Diagnosis & Treatment of TB Infection

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TB Intensive
September 13 – 15, 2023
Richmond, TX

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Aurelia Schmalstieg, MD has the following disclosures to make:

- No conflict of interests
- No relevant financial relationships with any commercial companies pertaining to this educational activity

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SCREENING, DIAGNOSIS AND TREATMENT OF TB INFECTION

Aurelia Schmalstieg MD

I have no conflicts of interest or financial relationships with interests discussed in this educational activity

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WHY IS THIS TOPIC IMPORTANT?

"TB incidence is returning to prepandemic levels. TB diagnosis and treatment to interrupt transmission and prevention of TB through treatment of latent TB infection are critical to U.S. TB elimination efforts."

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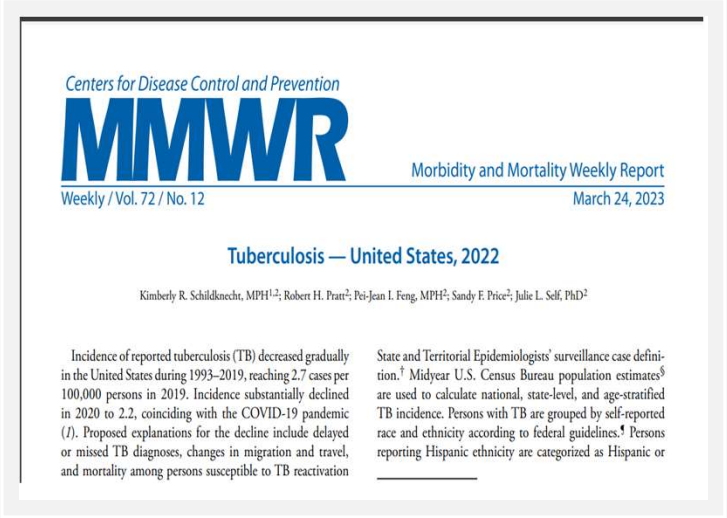

Centers for Disease Control and Prevention

MMWR

Morbidity and Mortality Weekly Report

Weekly / Vol. 72 / No. 12 March 24, 2023

Tuberculosis — United States, 2022

Kimberly R. Schildknecht, MPH[1,2]; Robert H. Pratt[2]; Pei-Jean I. Feng, MPH[2]; Sandy F. Price[2]; Julie L. Self, PhD[2]

Incidence of reported tuberculosis (TB) decreased gradually in the United States during 1993–2019, reaching 2.7 cases per 100,000 persons in 2019. Incidence substantially declined in 2020 to 2.2, coinciding with the COVID-19 pandemic (*1*). Proposed explanations for the decline include delayed or missed TB diagnoses, changes in migration and travel, and mortality among persons susceptible to TB reactivation

State and Territorial Epidemiologists' surveillance case definition.† Midyear U.S. Census Bureau population estimates§ are used to calculate national, state-level, and age-stratified TB incidence. Persons with TB are grouped by self-reported race and ethnicity according to federal guidelines.¶ Persons reporting Hispanic ethnicity are categorized as Hispanic or

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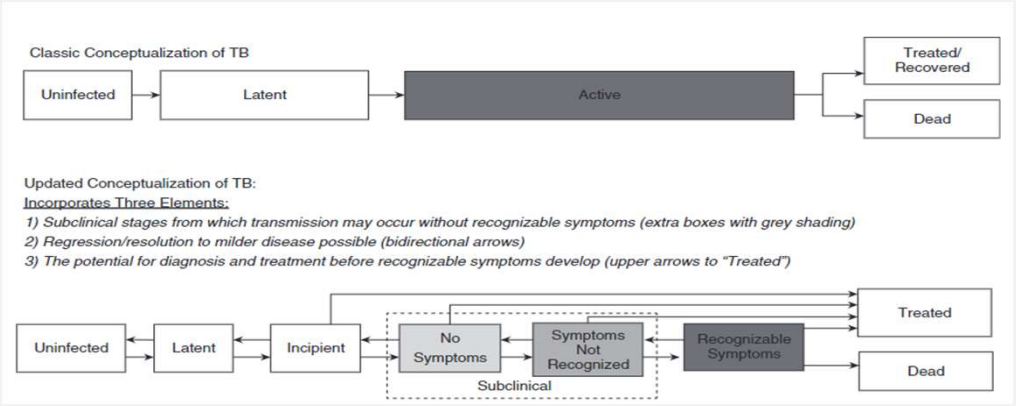

Am J Respir Crit Care Med 2021

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- Based on NHANES data, CDC estimates that up to 13 million people in the US have latent TB infection
- More than 80% of TB cases in the US result from longstanding, untreated latent TB infection

CDC 2022

Age-Associated Risk of Progression From TBI to TB Disease

Age	Risk of Progression from TBI to Disease if Untreated, %
<12 mo	40–50
1–2 y	25
School-aged	5–10
Adolescents	10–15
Adults	5–10

Risk of progression is also increased in immunocompromised individual and those recently infected with *M tuberculosis*.

