MAYO CLINIC

Center for Tuberculosis

Fundamentals of Tuberculosis

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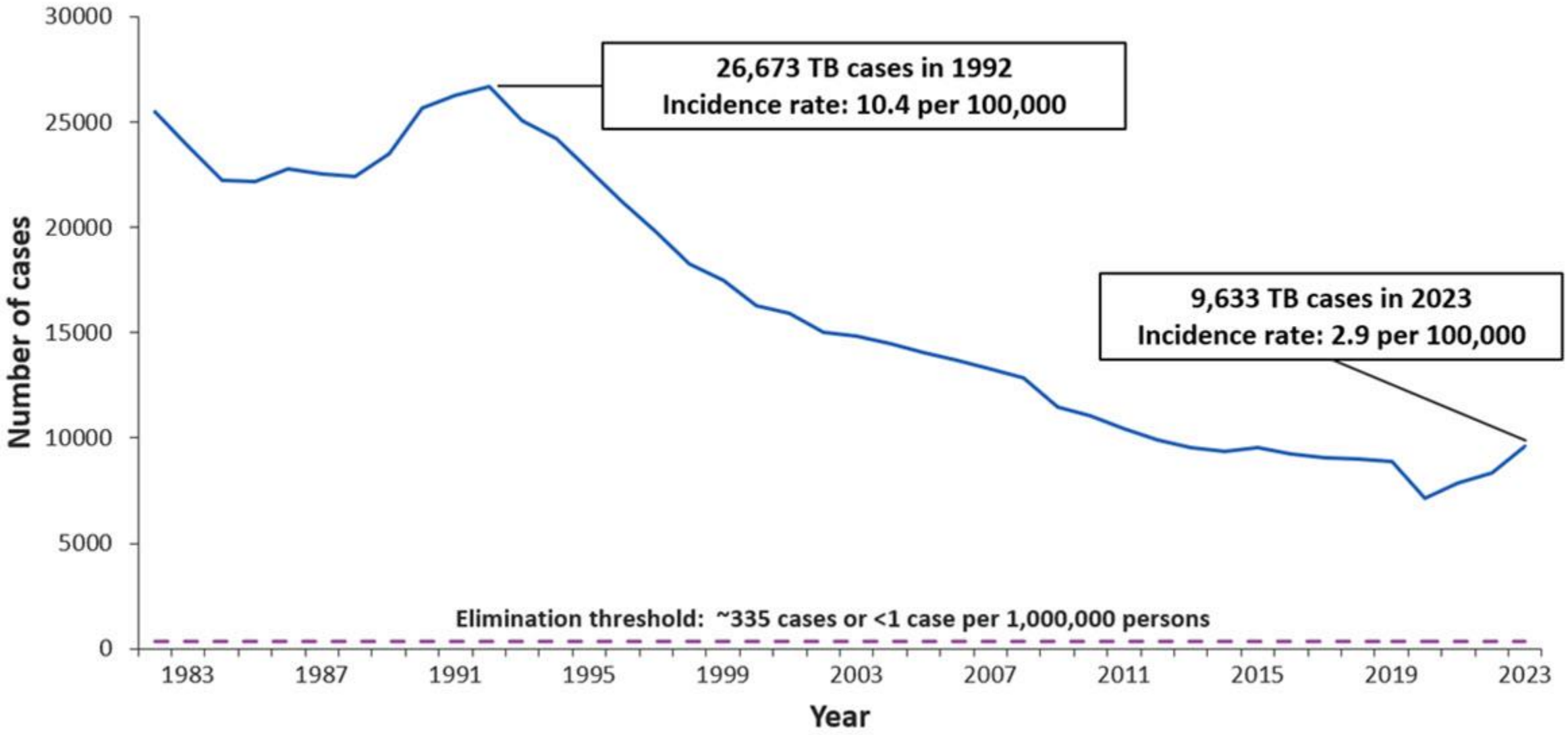
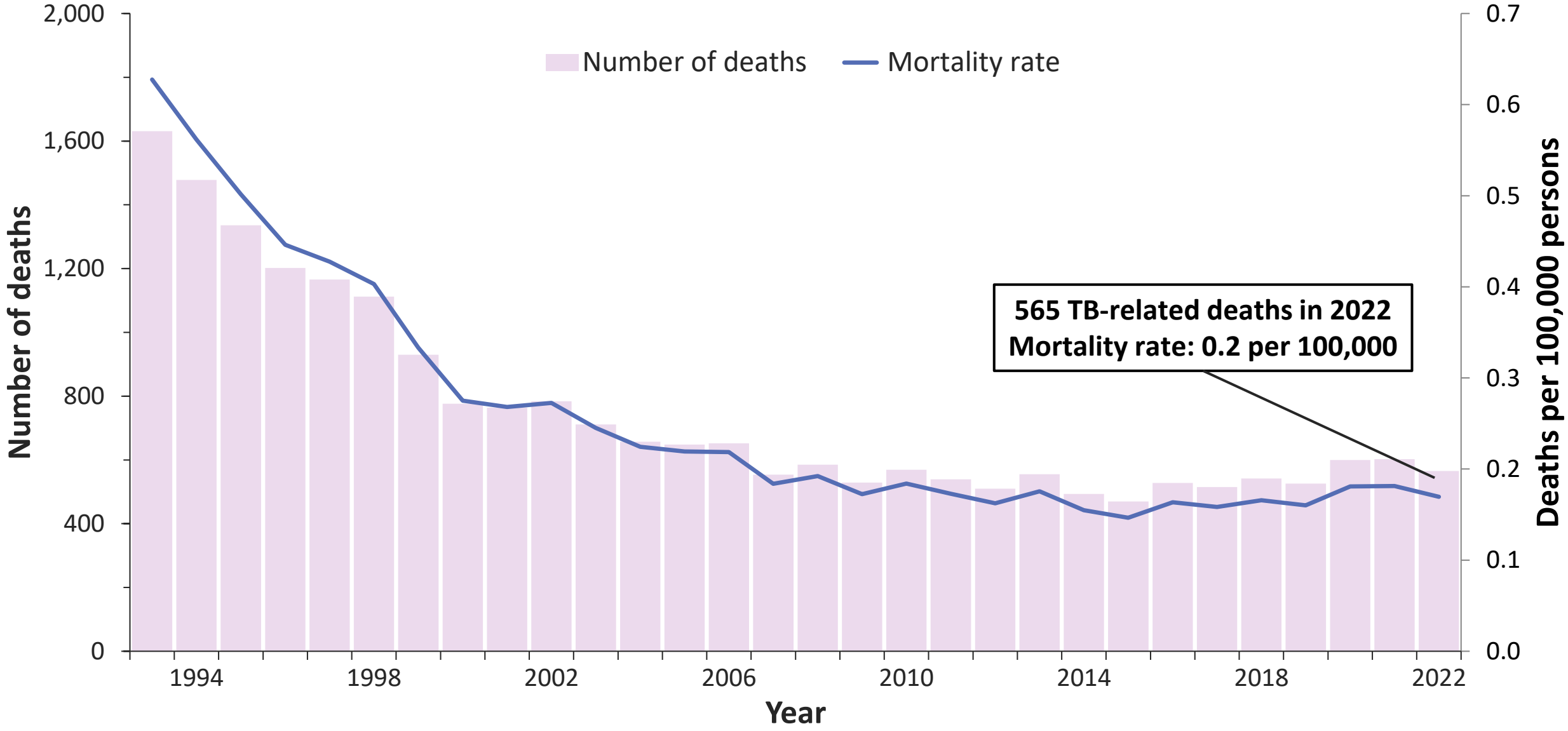
Progress Towards TB Elimination, United States, 1982–2023



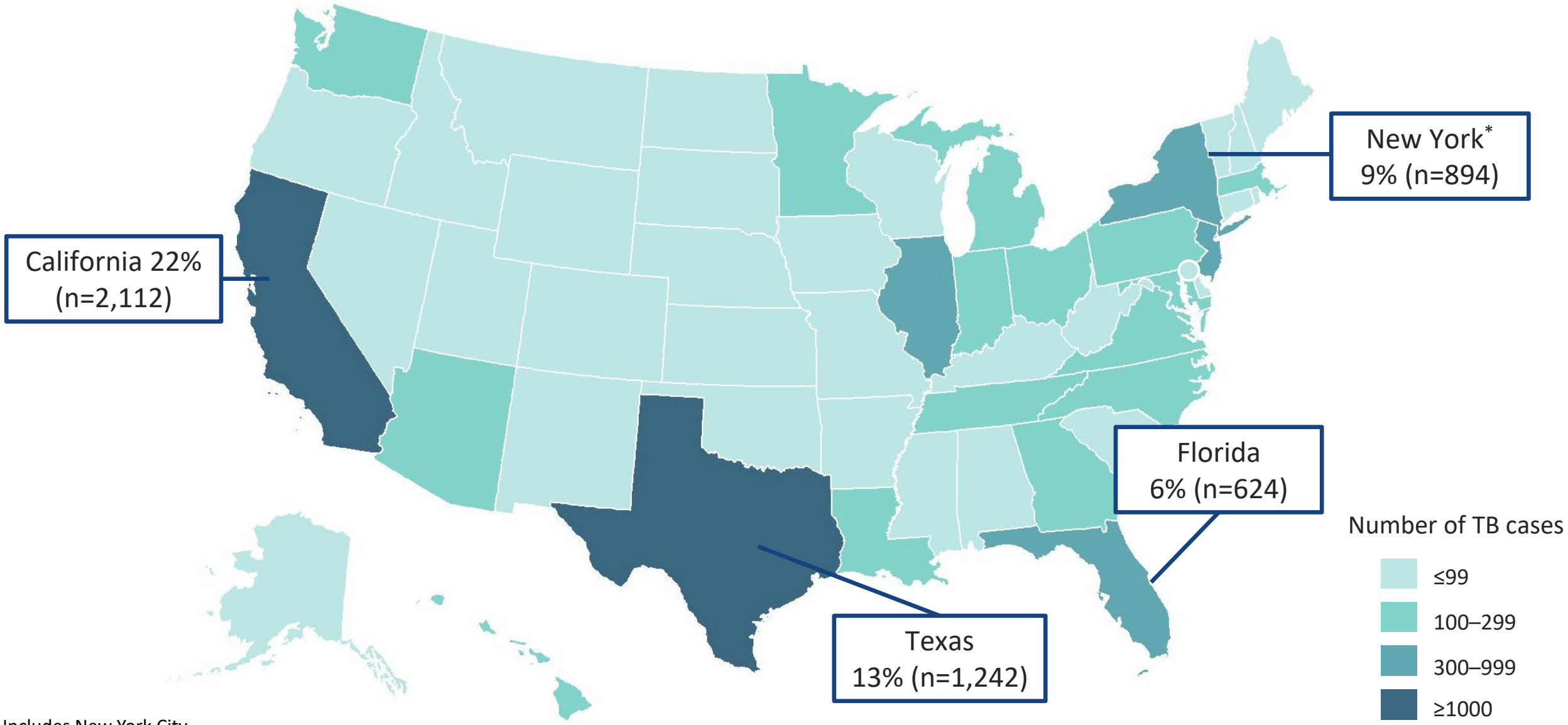
https://www.cdc.gov/tb-surveillance-report-2023/summary/index.html

