



Center for
Tuberculosis

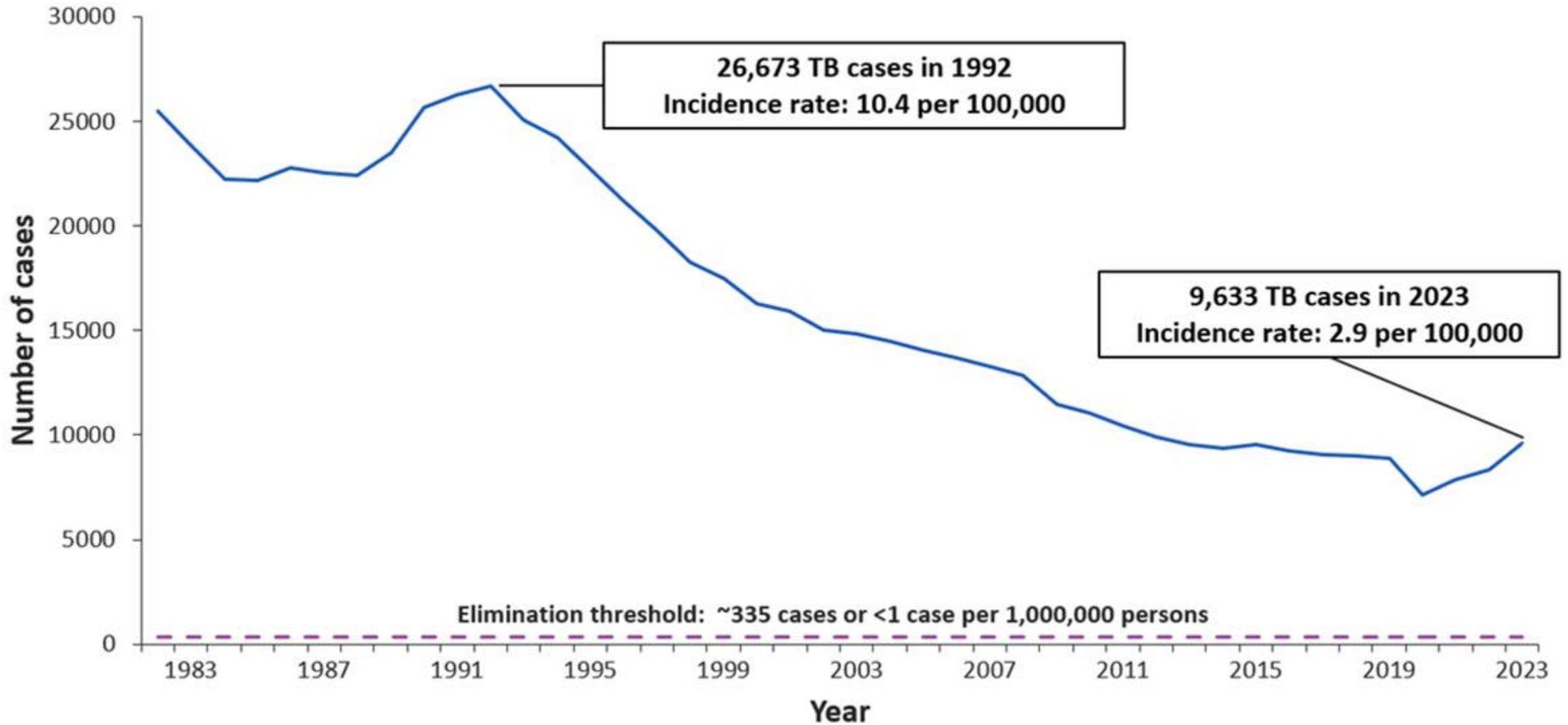
Fundamentals of Tuberculosis

James Gaensbauer, MD MScPH

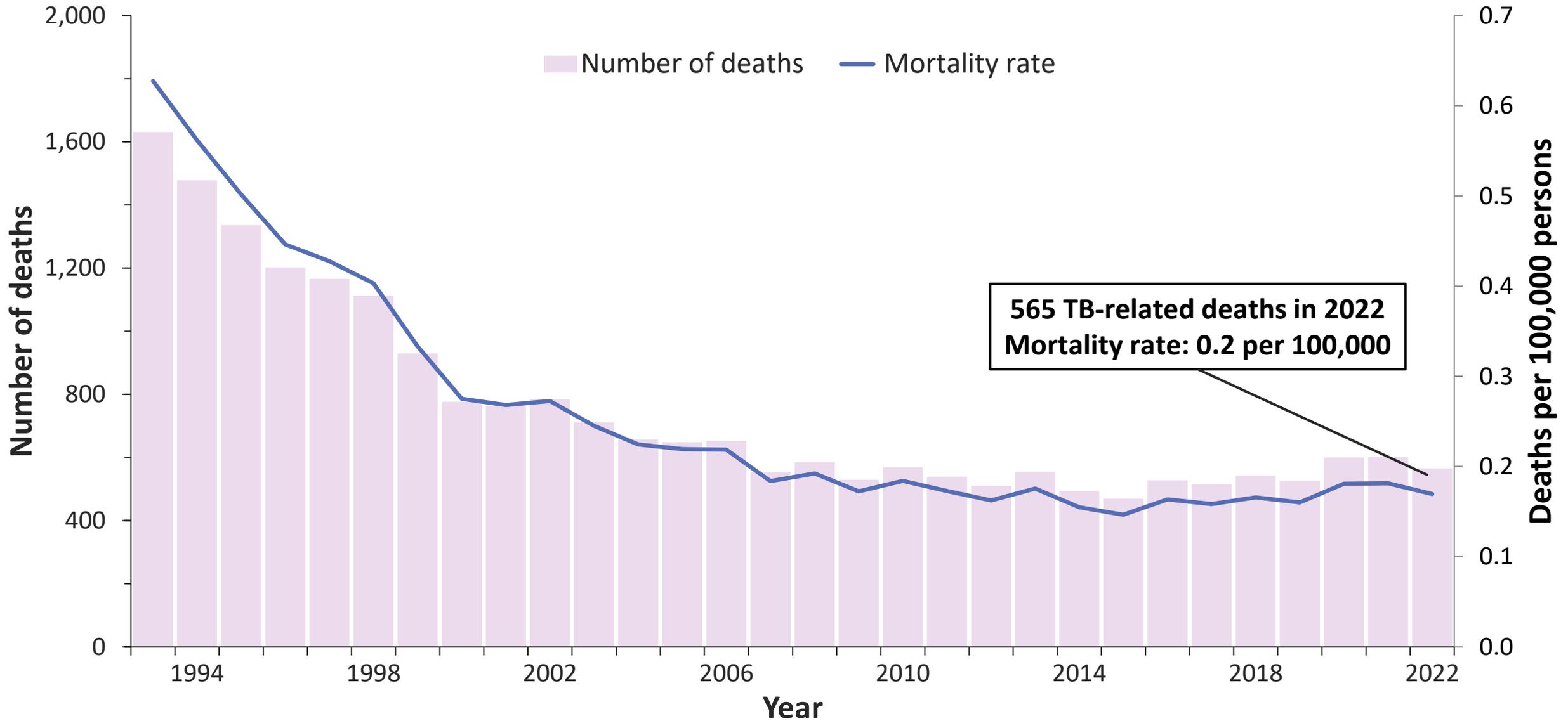
Associate Professor of Pediatric and Adolescent Medicine

