician information to help inform and guide patient and clinician conversations and other LTBI communications (https://www.cdc.gov/thinktesttreattb/index.html).
Where to read the full recommendation statement?	Visit the USPSTF website (https://www.uspreventiveservicestaskforce.org/uspstf/) or the *JAMA* website (https://jamanetwork.com/collections/44068/united-states-preventive-services-task-force) to read the full recommendation statement. This includes more details on the rationale of the recommendation, including benefits and harms; supporting evidence; and recommendations of others.

The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decision-making to the specific patient or situation.

risk in their community, since local demographic patterns may vary across the US.

In 2020, 71.5% of all cases of active tuberculosis in the US occurred among persons born outside the US.[13] According to the CDC, tuberculosis disease is common in most countries in Latin America, the Caribbean, Africa, Asia, Eastern Europe, and Russia.[14] In 2020, among persons with new tuberculosis living in the US who were born outside the US, the most common countries of birth were Mexico (18.0%), the Philippines (12.5%), India (10.4%), Vietnam (8.2%), and China (5.1%), accounting for 54.2% of total cases.[15] Most of these cases are believed to be due to progression of latent infection to active tuberculosis disease rather than new transmission within communities.[16-21]

Persons who live, or have lived, in high-risk congregate settings also have a higher prevalence rate of active tuberculosis and an increased risk for exposure. In 2020, 4.3% of tuberculosis disease cases diagnosed in persons 15 years or older occurred in persons experiencing homelessness and 2.6% occurred in residents of correctional facilities.[22] It is estimated that persons experiencing homelessness have an 11 times higher incidence of tuberculosis disease compared with persons who are not experiencing homelessness (36 cases per 100 000 population vs 2.9 cases per 100 000 population, respectively, during 2011 to 2016).[23]

Other populations at increased risk for LTBI or progression to active disease include persons who have immunosuppression (eg, persons living with HIV, patients receiving immunosuppressive medications such as chemotherapy or tumor necrosis factor inhibitors, and patients who have received an organ transplant) and patients with silicosis (a lung disease).[9] However, given that screening in these populations may be considered standard care as part of disease management or indicated prior to the use of certain medications, the USPSTF did not review evidence on screening in these populations. Information on testing in these populations is provided by other groups, such as the Office of AIDS Research at the National Institutes of Health,[24] and in a guideline issued jointly by the American Thoracic Society, Infectious Diseases Society of America, and CDC.[25] Some evidence from observational studies has explored the association between poorly controlled diabetes and progression of LTBI to active disease. However, there is insufficient evidence on screening for and treatment of LTBI in persons with diabetes for the USPSTF to make a separate recommendation for this important population.[9,26]

Persons who are contacts of individuals with active tuberculosis, health care workers, and workers in high-risk congregate settings may also be at increased risk of exposure. Because screening in these populations is conducted as part of public health or employee health surveillance, the USPSTF did not review the evidence in these populations. Clinicians seeking further information about testing for tuberculosis in these populations can refer to the Additional Tools and Resources and Recommendations of Others sections.

Screening Tests

Two types of screening tests for LTBI are currently available in the US: the tuberculin skin test (TST) and the interferon-gamma release assay (IGRA). The TST requires trained personnel to administer intradermal purified protein derivative and interpret the response 48 to 72 hours later.[25,27] The IGRA requires a single venous blood sample that measures the CD4 T-cell response to specific *M tuberculosis* antigens and laboratory processing within 8 to 30 hours after collection. Three types of IGRA are currently approved by the US Food and Drug Administration: T-SPOT.*TB* (Oxford Immunotec Global), QuantiFERON-TB Gold In-Tube (Qiagen), and QuantiFERON-Gold Plus (Qiagen).[9,28]

Diagnosis of LTBI is based on further clinical assessment of positive screening results and ruling out active tuberculosis. Consistent with CDC guidelines, tuberculosis disease is diagnosed by medical history, physical examination, chest radiograph, and other laboratory tests. These additional examinations, diagnostics, and tests are essential to completing a diagnosis of LTBI.