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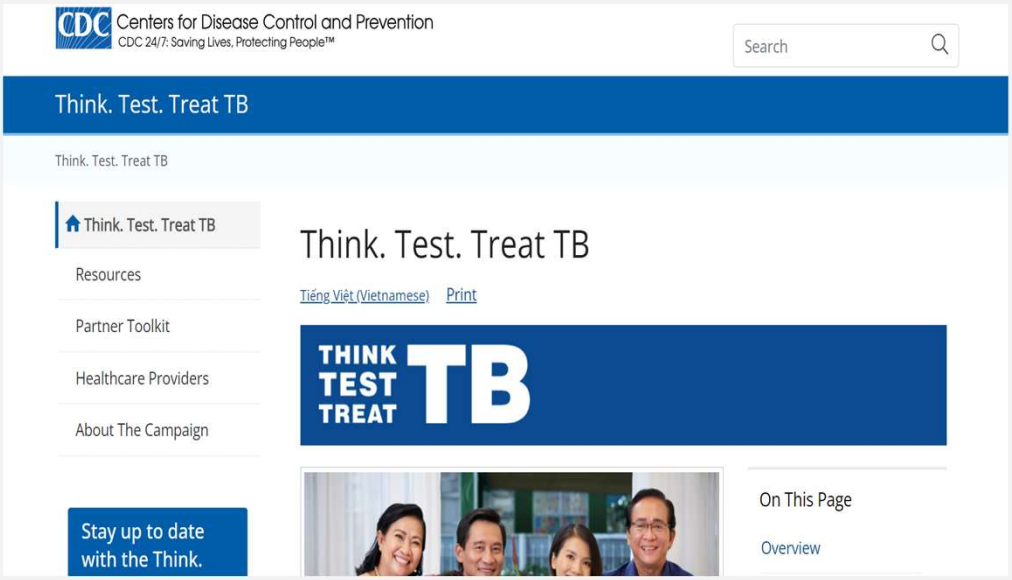

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OBJECTIVES FOR THIS SESSION:

1. Discuss the TB screening process and diagnostic criteria of tuberculosis infection
   - review diagnostic tests that are used for screening and diagnosis of tuberculosis infection
   - identify high priority candidates for screening for tuberculosis infection
   - summarize current treatments for latent tuberculosis infection

2. Discuss the ATS/CDC guidance for treating latent tuberculosis infection
   - monitoring while on treatment
   - DOT (DOPT)

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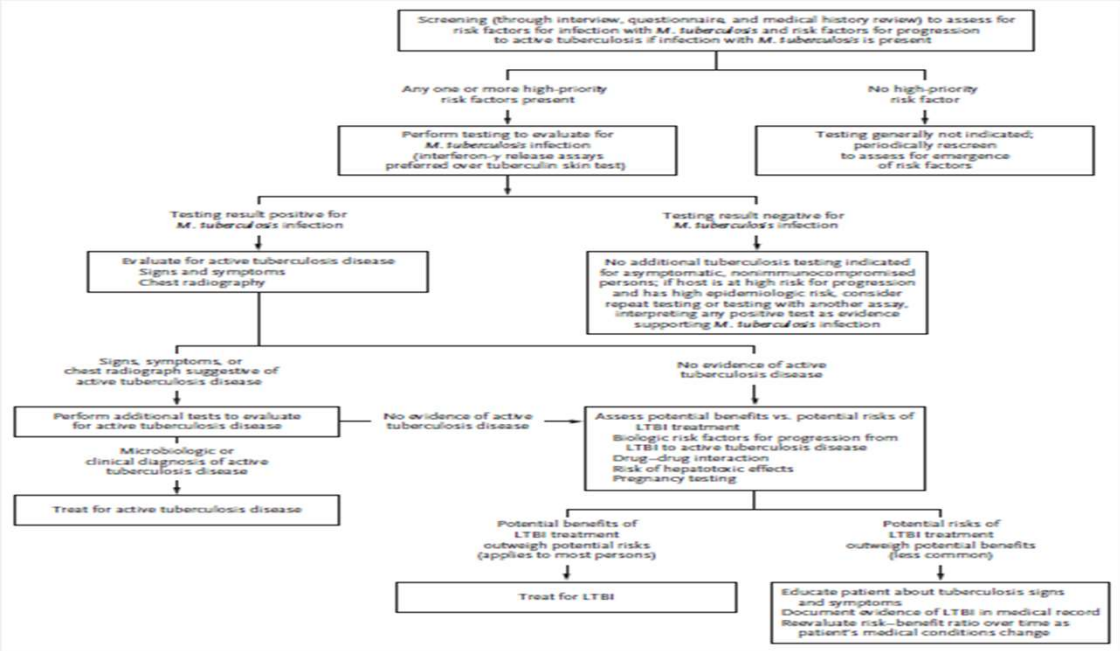

NEJM 2021 Shah M, S Dorman

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WHY IS THIS PERSON BEING EVALUATED FOR TUBERCULOSIS?

- Have they been named as being a contact to someone with active tuberculosis disease?
- Are they currently seeking care for another medical condition that makes them more likely to develop tuberculosis disease?
- Are they spending time in an occupational or residential setting that makes it more likely for them to have been exposed to tuberculosis?

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OBJECTIVE 1. DISCUSS THE PROCESS OF SCREENING FOR TB

Is the person having symptoms of tuberculosis disease?