Medical Director of Education and Training, Mayo Clinic Center for Tuberculosis

Progress Towards TB Elimination, United States, 1982–2023

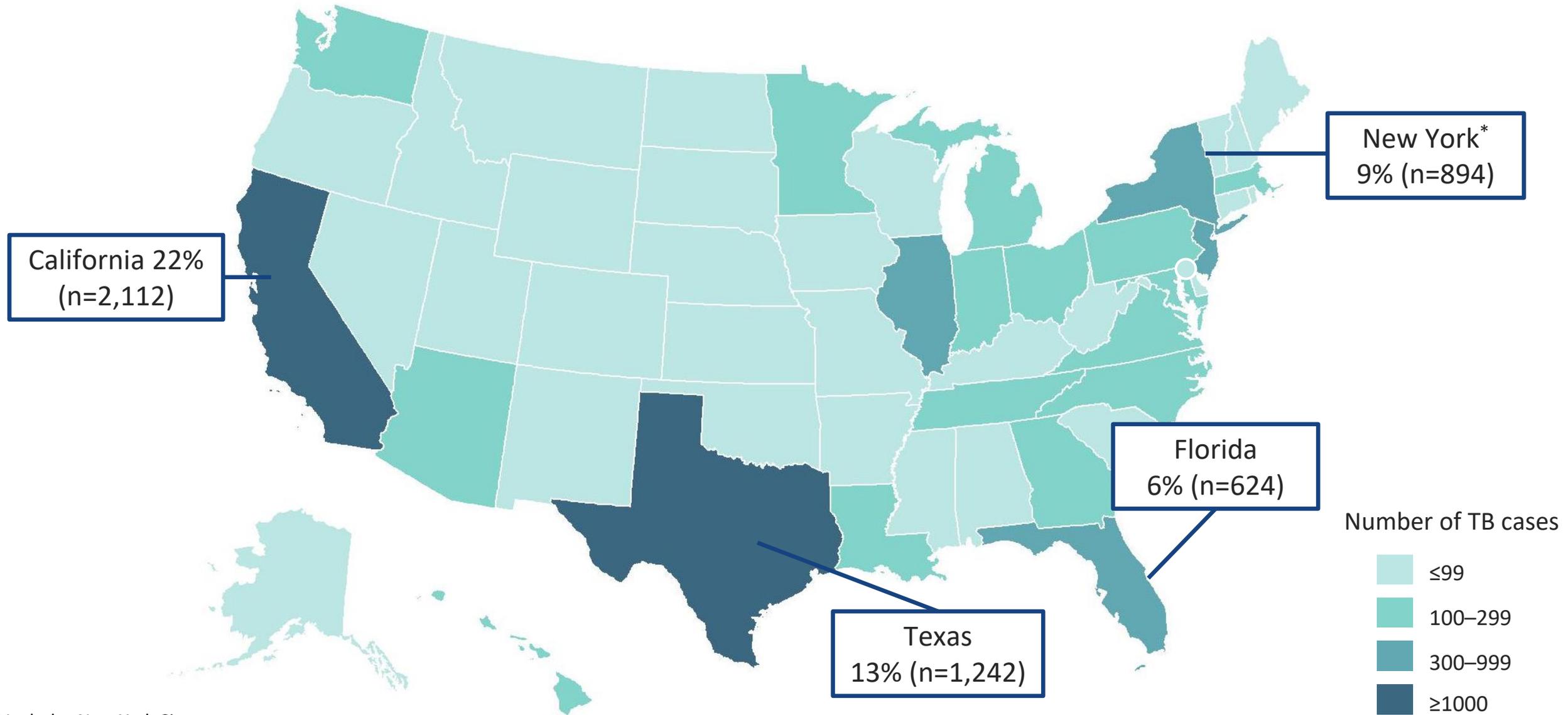


TB-Related Deaths* and Mortality Rates, United States, 1993–2022



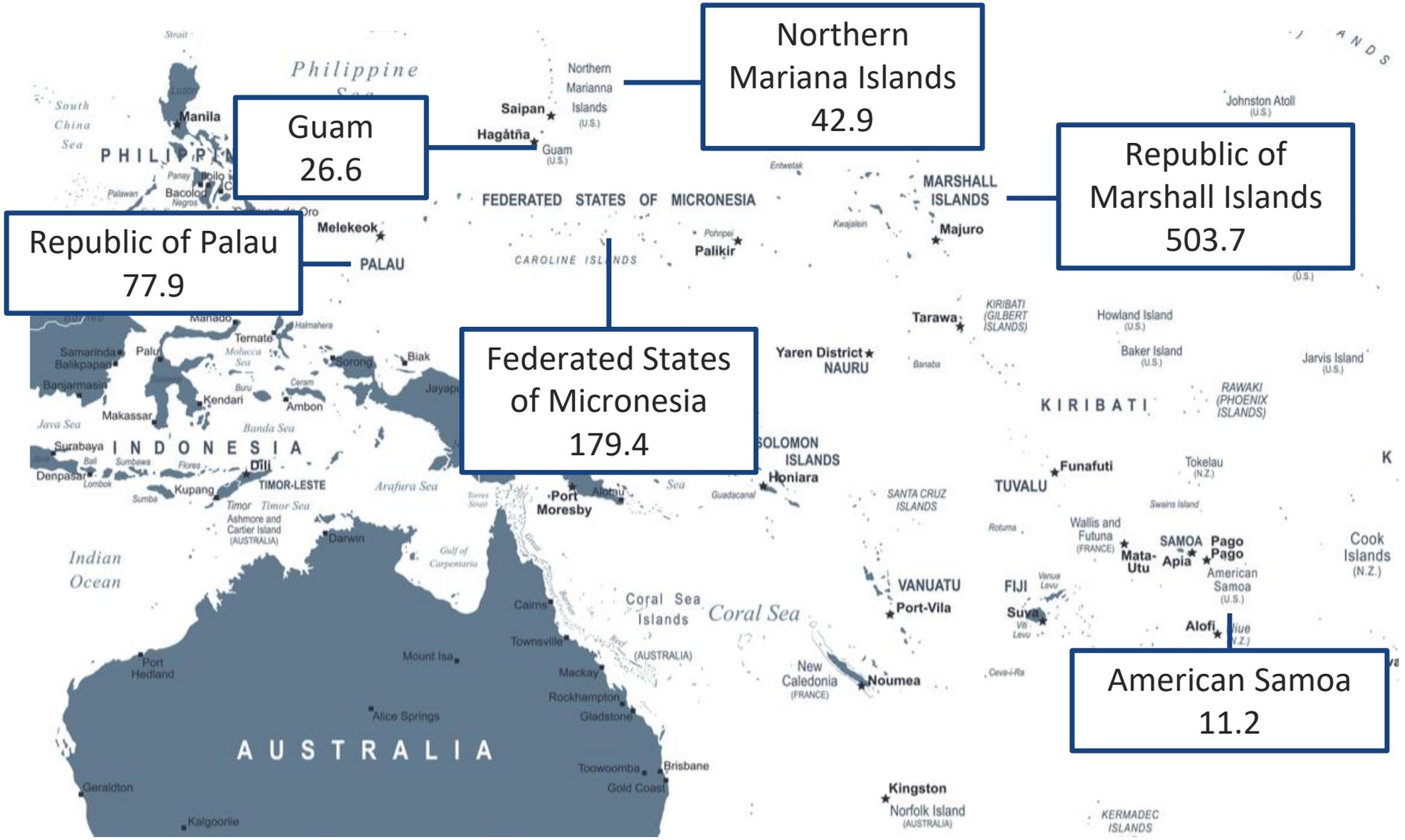
*National Vital Statistics System Underlying Cause of Death (based on deaths reported through 2022)