Screening Intervals

The USPSTF found no evidence on the optimal frequency of screening for LTBI. In the absence of evidence, a reasonable approach is to repeat screening based on specific risk factors; screening frequency could range from 1-time only screening among persons at low risk for future tuberculosis exposure to annual screening among those at continued risk of exposure.

Treatment

Several antibiotics are available for the treatment of LTBI. Isoniazid was the first medication shown to prevent progression to active tuberculosis; however, concerns about hepatotoxicity and drug resistance resulting from low adherence with long courses of treatment have prompted recommendations of shorter courses and that it be used in combination with other medications such as rifapentine and rifampin. Current recommendations for the treatment of LTBI are available from the CDC.[29]

Implementation

Screening with the TST requires that patients return 48 to 72 hours after administration of the skin test for interpretation of results. When placing a TST, clinicians should plan with patients accordingly to ensure they can return in time and that the facility is able to interpret the test results within the proper time frame.

Screening with an IGRA requires obtaining a single venous blood sample, and patients do not need to return for interpretation of results. However, clinicians should be aware of processing requirements for blood samples and ensure that venous blood samples are drawn and can reach the laboratory for processing within the appropriate time frame (8 to 30 hours, depending on the test). Consistent with CDC guidelines, testing with IGRA may have advantages over TST for persons who have received a BCG vaccination, because IGRA does not cross-react with the vaccine, and also for persons who may be unlikely to return for TST interpretation.[25]

With the exception of twice-weekly isoniazid monotherapy, CDC-recommended regimens can be self-administered, including once-weekly combination therapy with isoniazid and rifapentine taken for 3 months.[30]

Additional Tools and Resources

The CDC offers expert medical consultation to US clinicians with questions about patients being evaluated for tuberculosis or LTBI (https://www.cdc.gov/tb/education/tb_coe/default.htm). In addition, the CDC maintains several resources and continuing education activities on LTBI for clinicians (https://www.cdc.gov/tb/education/provider_edmaterials.htm), a guide for primary health care clinicians (https://www.cdc.gov/tb/publications/ltbi/pdf/LTBIbooklet508.pdf), and an online resource hub for information about LTBI (https://www.cdc.gov/tb/publications/ltbi/ltbiresources.htm). Also, the CDC's "Think.Test.Treat TB" campaign offers community and clinician information to help inform and guide patient and clinician conversations and other LTBI communications (https://www.cdc.gov/thinktesttreattb/index.html). Partnerships between primary care clinicians, federally qualified health centers, and communities at increased risk for LTBI and tuberculosis, as well as organizations that serve these communities, are important tools for working toward tuberculosis prevention and elimination.

Resources for tuberculosis screening of health care personnel are also available (https://www.cdc.gov/tb/topic/infectioncontrol/healthCarePersonnel-resources.htm).

Information on estimated tuberculosis burden by country is available from the World Health Organization at its website (https://worldhealthorg.shinyapps.io/tb_profiles/?_inputs_&entity_type=%22country%22&lan=%22EN%22&iso2=%22AF%22) and through its annual Global Tuberculosis Report (https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2022).

Guidelines for the prevention and treatment of opportunistic infections in adults and adolescents with HIV are available through HIV.gov (https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-opportunistic-infections/mycobacterium-0?view=full).

Update of Previous USPSTF Recommendation

This recommendation replaces the 2016 USPSTF recommendation on LTBI screening. In 2016, the USPSTF recommended screening for LTBI in populations at increased risk (B recommendation).[31] The current recommendation is consistent with the 2016 USPSTF recommendation.