TB-Related Deaths* and Mortality Rates, United States, 1993–2022



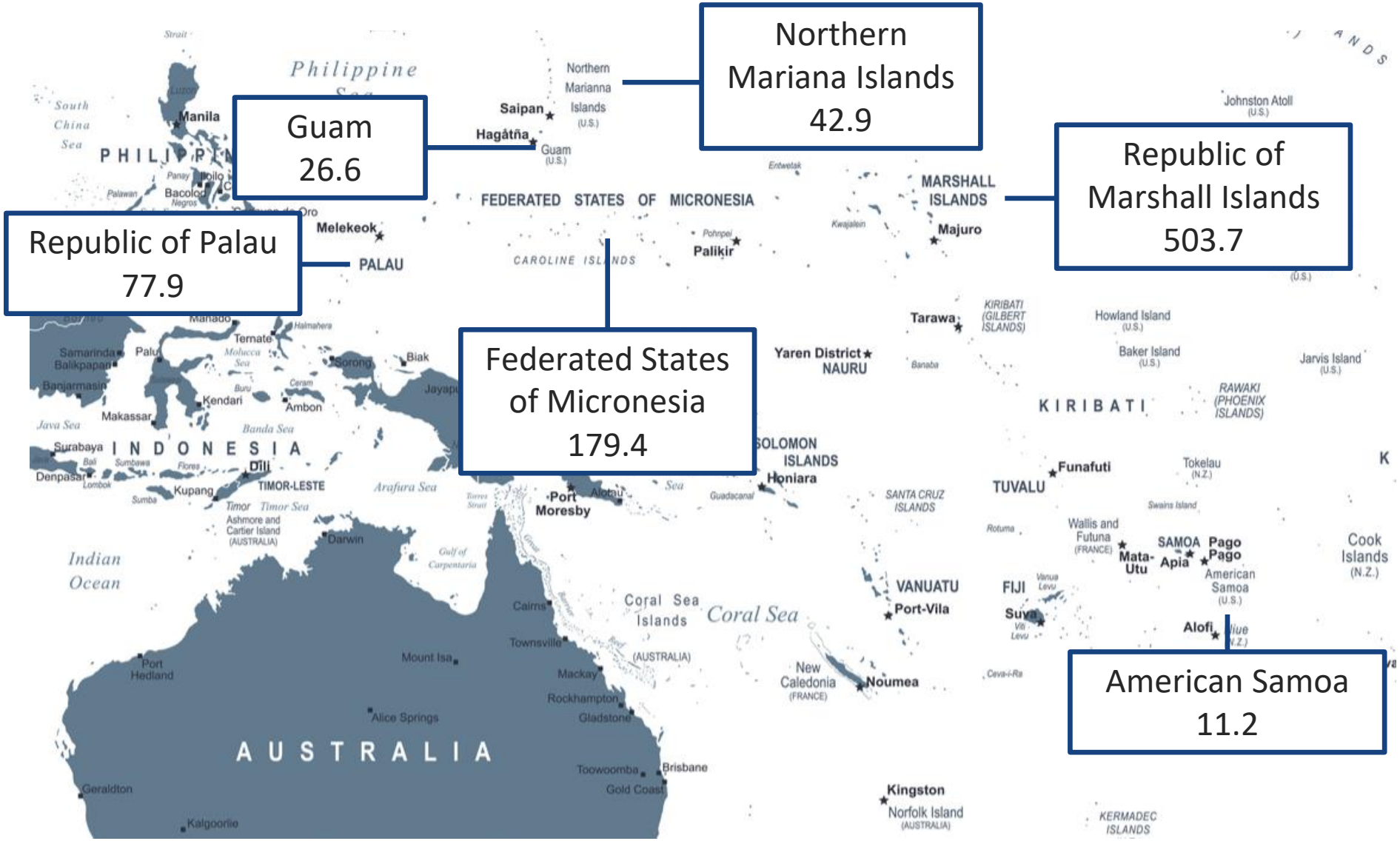
*National Vital Statistics System Underlying Cause of Death (based on deaths reported through 2022)

TB Cases and Percentages by Reporting Area, United States, 2023 (N=9,633)