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



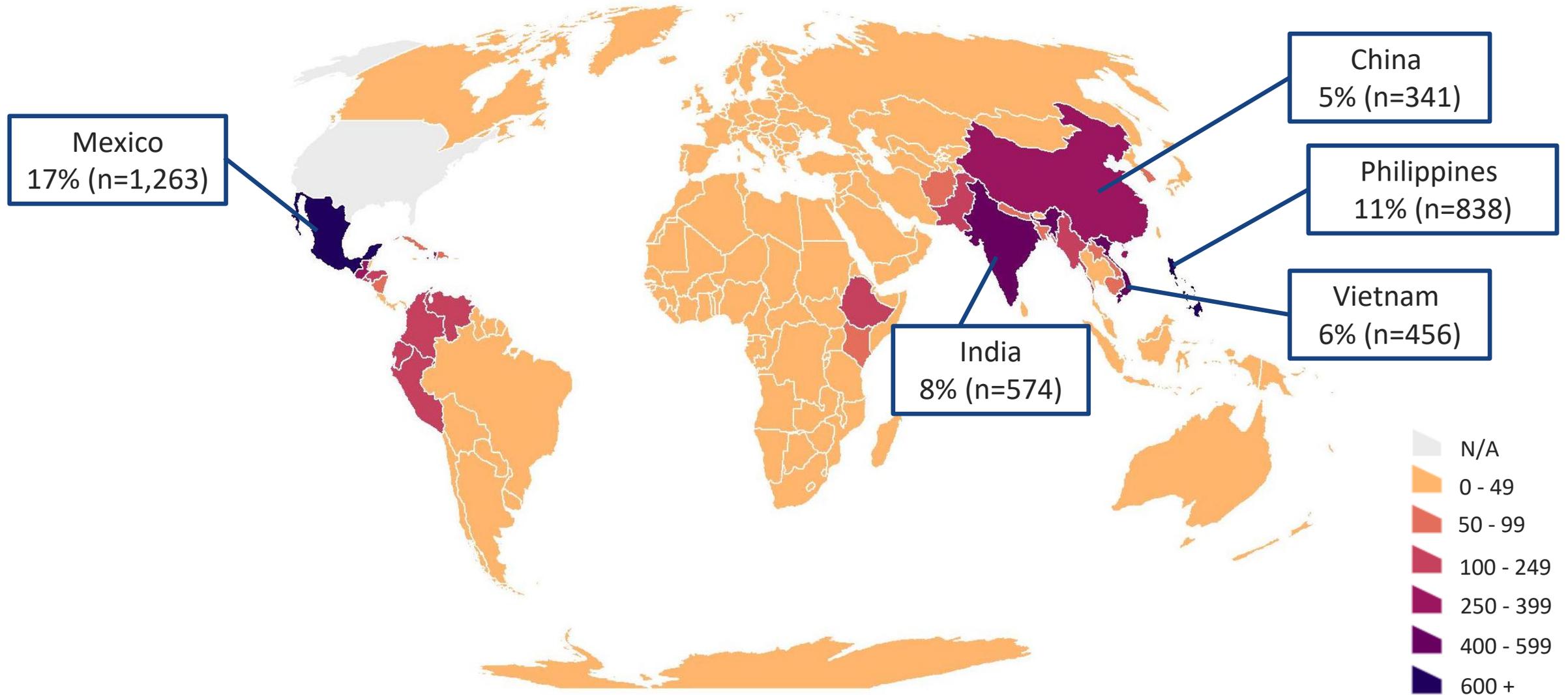
* Includes New York City

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



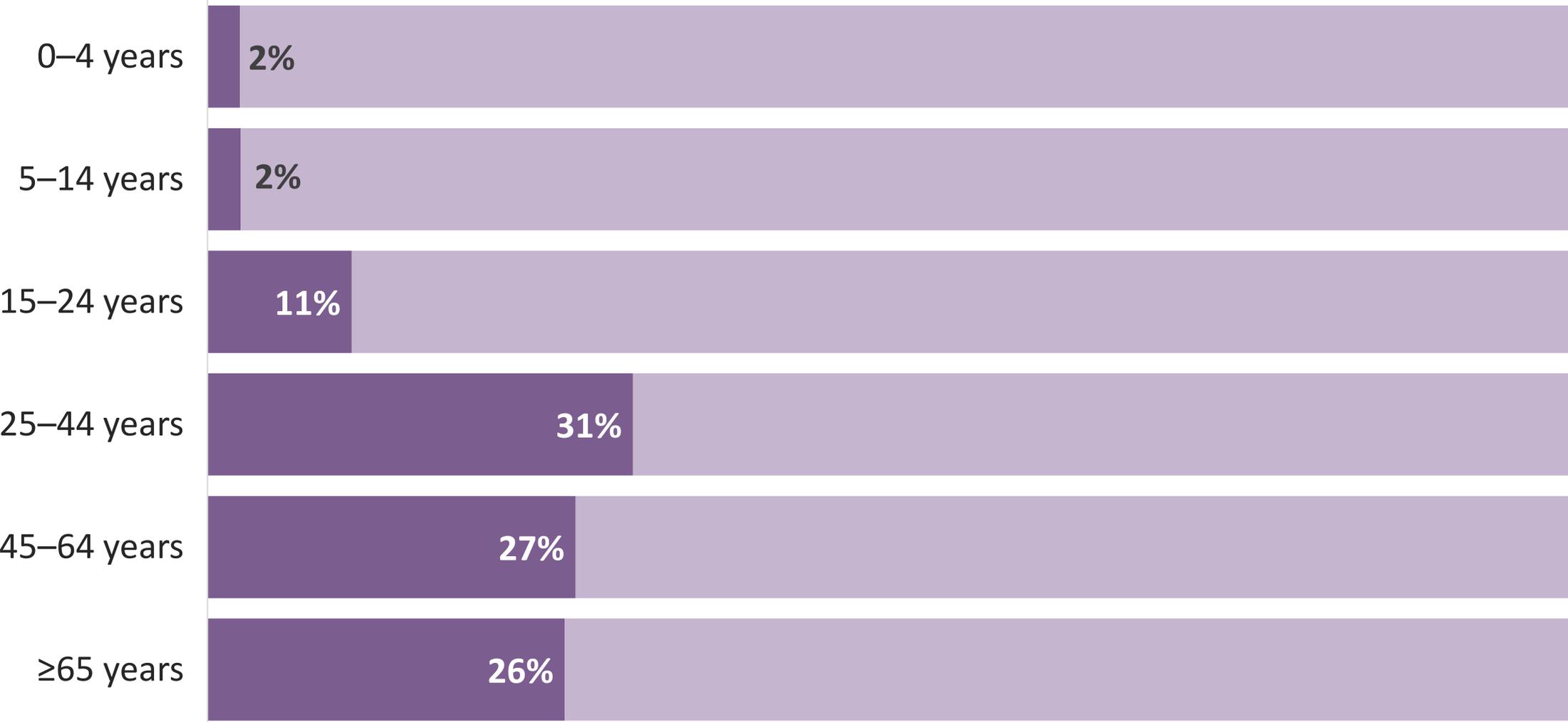
*Cases per 100,000 persons

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



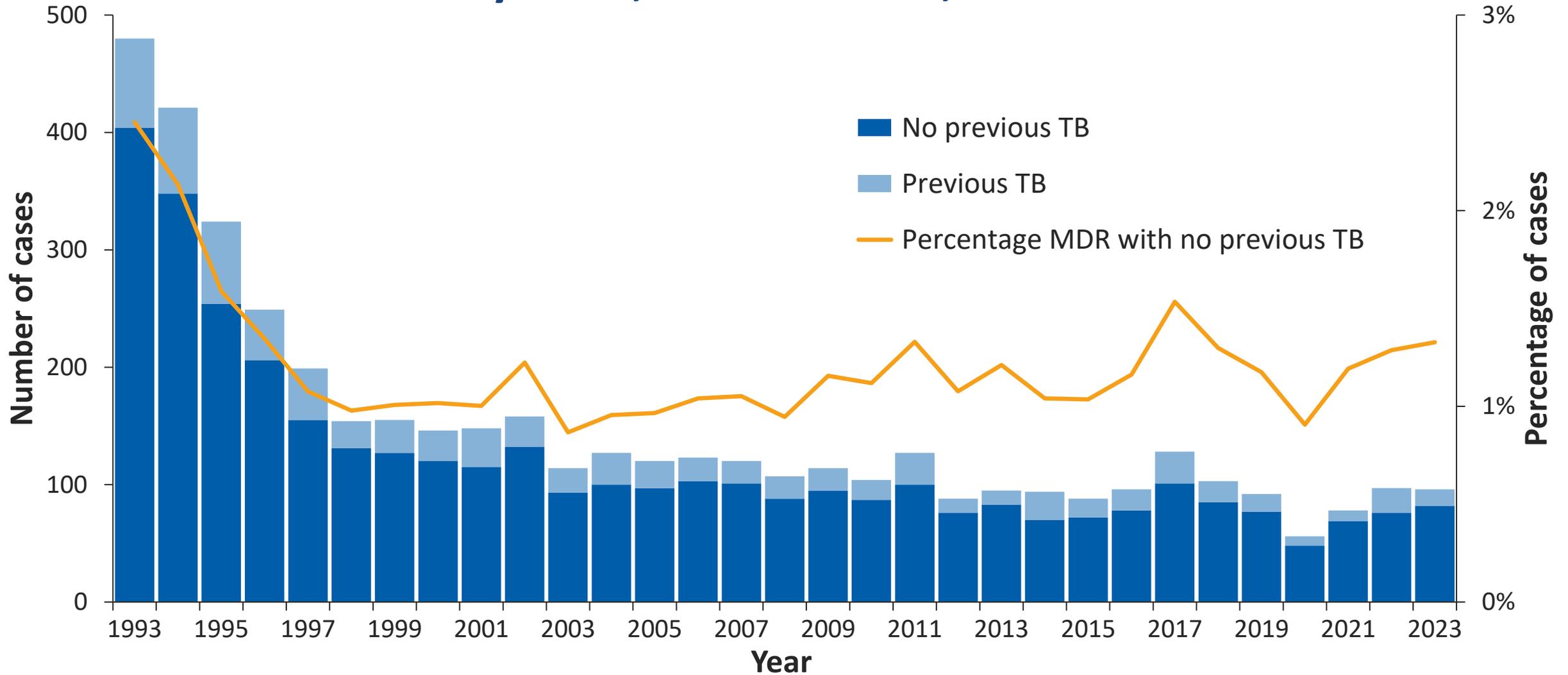
*Persons born in the United States, certain U.S. territories, or elsewhere to at least one U.S. citizen parent are categorized as U.S.-born. All other persons are categorized as non-U.S.–born.