Supporting Evidence

Scope of Review

The USPSTF commissioned a systematic evidence review[9,28] to update its 2016 recommendation on screening for LTBI. The review focused on the benefits and harms of LTBI screening and treatment in asymptomatic adults seen in primary care, as well as the accuracy of LTBI screening tests. It did not include evidence on screening in persons for whom LTBI screening would be considered management of a specific condition (eg, persons living with HIV), public health surveillance (ie, tracing contacts of persons with active tuberculosis disease), surveillance of employees working in high-risk settings, or screening indicated prior to the use of specific immunosuppressive medications.

Accuracy of Screening Tests

There is no direct test for the diagnosis of latent infection with *M tuberculosis*. In the absence of a reference standard for detection of LTBI, screening test performance is based on detection of disease in persons with known active tuberculosis and nondetection of disease in populations at low risk for the disease and presumed not to have LTBI or active tuberculosis.

Currently available TST and IGRA screening tests are moderately sensitive and highly specific for LTBI.[9,28] The sensitivity and specificity of TST depends on the threshold used to determine positivity. Using a threshold of 5-mm induration, the pooled sensitivity of TST was 80% (12 studies; n = 1323) and the pooled specificity was 95% (3 studies; n = 5149).[9,28] Using a threshold of 10-mm induration, the pooled sensitivity was 81% (15 studies; n = 1427) and the pooled specificity was 98% (8 studies; n = 9604).[9,28] Last, using a threshold of 15-mm induration, the pooled sensitivity was 60% (9 studies; n = 1004) and the pooled specificity was 99% (10 studies; n = 9563).[9,28]

For IGRA tests, pooled sensitivity of the T-SPOT.*TB* test was 90% (37 studies; n = 5367) and pooled specificity ranged from 95% to 97% (2 studies; n = 1664).[9,28] For QFT-GIT, pooled sensitivity was 81% (48 studies; n = 7055) and pooled specificity was 99% (3 studies; n = 2090).[9,28] For QFT-Gold Plus, pooled sensitivity was 89% (11 studies; n = 939) and specificity was 98%, based on a single study (n = 211).[9,28] No eligible studies reported on the accuracy of sequential testing (TST followed by IGRA or IGRA followed by TST).

Additional studies reporting on the reliability of TST and IGRA screening tests suggest moderate to substantial agreement between 2 observers.[9] Interrater reliability was higher for IGRA and varied by whether results were read manually or by automation.[9]

Benefits of Early Detection and Treatment

The USPSTF identified no randomized clinical trials that directly compared the benefits on health outcomes of LTBI-screened populations compared with unscreened populations. The International Union Against Tuberculosis (IUAT) trial,[32] a randomized clinical trial of LTBI treatment published in 1982, compared isoniazid with placebo in 27 830 European adults with fibrotic pulmonary lesions (but not active tuberculosis). Treatment with isoniazid (300 mg daily for 24 weeks) was associated with a decreased risk of developing active tuberculosis (relative risk [RR], 0.35 [95% CI, 0.24-0.52]), which translates to a number needed to treat of 112. The IUAT trial also suggested a potential reduction of risk of death from tuberculosis at 5 years with isoniazid treatment (RR, 0.14 [95% CI, 0.01-2.78]).

More recent comparative effectiveness trials have compared other treatment regimens with isoniazid alone to establish the noninferiority of other regimens in asymptomatic persons with positive TST or IGRA results.[9] Two clinical trials compared treatment of LTBI with rifampin vs isoniazid (n = 6910)[9,28,33,34]: 8 vs 9 participants developed active tuberculosis in the rifampin group vs isoniazid group, and there were 22 deaths (all-cause mortality) in the rifampin group compared with 15 deaths in the isoniazid group. Two clinical trials (n = 7149) have compared treatment of LTBI with rifapentine plus isoniazid vs isoniazid alone[9,28,35,36]: 30 vs 34 deaths (all-cause mortality) in rifapentine plus isoniazid vs isoniazid-alone groups were reported across both studies, and 1 trial (n = 6886)[35] reported 5 vs 10 cases of subsequent active tuberculosis in the rifapentine plus isoniazid group vs isoniazid-alone group. None of the treatment studies reported on transmission rates of tuberculosis.

