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TUBERCULOSIS (TB) UPDATE

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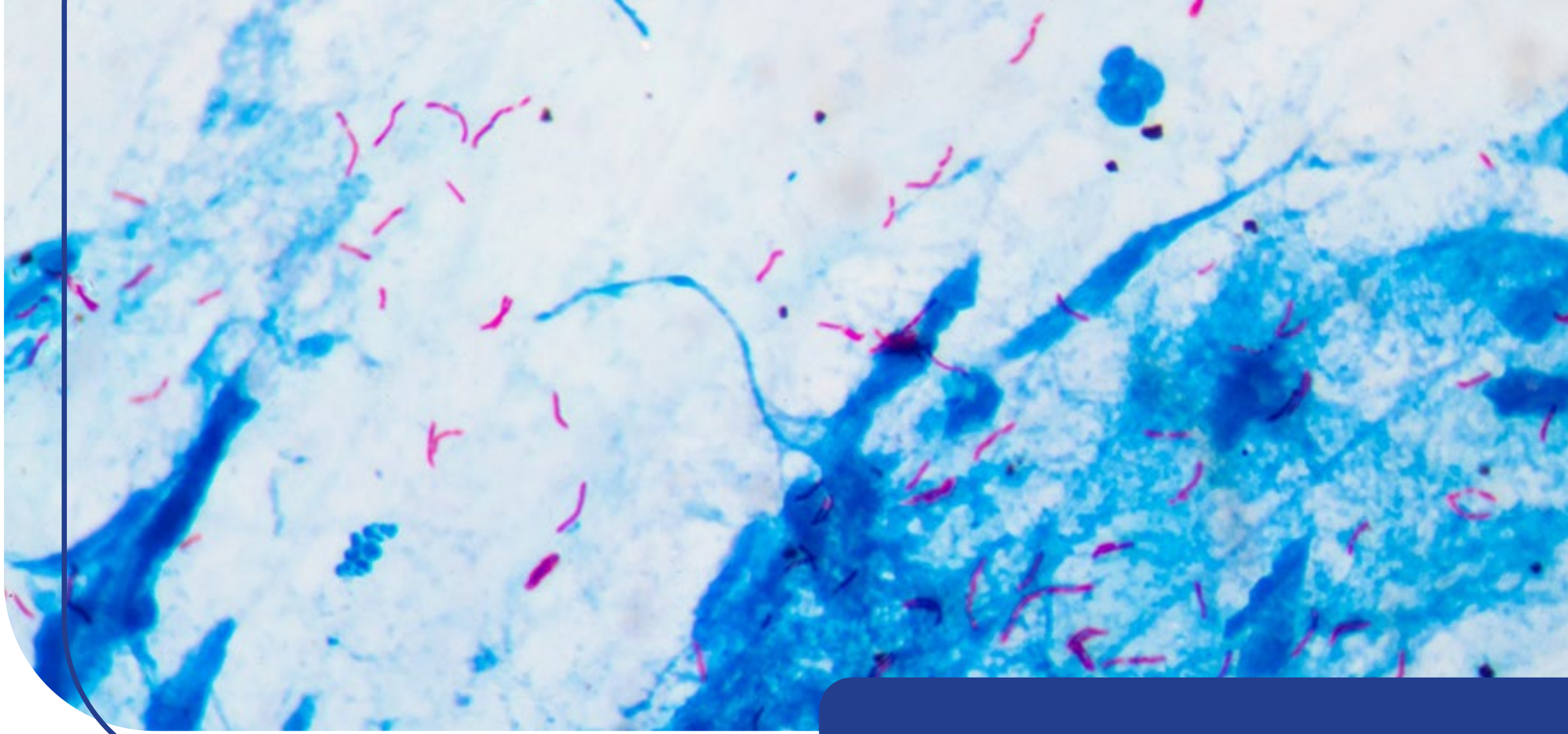
12/18/2023



BASICS OF TB

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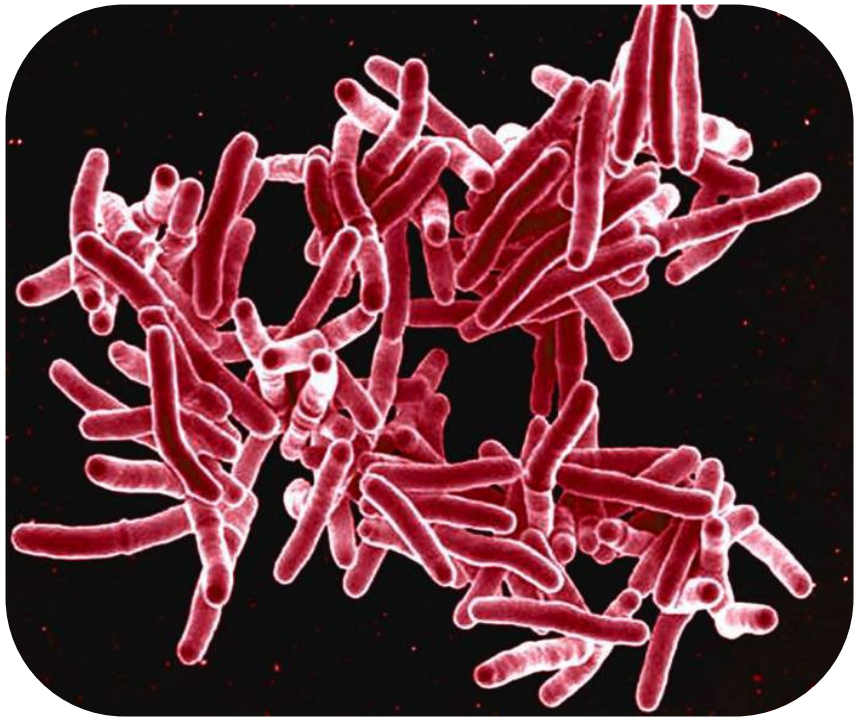
Tuberculosis

- Tuberculosis (TB) is caused by the bacterium *Mycobacterium tuberculosis*
- Usually affects the lungs, but can attack any part of the body
- Divides at a slow rate
- Can persist as **latent** infection
- Requires a complex and extended treatment course



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TB Disease Basics

- How does it spread?
  - Person-to-person through the air
  - The bacteria is expelled via coughing, speaking, or singing

- Signs and symptoms of TB disease?
  - Cough greater than three weeks
  - Illustration to the right shows other symptoms

Patients may have one or more of these signs and symptoms.

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Extrapulmonary TB

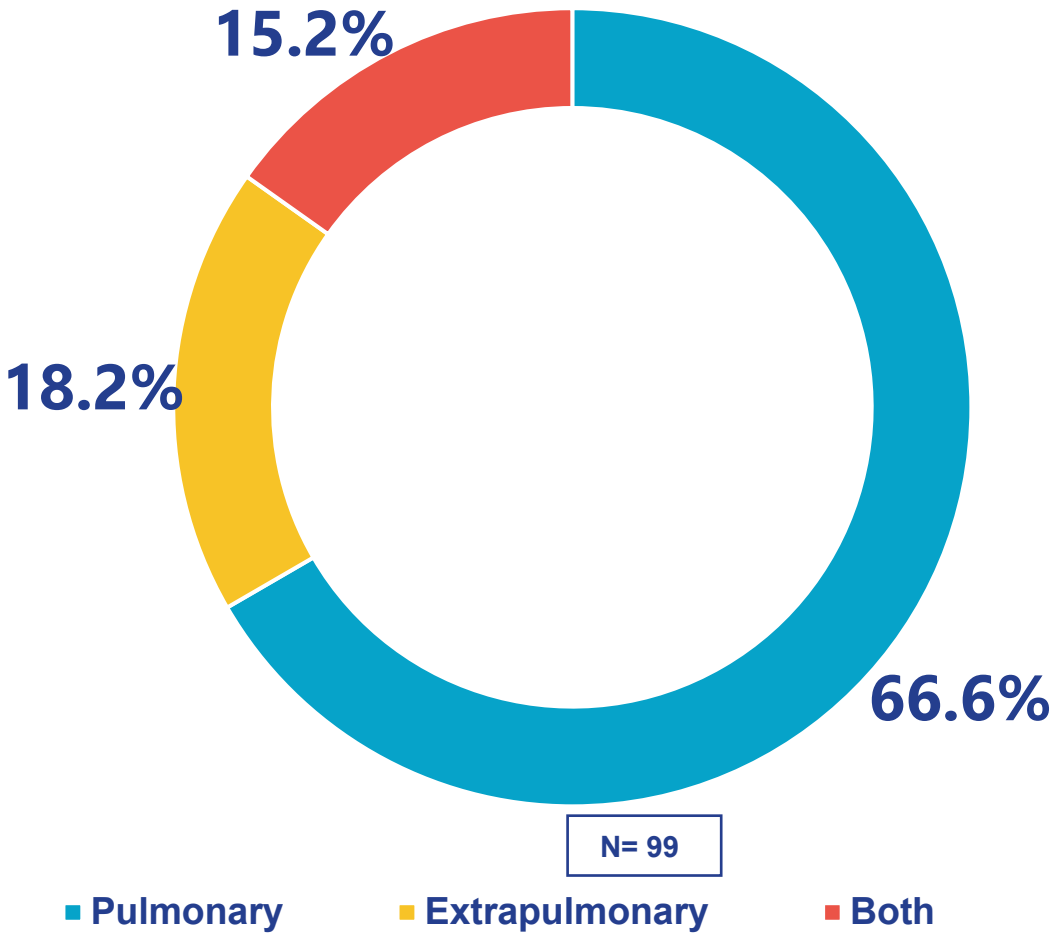
- Refers to TB involving organs other than the lungs:
  - 20 percent of cases are extrapulmonary - including pleural
  - 10 percent are both

- **Symptoms:**
  - Depends on location:
    - Lymph nodes
    - Bone and joints – Pott's
    - Headaches/CNS - slow onset basilar meningitis
    - Visual – uveitis/scleritis
    - Abdominal pain/ascites
    - GI/GU - "Sterile pyuria"
    - Skin rashes

TB Cases by Site of Disease, Indiana, 2022

Extrapulmonary sites include:

- Lymphatic (35.0%), *adenitis*
- Pleural (22.5%)
- Meningeal (10.0%)
- Peritoneal (7.5%)
- Eye and Ear Appendages (5.0%)