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.

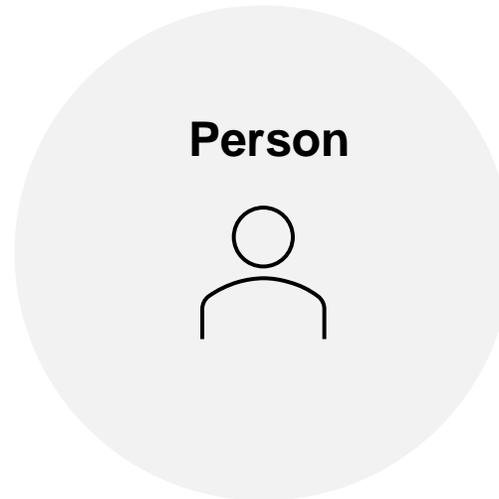
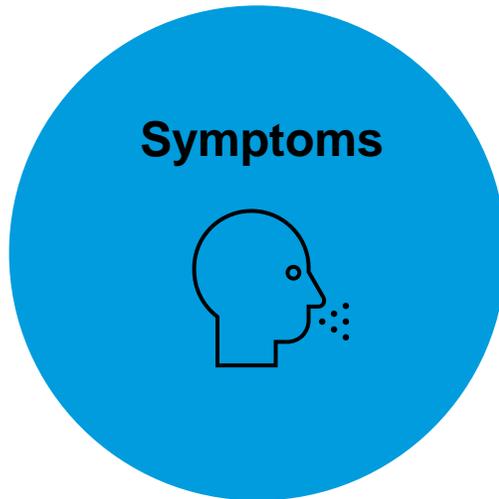
Number and Percentage of Multidrug-Resistant (MDR)* TB Cases† by History of TB, United States, 1993–2023



*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 of Tuberculosis

Non-specific Constitutional Symptoms

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

Respiratory Symptoms

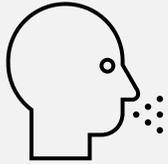
- Prolonged cough (3 weeks or longer)
- Shortness of breath
- Hemoptysis
- Chest pain