- Symptoms of pulmonary tuberculosis disease include (but are not limited to) :

  Cough, fever, fatigue, night sweats, chest pain, malaise, unexplained weight loss

- Symptoms of extra-pulmonary tuberculosis disease may include:

  Blood in the urine, headache and confusion, back pain, hoarseness, lack of appetite, unexplained weight loss, night sweats, fever, fatigue, infertility

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ALSO, NEED TO KNOW…

- Have they ever had tuberculosis in the past?
- Been around someone with tuberculosis?
- Had a positive test for tuberculosis in the past?

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NEXT, ASSESS THE PERSON'S RISK FOR HAVING TB INFECTION AND PROGRESSION TO ACTIVE DISEASE

Clues in the person's history that predict high risk for infection with tuberculosis:

- Being a household or close contact of someone with active TB
- Birth, residence or prolonged travel (>1 month) in a setting in which TB disease is common (most countries in Africa, Asia, Eastern Europe, Latin America, and the Pacific Islands)
- Other circumstances based on local epidemiology (correctional facilities and homeless shelters)
- Immunosuppression

Biologic factors that can increase risk of progression to tuberculosis disease:

- Diabetes mellitus
- Silicosis
- Chronic kidney disease
- Chronic malabsorption, gastrectomy, or intestinal bypass
- Age less that 5 years
- A BMI of 20 or less
- Current or former smoker
- Leukemia/lymphoma, cancer of the head and neck

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HIGH PRIORITY CANDIDATES FOR SCREENING:

HIGH RISK OF TUBERCULOSIS INFECTION:

- Persons who have spent time with someone who had TB disease
- Persons from a country in which TB is common
- Live or work in high risk settings like correctional facilities, nursing homes, shelters for people experiencing homelessness
- Healthcare workers who care for people at increased risk for TB disease
- Mycobacteriology lab personnel
- Infants, children and adolescents exposed to adults who are at increased risk for Tb infection or disease

MORE LIKELY TO DEVELOP TUBERCULOSIS DISEASE:

- Persons living with HIV
- Persons who became infected with TB bacteria in the last 2 years
- Babies and children
- Persons who use IV drugs
- Persons who have other conditions that weaken the immune system
- Persons with a history of inadequately treated TB
- Elderly persons
- Persons with renal failure, diabetes mellitus and silicosis

"Flexibility should be used in defining high-risk groups for testing…definitions should be made at the local level according to local demographics and TB epidemiology"

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"TARGETED TESTING"

People at High Risk for Exposure to or Infection with *M. tuberculosis*	People at High Risk for Developing TB Disease after Infection with *M. tuberculosis*
• **Contacts** of people known or suspected to have TB disease • People born in or who frequently travel to countries where TB disease is common, including Mexico, the Philippines, Vietnam, India, China, Haiti, and Guatemala, or other countries with high rates of TB • People who live in, or have lived in, high-risk congregate settings (for example, homeless shelters or correctional facilities) • Employees of high-risk congregate settings • Health care workers who serve patients with TB disease • Populations defined locally as having an increased incidence of LTBI or TB disease, possibly including medically underserved, low-income populations, or persons who abuse drugs or alcohol • Infants, children, and adolescents exposed to adults who are at increased risk for LTBI or TB disease	• People living with HIV • Children younger than 5 years of age • People recently infected with *M. tuberculosis* (within the past 2 years) • People with a history of untreated or inadequately treated TB disease • Persons who are receiving immunosuppressive therapy such as tumor necrosis factor-alpha (TNF) antagonists, systemic corticosteroids equivalent to/greater than 15 mg of prednisone per day, or immunosuppressive drug therapy following organ transplantation • Persons with silicosis, diabetes mellitus, chronic renal failure, leukemia, or cancer of the head, neck, or lung • Persons who have had a gastrectomy or jejunoileal bypass • Low body weight • Cigarette smokers and persons who abuse drugs or alcohol • Populations defined locally as having an increased incidence of disease due to *M. tuberculosis*, including medically underserved, low-income populations

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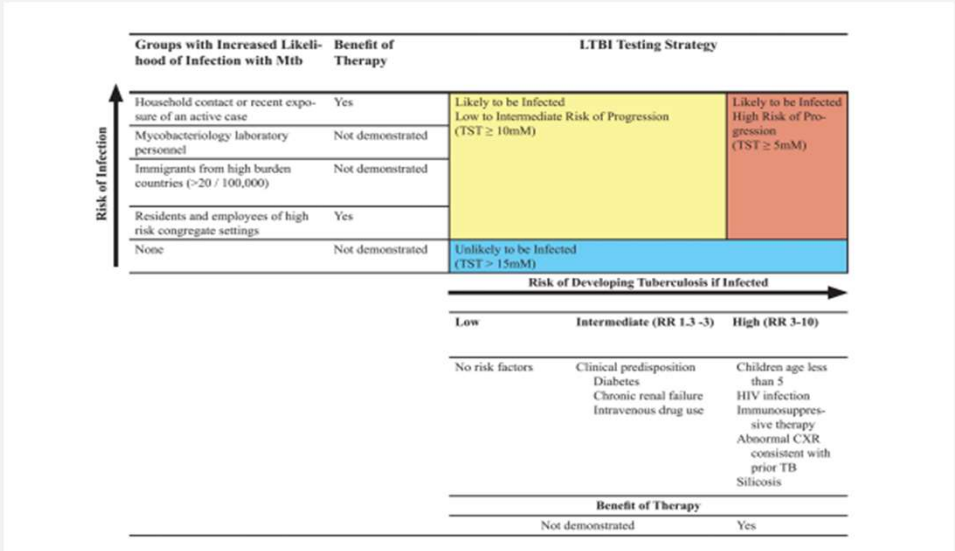