Harms of Screening and Treatment

The USPSTF identified no studies that directly reported on the harms of screening. Potential hypothesized harms of screening include stigma associated with screening and diagnostic workup, as well as treatment of false-positive results. The IUAT trial reported on harms of treatment of LTBI with isoniazid compared with placebo.[32,37] An increased risk of hepatoxicity with isoniazid (300 mg for 24 weeks of treatment) was reported in the IUAT trial (RR, 4.59 [95% CI, 2.03-10.39]), translating to a number needed to harm of 279.

Deaths due to hepatoxicity were rare; increased risk of death from hepatotoxicity was reported with an RR of 2.35 (95% CI, 0.12-45.46), translating to a number needed to harm of 6947. There was also a greater risk of treatment discontinuation because of adverse events reported with isoniazid (RR, 1.50 [95% CI, 1.18-1.89]) and a greater risk of gastrointestinal adverse events (RR, 1.33 [95% CI, 1.01-1.75]).

More recent trials have evaluated whether other treatment regimens, including lower doses or shorter durations of isoniazid in combination with other medications, may be associated with lower risk of hepatotoxicity. Meta-analysis of 3 trials (n = 7339) that compared isoniazid vs rifampin found a higher pooled RR of hepatotoxicity with isoniazid (pooled RR, 4.22 [95% CI, 2.21-8.06])[9,28,33,34,38,39]; deaths from hepatotoxicity were not reported in any treatment groups. Two trials reported on harms of rifapentine plus isoniazid vs isoniazid alone.[9,28,35,36,40] The PREVENT TB study (n = 7731)[35] reported a statistically nonsignificant difference in grade 3 or 4 hepatotoxicity between participants receiving rifapentine plus isoniazid and those taking isoniazid alone (RR, 0.90 [95% CI, 0.75-1.08]); post hoc analyses showed a smaller number of cases of hepatotoxicity attributable to the study drug in the rifapentine plus isoniazid group compared with the isoniazid-alone group (RR, 0.16 [95% CI, 0.10-0.28]).[40] The second trial (n = 263)[36] reported a statistically nonsignificant decreased risk of clinically relevant hepatotoxicity in the rifapentine plus isoniazid group compared with the isoniazid-alone group (RR, 0.28 [95% CI, 0.06-1.34]); no deaths due to hepatoxicity were reported in either treatment group.

Recent trials also reported on discontinuation due to adverse events. There was a statistically nonsignificant increase in discontinuation due to adverse events in a meta-analysis of 3 trials of isoniazid vs rifampin (pooled RR, 2.25 [95% CI, 0.90-5.59]; 3 trials; n = 7339). Both the PREVENT TB study and a second trial of participants receiving rifapentine plus isoniazid vs isoniazid alone reported increased discontinuation due to adverse events in study participants in the rifapentine plus isoniazid group compared with isoniazid alone; however, this was statistically significant in only 1 trial.[9,28] Overall, study reports of gastrointestinal adverse events other than hepatotoxicity were heterogeneous, with mixed results.[9,28]

Response to Public Comment

A draft version of this recommendation statement was posted for public comment on the USPSTF website from November 22, 2022, to December 27, 2022. Most commenters agreed with the conclusions of the USPSTF. Several commenters requested that the USPSTF highlight that TST and IGRA screening tests should not be used to screen for active tuberculosis and that in certain scenarios, IGRA may have advantages over TST. In response, the USPSTF added information to make clear that clinical assessment, physical examination, and diagnostic workup are necessary for the diagnosis of LTBI. The USPSTF also clarified scenarios in which IGRA could be preferable to TST. Other commenters sought additional information on persons at increased risk for LTBI or requested that the USPSTF identify additional populations at increased risk for LTBI in the recommendation. The USPSTF outlined evidence of persons at increased risk in the Assessment of Risk section of the recommendation. Given regional variations in the local populations considered at increased risk for tuberculosis, clinicians may consult their local or state public health agency for additional details on specific populations at increased risk in their community. Last, the USPSTF added clarifications to the Practice Considerations section and materials to the Additional Tools and Resources section to assist and guide clinicians in screening for and treatment of LTBI, as well as the need for community partnerships to prevent and eliminate LTBI and tuberculosis.