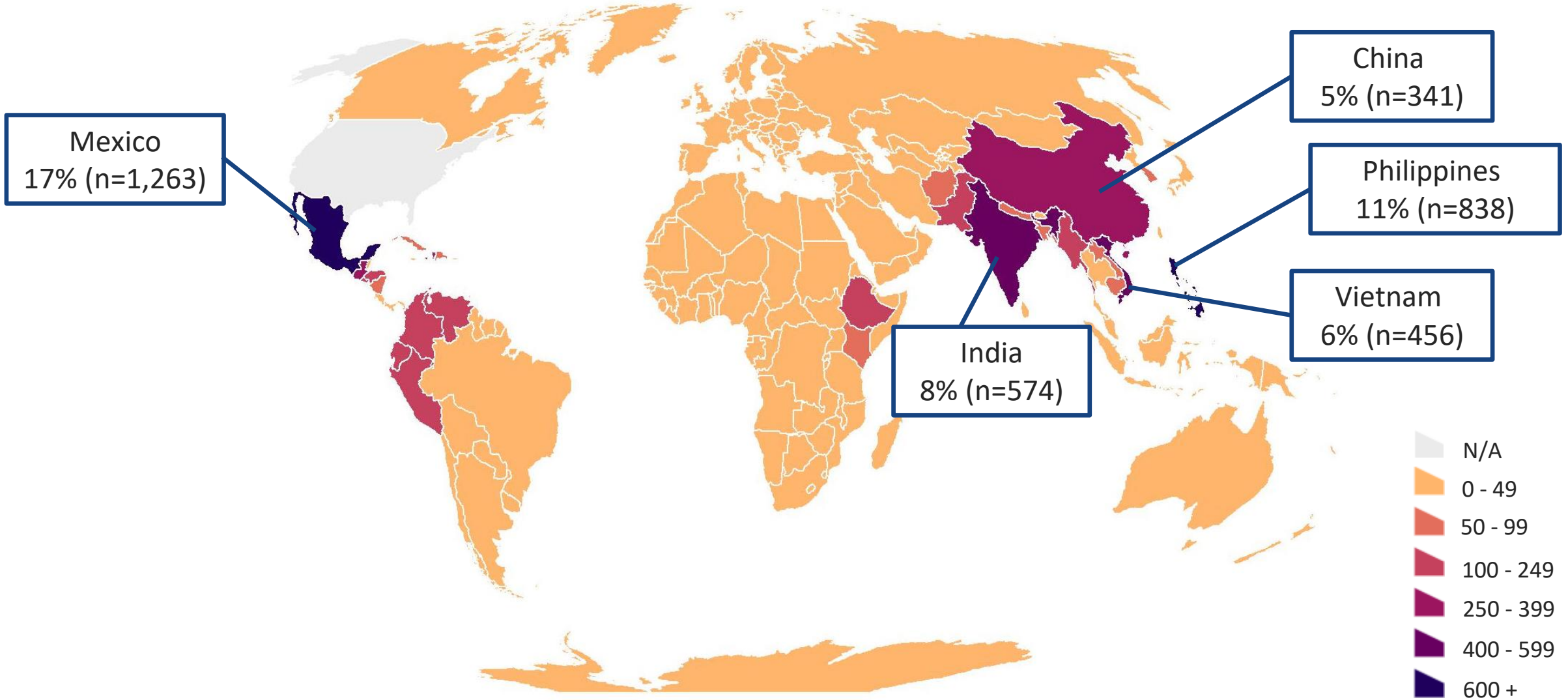
* Includes New York City

TB Incidence Rates* by U.S.-Affiliated Pacific Islands, 2023



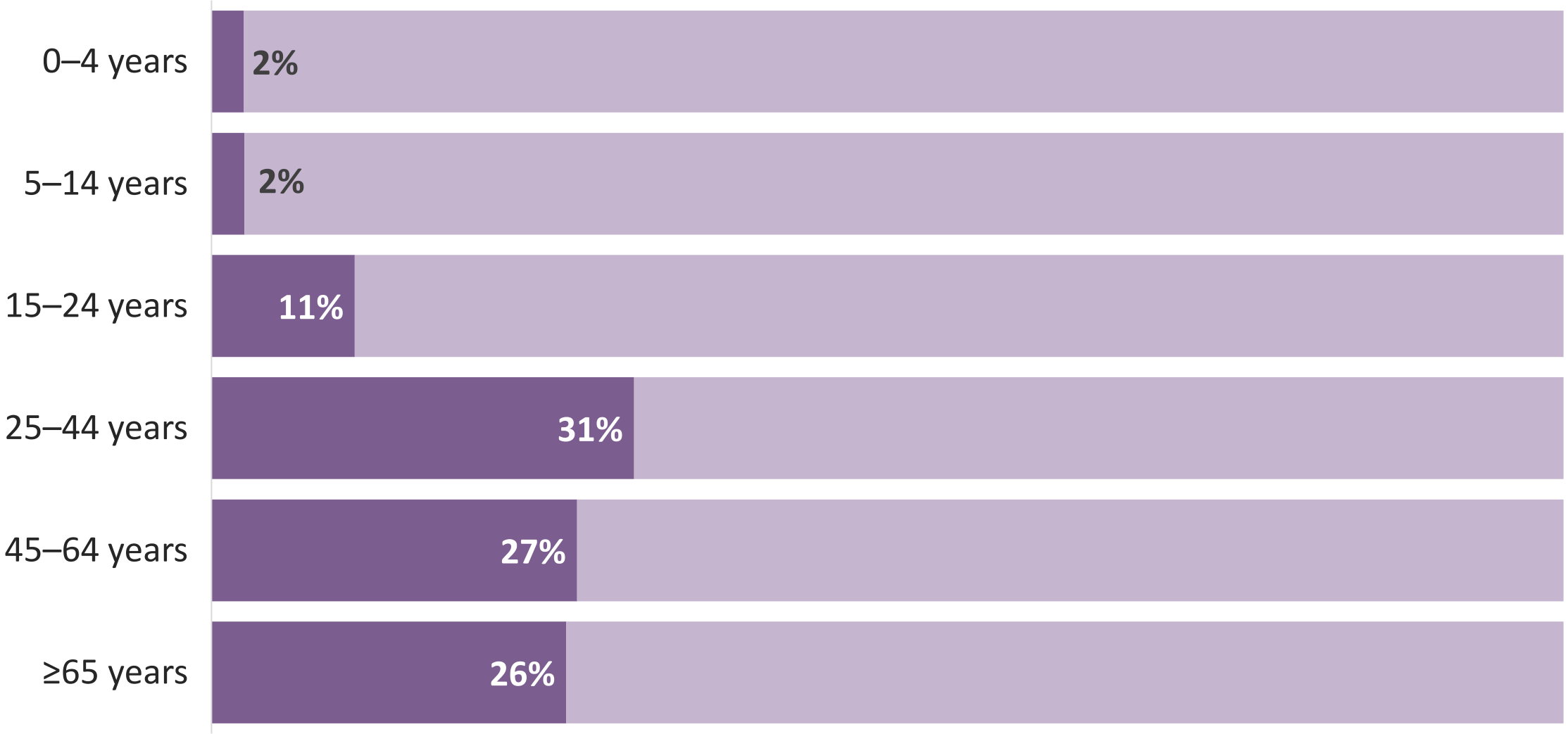
*Cases per 100,000 persons

TB Cases by Countries of Birth Among Non-U.S.–Born* Persons, United States, 2023 (N=7,299)



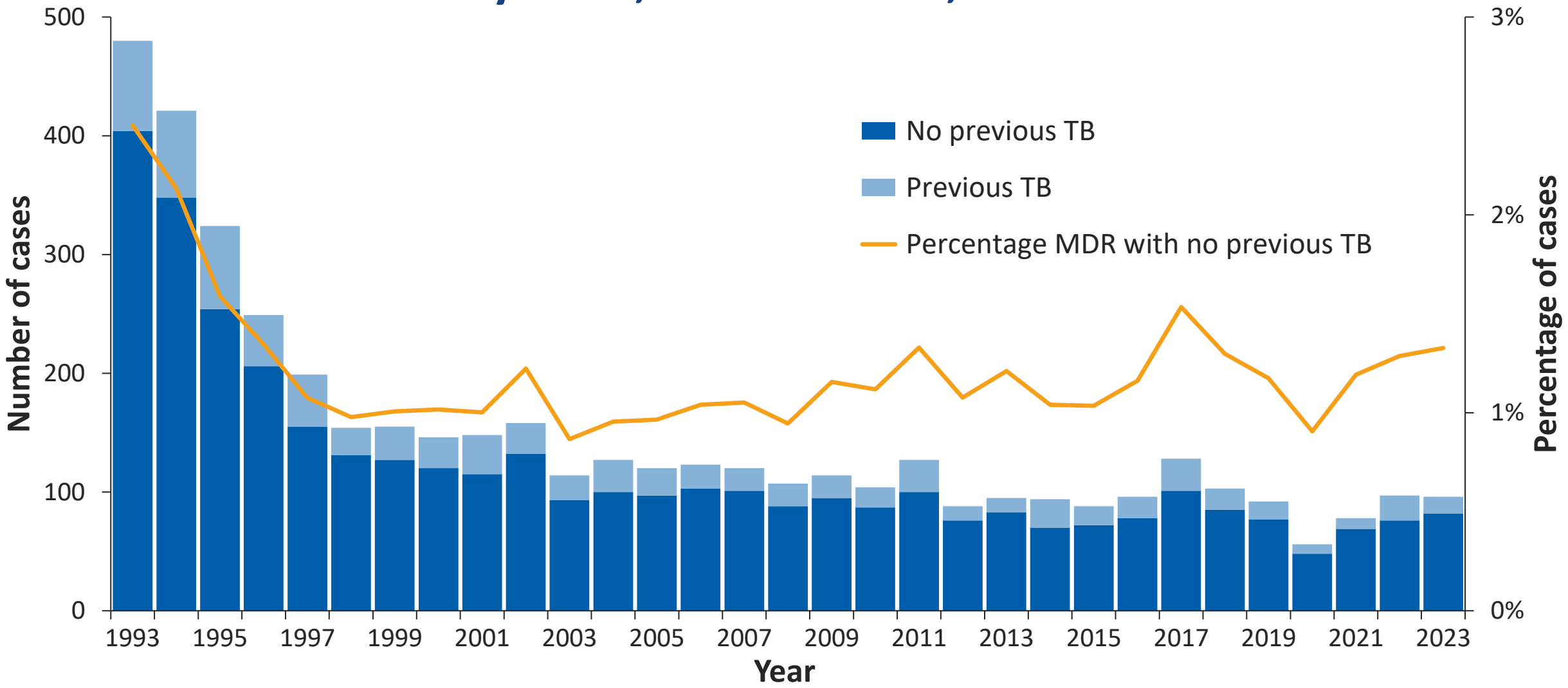
*Persons born in the United States, certain U.S. territories, or elsewhere to at least one U.S. citizen parent are categorized as U.S.-born. All other persons are categorized as non-U.S.–born.

Percentage of TB Cases by Age Group, United States, 2023 (N=9,633*)



*This total includes two TB cases with missing or unknown age. Percentages do not add up to 100% due to rounding.

Number and Percentage of Multidrug-Resistant (MDR)* TB Cases† by History of TB, United States, 1993–2023

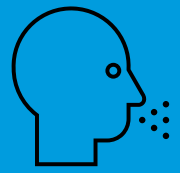


*Starting in 2023, information on drug resistance included results of molecular drug susceptibility testing in addition to growth-based susceptibility testing for isoniazid and rifampin. An isolate is considered resistant to isoniazid or rifampin if either the growth-based test or molecular test detects resistance.

†Excludes persons with unknown origin of birth.

When should we suspect TB?

Symptoms



Person

Tests

Symptoms of Tuberculosis

Non-specific Constitutional Symptoms

- Loss of appetite
- unexplained weight loss
- Night sweats,
- fever
- Fatigue

Respiratory Symptoms

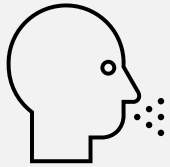
- Prolonged cough (3 weeks or longer)
- Shortness of breath
- Hemoptysis
- Chest pain

Symptoms Of Possible Extra-pulmonary TB

- Blood in the urine (TB of the kidney)
- Headache/confusion (TB meningitis)
- Back pain (TB of the spine)
- Hoarseness (TB of the larynx)

When should we suspect TB?