CID 2017

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IF INTERFERON GAMMA RELEASE TEST OR TUBERCULIN SKIN TEST IS POSITIVE…

Review signs and symptoms again

and

Perform chest radiography

- Collect sputum for AFB smear, culture and MTB NAAT if there are signs and symptoms of TB and/or chest xray is abnormal

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DIAGNOSTIC CRITERIA FOR LATENT TB INFECTION:

Lack of signs and symptoms of TB disease (pulmonary or extra-pulmonary)

+

Normal chest xray (2 views)

+

A positive interferon release assay or tuberculin skin test

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WHEN DISCUSSING THE RISKS AND BENEFITS OF LTBI TREATMENT:

- Consider the person's risk for getting TB, and their underlying biologic risk factors for progression to active TB disease
- Consider drug-drug interactions with current medications the person is taking for other medical conditions
- Consider the risk of hepatotoxicity based on the treatment regimen being considered, and other concurrent medical conditions
- Pregnancy status

A regimen of shorter duration is more likely to be successfully completed

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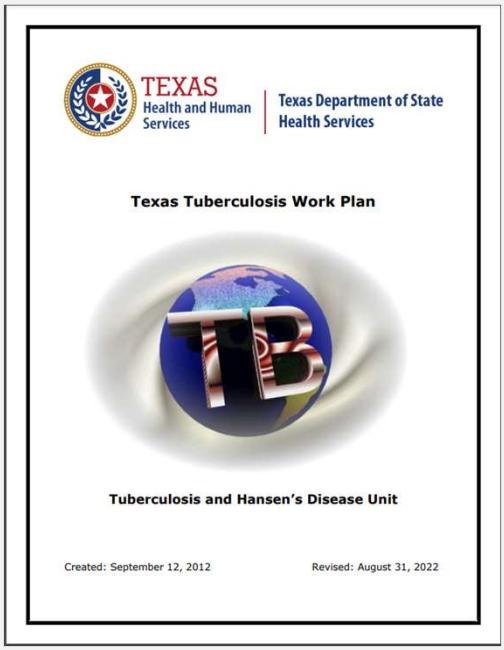

For patients age 12 years and older, screen for HIV infection using an approved laboratory-based HIV immunoassay.

For patients younger than 12 years old, screen for HIV infection using an approved laboratory-based HIV immunoassay if risk factors for HIV infection are present (including known or self-reporting of: mother with HIV infection and no documentation of child's status; history of blood transfusion outside the United States; history of sexually transmitted infection (STI), sexual activity, pregnancy, intravenous drug abuse).

https://www.dshs.texas.gov/sites/default/files/LIDS-TB/policies/TBWorkPlan.pdf

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SCREENING FOR TUBERCULOSIS FOR PEOPLE WITH HIV

- All persons with HIV should be evaluated for LTBI at the time of HIV diagnosis, regardless of their epidemiological risk of TB exposure **(AII)**
- Persons with advanced HIV infection (CD4 count <200 cells/mm^3) and negative diagnostic tests for LTBI, without indications for initiating empiric LTBI treatment (i.e., no recent exposure to a culture-confirmed TB case), should be retested for LTBI once they start ART and attain a CD4 count ≥200 cells/mm^3 to ensure that the initial test result was a true negative result.

https://clinicalinfo.hiv.gov/en/guidelines/adult-andadolescent-opportunistic-infection. Accessed (August 26, 2023) [pp X-1]

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GUIDANCE FOR LTBI TREATMENT FOR PEOPLE LIVING WITH HIV

Treating LTBI to Prevent TB Disease in People with HIV

Indications

- Positive screening test[a] for LTBI, no evidence of active TB disease, and no prior history of treatment for active disease or latent TB infection **(AI)**
- Close contact with a person with infectious TB, regardless of screening test result **(AII)**

https://clinicalinfo.hiv.gov/en/guidelines/adult-andadolescent-opportunistic-infection. Accessed (August 26, 2023) [pp X-1]

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WINDOW PROPHYLAXIS

Once TB disease has been ruled out, children who are younger than 5 years of age who have been exposed to TB should receive LTBI treatment, even if they have an initial negative TST result.

Children should be retested 8 to 10 weeks after they were last exposed to TB.