Research Needs and Gaps

More research is needed on the following.

- Although risk factors for active tuberculosis disease are well described, studies are needed on the accuracy of risk assessment tools to help clinicians identify who is at increased risk for LTBI and who should receive screening.
- Evidence is needed to inform which populations should receive repeat screening for LTBI and how frequently.
- More research is needed to inform which screening strategies are more effective for specific patient populations.

Recommendations of Others

The CDC, together with the American Thoracic Society and the Infectious Diseases Society of America, recommends screening for LTBI to identify persons who may benefit from treatment before progression to active tuberculosis infection.[25,41] Joint guidelines from the American Academy of Pediatrics and American College of Obstetricians and Gynecologists recommend screening for latent tuberculosis in early pregnancy for women at high risk for tuberculosis, including those with recent tuberculosis exposure, HIV infection, risk factors increasing risk of progression to active disease (such as diabetes, lupus, cancer, alcoholism, and drug addiction), use of immune-suppressing drugs such as tumor necrosis factor inhibitors or chronic steroids, kidney failure with dialysis, homelessness, living or working in long-term care facilities such as nursing homes and prisons, being medically underserved, and being born in a country with high prevalence of tuberculosis.[42] The American Academy of Family Physicians supports the 2016 USPSTF recommendation on screening for LTBI.[43]

ARTICLE INFORMATION

Accepted for Publication: March 16, 2023.

The US Preventive Services Task Force (USPSTF) Members: Carol M. Mangione, MD, MSPH; Michael J. Barry, MD; Wanda K. Nicholson, MD, MPH, MBA; Michael Cabana, MD, MPH; David Chelmow, MD; Tumaini Rucker Coker, MD, MBA; Esa M. Davis, MD, MPH; Katrina E. Donahue, MD, MPH; Carlos Roberto Jaén, MD, PhD, MS; Li Li, MD, PhD, MPH; Gbenga Ogedegbe, MD, MPH; Goutham Rao, MD; John M. Ruiz, PhD; James Stevermer, MD, MSPH; Sandra Millon Underwood, PhD, RN; John B. Wong, MD.

Affiliations of The US Preventive Services Task Force (USPSTF) Members: University of California, Los Angeles (Mangione); Harvard Medical School, Boston, Massachusetts (Barry); George Washington University, Washington, DC (Nicholson); Albert Einstein College of Medicine, New York, New York (Cabana); Virginia Commonwealth University, Richmond (Chelmow); University of Washington, Seattle (Coker); University of Pittsburgh, Pittsburgh, Pennsylvania (Davis); University of North Carolina at Chapel Hill (Donahue); The University of Texas Health Science Center, San Antonio (Jaén); University of Virginia, Charlottesville (Li); New York University, New York, New York (Ogedegbe); Case Western Reserve University, Cleveland, Ohio (Rao); University of Arizona, Tucson (Ruiz); University of Missouri, Columbia (Stevermer); University of Wisconsin, Milwaukee (Underwood); Tufts University School of Medicine, Boston, Massachusetts (Wong).

Author Contributions: Dr Mangione had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. The USPSTF members contributed equally to the recommendation statement.