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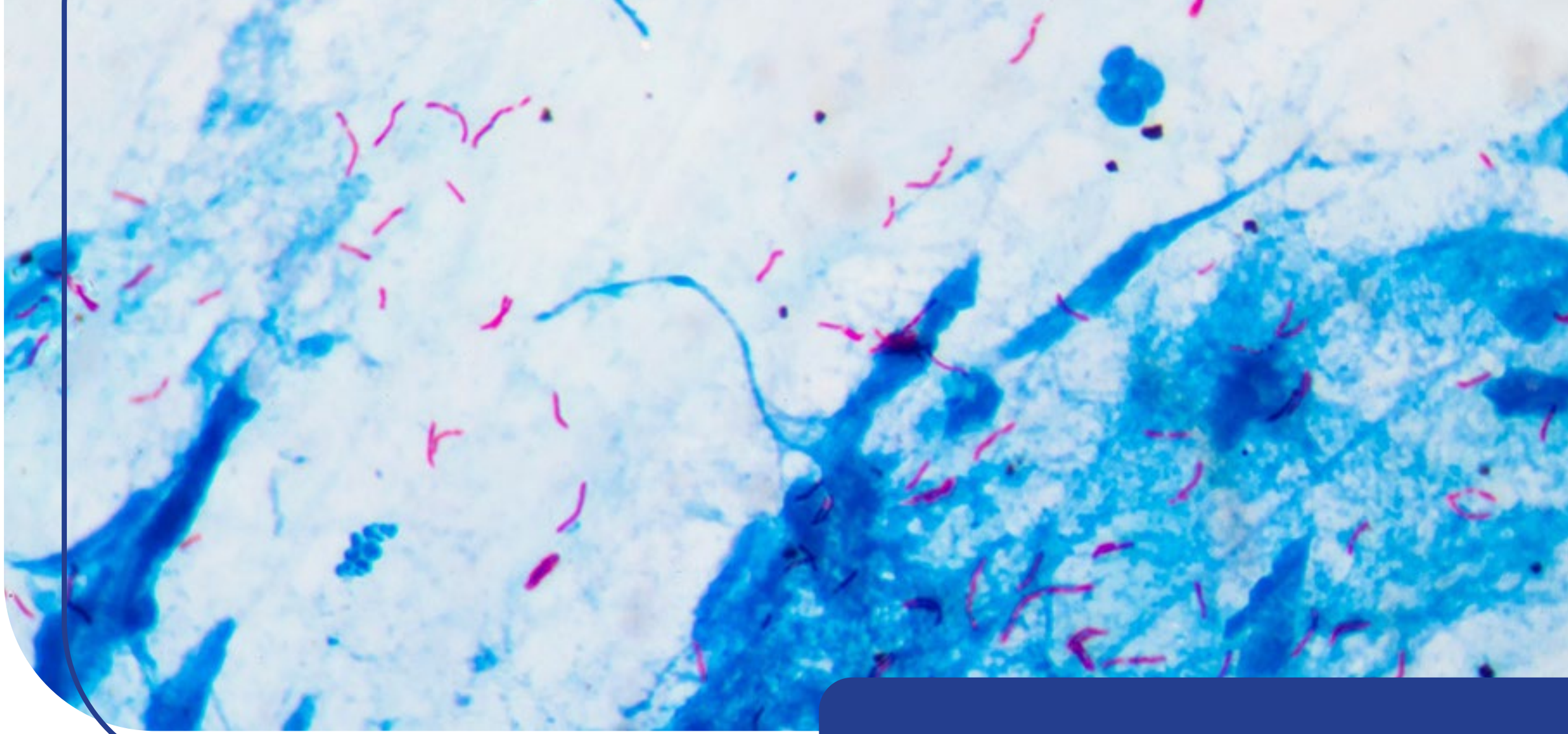

TB IN INDIANA

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Indiana TB 10-Year Trend, 2013-2022

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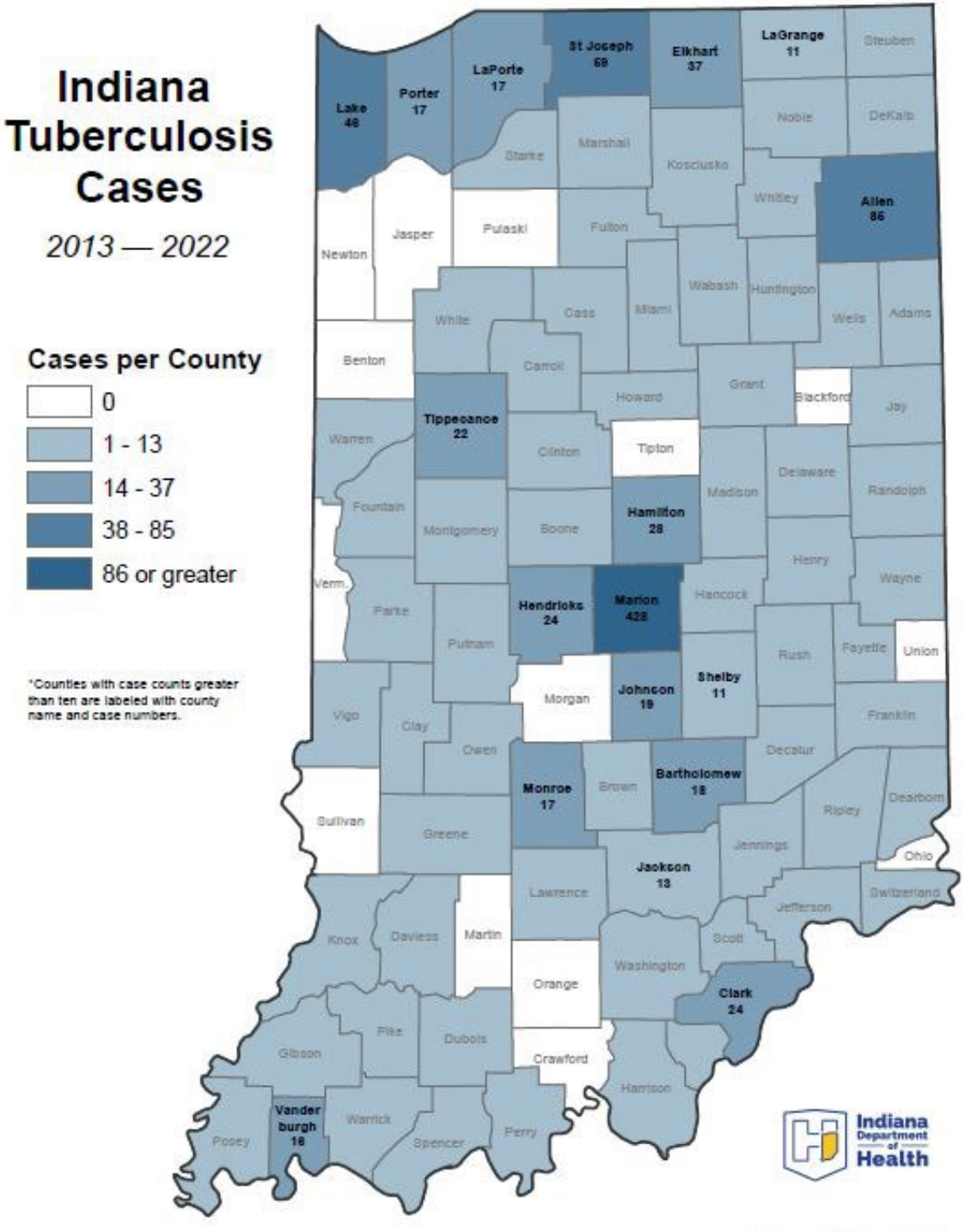
Indiana Cases = 99

Incidence Rate = **1.5**/100,000

Compare to U.S. incidence of 2.5

Indiana Tuberculosis Cases

2013 — 2022



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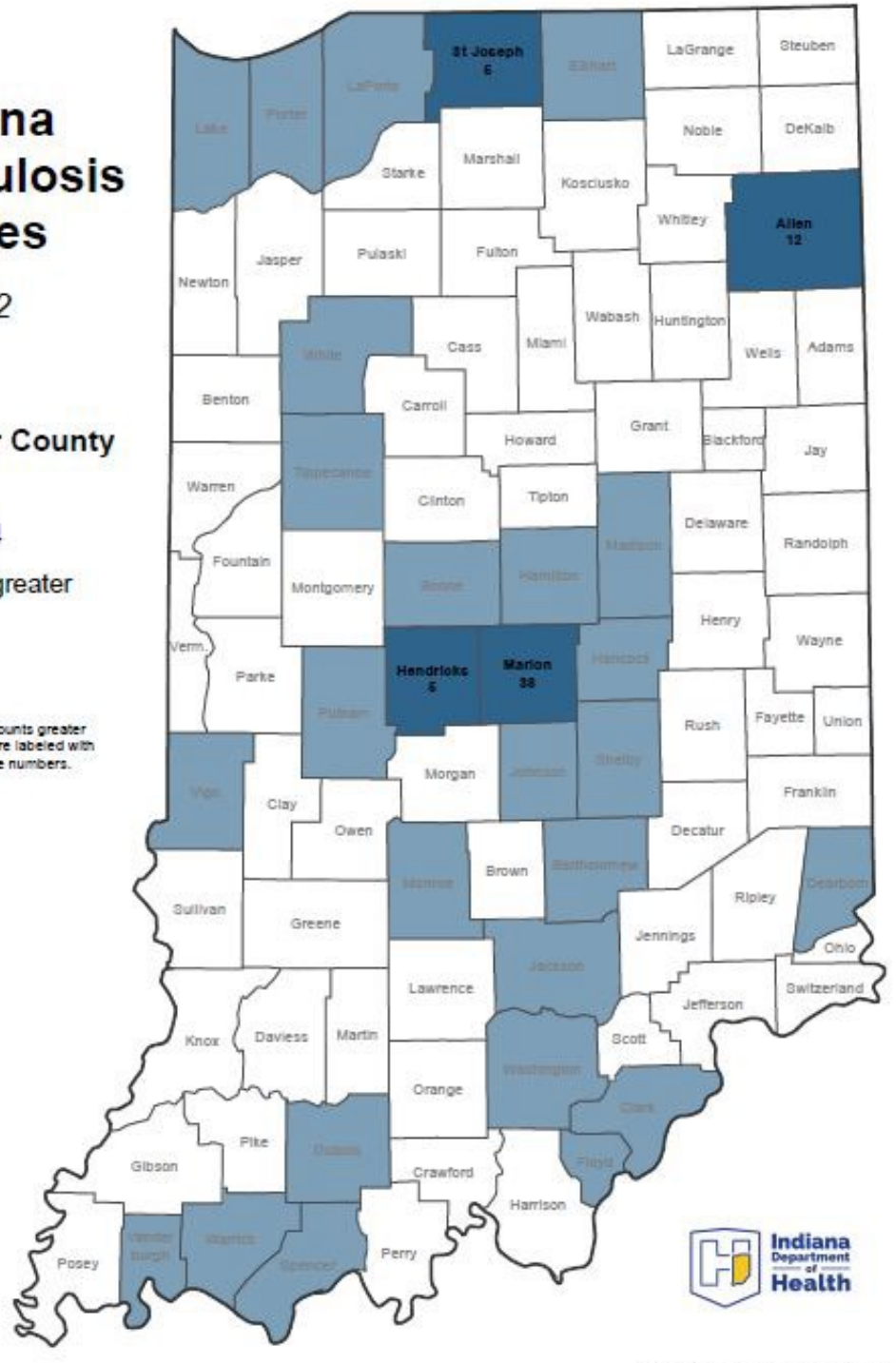
Indiana Tuberculosis Cases

2022

Cases per County

- 0
- 1 to 4
- 5 or greater

*Counties with case counts greater than or equal to five are labeled with county name and case numbers.