Window prophylaxis can be stopped only if: the child is now older than 6 months, repeat TST is negative, and repeat TST was collected at least 8 weeks after last contact with the infectious person

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IF THE PATIENT DECIDES NOT TO START TREATMENT FOR LTBI

- If treatment is not initiated, provide education to the patient about the signs and symptoms of TB
- Discuss the test results with the patient and document them clearly
- Continue to perform risk- benefit assessments in the future

In general, an "intention to test should be an intention to treat" so be sure to document reason why treatment is not being initiated

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AFTER COMPLETION OF THERAPY:

- Make sure the person is given documentation of their positive test and completion of treatment
- Educate them that they would be expected to have a positive test for TB in the future, but this does not mean that their treatment didn't work

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TESTS USED IN IDENTIFYING LTBI:

Both of these tests really just tell us that the host immune response has been sensitized to antigens, and is working well enough to indicate this prior sensitization

1. Interferon-Gamma Release Assays:
   - QuantiFERON-TB Gold assay
   - T-SPOT TB assay
2. Tuberculin skin test (TST)

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TUBERCULIN SKIN TEST

- The TST is the preferred method of testing for children younger than age 2
- TST's are not recommended for people who won't be able to return in 48-72 hours, or for people who have a history of TB, a positive TB test in the past, or for most people with known BCG immunization in the past.
- TST interpretation is subjective and positivity thresholds are risk stratified

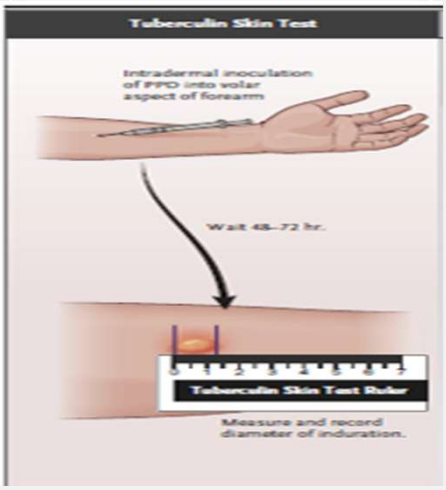

Image: NEJM 2021

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TST RESULT STRATIFICATION:

5 or more millimeters	10 or more millimeters	15 or more millimeters
An induration of 5 or more millimeters is considered positive for • People living with HIV • Recent contacts of people with infectious TB • People with chest x-ray findings suggestive of previous TB disease • People with organ transplants • Other immunosuppressed patients (for example, patients on prolonged therapy with corticosteroids equivalent to/ greater than 15 mg per day of prednisone or those taking TNF-alpha antagonists)	**An induration of 10 or more millimeters is considered positive for** • People born in countries where TB disease is common, including Mexico, the Philippines, Vietnam, India, China, Haiti, and Guatemala, or other countries with high rates of TB • People who abuse drugs • Mycobacteriology laboratory workers • People who live or work in high-risk congregate settings (for example, nursing homes, homeless shelters, or correctional facilities) • People with certain medical conditions that place them at high risk for TB (for example, silicosis, diabetes mellitus, severe kidney disease, certain types of cancer, and certain intestinal conditions) • Children younger than 5 years of age • Infants, children, and adolescents exposed to adults in high-risk categories	**An induration of 15 or more millimeters is considered positive for** • People with no known risk factors for TB

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MISLEADING TST RESULTS CAN OCCUR:

FALSE POSITIVE RESULT

- Infection with non- tuberculous mycobacteria
- BCG vaccination
- Incorrect administration
- Incorrect measurement or interpretation of the reaction

FALSE NEGATIVE RESULT

- Immunosuppression
- Tuberculosis infection occurred within the last 8-10 weeks
- Age <6 months
- Incorrect administration
- Live virus vaccination within the last 4 weeks

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IGRA vs. TST

- Laboratory instruments are required
- One patient encounter is sufficient
- Little subjectivity
- Does not cross-react with BCG
- Previous IGRA does not boost IGRA
- Results can be available within 24hrs
- Generally more expensive
- Blood must be processed within 8 – 32 hours after collection

- No lab instruments are required
- Required two visits to complete test
- Interpretation is subjective
- Cross-reacts with BCG
- Can boost subsequent TST or IGRA
- Results available in 48-72 hrs
- Generally lower cost

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T-SPOT IGRA:

- In vitro enzyme-linked immunosorbent spot assay
- Antigens: ESAT-6 and CFP-10
- Process whole blood cells within 8-32 hours
- Reports the actual number of interferon gamma-releasing T-lymphocytes detected
- Possible results: Positive, Negative, Invalid, or Borderline

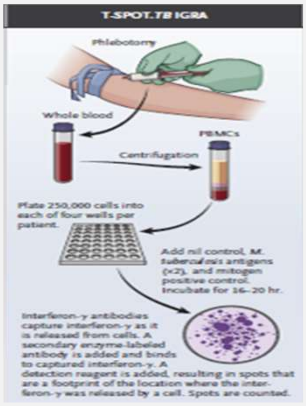

Image: NEJM 2021

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QUANTIFERON TB GOLD PLUS IGRA:

- In vitro ELISA
- Antigens: ESAT-6 and CFP-10
- Process whole blood within 16 hours
- Detects concentration of interferon gamma
- Possible results: Positive, Negative, Indeterminate