Conflict of Interest Disclosures: Authors followed the policy regarding conflicts of interest described at https://www.uspreventiveservicestaskforce.org/Page/Name/conflict-of-interest-disclosures. Dr Donahue reported that she is the vice chair of the University of North Carolina Evidence-based Practice Center, where faculty and primary care research fellows worked on the systematic evidence review for this topic. Dr Barry reported receiving grants from Healthwise, a nonprofit. Dr Wong reported authoring a publication involving isoniazid treatment for adults with positive tuberculin reactions and no other risk factors. No other disclosures were reported. All members of the USPSTF receive travel reimbursement and an honorarium for participating in USPSTF meetings.

Funding/Support: The USPSTF is an independent, voluntary body. The US Congress mandates that the Agency for Healthcare Research and Quality (AHRQ) support the operations of the USPSTF.

Role of the Funder/Sponsor: AHRQ staff assisted in the following: development and review of the research plan, commission of the systematic evidence review from an Evidence-based Practice Center, coordination of expert review and public comment of the draft evidence report and draft recommendation statement, and the writing and preparation of the final recommendation statement and its submission for publication. AHRQ staff had no role in the approval of the final recommendation statement or the decision to submit for publication.

Disclaimer: Recommendations made by the USPSTF are independent of the US government. They should not be construed as an official position of AHRQ or the US Department of Health and Human Services.

Additional Contributions: We thank Sheena Harris, MD, MPH (AHRQ), and Tina Fan, MD, MPH, who contributed to the writing of the manuscript, and Lisa Nicolella, MA (AHRQ), who assisted with coordination and editing.

Additional Information: Published by JAMA®—Journal of the American Medical Association under arrangement with the Agency for Healthcare Research and Quality (AHRQ).

REFERENCES

1. 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. *PLoS One*. 2015;10(11):e0140881. doi:10.1371/journal.pone.0140881

2. Centers for Disease Control and Prevention. Latent TB infections in the United States—published estimates. Published January 21, 2022. Accessed March 9, 2023. https://www.cdc.gov/tb/statistics/ltbi.htm

3. Grzybowski S, Barnett GD, Styblo K. Contacts of cases of active pulmonary tuberculosis. *Bull Int Union Tuberc*. 1975;50(1):90-106.

4. Marks SM, Taylor Z, Qualls NL, Shrestha-Kuwahara RJ, Wilce MA, Nguyen CH. Outcomes of contact investigations of infectious tuberculosis patients. *Am J Respir Crit Care Med*. 2000;162(6):2033-2038. doi:10.1164/ajrccm.162.6.2004022

5. American Thoracic Society. Targeted tuberculin testing and treatment of latent tuberculosis infection. *MMWR Recomm Rep*. 2000;49(RR-6):1-51.

6. Ferebee SH. Controlled chemoprophylaxis trials in tuberculosis: a general review. *Bibl Tuberc*. 1970;26:28-106.

7. Reported tuberculosis in the United States, 2020; Table 2: tuberculosis cases, percentages, and incidence rates per 100,000 population by Hispanic ethnicity and non-Hispanic race: United States, 1993-2020. Centers for Disease Control and Prevention. Accessed March 9, 2023. https://www.cdc.gov/tb/statistics/reports/2020/table2.htm

8. Reported tuberculosis in the United States, 2020; Table 29: tuberculosis cases and incidence rates per 100,000 population, ranked and grouped by number of cases: United States and the District of Columbia, 2020 and 2019. Centers for Disease Control and Prevention. Accessed March 9, 2023. https://www.cdc.gov/tb/statistics/reports/2020/table29.htm

9. Jonas DE, Riley S, Lee L, et al. *Screening for Latent Tuberculosis Infection in Adults: An Evidence Review for the US Preventive Services Task Force. Evidence Synthesis No. 226*. Agency for Healthcare Research and Quality; 2023. AHRQ publication 22-05298-EF-1.