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

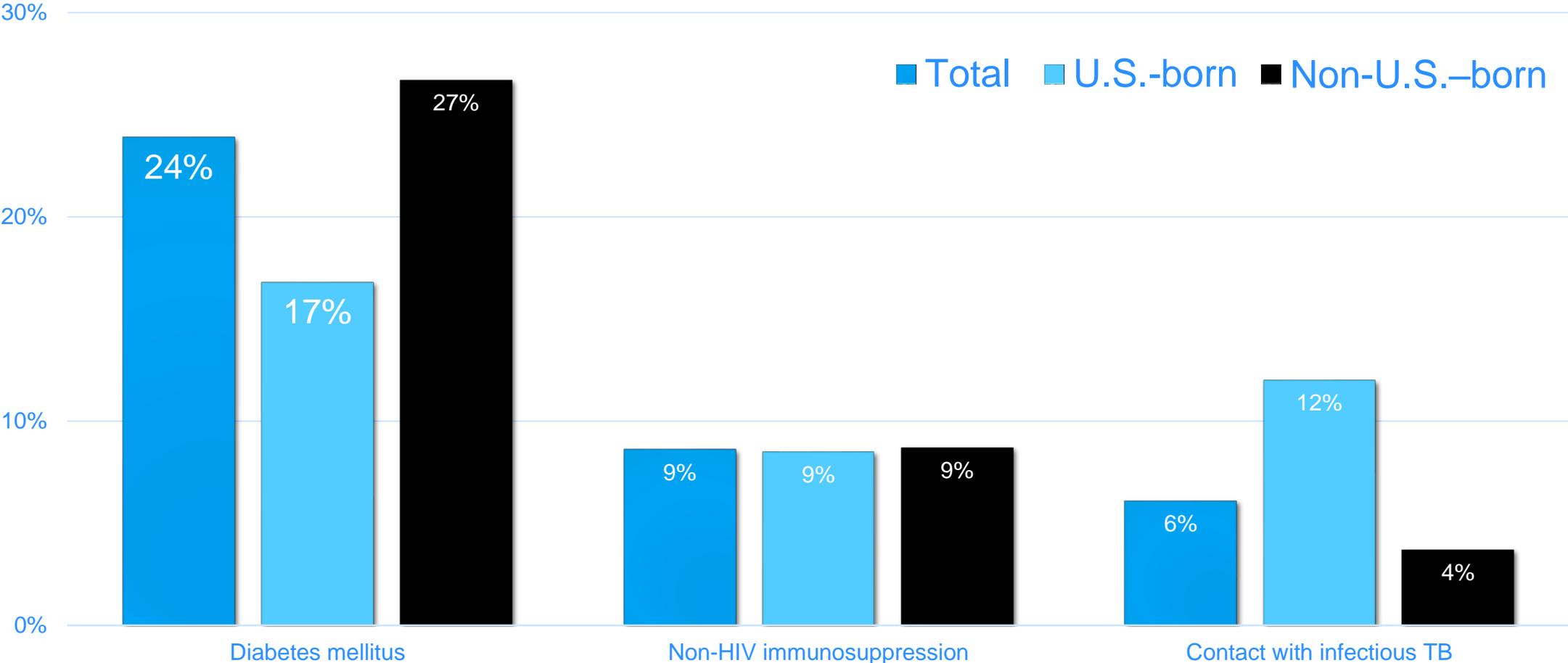
Increased Likelihood of Exposure to Persons with TB Disease

- 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 jejunioileal bypass

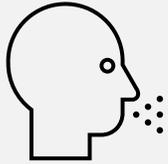
Percentage of Selected Risk Factors Among Persons with TB by Origin of Birth,* United States, 2021



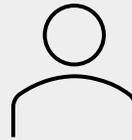
*Persons born in the United States, certain U.S. territories, or elsewhere to at least one U.S. citizen parent are categorized as U.S.-born. All other persons are categorized as non-U.S.-born.

When should we suspect TB?

Symptoms



Person



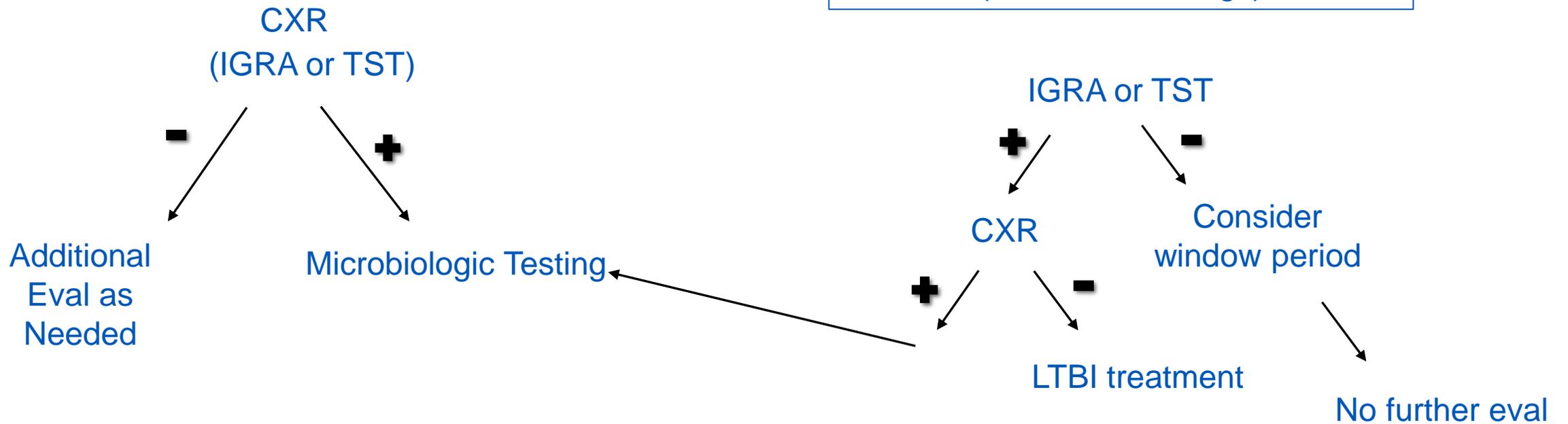
Tests



Tuberculosis Tests

TB suspect based on clinical findings

LTBI suspect based on epidemiologic risk or contact with active case (no clinical findings)



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

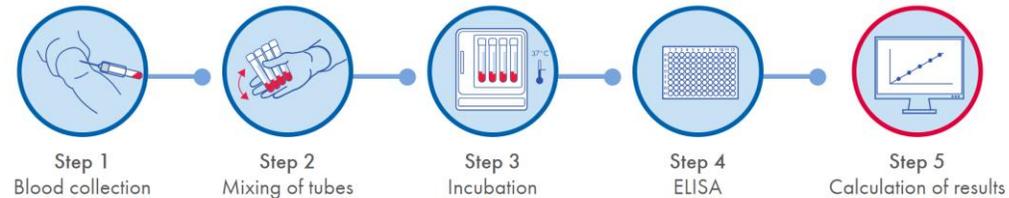


Tuberculin skin test (TST)

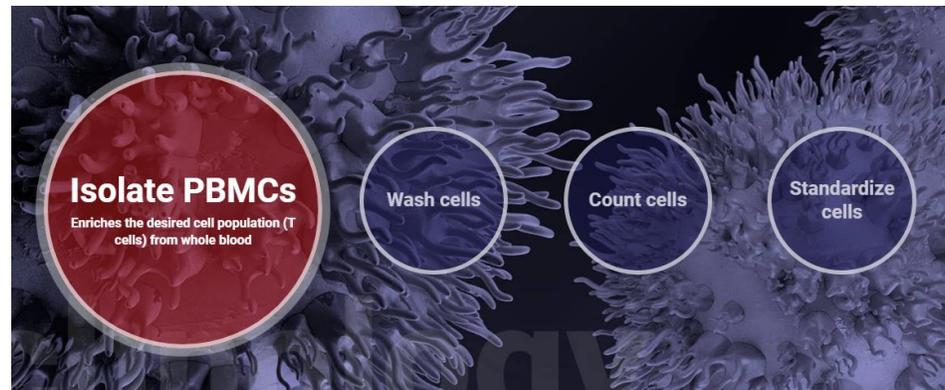
Interferon-gamma release assays

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:



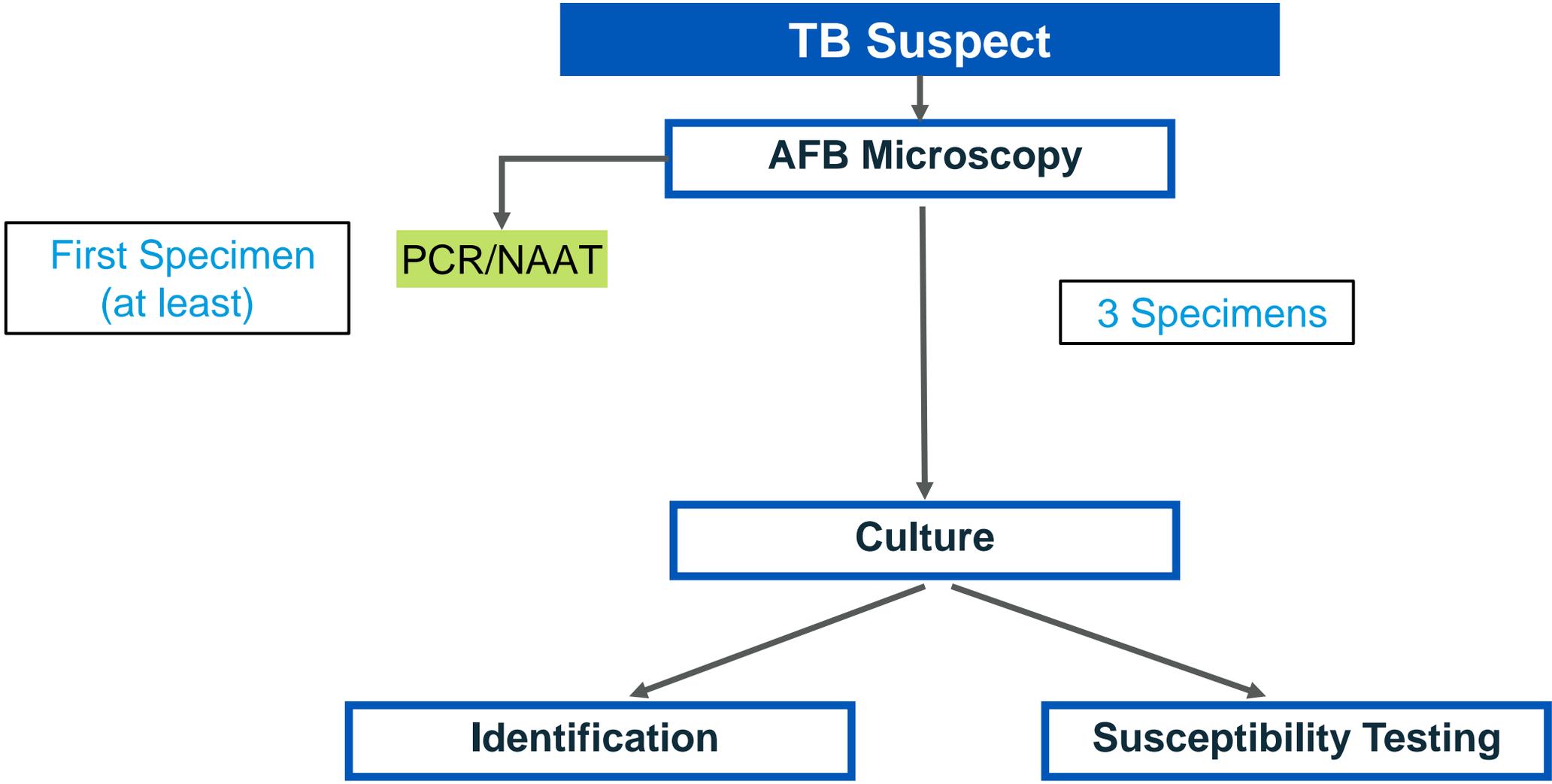
T-SPOT[®].TB



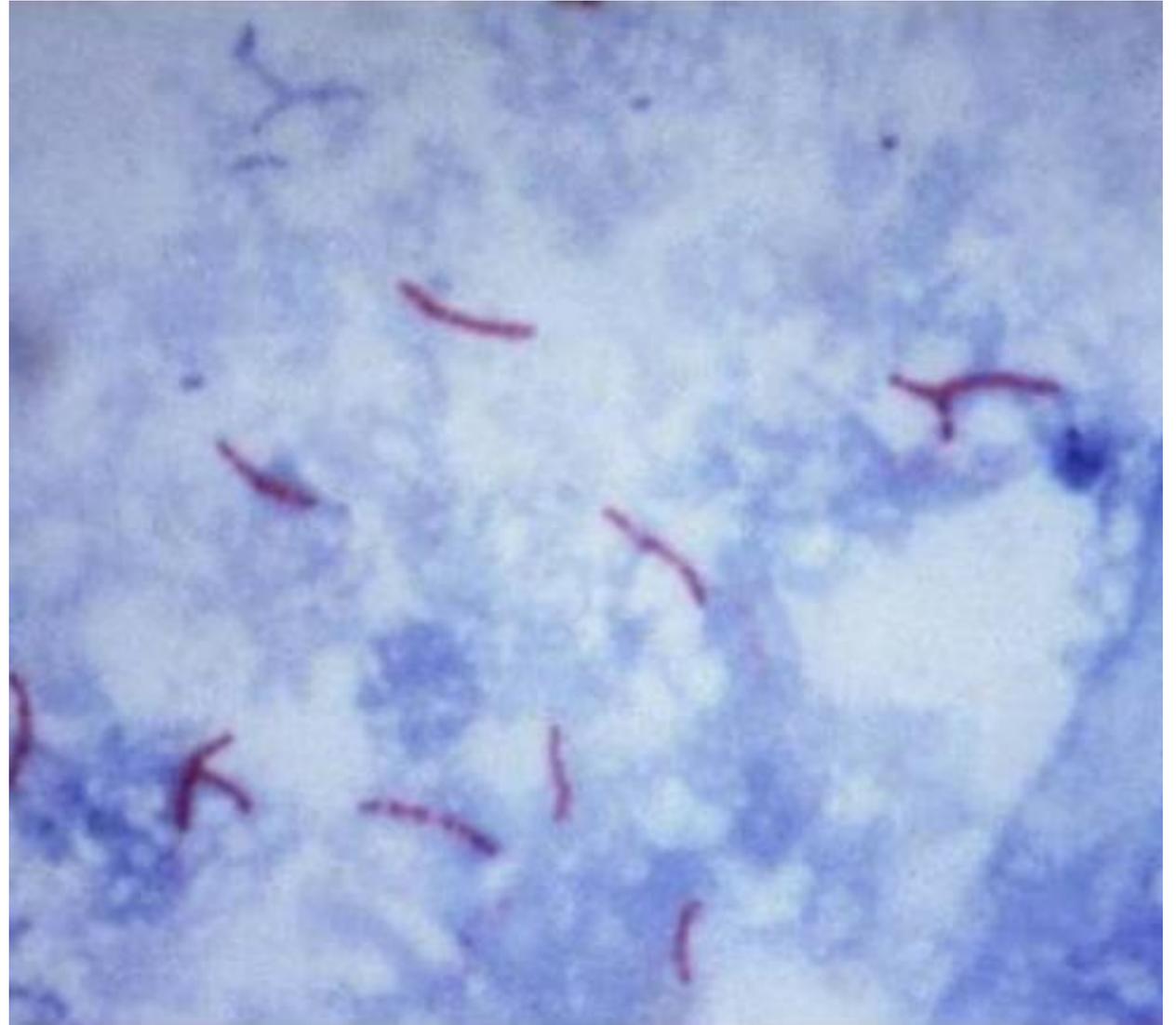
TB Radiology



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).