Symptoms



Person

Tests

Persons at Risk for Developing TB Disease

1

Those who have an increased likelihood of exposure to persons with TB disease

2

Those with clinical conditions that increase their risk of progressing from LTBI to TB disease

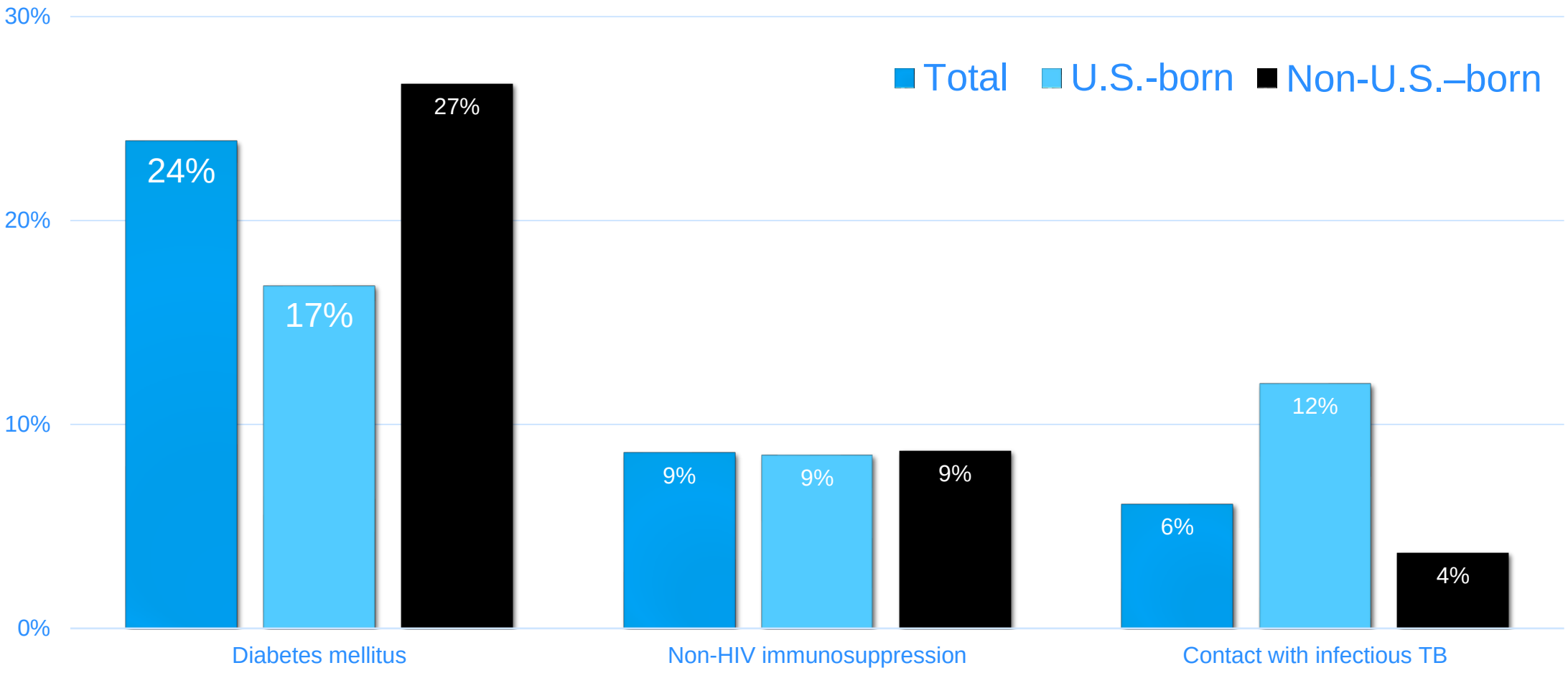
Increased Likelihood of Exposure to Persons with TB Disease

- Close contacts to person with infectious TB
- Residents and employees of high-risk congregate settings (e.g., correctional facilities, homeless shelters, health care facilities)
- Recent immigrants from TB-endemic regions of the world

Increased Risk for Progression to TB Disease

- HIV-infected persons
- Those with a history of prior, untreated TB or fibrotic lesions on chest radiograph
- Children ≤ 5 years with a positive skin test for latent tuberculosis
- Underweight or malnourished persons
- Substance abusers (such as smoking, alcohol abusers, or injection drug use)
- Those receiving biologics
- Those with certain medical conditions
  - Silicosis
  - Diabetes mellitus
  - Chronic renal failure/hemodialysis
  - Solid organ transplantation
  - Carcinoma of head or neck
  - Gastrectomy or jejunoileal bypass

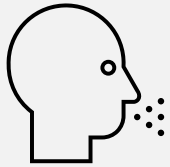
Percentage of Selected Risk Factors Among Persons with TB by Origin of Birth,* United States, 2021



*Persons born in the United States, certain U.S. territories, or elsewhere to at least one U.S. citizen parent are categorized as U.S.-born. All other persons are categorized as non-U.S.–born.

When should we suspect TB?

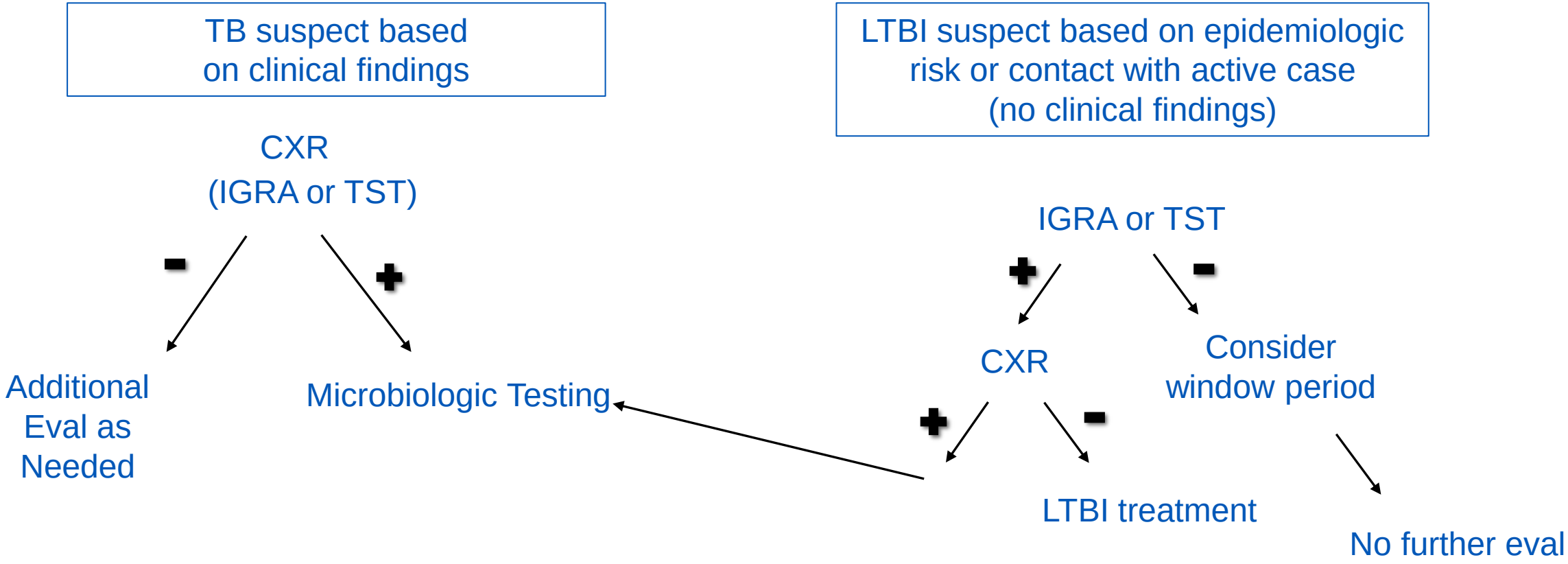
Symptoms



Person

Tests

Tuberculosis Tests



TB infection vs TB disease

LTBI

- No symptoms
- No abnormal clinical findings
- Normal x-ray
- Immunologic evidence of past infection (TST or IGRA)

TB DISEASE

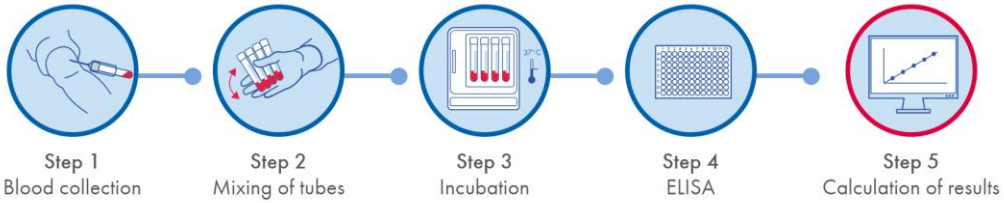
- Clinical signs or symptoms and/or
- Abnormal x-ray
- May or may not have positive immunologic testing
- Possible microbiologic confirmation

Tuberculin skin test (TST)