10. Health disparities in TB. Centers for Disease Control and Prevention. Accessed March 9, 2023. https://www.cdc.gov/tb/topic/populations/healthdisparities/default.htm

11. US Preventive Services Task Force Procedure Manual. US Preventive Services Task Force. Updated August 2022. Accessed March 9, 2023. https://uspreventiveservicestaskforce.org/uspstf/about-uspstf/methods-and-processes/procedure-manual

12. TB terms. Centers for Disease Control and Prevention. Accessed March 9, 2023. https://www.cdc.gov/tb/topic/basics/glossary.htm

13. Reported tuberculosis in the United States, 2020; table 5: tuberculosis cases, percentages, and incidence rates per 100,000 population by origin of birth: United States, 1993-2020. Centers for Disease Control and Prevention. Accessed March 9, 2023. https://www.cdc.gov/tb/statistics/reports/2020/table5.htm

14. Who should be tested for TB infection. Centers for Disease Control and Prevention. Updated April 14, 2016. Accessed March 9, 2023. https://www.cdc.gov/tb/topic/testing/whobetested.htm

15. Reported tuberculosis in the United States, 2020; Table 6A: tuberculosis cases and percentages among non-US–born persons by the top 30 countries of birth: United States, 2016-2020. Centers for Disease Control and Prevention. Accessed March 9, 2023. https://www.cdc.gov/tb/statistics/reports/2020/table6a.htm

16. Geng E, Kreiswirth B, Driver C, et al. Changes in the transmission of tuberculosis in New York City from 1990 to 1999. *N Engl J Med*. 2002;346(19):1453-1458. doi:10.1056/NEJMoa012972

17. Chin DP, DeRiemer K, Small PM, et al. Differences in contributing factors to tuberculosis incidence in U.S.-born and foreign-born persons. *Am J Respir Crit Care Med*. 1998;158(6):1797-1803. doi:10.1164/ajrccm.158.6.9804029

18. Talbot EA, Moore M, McCray E, Binkin NJ. Tuberculosis among foreign-born persons in the United States, 1993-1998. *JAMA*. 2000;284(22):2894-2900. doi:10.1001/jama.284.22.2894

19. Borgdorff MW, Behr MA, Nagelkerke NJ, Hopewell PC, Small PM. Transmission of tuberculosis in San Francisco and its association with immigration and ethnicity. *Int J Tuberc Lung Dis*. 2000;4(4):287-294.

20. Jasmer RM, Ponce de Leon A, Hopewell PC, et al. Tuberculosis in Mexican-born persons in San Francisco: reactivation, acquired infection and transmission. *Int J Tuberc Lung Dis*. 1997;1(6):536-541.

21. Walter ND, Jasmer RM, Grinsdale J, Kawamura LM, Hopewell PC, Nahid P. Reaching the limits of tuberculosis prevention among foreign-born individuals: a tuberculosis-control program perspective. *Clin Infect Dis*. 2008;46(1):103-106. doi:10.1086/523733

22. Reported tuberculosis in the United States, 2020: risk factors. Centers for Disease Control and Prevention. Accessed March 9, 2023. https://www.cdc.gov/tb/statistics/reports/2020/risk_factors.htm

23. Self JL, McDaniel CJ, Bamrah Morris S, Silk BJ. Estimating and evaluating tuberculosis incidence rates among people experiencing homelessness, United States, 2007-2016. *Med Care*. 2021;59(suppl 2):S175-S181. doi:10.1097/MLR.0000000000001466

24. Panel on Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents With HIV. Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents With HIV. Accessed March 9, 2023. https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/adult-adolescent-oi/guidelines-adult-adolescent-oi.pdf

25. 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):e1-e33. doi:10.1093/cid/ciw694

26. Kahwati LC, Feltner C, Halpern M, et al. *Screening for Latent Tuberculosis Infection in Adults: An Evidence Review for the US Preventive Services Task Force. Evidence Synthesis No 142*. Agency for Healthcare Research and Quality; 2016. AHRQ publication 14-05212-EF-1.