Mycobacterial Culture

MYCOBACTERIA GROWTH
INDICATOR TUBE (MGIT)



SOLID MEDIA



Drug resistance and susceptibility testing

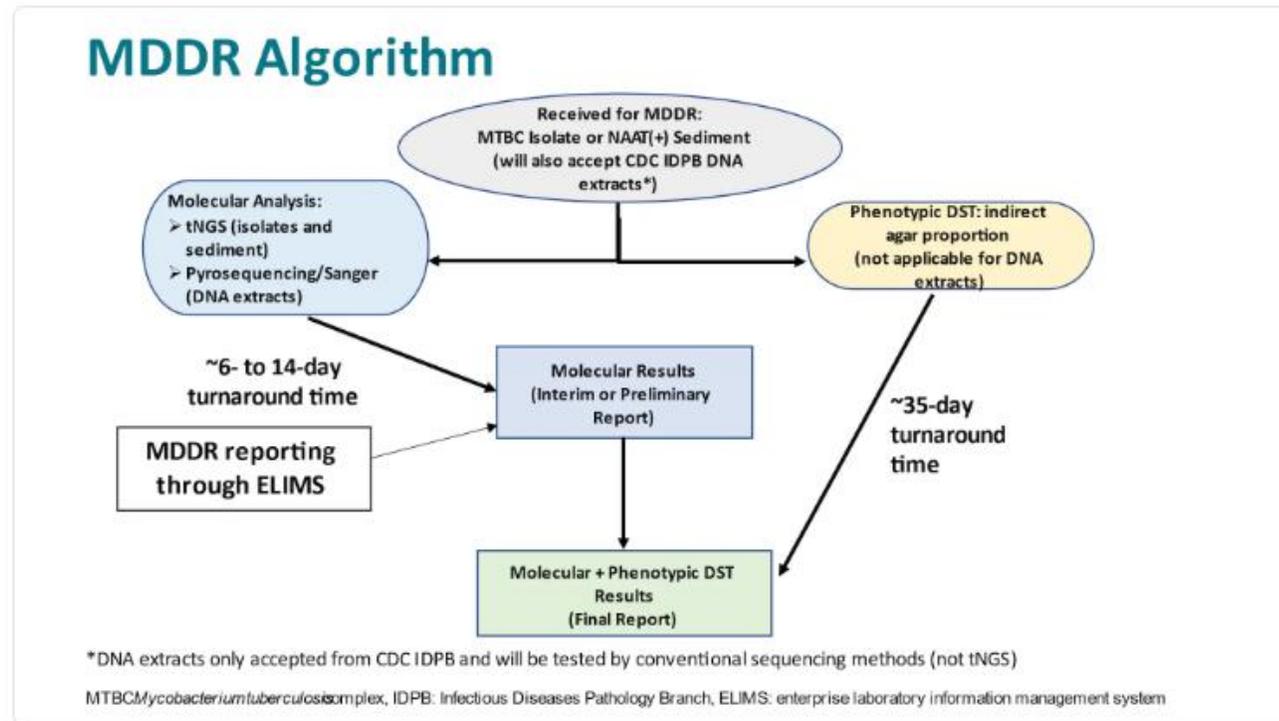
When to suspect drug-resistance?

- 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

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

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

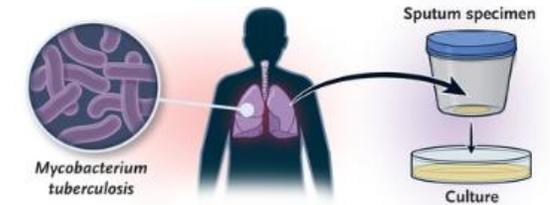
RESEARCH SUMMARY

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 rifampin-based antimicrobial regimen. A more potent regimen with improved rifampin exposure might shorten treatment duration, potentially improving adherence and reducing adverse effects and costs.



CLINICAL TRIAL

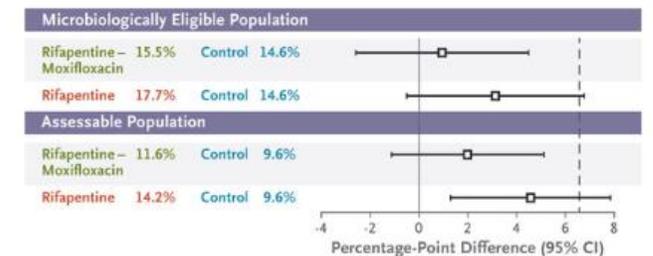
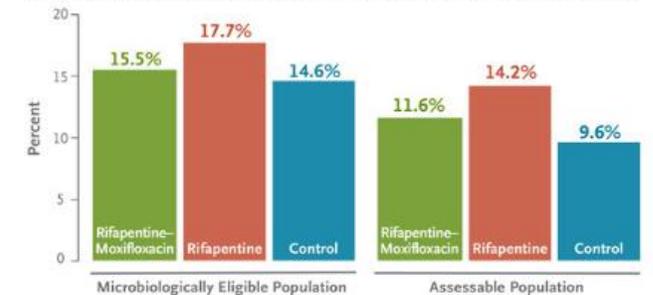
Design: A randomized, open-label, noninferiority trial of two 4-month rifapentine-containing regimens, as compared with a standard 6-month rifampin-containing regimen, for the treatment of drug-susceptible tuberculosis.

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.

Absence of tuberculosis disease–free survival at 12 months after randomization



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-

Unfavorable Outcome in Modified Intention-to-Treat Analysis



LTBI and
importance of
public
health/healthcare
partnership

THINK
TEST
TREAT **TB**

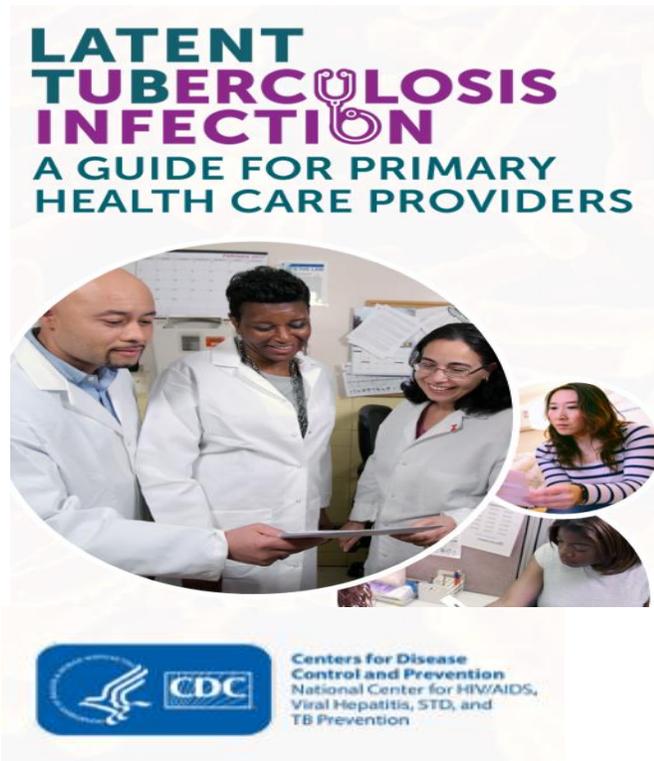
Don't let patients
walk out of your
clinic with **latent
TB infection.**



The illustration shows a woman with dark hair in a ponytail, wearing a white short-sleeved shirt and dark pants, walking away from an open doorway. The doorway is on the right side of the frame, and the woman is walking towards the left. The background is a light blue gradient with a subtle pattern of hexagons and dots.