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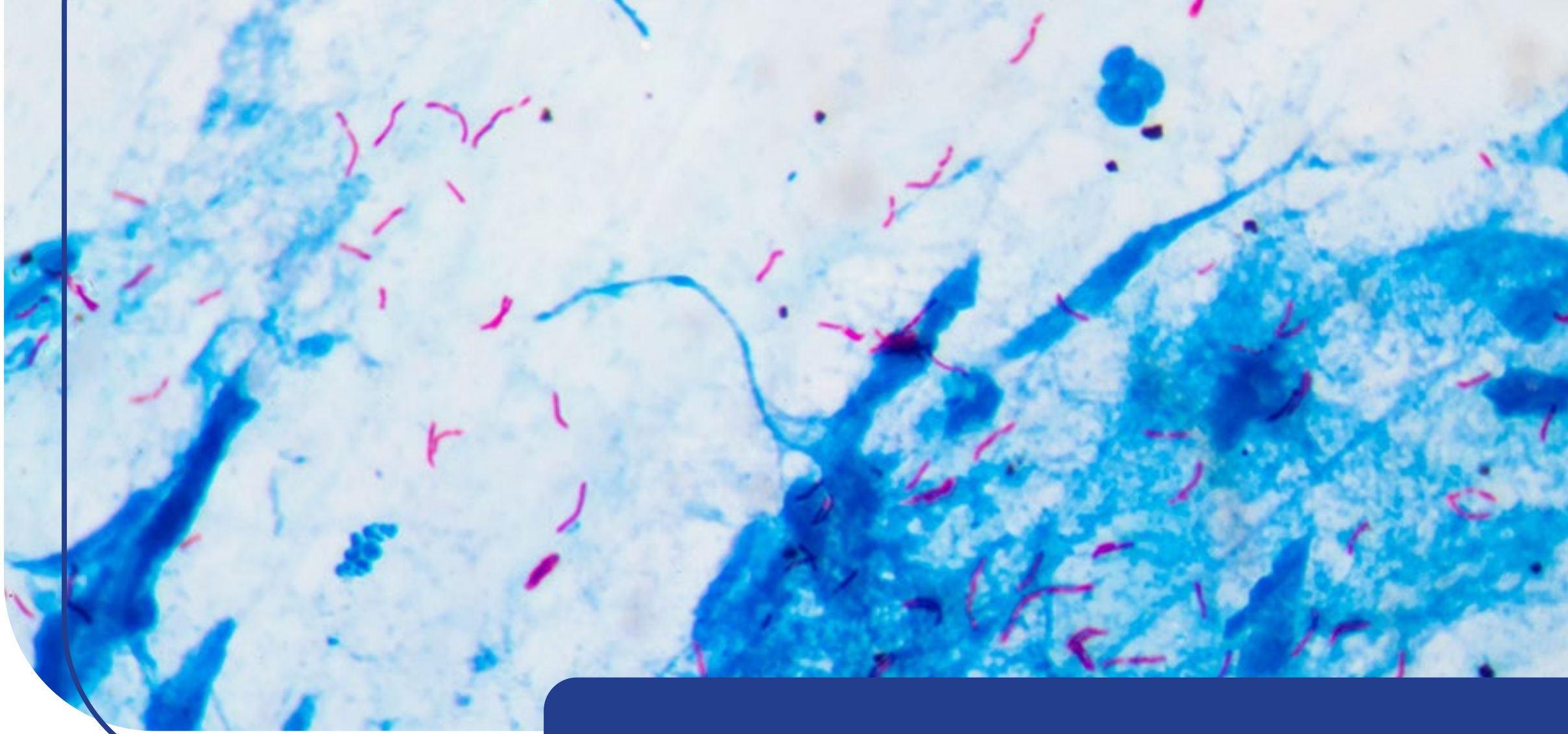

TB IN MARSHALLESE

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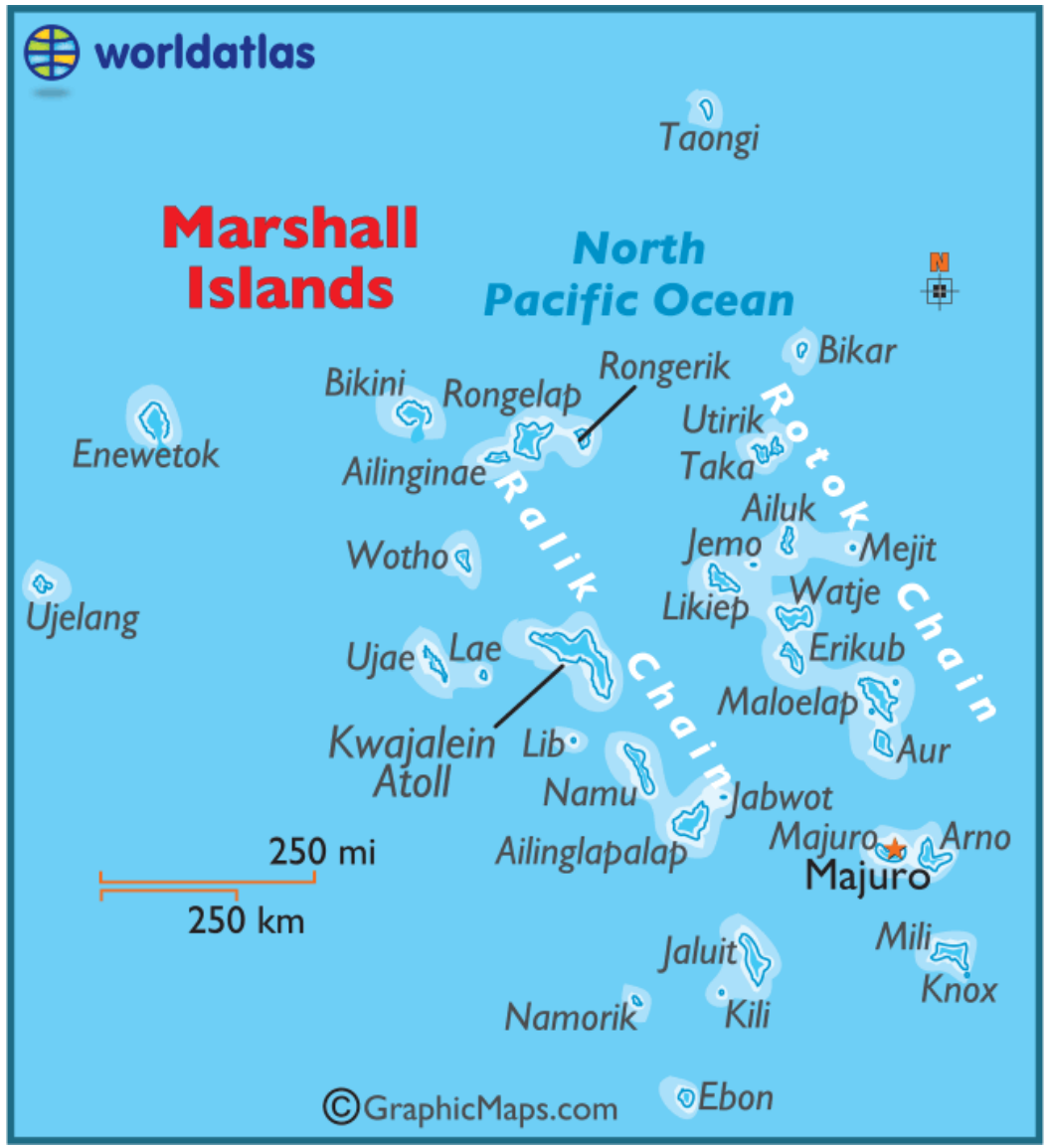

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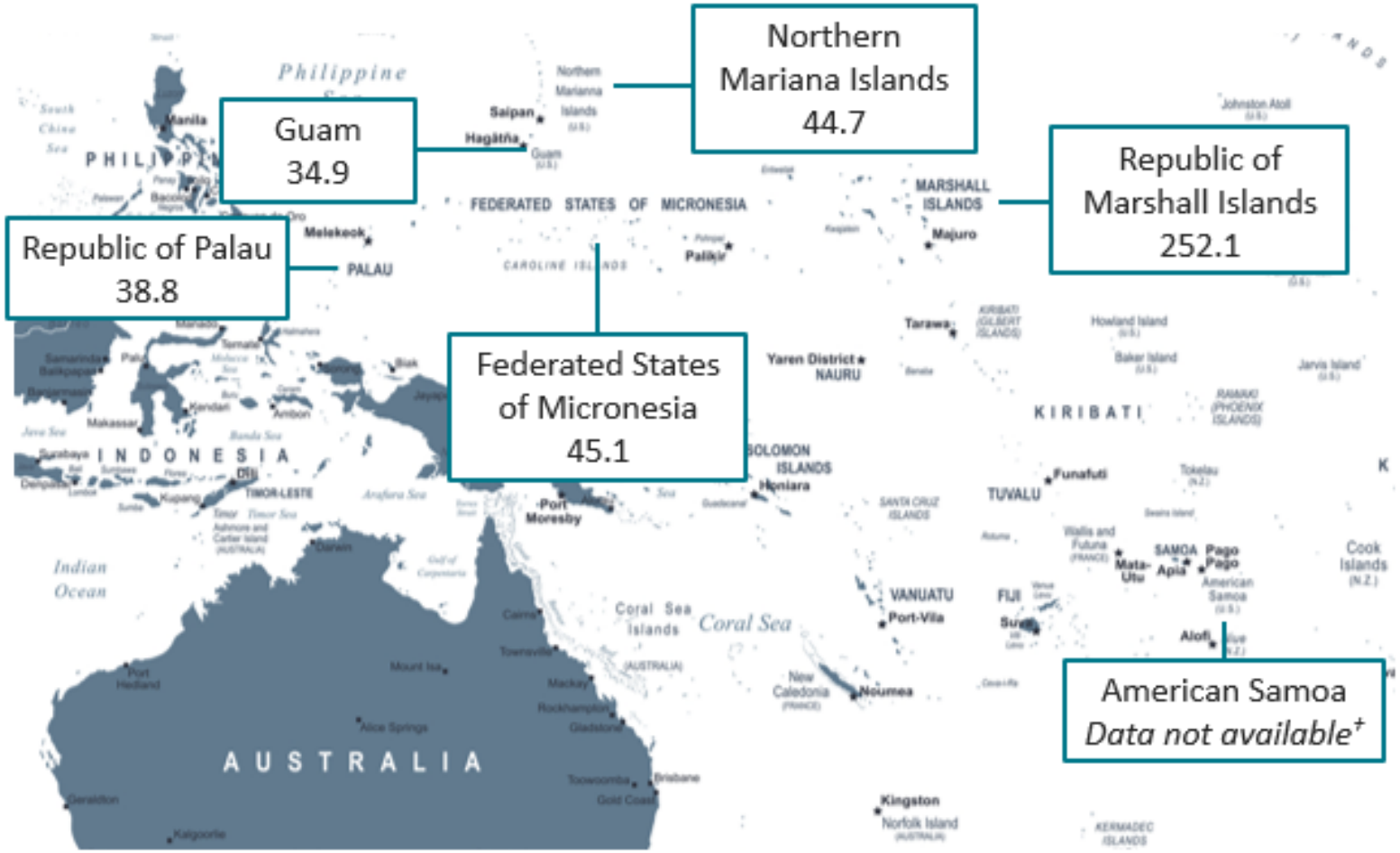
Photos: www.worldatlas.com