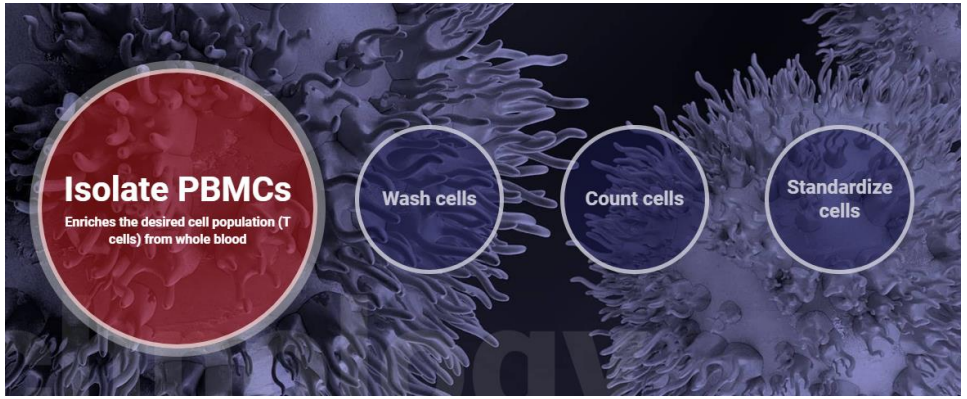
Interferon-gamma release assays

The QFT-Plus assay

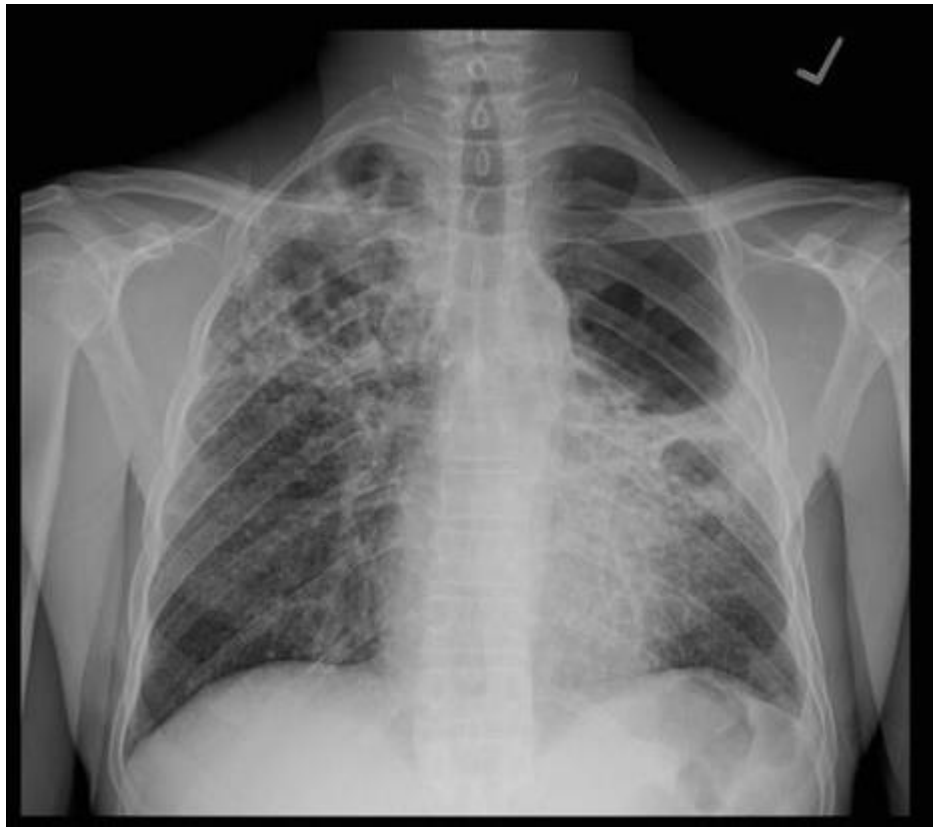
The QFT-Plus assay is an in-vitro diagnostic laboratory test that aids in the indirect detection of infection with MTB. It uses human whole blood, with patented assay technology based on the measurement of Interferon-gamma (IFN-γ) secreted from stimulated T-cells previously exposed to MTB. It is a straightforward laboratory test that involves the following steps:

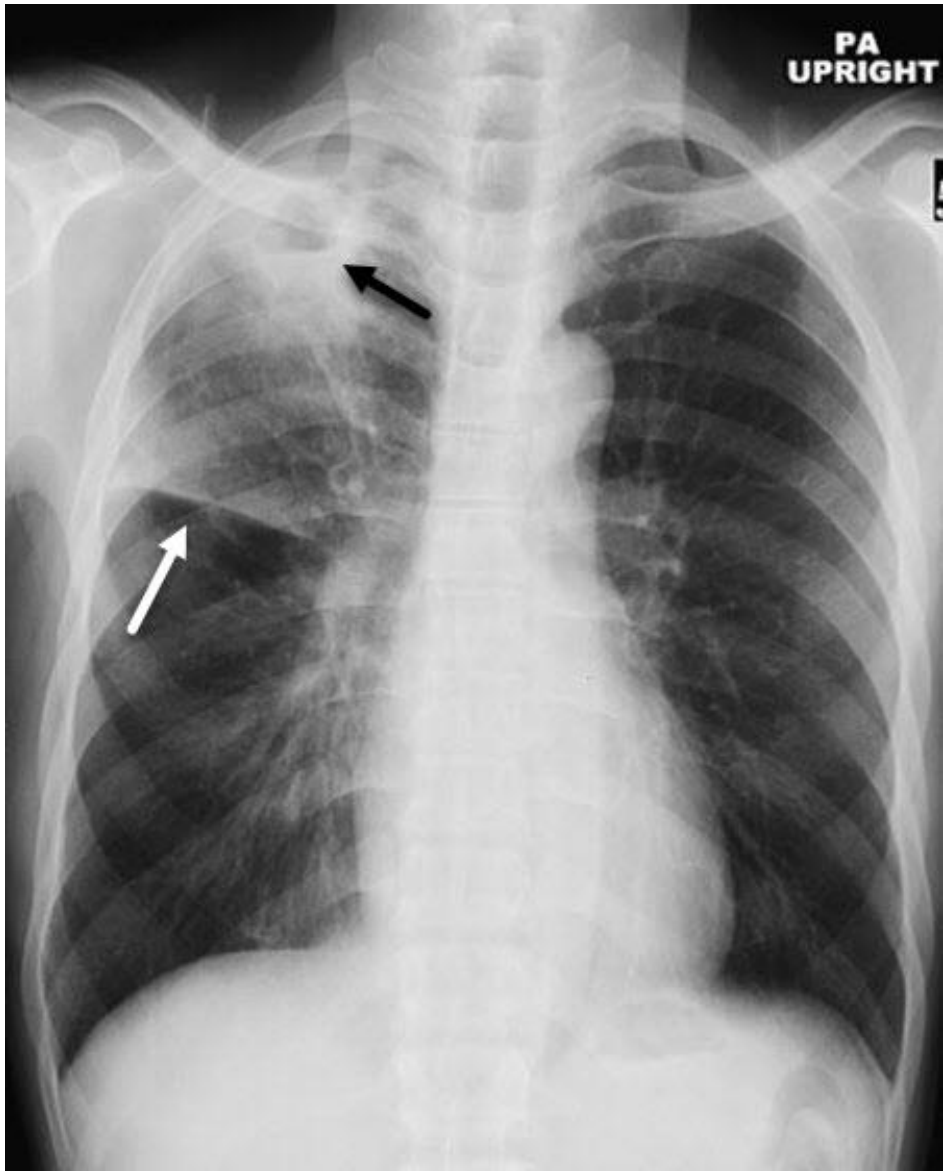


T-SPOT.TB

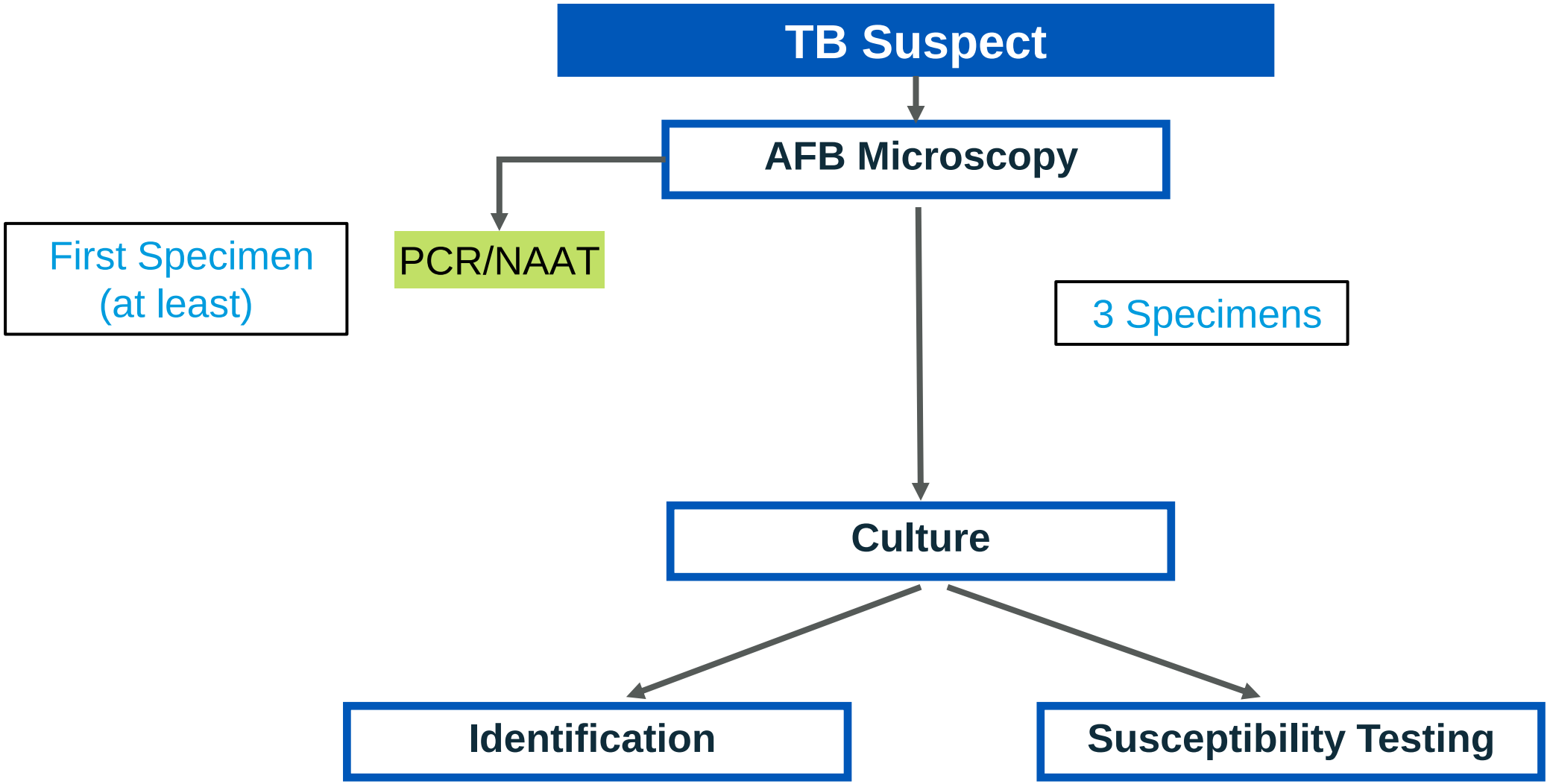


TB Radiology

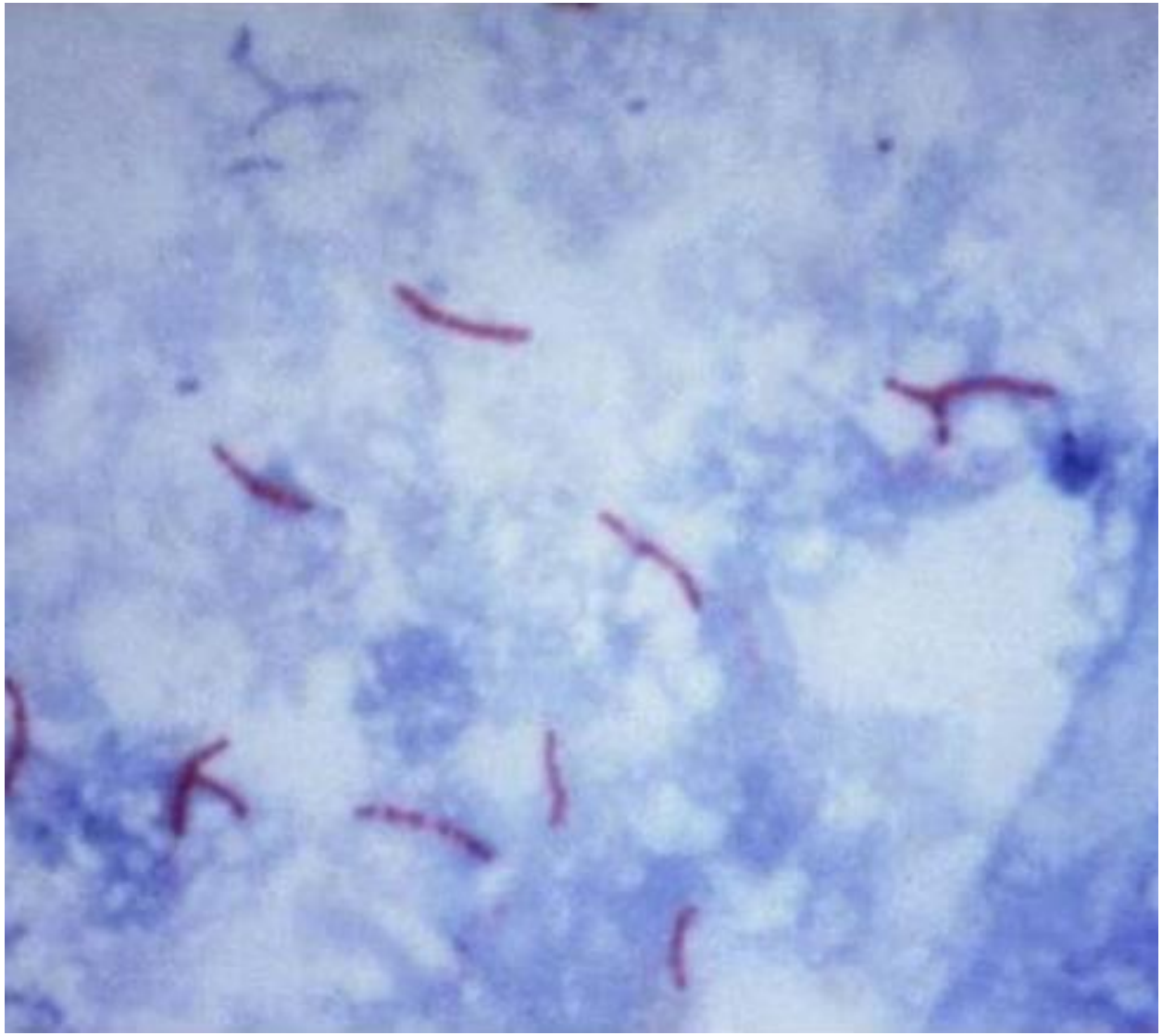




TB Diagnostic Algorithm



AFB smear



Xpert MTB/RIF Assay

A Tool to Diagnose Tuberculosis

KEY POINTS

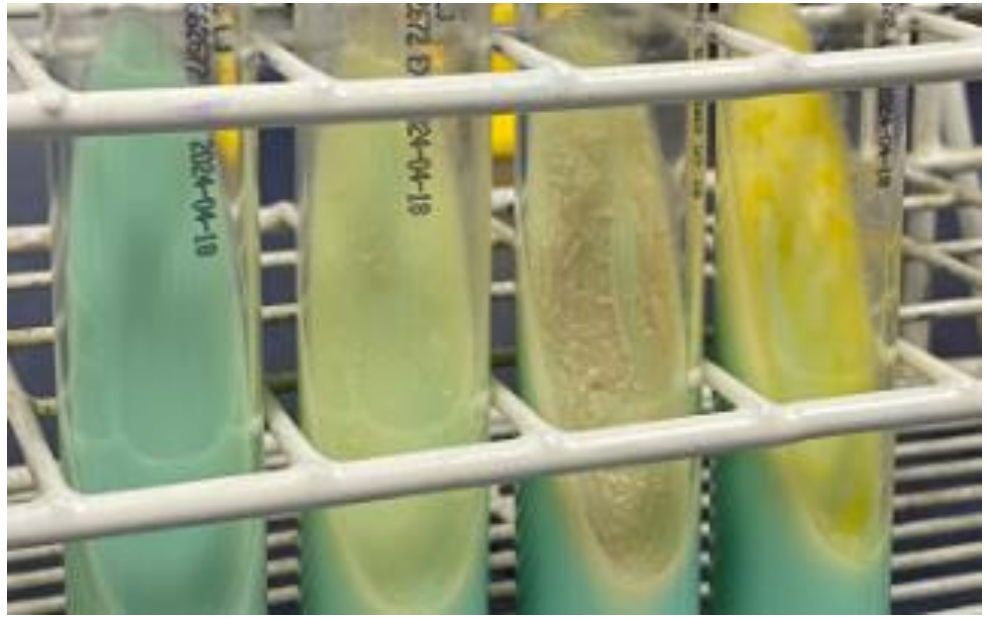
The Xpert MTB/RIF assay is a test that simultaneously detects *Mycobacterium tuberculosis* complex (MTBC) and resistance to rifampin (RIF), one of the most effective drugs used to treat tuberculosis (TB).

https://www.cdc.gov/tb/php/laboratory-information/xpert-mtb-rif-assay.html

Mycobacterial Culture

MYCOBACTERIA GROWTH INDICATOR TUBE (MGIT)

SOLID MEDIA



Drug resistance and susceptibility testing

When to suspect drug-resistance?

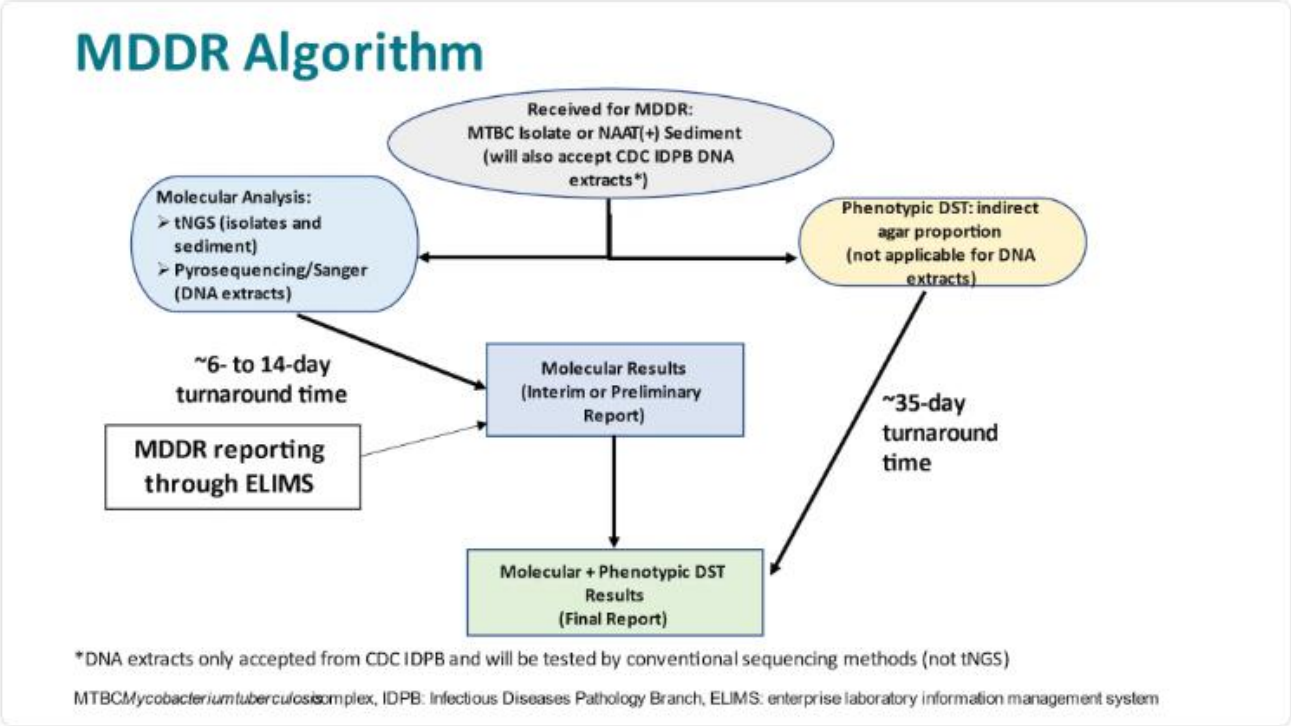
- Rifampin resistance detected on initial NAAT

