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**Clinical Advisory:**

**Latent Tuberculosis Infection Testing and Treatment for High-Risk Populations**

**July 1, 2018**

In September 2016, the United States Preventive Services Task Force (USPSTF) published the [Final Recommendation Statement](https://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/latent-tuberculosis-infection-screening) on testing for latent tuberculosis (TB) infection, also referred to as LTBI. The USPSTF recommends and assigns a “B” grade to the following clinical preventive service:

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| --- | --- |
| Population | Asymptomatic adults at increased risk for infection |
| Recommendation | Screen for latent tuberculosis infection  |

A “B” grade means that providers will have increased opportunities to seek reimbursement for the service. Screening for latent TB infection will be covered by most private and public health insurance in 2018. The Affordable Care Act (ACA) requires that private insurance plans cover USPSTF recommendations that receive an “A” or “B” grade, and to do so without patient co-payment or deductibles.

The USPSTF recommendation applies to adult patients. The complementary pediatric recommendation for risk-based latent TB infection testing is included in the [Recommendations for Preventive Pediatric Health Care](https://www.aap.org/en-us/Documents/periodicity_schedule_oral_health.pdf) published by Bright Futures and the American Academy of Pediatrics (AAP), based on recommendations of the Committee on Infectious Diseases, published in the AAP “Red Book”.

The Massachusetts Department of Public Health (MDPH) strongly endorses screening for latent TB infection in primary care due to the individual and public health benefits associated with identification of persons infected with TB and linkage with medical evaluation and treatment services.

Key recommendations for screening patients for latent TB infection include:

1. **Use a TB Risk Assessment to identify patients at increased risk for infection.**
2. **Choose a diagnostic test for TB infection that is appropriate for your patient.**
3. **Provide patients who test positive for TB infection with medical evaluation to rule out active TB disease or refer such patients for such evaluation.**
4. **Report cases of latent TB infection or active TB disease to MDPH.**
5. **Review treatment options and focus on shorter regimens.**
6. **Provide education and adherence support to assist patients in completing treatment for latent TB infection.**

This MDPH Advisory will review each of these elements and provide links to resources and additional information.

1. **Use a TB Risk Assessment to identify patients at increased risk for infection.**

MDPH, in collaboration with the Medical Advisory Committee for the Elimination of Tuberculosis, has developed Massachusetts TB Risk Assessment and accompanying User Guide for all ages, as well as pediatric versions. The purpose of the TB Risk Assessment is to identify asymptomatic children and adults for testing for latent TB infection. Testing is indicated if risk is identified through any of these three key questions:

* Was your patient born in or has s/he lived in a country with an elevated TB rate (i.e., any country other than the US, Canada, Australia, New Zealand, or a country in western or northern Europe)?
* Does your patient have immune suppression currently, or is immune suppression anticipated (e.g., due to a medical condition or therapy with a drug or biologic agent)?
* Has your patient had close contact to a person with known or suspected infectious tuberculosis since the last risk assessment?

Persons at low risk for latent TB infection and disease progression should not be tested. Testing among low risk populations in the absence of new exposure may result in unnecessary evaluation and treatment because of false positive test results.

**Resources:**

[**Massachusetts Tuberculosis Risk Assessment**](https://www.mass.gov/media/1816491/download)

[**Massachusetts Tuberculosis Risk Assessment User Guide**](https://www.mass.gov/media/1816501/download)

[**Massachusetts Tuberculosis Risk Assessment: Pediatrics**](https://www.mass.gov/media/1884106/download)

[**Massachusetts Pediatric Tuberculosis Risk Assessment**](https://www.mass.gov/media/1883941/download)

1. **Choose a diagnostic TB test that is appropriate for your patient.**

Screening tests include the interferon-gamma release assays (IGRAs) and Mantoux tuberculin skin test (TST). The primary care provider’s choice of TB test should be based on several factors, including patient age, other medical conditions, test availability, cost, and logistics required for TST reading. The TST requires a return visit by the patient in 48-72 hours to have the test read by a trained professional.

Because IGRAs have increased specificity for TB infection in persons vaccinated with bacille Calmette-Guerin (BCG), an IGRA is preferred over the TST for patients two years of age and older with a history of BCG vaccination or who are from countries where BCG vaccination is routinely practiced. The primary care provider may presume that most persons born outside the United States may have been vaccinated with BCG.

An IGRA is the preferred test if the patient is not likely or able to return for the TST reading.

The TST is an acceptable test, and is preferred if the cost of IGRA would preclude testing (e.g., the patient is uninsured) or if an IGRA is not available.

The TST should be used for children under two years of age.

In general, it is **not** recommended to test a person with both a TST and an IGRA. However, for patients who are at high risk for infection and at high risk for progression to disease, the increased sensitivity in considering a positive result with *either* test to be positive (i.e., indicative of infection) may be useful. In such situations, a negative TST (i.e., <5 mm induration) would be followed by an IGRA and vice versa.