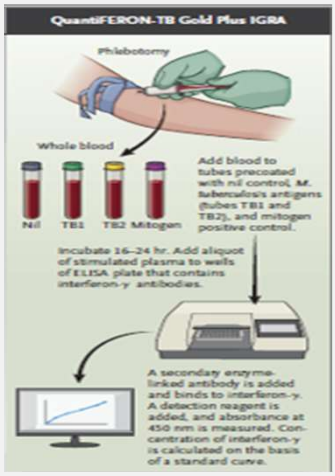

Image: NEJM 2021

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- Negative IGRA results for contacts to persons with infectious TB should be confirmed with a repeat test 8 to 10 weeks after their last exposure to TB.
- A positive IGRA result can be caused by certain non-tuberculous mycobacteria (M. kansasii, M. szulgai, M. marinum)

IGRA Result	Interpretation
Positive	*M. tuberculosis* infection likely
Negative	*M. tuberculosis* infection unlikely, but cannot be excluded especially if 1. Patient has signs and symptoms of TB 2. Patient has a high risk for developing TB disease once infected with *M. tuberculosis*
Indeterminate (QFT-Plus only)	The test did not provide useful information about the likelihood of *M. tuberculosis* infection. Repeating an IGRA or performing a TST may be useful.
Invalid or Borderline (T-Spot only)	The test did not provide useful information about the likelihood of *M. tuberculosis* infection. Repeating an IGRA or performing a TST might be useful.

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CLINICAL SCENARIO:

A 54 yo nurse has started a new job in her local TB clinic and upon employment has a negative TST. She does not recall having a TB test in the past.

At her next annual employment screening, her TST is positive.

Does this mean that she was exposed to TB at the nursing home?

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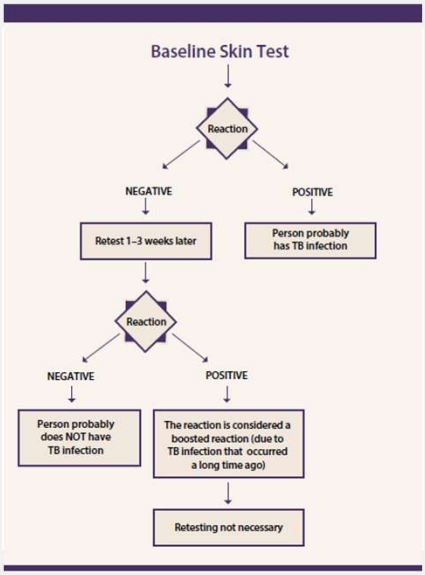
TWO-STEP TESTING

- Two-step testing should be used for the initial TB skin testing of persons who will be retested periodically.
- Note: A TST can boost a subsequent IGRA. IGRAs do not boost subsequent test results because, unlike the TST, the patient is not exposed to the *M. tuberculosis* antigens.



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SUMMARY OF THE CURRENT TREATMENTS FOR LTBI:

- Encourage people with who are at increased risk for TB infection and/or progression to TB disease and are found to have LTBI to take a course of preventative treatment.
- The shorter the regimen, the great the likelihood that they will complete the treatment.
- The current preferred treatments for TB infection is weekly Isoniazid and Rifapentine (12 doses), which can be completed in 3 months, Rifampin daily for 4 months, and Rifampin and INH daily for three months.

  Note some exceptions for special groups:

  - people younger than 2 years old
  - pregnant people
  - people who are thought to be infected with INH or rifampin resistant TB
  - people with HIV whose ART regimen is not compatible with rifapentine

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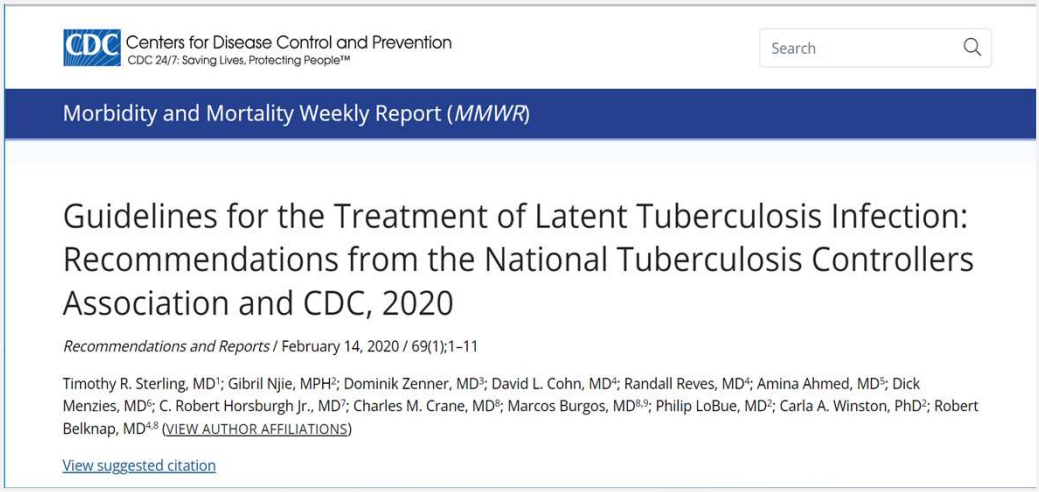
OBJECTIVE 2: REVIEW THE CURRENT ATS/CDC GUIDANCE FOR TREATING LTBI



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Morbidity and Mortality Weekly Report (*MMWR*)

Guidelines for the Treatment of Latent Tuberculosis Infection: Recommendations from the National Tuberculosis Controllers Association and CDC, 2020