The most important predictors of drug-resistant TB are:

- **Previous episode(s)** of TB treatment
- **Worsening clinical and/or radiographic findings** while on TB therapy
- History of **residence** in, or frequent travel to, a **region or country with a high prevalence of drug-resistant TB** (see **Chapter 1, *Epidemiology***)
- **Exposure to a person with known (or highly suspected) infectious drug-resistant TB,** or exposure to individuals in congregate settings where drug resistance has been documented

HTTPS://WWW.CURRYTBCENTER.UCSF.EDU/PRODUCTS/PAGE/CHAPTER-2-DIAGNOSIS

Molecular Detection of Drug Resistance (MDDR) in Mycobacterium tuberculosis Complex by DNA Sequencing User Guide



Testing algorithm for the Molecular Detection of Drug Resistance (MDDR) service

tNGS: targeted next generation sequencing assay, NAAT: nucleic acid amplification testing

https://www.cdc.gov/tb/php/laboratory-information/mddr-user-guide.html

Treatment of TB: RIPE

Drug Regimens for Microbiologically Confirmed Pulmonary Tuberculosis Caused by Drug-Susceptible Organisms

Regimen	Intensive Phase		Continuation Phase		Range of Total Doses
	Drug[a]	Interval and Dose[b] (Minimum Duration)	Drugs	Interval and Dose[b,c] (Minimum Duration)	
1	INH RIF PZA EMB	7 d/wk for 56 doses (8 wk), or 5 d/wk for 40 doses (8 wk)	INH RIF	7 d/wk for 126 doses (18 wk), or 5 d/wk for 90 doses (18 wk)	182–130

Treatment of TB: 4-month rifapentine with moxifloxacin

RESEARCH SUMMARY

Four-Month Rifapentine Regimens with or without Moxifloxacin for Tuberculosis

Dorman SE et al. DOI: 10.1056/NEJMoa2033400

CLINICAL PROBLEM

The standard treatment of drug-susceptible pulmonary tuberculosis is a 6-month course of a daily rifamycin-based antimicrobial regimen. A more potent regimen with improved rifamycin exposure might shorten treatment duration, potentially improving adherence and reducing adverse effects and costs.

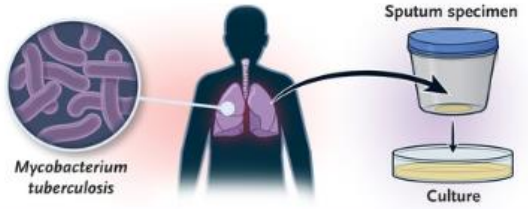
CLINICAL TRIAL

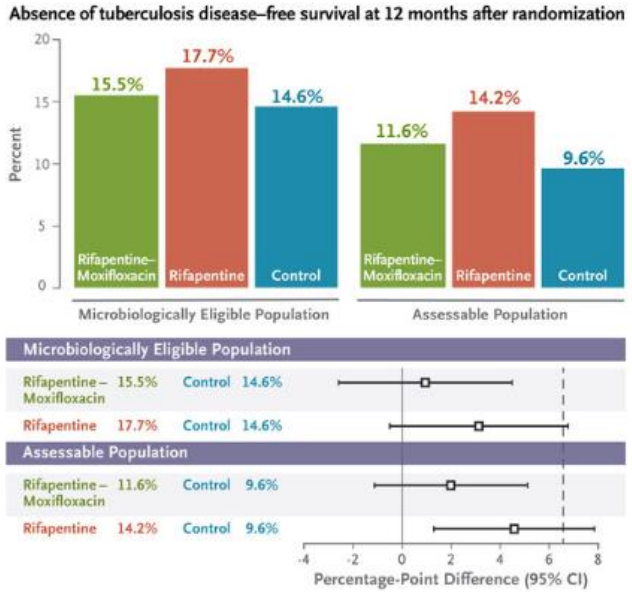
Design: A randomized, open-label, noninferiority trial of two 4-month rifapentine-containing regimens, as compared with a standard 6-month rifampin-containing regimen, for the treatment of drug-susceptible tuberculosis.

Intervention: 2516 participants 12 years of age or older with newly diagnosed tuberculosis were randomly assigned to a 6-month control regimen, a 4-month regimen in which rifampin was replaced with rifapentine (rifapentine group), or a 4-month regimen in which rifampin was replaced with rifapentine and ethambutol with moxifloxacin (rifapentine–moxifloxacin group). The primary efficacy outcome was survival free of tuberculosis at 12 months after randomization, and safety was assessed through day 14 after the last dose of a trial drug.

RESULTS

Efficacy: The rifapentine–moxifloxacin regimen, but not the rifapentine regimen, was shown to be noninferior to the control regimen.





The NEW ENGLAND JOURNAL of MEDICINE

RESEARCH SUMMARY

A 24-Week, All-Oral Regimen for Rifampin-Resistant Tuberculosis

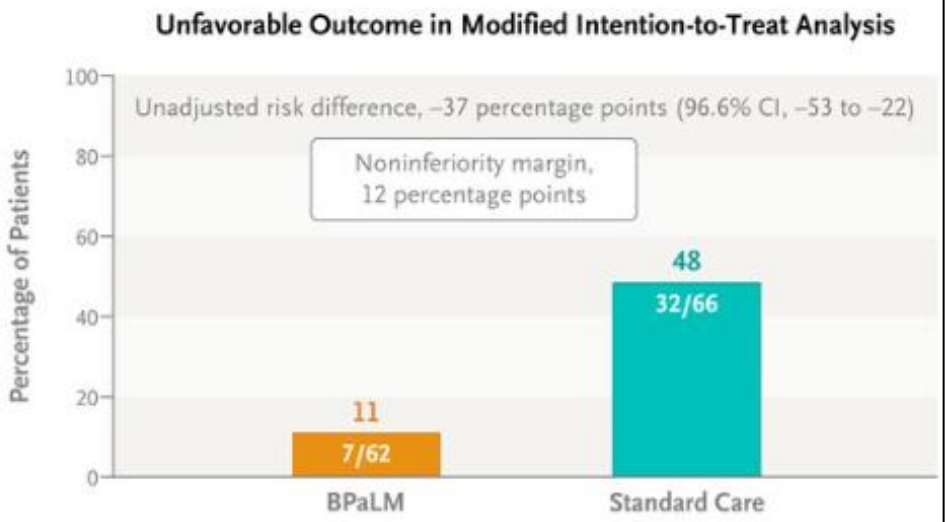
Nyang'wa B-T et al. DOI: 10.1056/NEJMoa2117166

CLINICAL PROBLEM

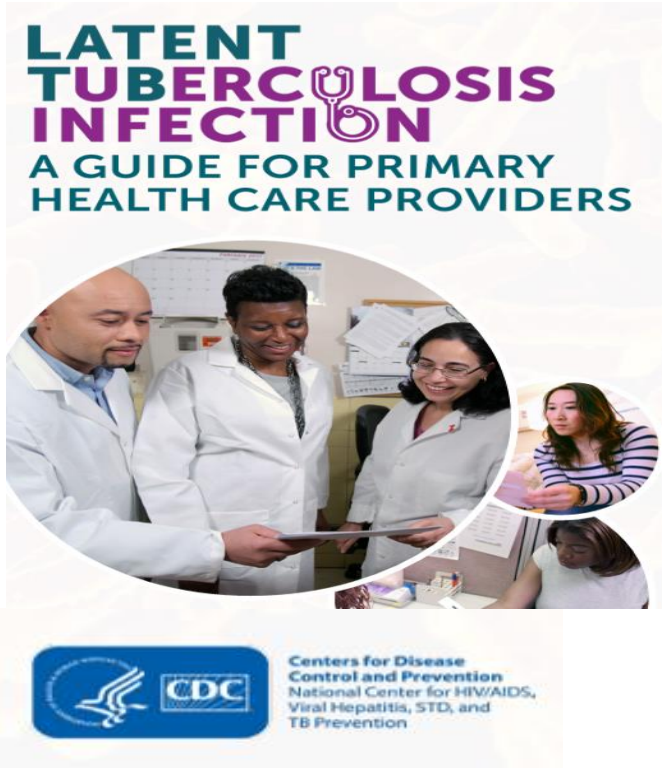
The currently recommended duration of treatment for rifampin-resistant tuberculosis is 9 to 20 months, and treatment involves up to 20 tablets per day; unfavorable outcomes are common. Effective treatments of shorter duration are needed.