TB Incidence Rates* by U.S.-Affiliated Pacific Islands, 2022



Indiana 1.5

U.S. 2.5

Australia 6.5

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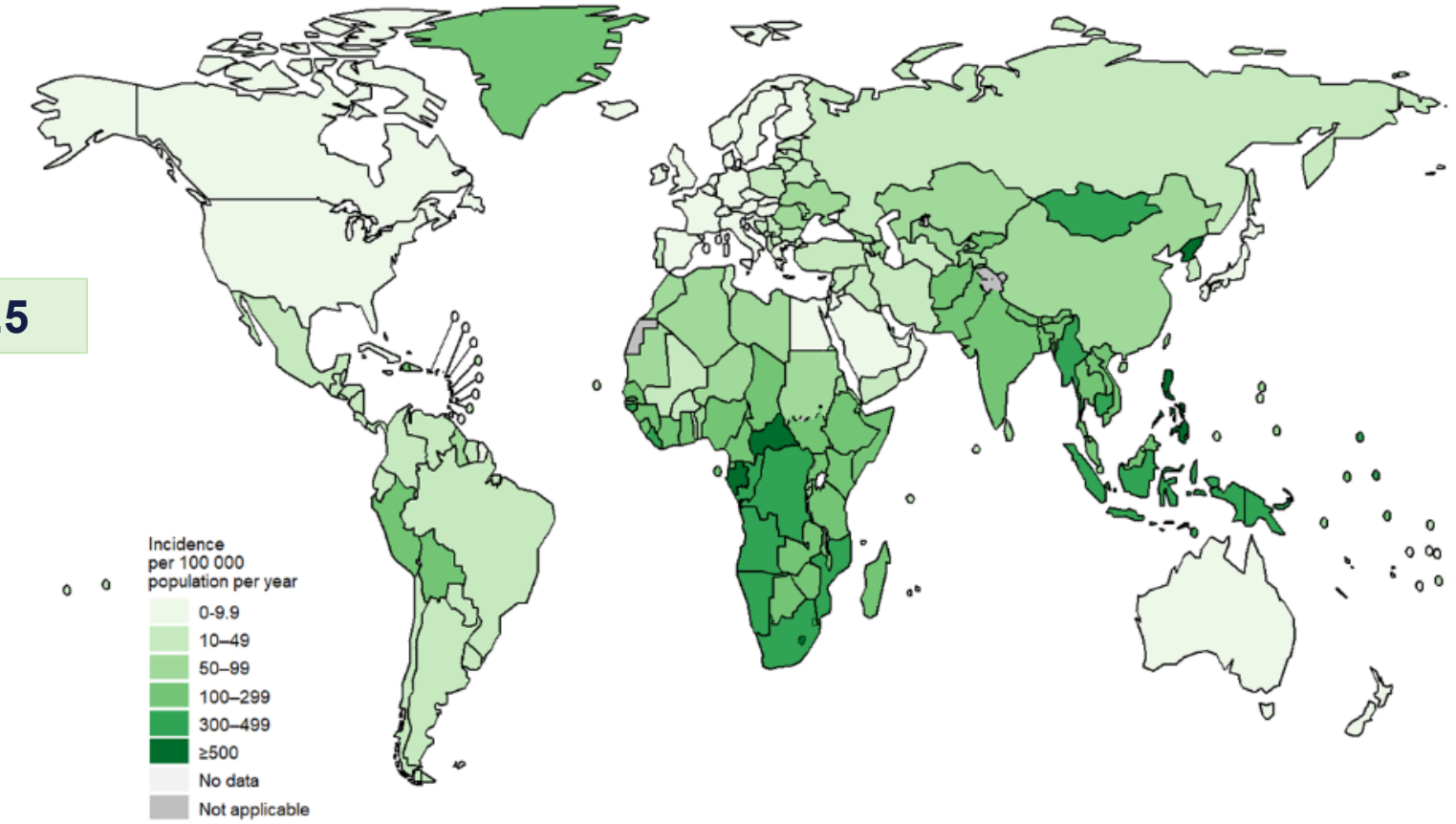
*Cases per 100,000 persons
+American Samoa data not submitted for 2022

Estimated Tuberculosis Incidence Rates, Worldwide, 2022

U.S.	2.5



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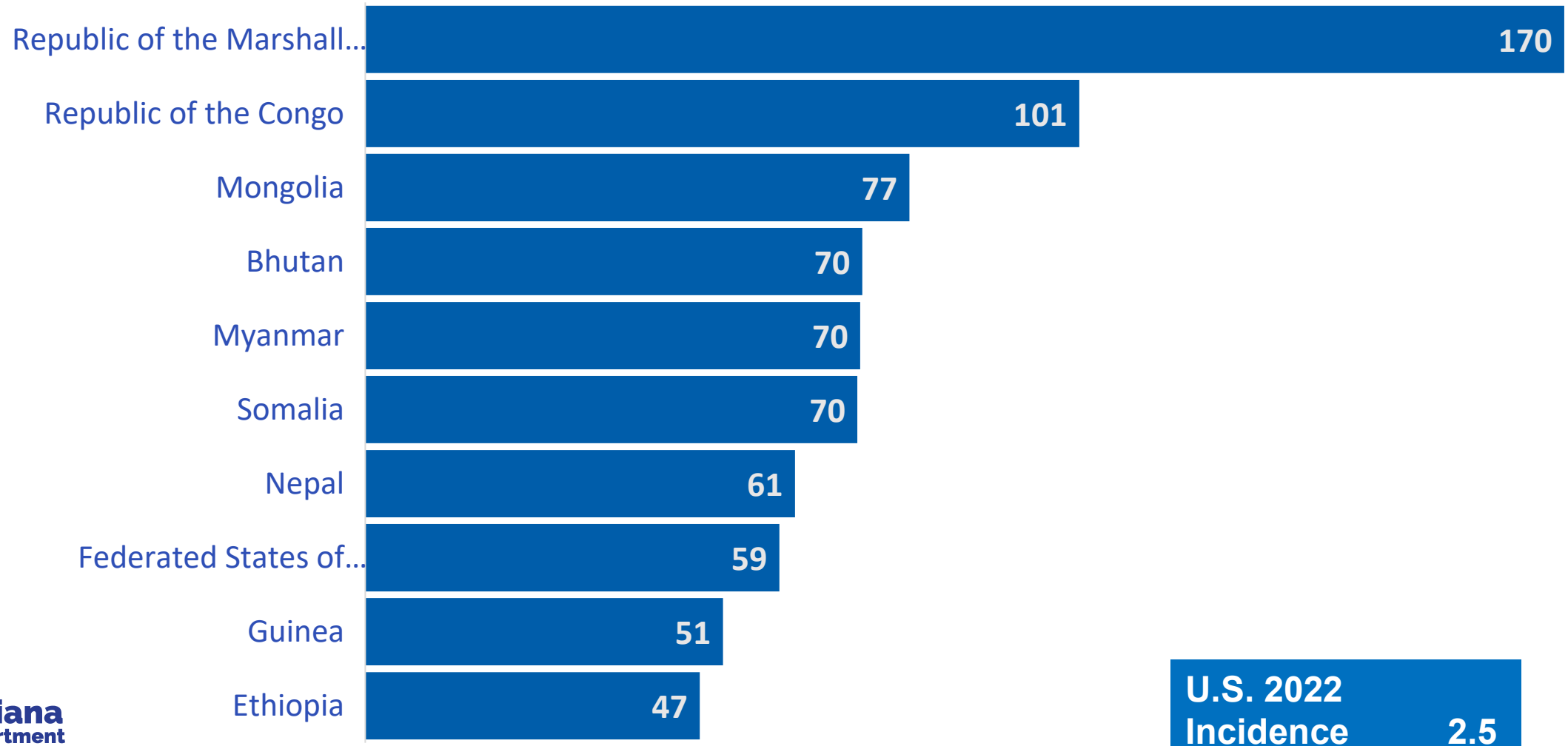
Top 10 TB Incidence Rates* by Country of Birth, diagnosed while living in the United States, 2017–2021