Recommendations and Reports / February 14, 2020 / 69(1);1–11

Timothy R. Sterling, MD[1]; Gibril Njie, MPH[2]; Dominik Zenner, MD[3]; David L. Cohn, MD[4]; Randall Reves, MD[4]; Amina Ahmed, MD[5]; Dick Menzies, MD[6]; C. Robert Horsburgh Jr., MD[7]; Charles M. Crane, MD[8]; Marcos Burgos, MD[8,9]; Philip LoBue, MD[2]; Carla A. Winston, PhD[2]; Robert Belknap, MD[4,8] (VIEW AUTHOR AFFILIATIONS)

View suggested citation

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TABLE 3. Recommendations for regimens to treat latent tuberculosis infection

Priority rank*	Regimen	Recommendation (strong or conditional)	Evidence (high, moderate, low, or very low)
Preferred	3 mos isoniazid plus rifapentine given once weekly	Strong	Moderate
Preferred	4 mos rifampin given daily	Strong	Moderate (HIV negative)†
Preferred	3 mos isoniazid plus rifampin given daily	Conditional	Very low (HIV negative)
		Conditional	Low (HIV positive)
Alternative	6 mos isoniazid given daily	Strong§	Moderate (HIV negative)
		Conditional	Moderate (HIV positive)
Alternative	9 mos isoniazid given daily	Conditional	Moderate

Abbreviation: HIV = human immunodeficiency virus.
* *Preferred:* excellent tolerability and efficacy, shorter treatment duration, higher completion rates than longer regimens and therefore higher effectiveness; *alternative:* excellent efficacy but concerns regarding longer treatment duration, lower completion rates, and therefore lower effectiveness.
† No evidence reported in HIV-positive persons.
§ Strong recommendation for those persons unable to take a preferred regimen (e.g., due to drug intolerability or drug-drug interactions).

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TABLE 4. Dosages for recommended latent tuberculosis infection treatment regimens

Drug	Duration	Dose and age group	Frequency	Total doses
Isoniazid* and rifapentine†	3 mos	**Adults and children aged ≥12 yrs** Isoniazid: 15 mg/kg rounded up to the nearest 50 or 100 mg; 900 mg maximum Rifapentine: 10–14.0 kg, 300 mg 14.1–25.0 kg, 450 mg 25.1–32.0 kg, 600 mg 32.1–49.9 kg, 750 mg ≥50.0 kg, 900 mg maximum **Children aged 2–11 yrs** Isoniazid*: 25 mg/kg; 900 mg maximum Rifapentine†: see above	Once weekly	12
Rifampin¶	4 mos	**Adults:** 10 mg/kg **Children:** 15–20 mg/kg** **Maximum dose:** 600 mg	Daily	120
Isoniazid* and rifampin¶	3 mos	**Adults** Isoniazid*: 5 mg/kg; 300 mg maximum Rifampin¶: 10 mg/kg; 600 mg maximum **Children** Isoniazid*: 10–20 mg/kg††; 300 mg maximum Rifampin¶: 15–20 mg/kg; 600 mg maximum	Daily	90
Isoniazid*	6 mos	**Adults:** 5 mg/kg **Children:** 10–20 mg/kg†† **Maximum dose:** 300 mg	Daily	180
		Adults:15 mg/kg **Children:** 20–40 mg/kg†† **Maximum dose:** 900 mg	Twice weekly§	52
	9 mos	**Adults:** 5 mg/kg **Children:** 10–20 mg/kg†† **Maximum dose:** 300 mg	Daily	270
		Adults: 15 mg/kg **Children:** 20–40 mg/kg†† **Maximum dose:** 900 mg	Twice weekly§	76

* Isoniazid is formulated as 100-mg and 300-mg tablets.
† Rifapentine is formulated as 150-mg tablets in blister packs that should be kept sealed until use.
§ Intermittent regimens must be provided via directly observed therapy (i.e., a health care worker observes the ingestion of medication).
¶ Rifampin (rifampicin) is formulated as 150-mg and 300-mg capsules.
** The American Academy of Pediatrics acknowledges that some experts use rifampin at 20–30 mg/kg for the daily regimen when prescribing for infants and toddlers (**Source:** American Academy of Pediatrics. Tuberculosis. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. Red Book: 2018 Report of the Committee on Infectious Diseases. 31st ed. Itasca, IL: American Academy of Pediatrics; 2018:829–53).
†† The American Academy of Pediatrics recommends an isoniazid dosage of 10–15 mg/kg for the daily regimen and 20–30 mg/kg for the twice-weekly regimen.

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TREATMENT OF CONTACTS EXPOSED TO MDR TB:

May offer treatment for LTBI vs following with observation alone

For treatment of MTB LTBI, we suggest 6 to 12 months treatment with a fluoroquinolone alone or with a second drug, on the basis of sourse-case isolate DST.

Randomized, clinical trials on the effectiveness of shorter, safer, more effective regimens for MDR LTBI are underway.