CLINICAL TRIAL

Design: In the second stage of a phase 2–3, multicenter, open-label, randomized, controlled, noninferiority trial, the efficacy and safety of a 24-week, all-oral regimen containing bedaquiline, pretomanid, linezolid, and moxifloxacin (BPaLM) in patients with rifampin-resistant tu-



LTBI and importance of public health/healthcare partnership



Treatment Regimens

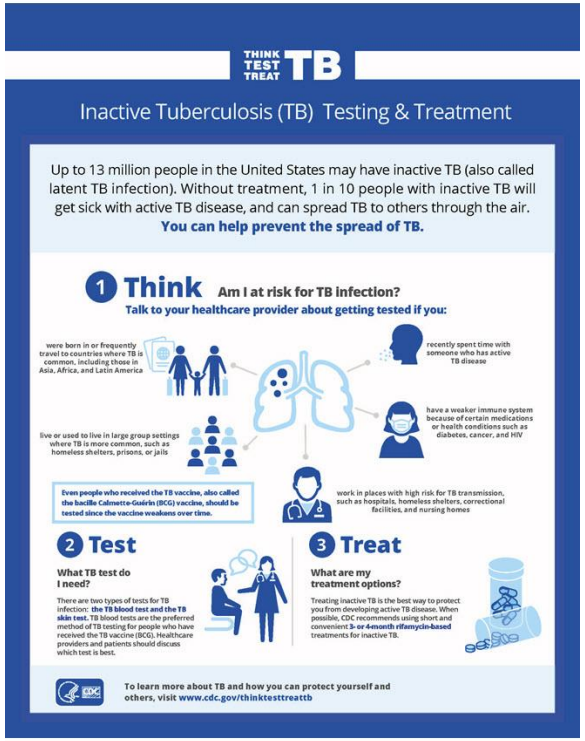
- **Three Months of Once-weekly Isoniazid (INH) plus Rifapentine (RPT) Regimen (3HP)**
- **Four Months of Daily Rifampin (RIF) Regimen (4R)**
- **Six or Nine Months of Daily Isoniazid (INH) Regimens (6H or 9H)**

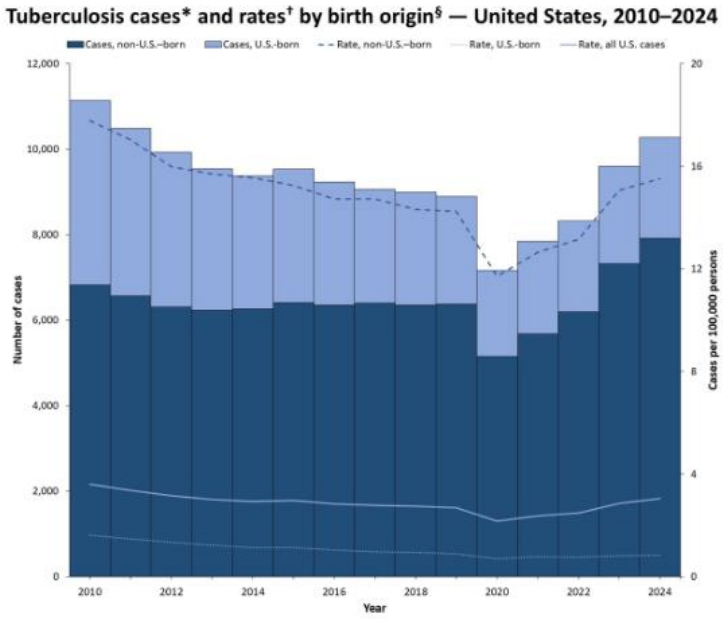
Organization of TB Services in the United States

National TB Program

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

David M. Lewinsohn,[1,a] Michael K. Leonard,[2,a] Philip A. LoBue,[3,a] David L. Cohn,[4] Charles L. Daley,[5] Ed Desmond,[6] Joseph Keane,[7] Deborah A. Lewinsohn,[1] Ann M. Loeffler,[8] Gerald H. Mazurek,[3] Richard J. O'Brien,[9] Madhukar Pai,[10] Luca Richeldi,[11] Max Salfinger,[12] Thomas M. Shinnick,[3] Timothy R. Sterling,[13] David M. Warshauer,[14] and Gail L. Woods[15]





- Most core activities of the National TB Program are administered by the CDC

National TB Program

- Division of Tuberculosis Elimination provides categorical funding for 67 programs through cooperative agreements with
- All 50 states
- 9 large cities (including Washington DC)
- 5 U.S. territories (Guam, AS, CNMI, PR, USVI)
- 3 freely-associated nations (FSM, RMI, Palau)

U.S. National TB Program jurisdictions

- 100+ metropolitan areas with pops. >500,000
- 3,143 counties

Local TB Jurisdiction Functions

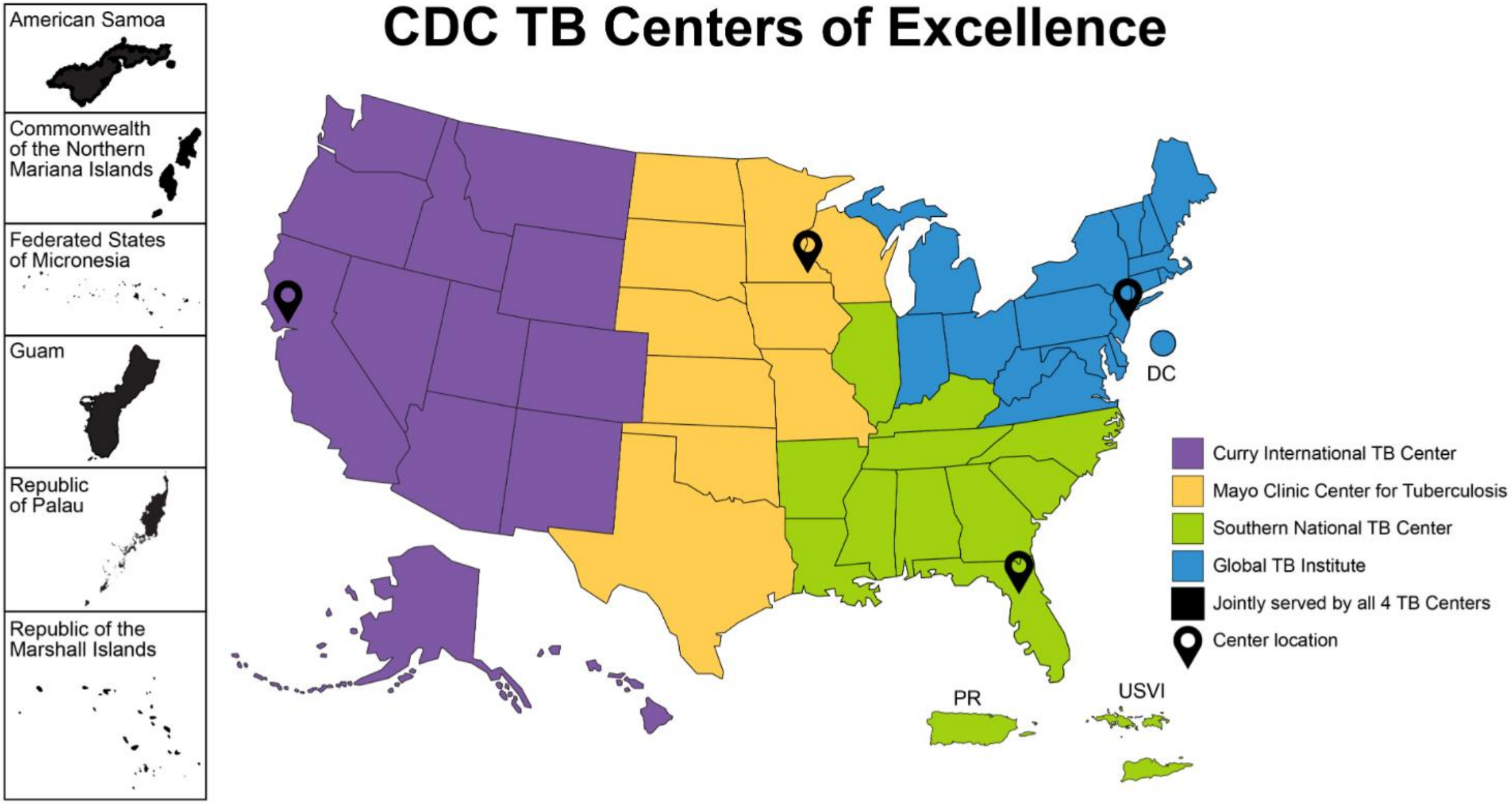
- Case management
  - DOT
- Contact investigations
- Collaboration with private medical providers
- Direct medical care, at many sites
- Program evaluation
- TB surveillance

Public/Private Partnership

- **Diagnosis and treatment of LTBI**
- Patient monitoring/management of co-morbidities
- Social and psychological support
- Alignment of messaging
- Pediatric co-management

- 55% of TB patients receive some TB care in private sector

CDC TB Centers of Excellence



TB Support

CDC and its domestic and international partners are working together to eliminate this deadly disease.

- National TB Controllers Association
- Stop TB USA, We Are TB
- TB Elimination Alliance
- Stop TB Partnership

Thank you