[**Guidelines on the Use of Interferon-Gamma Release Assays and the Tuberculin Skin Test in Massachusetts**](https://www.mass.gov/media/1884126/download)

1. **Provide patients who test positive for TB infection with medical evaluation to rule out active TB disease or refer such patients for further evaluation.**

The TST and IGRA cannot distinguish active from latent tuberculosis. Thus, a medical evaluation and chest radiograph are essential for evaluating a positive IGRA or TST result. The primary care provider may perform this evaluation, but diagnostic questions may require referral. The evaluation includes a symptom screen, physical examination, chest radiograph, and, if indicated, smears, cultures, and nucleic acid amplification testing of sputum. ***Active disease must be excluded before treatment for latent TB infection is initiated because failure to do so may result in inadequate treatment and development of drug resistance.***

MDPH has contracts for TB outpatient services at facilities across the Commonwealth. These facilities may be appropriate for referrals for evaluation and treatment recommendations. The facilities will bill third party insurers when available, but MDPH is the payer of last resort.

[**Medical Evaluation for Persons with Positive Test Results Indicating TB Infection**](https://www.mass.gov/media/1884131/download)

1. **Report cases of latent TB infection or active TB disease to MDPH.**

Latent TB infection and Active/Suspected Active TB disease are reportable conditions as per Massachusetts regulation 105 CMR 300.180. Case reporting forms are [on-line](https://www.mass.gov/how-to/report-a-case-of-tuberculosis-disease-or-latent-tb-infection) or call 617-983-6801 for assistance.

[**Report a Case of Tuberculosis Disease or Latent TB Infection**](https://www.mass.gov/how-to/report-a-case-of-tuberculosis-disease-or-latent-tb-infection)

1. **Review treatment options and focus on shorter regimens.**

Because testing should be focused on persons at risk for TB infection who will benefit from treatment, patients who test positive for latent TB infection should generally be treated once active TB disease has been ruled out.

Patients are more likely to complete a shorter regimen for treating latent TB infection. For this reason, MDPH recommends their use when possible. The twelve-week/twelve-dose regimen via directly observed therapy has been shown to be as effective as nine months of daily self-administered isoniazid. Four months of daily self-administered rifampin recently has been shown to be as effective as nine months of isoniazid. However, because the shorter regimens include rifamycins, drug-drug interactions must be considered and are frequent reasons they are not used.

**Shorter duration latent TB infection treatment regimens**

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| **Regimen** | **Medications** | **Frequency** | **Duration** |
| 4R | Rifampin (RIF) | Daily | 4 months |
| 3HP | Isoniazid + Rifapentine\* | Weekly | 12 weeks |

\*MDPH recommends directly observed therapy (DOT) for this regimen.

With any latent TB infection treatment regimen, patients should undergo a clinical assessment at least monthly by a health care provider, including inquiries about adherence and side effects and a physical examination. In addition to the monthly clinical assessment, MDPH recommends review of side effects at each directly observed isoniazid + rifapentine dose.

[**Treatment Regimens for Latent Tuberculosis Infection in Massachusetts**](https://www.mass.gov/media/1884116/download)

1. **Provide education and adherence support to assist patients in completing treatment.**

The USPSTF noted adequate evidence that treatment of latent TB infection with regimens recommended by the CDC decreases progression to active tuberculosis. MDPH encourages primary care providers to discuss the importance of treating latent TB infection with patients for whom treatment is recommended. Health care providers play a key role in motivating patients to start, continue and complete treatment.

MDPH has developed patient materials that can support dialogue between patients and providers about latent TB infection, strategies to adhere to treatment, what to do if the patient experiences side effects, and appointment reminders for refills. These materials are available in in 22 languages in a bilingual format. [**TB Information for Your Patients**](https://www.mass.gov/lists/tb-information-for-your-patients-in-english-and-other-languages)

The CDC has informational materials on latent TB infection that may be appropriate for use with patients. [**CDC Latent Tuberculosis Infection Resources**](https://www.cdc.gov/tb/publications/ltbi/ltbiresources.htm)

**Resource: Current Procedure Terminology (CPT) and ICD-10 Codes for Latent Tuberculosis Infection**

Screening: CPT

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| **Step** | **Test Type** | **CPT** |
| Screening/Testing | TST | 86580 |
| Screening/Testing | QFT\* | 86480 |
| Screening/Testing  | T.Spot\*\* | 86481 |

\*QuantiFERON® test (IGRA)

\*\*T.spot-TB® test (IGRA)

Follow-up: ICD-10

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| **Diagnosis** | **Description** | **ICD-10** |
| TST-positive | Nonspecific reaction to TST without active tuberculosis. | R76.11 |
| IGRA-positive | Nonspecific reaction to IGRA without active tuberculosis. | R76.12 |