Am J Respir Crit Care Med 2015

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PREFERRED THERAPY FOR LTBI FOR PEOPLE WITH HIV

Preferred Therapy

- Rifapentine (see weight-based dosing below) PO once weekly plus isoniazid 15 mg/kg PO once weekly (900 mg maximum) plus pyridoxine 50 mg PO once weekly for 12 weeks **(AI).** Note: Rifapentine is recommended only for virally-suppressed patients receiving an efavirenz-, raltegravir-, or once-daily dolutegravir-based ARV regimen **(AI).**
  - Rifapentine Weekly Dose (maximum 900 mg)
    - *Weighing 32.1–49.9 kg*: 750 mg
    - *Weighing ≥50.0 kg*: 900 mg
- Isoniazid 300 mg PO daily plus rifampin 600 mg PO daily plus pyridoxine 25–50 mg PO daily **(AI)** for 3 months. See the Dosing Recommendations for Anti-TB Drugs table for the list of ARV drugs not recommended for use with rifampin and those which require dosage adjustment (i.e., raltegravir, dolutegravir, or maraviroc).

https://clinicalinfo.hiv.gov/en/guidelines/adult-andadolescent-opportunistic-infection. Accessed (August 26, 2023)

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ALTERNATIVE REGIMENS FOR LTBI TREATMENT FOR PEOPLE WITH HIV

Alternative Therapies

- Isoniazid 300 mg PO daily plus pyridoxine 25–50 mg PO daily for 6–9 months **(AII)** *or*
- Rifampin 600 mg PO daily for 4 months **(BI)** See the Dosing Recommendations for Anti-TB Drugs table (above) for the list of ARV drugs not recommended for use with rifampin and those which require dosage adjustment (i.e., raltegravir, dolutegravir, or maraviroc) *or*
- Isoniazid 300 mg PO daily plus rifapentine PO daily plus pyridoxine 25–50 mg PO daily for 4 weeks **(BI)** Note: Rifapentine is recommended only for patients receiving an efavirenz-based ARV regimen **(AI).**
  - Rifapentine Daily Dose (maximum 600 mg)
    - *Weighing <35 kg*: 300 mg
    - *Weighing 35–45 kg*: 450 mg
    - *Weighing >45 kg*: 600 mg

For persons exposed to drug-resistant TB, select drugs for prevention of TB after consultation with experts and with public health authorities **(AIII).**

https://clinicalinfo.hiv.gov/en/guidelines/adult-andadolescent-opportunistic-infection. Accessed (August 26, 2023)

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MONITORING DURING TREATMENT FOR LTBI:

For healthy adults with no underlying risk factors for hepatotoxicity, check in monthly to ask about
- adherence
- signs and symptoms of TB disease
- signs and symptoms of adverse medication reactions

For adults with risk factors for hepatotoxicity (pregnant or post partum, hepatitis, alcohol use, HIV, or concurrent use of other medications that can cause hepatotoxicity) check a baseline AST, ALT, total bilirubin, alk phos, albumin. If starting a rifamycin also check CBC. Check in monthly to ask about
- adherence
- signs and symptoms of TB disease
- signs and symptoms of adverse medication reactions
- recheck labs "periodically" if baseline was abnormal or there are any new signs or symptoms

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Potential adverse events of drugs used for latent tuberculosis infection (LTBI) treatment

Drug	Potential adverse effects	Comments
Isoniazid	Elevation of aminotransferases Symptomatic hepatitis Peripheral neuropathy	Close follow-up and caution in patients with baseline liver disease
Rifamycins (includes rifampin,rifapentine, and rifabutin)	Cutaneous rash Hematologic abnormalities Flu-like illness Elevation of aminotransferases Symptomatic hepatitis Orange discoloration of body fluids	Consider multiple potential drug-drug interactions (i.e., warfarin, anticonvulsants, opioids, antiretrovirals) Isoniazid-rifapentine not recommended in pregnant women or women expecting to be pregnant during treatment Isoniazid-rifapentine not recommended for children < 2 years of age

Clin Chest Med 2019

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DOT FOR LTBI

DOT is required for LTBI treatment if using an intermittent (twice weekly) INH regimen

Initially, DOT was required for 12 dose INH + rifapentine weekly regimen, but now this is considered optional in the guidance from the CDC depending on the setting and resources available

DOT for LTBI is recommended in any situation where the risk of progression to TB disease is very high if the preventive treatment is not taken (for example in children and adolescents).

It may also be considered if there is special concern for non-adherence to treatment

CDC 2020

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WHAT IF THERE IS AN INTERRUPTION IN THERAPY?

- Be sure to perform symptom review before restarting treatment for LTBI
- If the person is having any symptoms consistent with TB disease, repeat chest xray, perform physical exam, and collect sputum before considering restarting treatment

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THANK YOU!

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CDC Self-Study Modules on Tuberculosis, Module 3: *Targeted Testing and the Diagnosis of Latent Tuberculosis Infection and Tuberculosis Disease* and Module 4: *Treatment of Latent Tuberculosis Infection and Tuberculosis Disease*. https://www.cdc.gov/tb/education/ssmodules/default.htm

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QUESTIONS:

- Is there evidence to show how we can best communicate the benefits of LTBI treatment?
- How can we better determine who will progress to active disease?
- If a person has had several exposures to TB over time, how many times is it reasonable to recommend that they take preventive therapy? Is there a limit?
- If a person decides not to take treatment for LTBI what is the best evidence-based strategy to follow them for progression to tuberculosis disease?

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