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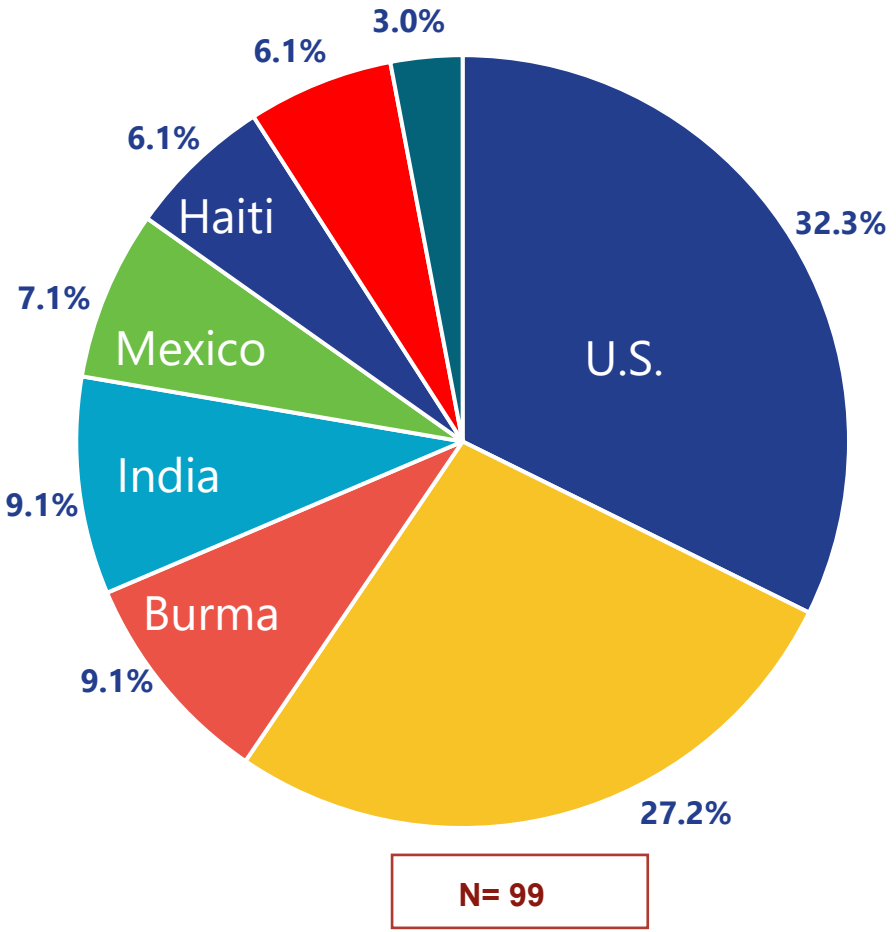
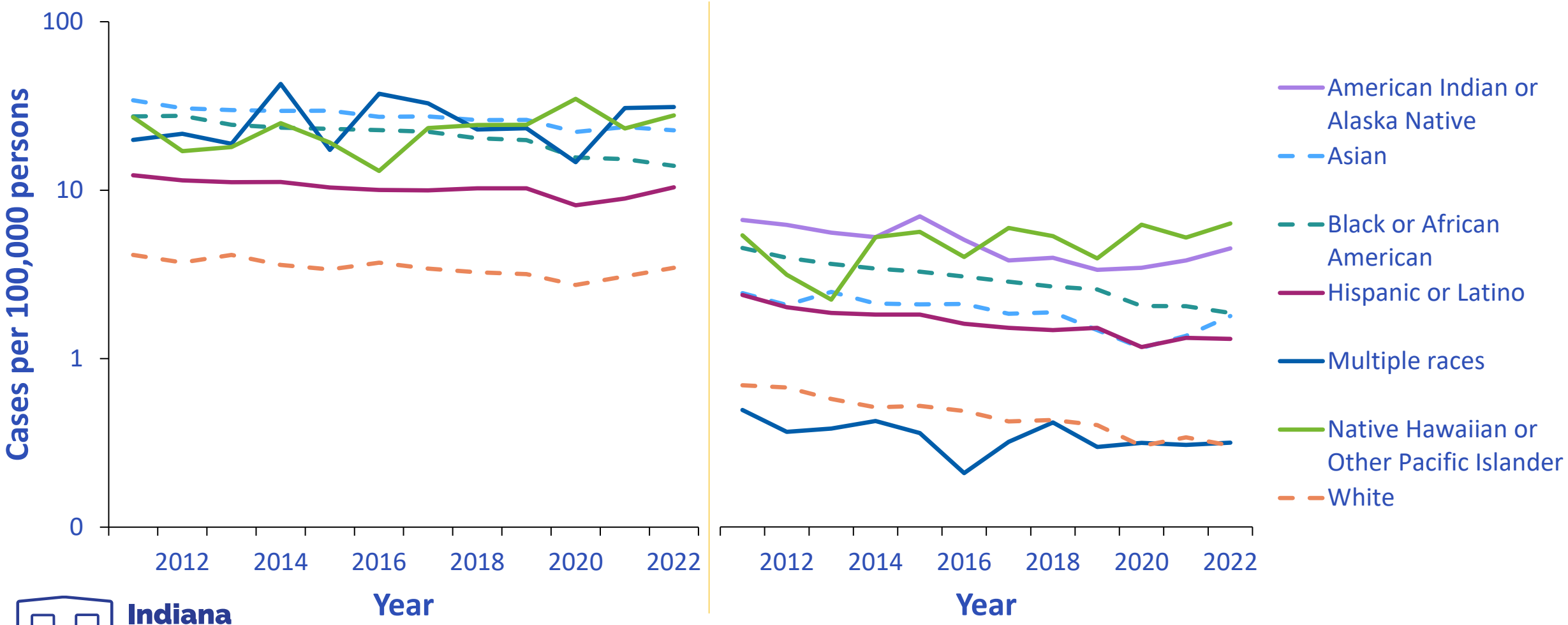
* Cases per 100,000 persons

TB Cases by Country of Birth, Indiana, 2022



Other than Burma/Myanmar, the Indiana trends are similar to U.S. representations

TB Incidence Rates Among Non-U.S.–Born and U.S.-Born* Persons by Race/Ethnicity,† United States, 2011–2022



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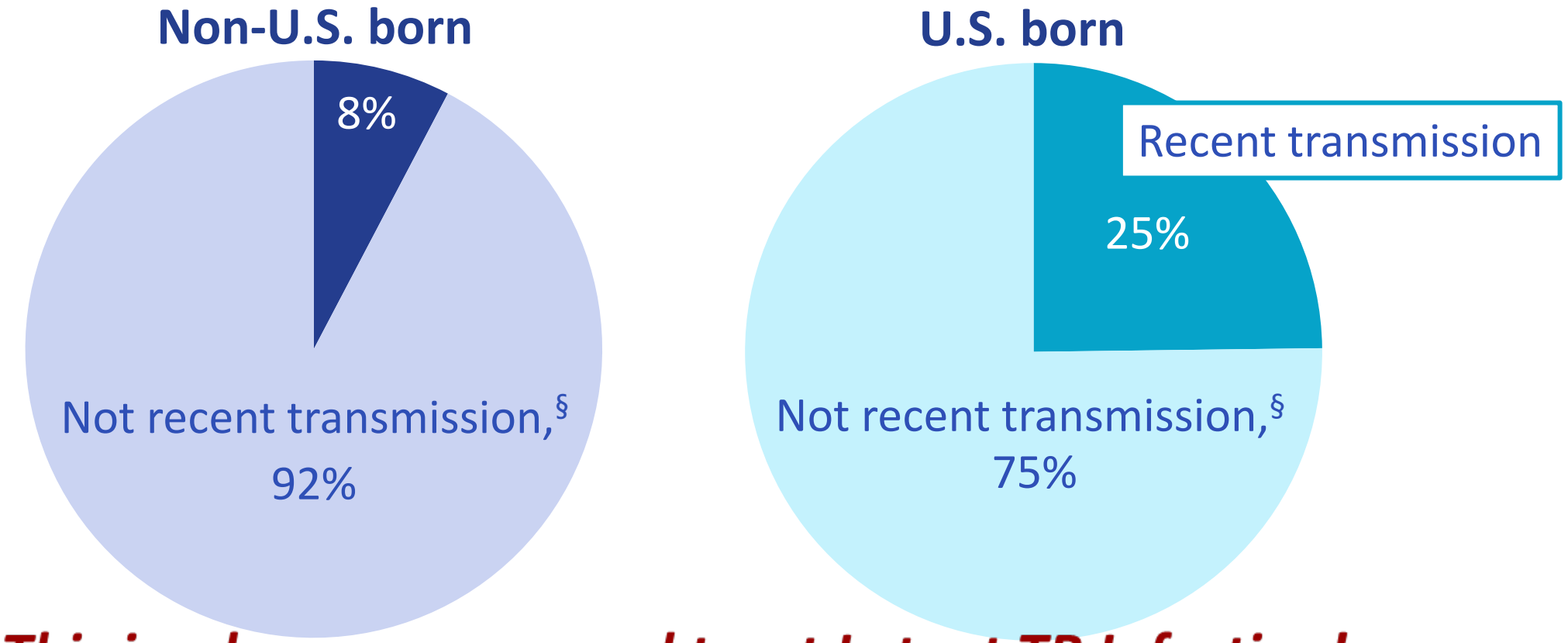
*Persons born in the United States, certain U.S. territories, or elsewhere to at least one U.S. citizen parent are categorized as U.S.-born. All other persons are categorized as non-U.S.–born.

†Persons who identified as Hispanic or Latino were categorized as "Hispanic," regardless of self-reported race. Persons who did not identify as Hispanic or Latino were categorized by self-reported race; if more than one race was reported, the person was categorized as "Multiple race."

§Non-U.S-born American Indian/Alaska Native are not displayed because some years have zero cases, which cannot be displayed in a log-scale graph.

Percentages of TB Cases Estimated to be Attributed and Not Attributed to Recent Transmission* by Origin of Birth,† 2020–2021



This is why we screen and treat Latent TB Infection!

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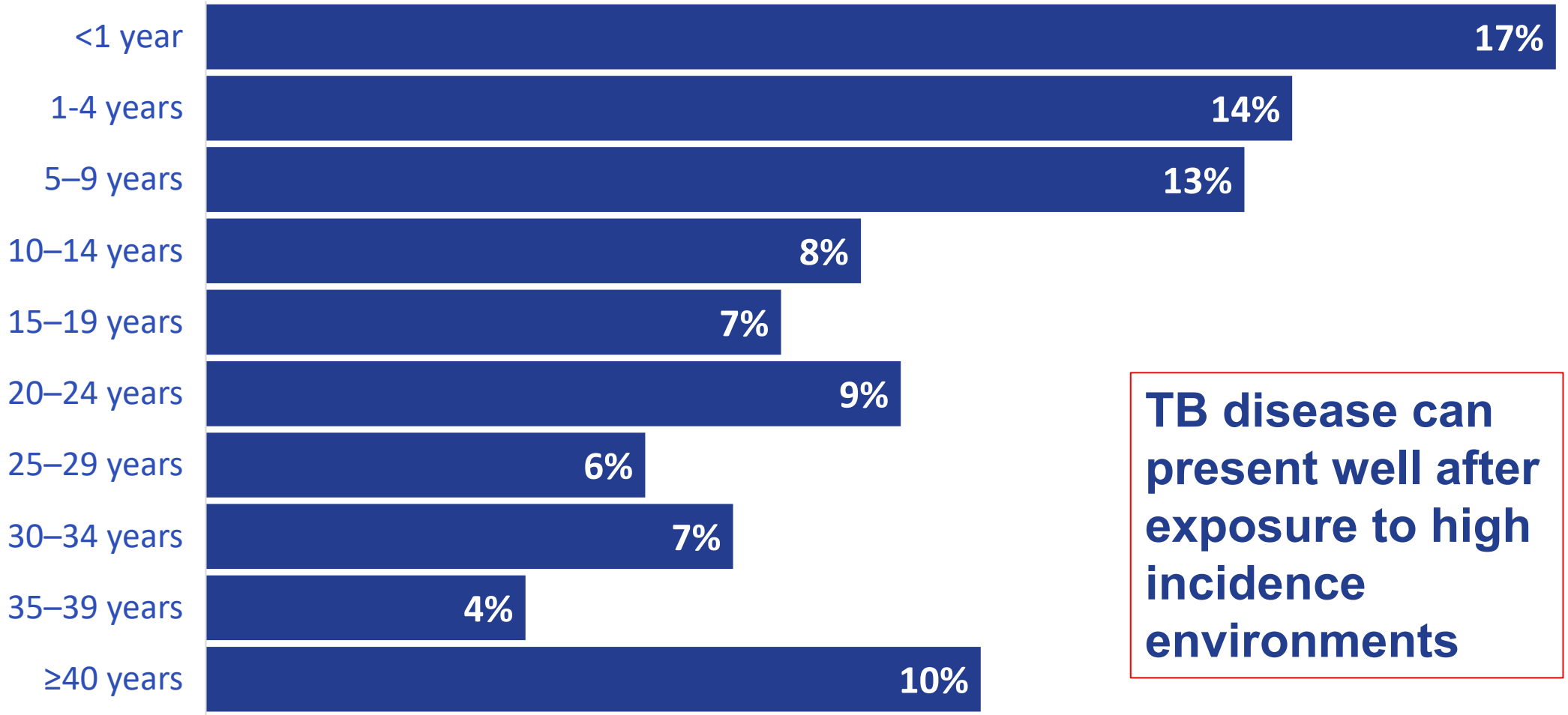
* Cases with unknown origin of birth not shown (n=40).
† A TB case is designated as attributed to recent transmission if a plausible source case can be identified in a person who i) has the same *M. tuberculosis* genotype, ii) has an infectious form of TB disease, iii) resides within 10 miles of the TB case, iv) is 10 years of age or older, and v) was diagnosed within 2 years before the TB case.
§ Cases not attributed to recent transmission may be misclassified in children <5 years old or indeterminate in persons with a recent U.S. arrival due to limitations of the plausible-source case method.