27. Yang H, Kruh-Garcia NA, Dobos KM. Purified protein derivatives of tuberculin—past, present, and future. *FEMS Immunol Med Microbiol*. 2012;66(3):273-280. doi:10.1111/j.1574-695X.2012.01002.x

28. Jonas DE, Riley SR, Lee LC, et al. Screening for latent tuberculosis infection in adults: updated evidence report and systematic review for the US Preventive Services Task Force. *JAMA*. Published May 2, 2023. doi:10.1001/jama.2023.3954

29. 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):1-11. doi:10.15585/mmwr.rr6901a1

30. 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(25):723-726. doi:10.15585/mmwr.mm6725a5

31. US Preventive Services Task Force. Screening for latent tuberculosis infection in adults: US Preventive Services Task Force recommendation statement. *JAMA*. 2016;316(9):962-969. doi:10.1001/jama.2016.11046

32. Thompson MJ; International Union Against Tuberculosis Committee on Prophylaxis. Efficacy of various durations of isoniazid preventive therapy for tuberculosis: five years of follow-up in the IUAT trial. *Bull World Health Organ*. 1982;60(4):555-564.

33. Menzies D, Long R, Trajman A, et al. Adverse events with 4 months of rifampin therapy or 9 months of isoniazid therapy for latent tuberculosis infection: a randomized trial. *Ann Intern Med*. 2008;149(10):689-697. doi:10.7326/0003-4819-149-10-200811180-00003

34. 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(5):440-453. doi:10.1056/NEJMoa1714283

35. Sterling TR, Villarino ME, Borisov AS, et al; TB Trials Consortium PREVENT TB Study Team. Three months of rifapentine and isoniazid for latent tuberculosis infection. *N Engl J Med*. 2011;365(23):2155-2166. doi:10.1056/NEJMoa1104875

36. Sun HY, Huang YW, Huang WC, et al. Twelve-dose weekly rifapentine plus isoniazid for latent tuberculosis infection: a multicentre randomised controlled trial in Taiwan. *Tuberculosis (Edinb)*. 2018;111:121-126. doi:10.1016/j.tube.2018.05.013

37. Krebs A. The IUAT trial on isoniazid preventive treatment in persons with fibrotic lung lesions. *Bull Int Union Tuberc*. 1976;51(1):193-201.

38. Menzies D, Dion MJ, Rabinovitch B, Mannix S, Brassard P, Schwartzman K. Treatment completion and costs of a randomized trial of rifampin for 4 months versus isoniazid for 9 months. *Am J Respir Crit Care Med*. 2004;170(4):445-449. doi:10.1164/rccm.200404-478OC

39. White MC, Tulsky JP, Lee JR, et al. Isoniazid vs. rifampin for latent tuberculosis infection in jail inmates: toxicity and adherence. *J Correct Health Care*. 2012;18(2):131-142. doi:10.1177/1078345811435973

40. Sterling TR, Moro RN, Borisov AS, et al; Tuberculosis Trials Consortium. Flu-like and other systemic drug reactions among persons receiving weekly rifapentine plus isoniazid or daily isoniazid for treatment of latent tuberculosis infection in the PREVENT Tuberculosis study. *Clin Infect Dis*. 2015;61(4):527-535. doi:10.1093/cid/civ323

41. Taylor Z, Nolan CM, Blumberg HM; American Thoracic Society; Centers for Disease Control and Prevention; Infectious Diseases Society of America. Controlling tuberculosis in the United States recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. *MMWR Recomm Rep*. 2005;54(RR-12):1-81.

42. Kilpatrick SJ, Papile LA, Macones GA; AAP Committee on Fetus and Newborn; ACOG Committee on Obstetric Practice. *Guidelines for Perinatal Care*. 8th ed. American Academy of Pediatrics; 2017.

43. Clinical practice guideline: tuberculosis infection, asymptomatic adults. American Academy of Family Physicians. Accessed March 9, 2023. https://www.aafp.org/family-physician/patient-care/clinical-recommendations/all-clinical-recommendations/tuberculosis.html