The CDC logo is located in the bottom right corner of the graphic. It features the text 'U.S. DEPARTMENT OF HEALTH & HUMAN SERVICES' around the top edge of a circular emblem, with the 'CDC' logo in the center.



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,^{1,2} Michael K. Leonard,^{2,3} 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. Woods¹⁵

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

THINK TEST TREAT TB

Inactive Tuberculosis (TB) Testing & Treatment

Up to 13 million people in the United States may have inactive TB (also called latent TB infection). Without treatment, 1 in 10 people with inactive TB will get sick with active TB disease, and can spread TB to others through the air.
You can help prevent the spread of TB.

1 Think Am I at risk for TB infection?
Talk to your healthcare provider about getting tested if you:

- were born in or frequently travel to countries where TB is common, including those in Asia, Africa, and Latin America
- recently spent time with someone who has active TB disease
- live or used to live in large group settings where TB is more common, such as homeless shelters, prisons, or jails
- have a weaker immune system because of certain medications or health conditions such as diabetes, cancer, and HIV
- work in places with high risk for TB transmission, such as hospitals, homeless shelters, correctional facilities, and nursing homes

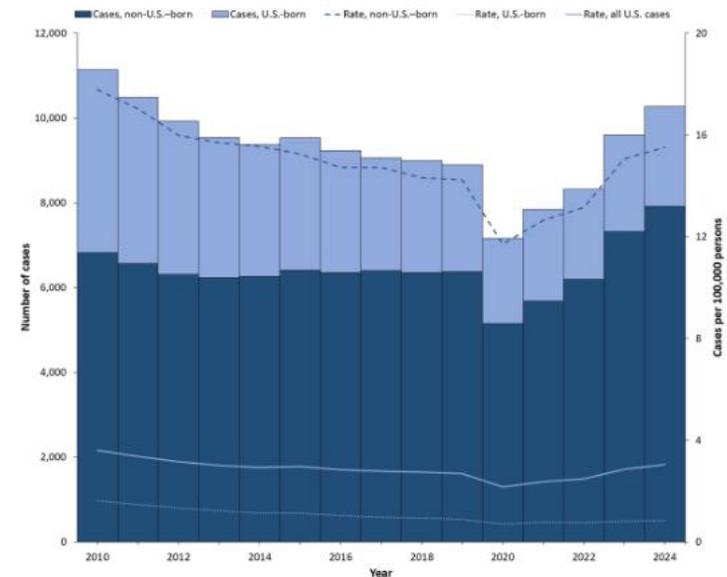
Even people who received the TB vaccine, also called the bacille Calmette-Guérin (BCG) vaccine, should be tested since the vaccine weakens over time.

2 Test What TB test do I need?
There are two types of tests for TB infection: the TB blood test and the TB skin test. TB blood tests are the preferred method of TB testing for people who have received the TB vaccine (BCG). Healthcare providers and patients should discuss which test to use.

3 Treat What are my treatment options?
Treating inactive TB is the best way to protect you from developing active TB disease. When possible, CDC recommends using short and convenient 3- or 4-month rifamycin-based treatments for inactive TB.

To learn more about TB and how you can protect yourself and others, visit www.cdc.gov/thinktesttreattb

Tuberculosis cases* and rates† by birth origin‡ — United States, 2010–2024



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

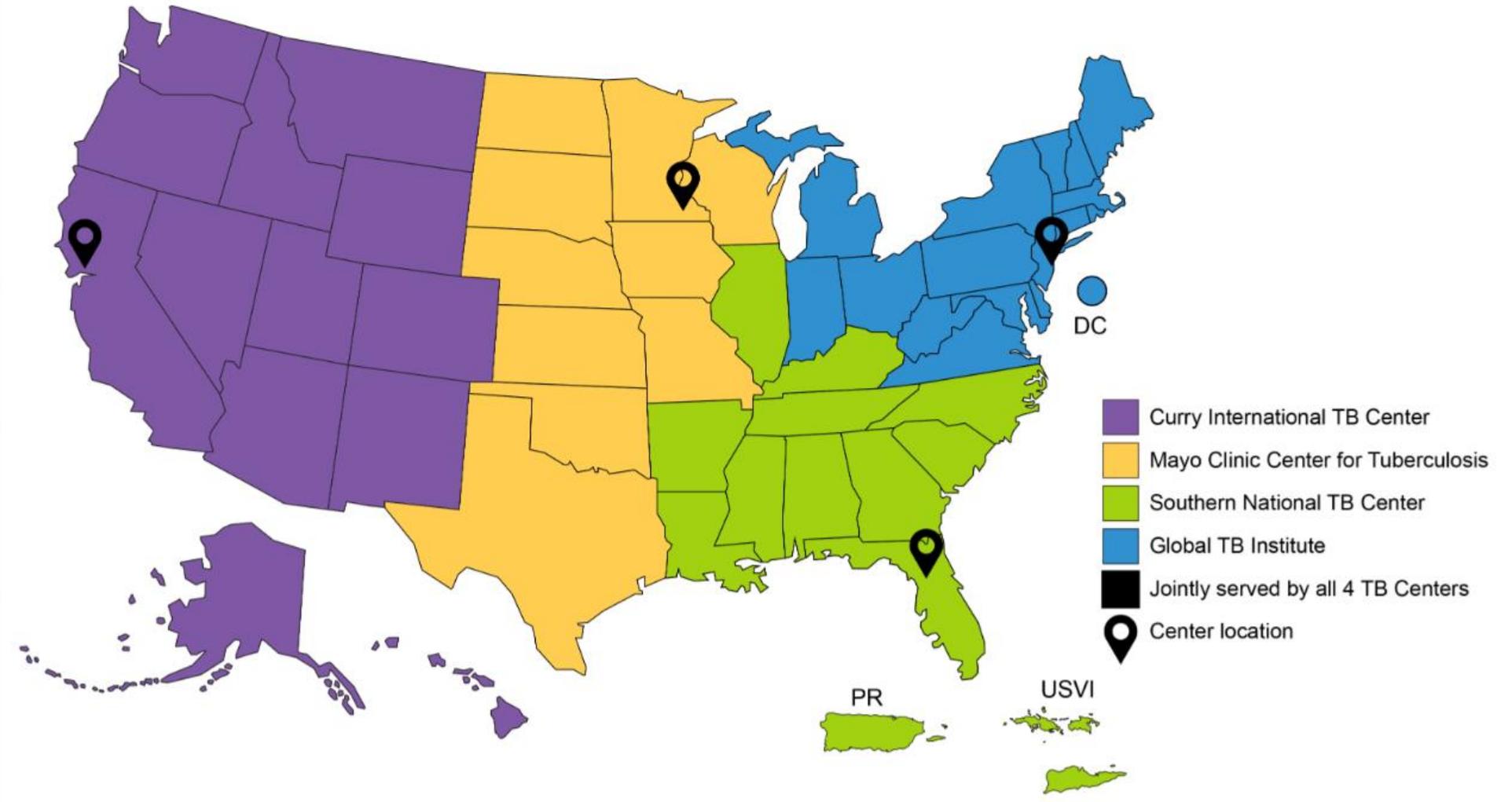
Public/Private Partnership

- **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

- American Samoa
- Commonwealth of the Northern Mariana Islands
- Federated States of Micronesia
- Guam
- Republic of Palau
- Republic of the Marshall Islands



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