Percentage of TB Cases Among Non-U.S.–Born* Persons by Years Since Initial Arrival in the United States at Diagnosis,† 2022 (N=6,148)



TB disease can present well after exposure to high incidence environments

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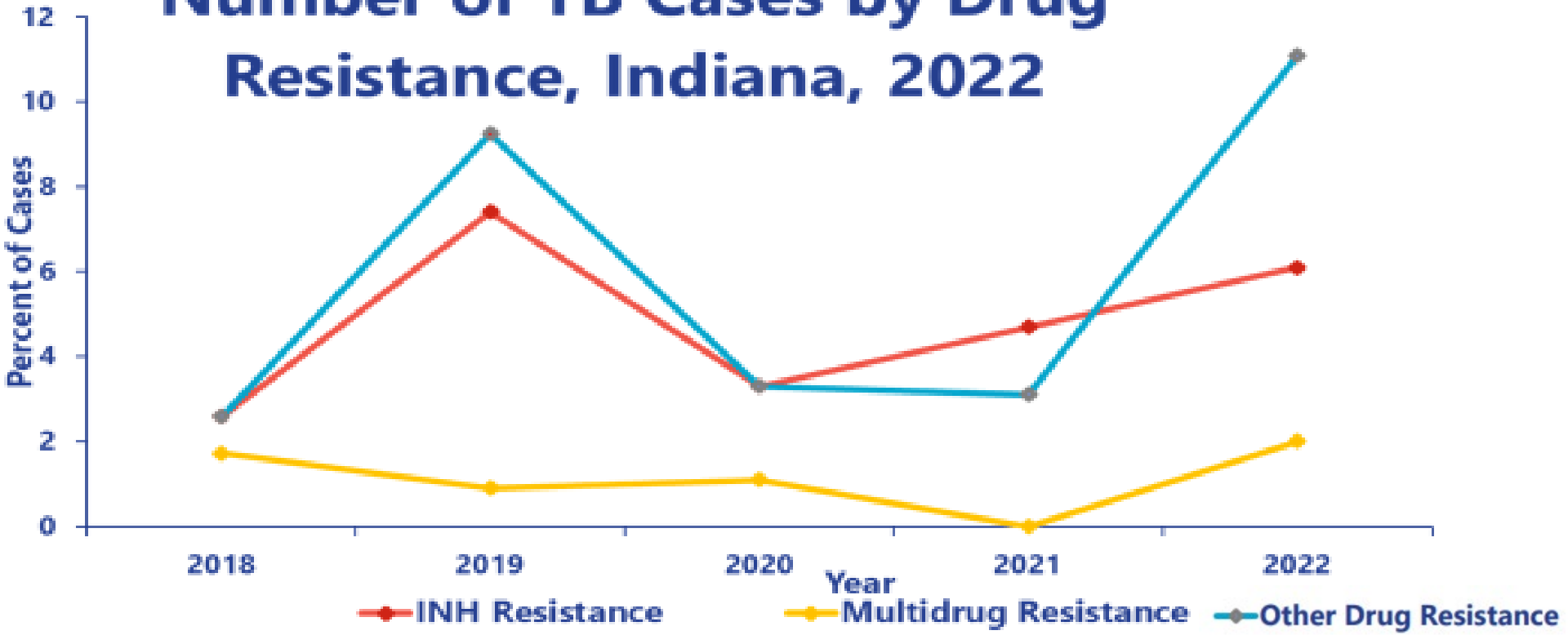
*Persons born in the United States, certain U.S. territories, or elsewhere to at least one U.S. citizen parent are categorized as U.S.-born. All other persons are categorized as non-U.S.–born.

†The number of years since initial arrival in the United States at diagnosis was unknown or missing for 7% of non-U.S.–born persons. These persons were included in the denominator when percentages were calculated.

Number of TB Cases by Drug Resistance, Indiana, 2022



Awareness of where the TB was acquired will impact the suspicion for drug resistance and alter empiric therapy regimen

TB CASE MANAGEMENT

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TB Case Management

- The **local health department** is responsible for investigating and case-managing patients with **suspected or confirmed TB disease**, including:
  - Verifying that **appropriate isolation** measures have been implemented
  - Determine the **infectious period** and possible sites of exposure
  - Assisting in **obtaining medication** through Purdue Pharmacy and ensuring that regimen, dosage, and length of treatment are per standard of care and given using **directly observed therapy (DOT)**
  - Conducting a **contact investigation** for all exposed contacts

TB Contact Investigation

- Ensure exposed **contacts are notified** of exposure and provide TB education as needed
- Provide and/or organize **testing of contacts** with TSTs or IGRAs
- Ensure **medical evaluations** are completed for contacts with positive tests
- **Coordinate and/or document LTBI treatment**
- Report all contacts, testing results, and outcomes to IDOH

Current Situation

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TB in Vanderburgh County

- Increase in TB cases especially among Marshallese population, including pediatric cases
- Multiple exposures in school settings

- **Vigilance recommended in at-risk populations**

Think TB

- Providers should have a **low threshold** to evaluate Marshallese* for **TB disease**, especially those with respiratory symptoms or findings consistent with extrapulmonary disease
- Providers should also screen for exposure and treat **latent TB** when identified
- Please reach out to Vanderburgh County LHD or IDOH for guidance

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*And patients from other higher-risk countries/environments

Higher-risk Countries/Environments

Certain individuals should be tested for TB infection because they are at higher risk for being infected with TB bacteria, including:

- People who have spent time with someone who has TB disease
- People from a country where TB disease is common (most countries in the Pacific Islands, Latin America, the Caribbean, Africa, Asia, Eastern Europe, and Russia)
- People who live or work in high-risk settings (i.e. homeless shelters, correctional facilities)
- Health-care workers who care for patients at increased risk for TB disease
- Infants, children, and adolescents exposed to adults who are at increased risk for latent TB infection or TB disease

Source: https://www.cdc.gov/tb/topic/testing/whobetested.htm

Evaluation for TB disease (active TB)

- Unexplained weight loss
- Loss of appetite
- Night sweats
- Fever
- Fatigue
- If TB disease is in the lungs (pulmonary), symptoms may include:
  - Coughing for longer than 3 weeks
  - Hemoptysis (coughing up blood)
  - Shortness of breath and chest pain
- Signs or symptoms of extrapulmonary TB disease
  - CNS, lymphatic, bone, GI, GU, skin, etc.

How to Evaluate Persons Suspected of TB Disease

A complete medical evaluation for active TB includes the following:

1. Medical History

Obtain the patient's history of TB exposure, infection, or disease – including demographic factors (e.g., country of origin, age, ethnic or racial group, occupation, hobbies and volunteer work) that may increase the risk for exposure to TB or to drug-resistant TB.

Also, screen for medical conditions (especially HIV infection, immunosuppression, diabetes) that increase the risk of progression from latent TB infection to TB disease which will impact how their TB will be treated.

2. Physical Examination

A physical exam can provide valuable information to suggest pulmonary and/or extrapulmonary TB disease.

TB Evaluation

3. Screening Tests for TB Infection

The Mantoux tuberculin skin test (TST) or the TB blood test can be used to test for *M. tuberculosis* infection. Additional tests are required to confirm TB disease.

The Mantoux tuberculin skin test is performed by injecting a small amount of fluid called tuberculin into the skin in the lower part of the arm. The test is read within **48 to 72 hours** by a trained health care worker, who looks for a reaction (induration) on the arm.

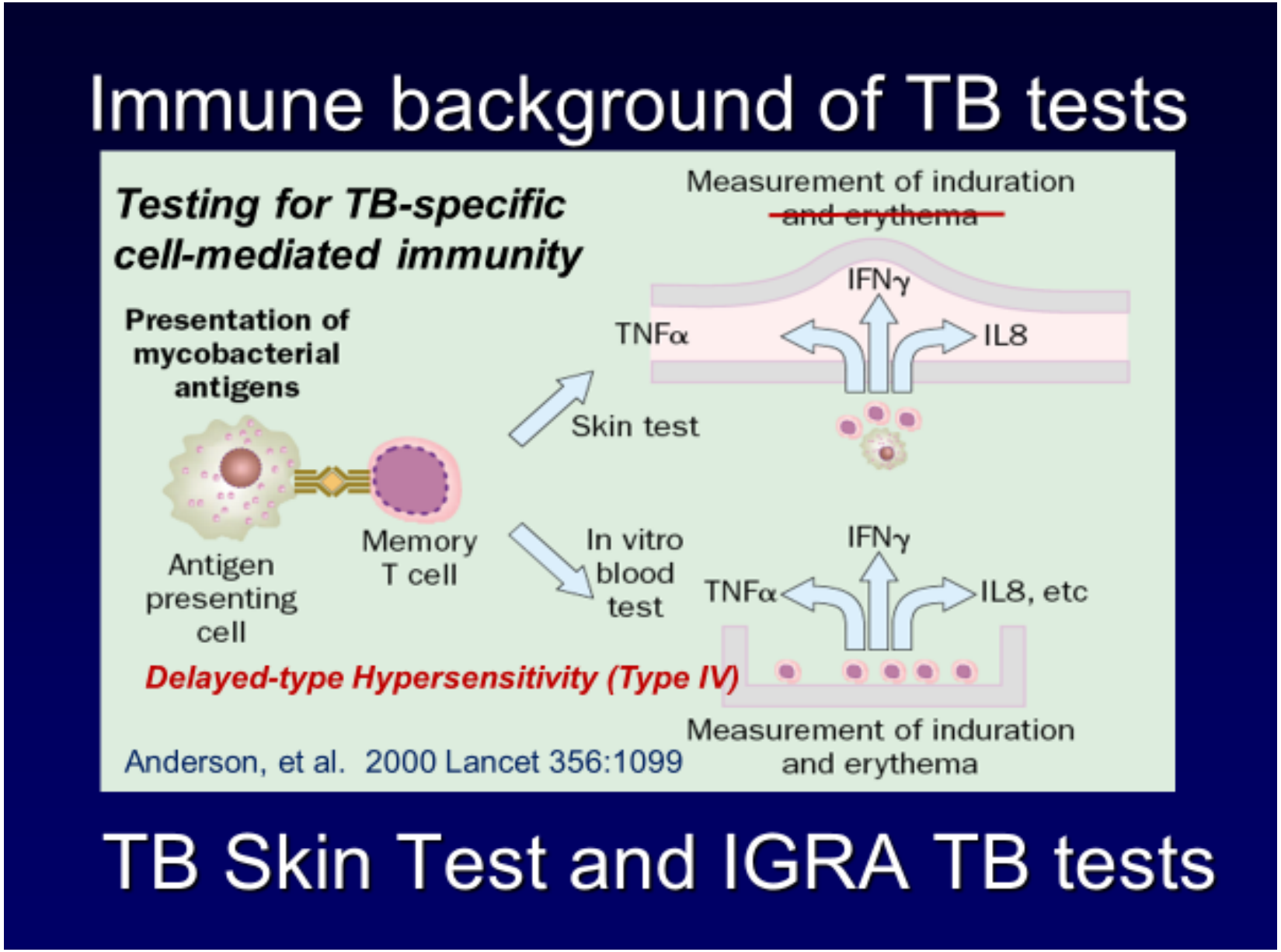
The TB blood tests measure the same evidence of immune system reaction to *M. Tuberculosis*.

It takes **2 to 8 weeks after initial infection** with *M. tuberculosis* for the immune system to be able to react to PPD and for the infection to be detected by the TST or blood test.

Recent Exposure requires repeat testing in 8-10 weeks after baseline testing.

Both TST and IGRA testing are only ~75% sensitive for TB infection, so a negative screening test should not end a diagnostic workup if the clinical suspicion of TB infection is high

Screening:


Immune background of TB tests
Testing for TB-specific cell-mediated immunity
Measurement of induration
and erythema
IFNγ
TNFα
IL8
Presentation of mycobacterial antigens
Skin test
Antigen presenting cell
Memory T cell
In vitro blood test
IFNγ
TNFα
IL8, etc
Delayed-type Hypersensitivity (Type IV)
Measurement of induration and erythema
Anderson, et al. 2000 Lancet 356:1099
TB Skin Test and IGRA TB tests

TB Evaluation

4. Chest Radiograph

A posterior-anterior chest radiograph is used to detect chest abnormalities.

Lesions may appear anywhere in the lungs and may differ in size, shape, density, and cavitation.

These abnormalities may suggest TB but cannot be used to definitively diagnose TB.

However, a chest radiograph may be used to rule out the possibility of pulmonary TB in a person who has had a positive reaction to a TST or TB blood test and no symptoms of disease.

Comparison to prior chest X-rays is extremely helpful to differentiate new abnormalities from older chronic changes in the lungs, often due to other diseases

TB Evaluation

5. Diagnostic Microbiology – *if indicated* by pulmonary symptoms or CXR abnormalities

The presence of acid-fast-bacilli (AFB) on a sputum smear (or other specimens for extrapulmonary disease suspicion) indicates TB disease. **Acid-fast microscopy** is easy and quick, but it does not confirm a diagnosis of TB because not all acid-fast-bacilli are *M. tuberculosis*. Therefore, a **culture** is done on all initial samples to confirm the diagnosis. If sputum obtained, three specimens should be obtained and at least one of the samples sent for **nucleic acid testing** to increase sensitivity

A positive culture for *M. tuberculosis* confirms the diagnosis of TB disease. Cultures should be completed on all specimens, regardless of AFB smear results. Laboratories should report positive results on smears and cultures within 1 working day by telephone or fax to the primary health care provider and to the state or local TB control program, as required by law.

A positive culture is not always necessary to begin or continue empiric treatment for TB if the clinical suspicion is high based on other factors.

TB Evaluation

6. TB Drug Sensitivity Testing/Drug Resistance

For all patients, the initial *M. tuberculosis* isolate should be tested for **routine TB drug sensitivity or resistance**. It is crucial to identify drug resistance as early as possible to ensure effective treatment.

Drug susceptibility patterns may be repeated for patients who do not respond adequately to treatment or who have positive culture results despite 3 months of therapy.

Susceptibility results from laboratories should be promptly reported to the primary health care provider and the state or local TB control program.

Initial empiric TB therapy may be based on the drug sensitivity profile of the likely source of TB exposure or based on the country of origin where they were likely exposed. Your TB Control Program can help obtain this information and give helpful guidance.

Testing Considerations: IGRAs

An Interferon Gamma Release Assay (IGRA) may be used in place of (but not in addition to) a TST in all situations in which CDC recommends a TST as an aid in diagnosing *M. tuberculosis* infection, with the following preferences and specific considerations. The most common IGRA tests currently available are the Quantiferon Gold Plus test and the T-Spot test.

- Preferred for testing persons from groups that historically have poor rates of return for TST reading in 48 to 72 hours after PPD placement
- Preferred for testing persons who have received BCG (as a vaccine or for cancer therapy)

TST	IGRA
Tuberculin is injected under the skin and produces a delayed-type hypersensitivity reaction if the person has been infected with *M. tuberculosis*	Blood is drawn for testing; test measures the immune response to the TB bacteria in whole blood
Requires two or more patient visits to conduct the test	Requires one patient visit to conduct the test
Results are available 48 to 72 hours later	Results can be available in 24 hours (depending on the batching of specimens by the laboratory and transport)
Can cause boosted reaction	Does **not** cause boosted reaction
Reading by HCW may be subjective	Laboratory test not affected by HCW perception or bias
BCG vaccination can cause false-positive result	BCG vaccination does **not** cause false-positive result and infection with most nontuberculous mycobacteria does **not** cause false-positive result
A negative reaction to the test does **not** exclude the diagnosis of LTBI or TB disease	A negative reaction to the test does **not** exclude the diagnosis of LTBI or TB disease

Testing Consideration: Pregnant Women

- TST and IGRAs are both safe and reliable throughout the course of pregnancy.
- No documented episodes of TST-related fetal harm have been reported since the test was developed, and no evidence exists that the TST has adverse effects on the pregnant mother.
- Pregnant women should receive a TB test if they have a specific risk factor for acquiring LTBI or for progression of LTBI to TB disease.

Testing Considerations: Pediatrics

- Young children have difficulty expectorating and they may require sputum induction or early morning gastric aspiration to obtain sample

- Children younger than 5 years of age are at high risk of rapidly developing severe forms of TB disease after infection and may need to be started on window prophylaxis while being tested after an exposure
    - (next slide)

Window Prophylaxis (Prophy) and Children

What is Window Prophylaxis?

- Prophylaxis with isoniazid (INH) or rifampin (RIF) during the window period to prevent the development of TB disease

What is the Window Period?

- The 8-10 weeks between the initial and repeat TB test (TST or IGRA) in a TB-exposed child

Infection Control

TB infection control plan is part of a general infection control program designed to ensure the following:

- Prompt detection of infectious TB patients
- Airborne precautions
- Treatment of people who have suspected or confirmed TB disease

Factors Associated with Infectious TB

The infectiousness of a TB patient depends on several factors.

In general, young children with pulmonary TB are less infectious than adults. Children are often unable to produce sputum and have paucibacillary TB.

For most patients, infectiousness declines rapidly after adequate and appropriate treatment is started; however, the rate of decline varies from patient to patient.

- Patients with extrapulmonary disease are usually noninfectious unless
  - Co-existent Pulmonary TB disease,
  - TB disease in the oral cavity or the larynx, or
  - Extrapulmonary disease that includes an open abscess or lesion with a high concentration of organisms.

Considerations for suspected TB patients evaluated in clinic, urgent care, or emergency departments

- Once a patient is identified as having risk factors of TB exposure or presents with signs or symptoms of active and contagious TB (respiratory complaints, cough, abnormal chest imaging), immediately take steps to minimize exposure to the health care team while the evaluation is in progress.
- Place the patient in a separate area, distanced from other patients in a well-ventilated area. If a separate room with a door or a negative pressure isolation room is available – even better.
- Ask the patient to wear a mask as soon as possible until other isolation steps can be arranged and for any time away from contained areas (trips to radiology, restroom, etc). An N-95 mask is preferred but a surgical mask is acceptable if no N-95 available.
- Minimize exposure of personnel by limiting the number of providers and time spent around the patient. Minimize aerosol generating procedures.
- Notify all care team members of the suspicion of TB so they can use caution and don N-95 masks
- Collect sputum samples asap and expedite delivery to the laboratory for AFB smear, culture and Nucleic Acid Amplification Testing (NAAT, increases sensitivity beyond smear and culture)

Isolation Recommendations

- Discuss the appropriate isolation and management of the suspect TB patient with your local Infection Control team in concert with the manager of the clinical area
- Consult your local Infectious Diseases or Pulmonary resources as indicated for guidance
- The Local/County Health Department or Indiana Department of Health TB Prevention and Care Program are ready to assist
- If TB smears are negative, the patient is a low contagious risk

Criteria to be Considered Non-Infectious for Patients with TB Disease

Patients no longer considered infectious if:

- They have 3 consecutive negative sputum smears
- Their symptoms have improved
- They are adhering to an adequate treatment regimen for at least 2 weeks

TB Infection Control in the Home

Patients can be sent home while still infectious ***if:***

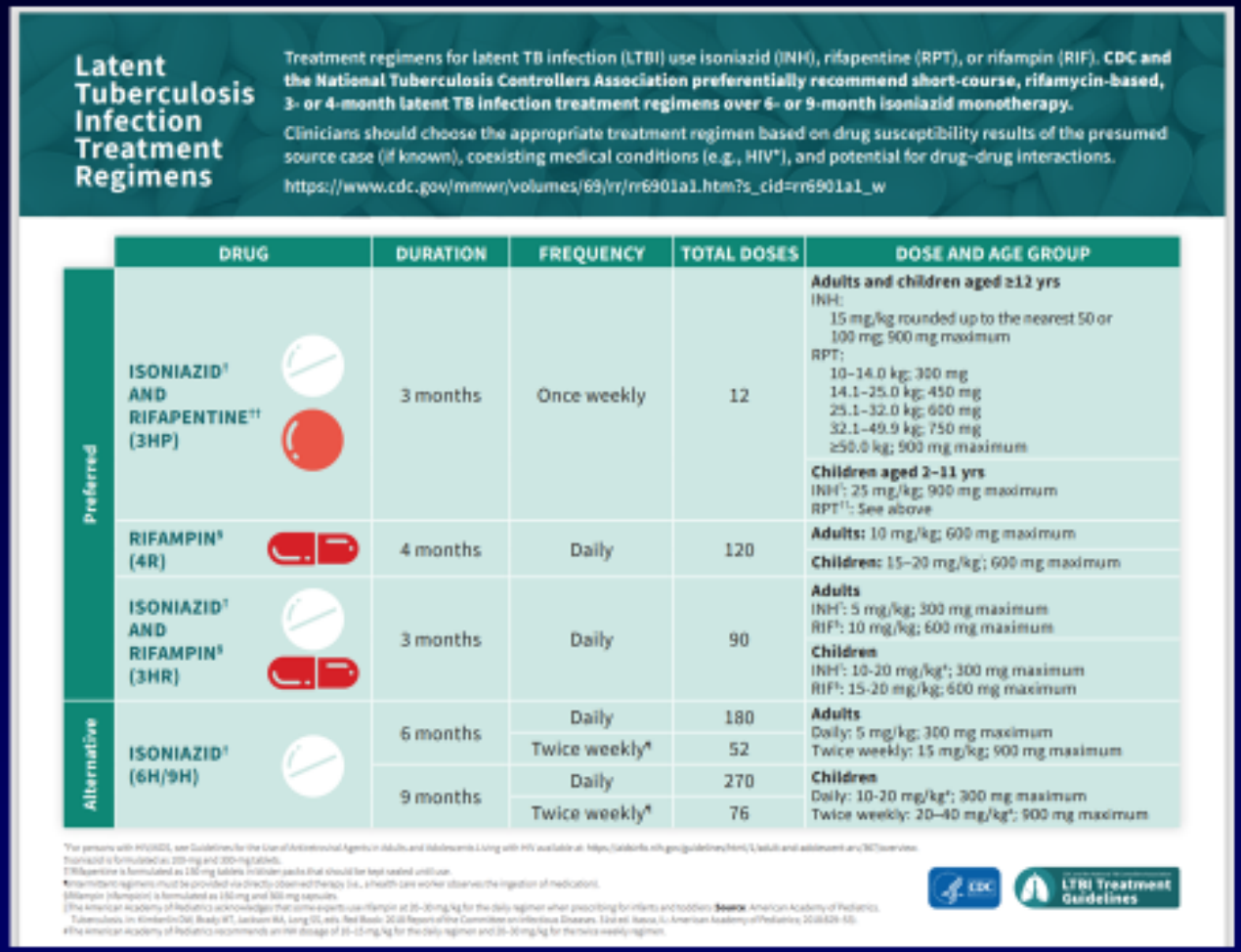
- A clear follow-up plan has been made and agreed on
- Patient is on standard treatment and DOT arranged
- No very young (under 4 years) or immunocompromised persons in household
- Patient is willing to refrain from travel outside the home except for healthcare visits and agrees to wear a mask

Latent TB Treatment:

Several options exist

Drug availability is sometimes a factor

Assess for possible drug interactions



Latent Tuberculosis Infection Treatment Regimens

Treatment regimens for latent TB infection (LTBI) use isoniazid (INH), rifapentine (RPT), or rifampin (RIF). **CDC and the National Tuberculosis Controllers Association preferentially recommend short-course, rifamycin-based, 3- or 4-month latent TB infection treatment regimens over 6- or 9-month isoniazid monotherapy.**

Clinicians should choose the appropriate treatment regimen based on drug susceptibility results of the presumed source case (if known), coexisting medical conditions (e.g., HIV*), and potential for drug–drug interactions.

https://www.cdc.gov/mmwr/volumes/69/rr/rr6901a1.htm?s_cid=rr6901a1_w

	DRUG	DURATION	FREQUENCY	TOTAL DOSES	DOSE AND AGE GROUP
Preferred	ISONIAZID† AND RIFAPENTINE†† (3HP)	3 months	Once weekly	12	**Adults and children aged ≥12 yrs** INH: 15 mg/kg rounded up to the nearest 50 or 100 mg; 900 mg maximum RPT: 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** INH†: 25 mg/kg; 900 mg maximum RPT††: See above
Preferred	RIFAMPIN§ (4R)	4 months	Daily	120	**Adults:** 10 mg/kg; 600 mg maximum **Children:** 15–20 mg/kg†; 600 mg maximum
Preferred	ISONIAZID† AND RIFAMPIN§ (3HR)	3 months	Daily	90	**Adults** INH†: 5 mg/kg; 300 mg maximum RIF§: 10 mg/kg; 600 mg maximum **Children** INH†: 10–20 mg/kg†; 300 mg maximum RIF§: 15–20 mg/kg; 600 mg maximum
Alternative	ISONIAZID† (6H/9H)	6 months	Daily	180	**Adults** Daily: 5 mg/kg; 300 mg maximum Twice weekly: 15 mg/kg; 900 mg maximum
			Twice weekly¶	52	
		9 months	Daily	270	**Children** Daily: 10–20 mg/kg†; 300 mg maximum Twice weekly: 20–40 mg/kg†; 900 mg maximum
			Twice weekly¶	76	

CDC | LTBI Treatment Guidelines

https://www.cdc.gov/tb/topic/treatment/pdf/LTBITreatmentRegimens.pdf

CDC

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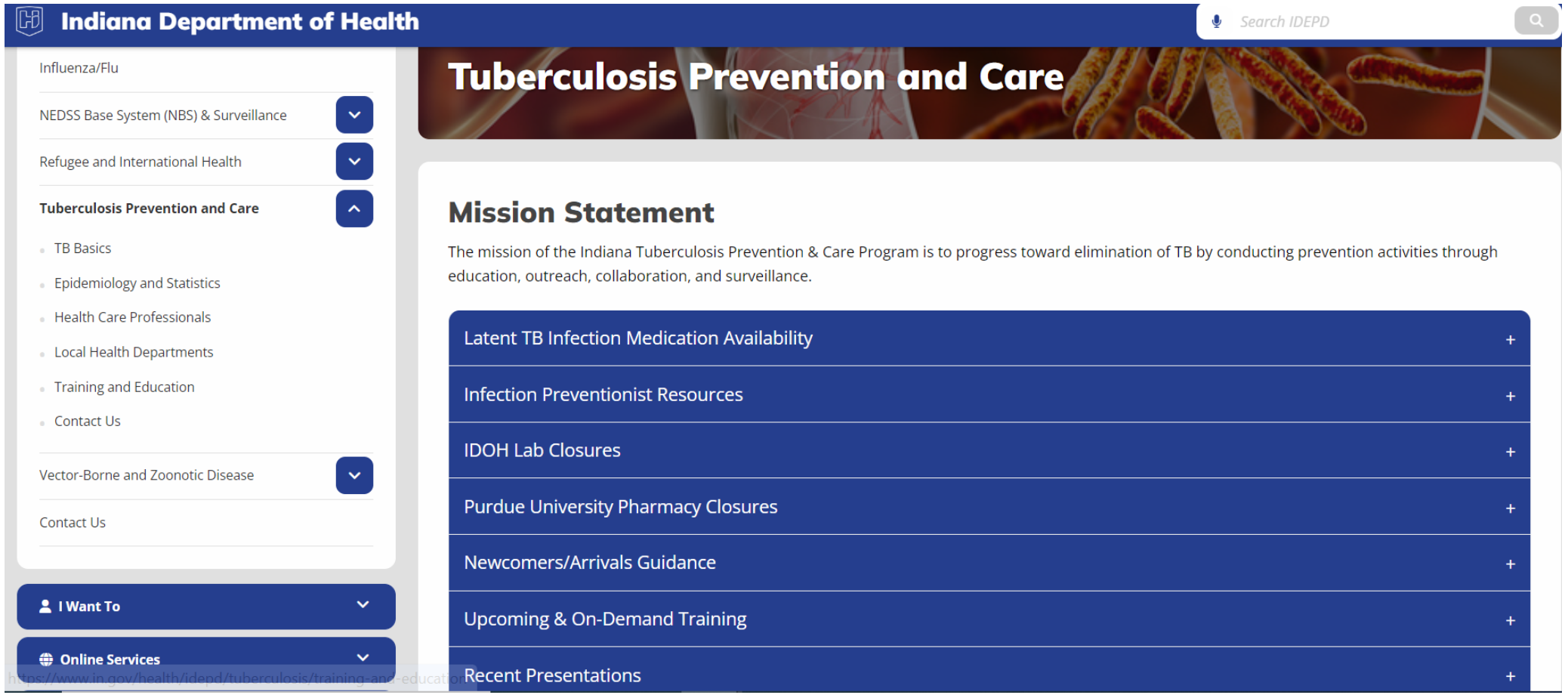
Treatment Regimens for TB Disease in United States

- CALL YOUR LOCAL ID, PULM, or Co. Health Dept
- 6 months duration for **routine** active pulmonary ds.
  - Initial phase: standard four drug regimens (INH, RIF, PZA, EMB), for 2 months
  - Continuation phase:
    - Additional 4 months with INH and RIF if susceptible strain and evidence of clinical response to initial treatment
- Adjustments often needed based on sensitivity of isolate and medication tolerance of the patient

Take-aways

- Think TB! in all patients with high-risk exposures
  - Racial/Ethnic groups, individuals experiencing homelessness
  - Diabetes, renal failure, immunosuppressive status
- Screen for TB infection with TST or IGRA testing
  - If positive, medical evaluation and CXR
  - Determine if Latent or TB disease
  - Treat LTBI. Contact trace active TB. Report both!
- Utilize your local TB expert and resources of the LHD and IDOH

IDOH TB Prevention and Care Resources



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https://www.in.gov/health/idepd/tuberculosis/

Contact Information

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Diagnosis of TB by Nucleic Acid Amplification (NAT)

- Direct amplification from clinical specimens
- Should be done on at least one of each set of 3 sputum samples to increase sensitivity
- 4 probes available
  1) MTB complex: *M. tuberculosis, M. bovis, M. bovis BCG, M. africanum, M. microti*
  2) MAC (avium-intracellulare complex)
  3) *M. kansasii*
  4) *M. gordonae*
- *Cannot distinguish viable from dead bacilli*
- *Probe for Rif resistance may predict MDR*