

Tuberculosis and Diabetes Mellitus

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Learning Objectives

- Learn tuberculosis (TB) pathogenesis and transmission
- Understand the impact of uncontrolled diabetes mellitus (DM) on TB infection and TB disease
- Recognize the importance of partnership between TB and DM programs
- Evaluate appropriate TB screening in clinical practice based on TB epidemiology

Audience Survey

- How many routinely screen foreign-born patients for TB?
- How many know the name and contact of your local TB PHN?
- How many have managed a patient that was then diagnosed with active TB disease?
- How many have assisted in management of active TB disease treatment?
- How many have assisted a patient in completing latent TB infection treatment?

New Terms

- acid-fast bacilli (AFB)
- Alveoli
- BCG—bacille Calmette-Guérin
- Cavity
- Culture
- directly observed therapy (DOT)
- disseminated TB
- droplet nuclei
- drug-resistant TB
- extensively drug-resistant TB (XDR TB)

New Terms

- extrapulmonary TB
- First-line TB treatment drugs
- Infectious
- interferon-gamma (IFN- γ)
- interferon-gamma release assay (IGRA)
- latent TB infection (LTBI)
- Mantoux tuberculin skin test (TST)
- multidrug-resistant TB (MDR TB)
- nucleic acid amplification (NAA)
- transmission

Mycobacterium Tuberculosis

Carried in airborne particles

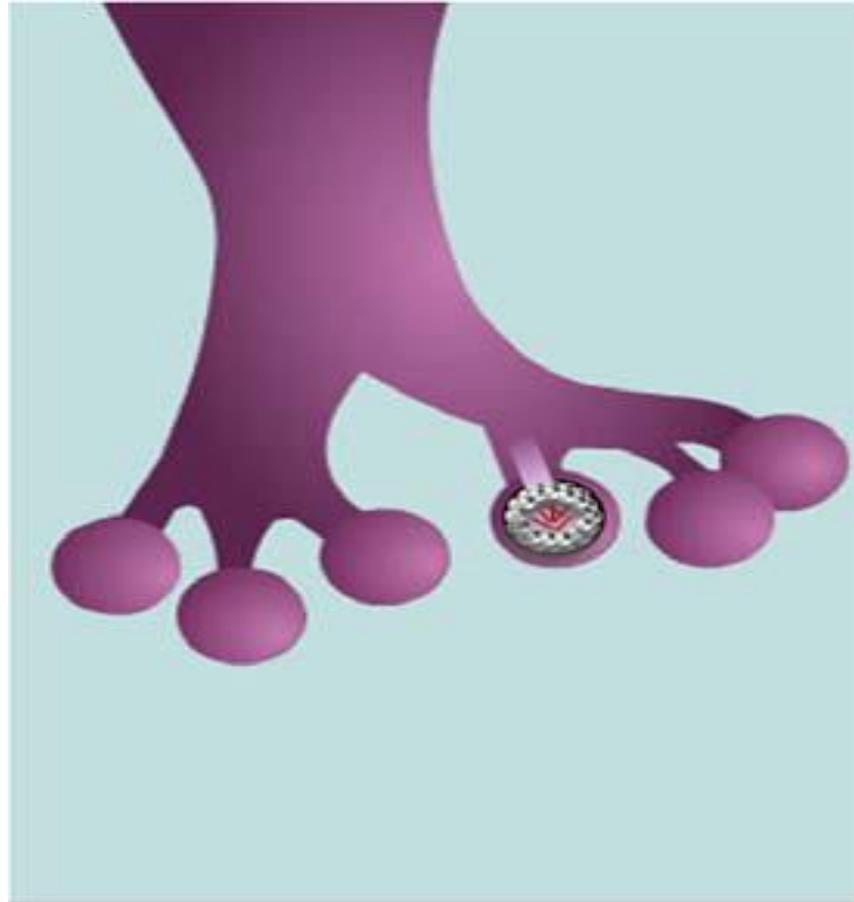
Infectious droplet nuclei

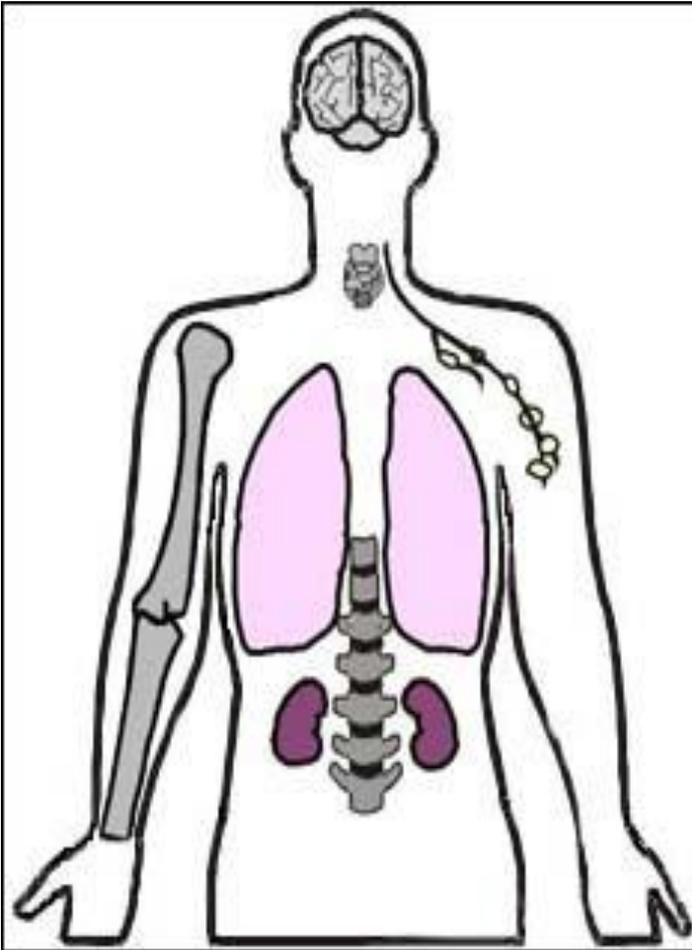
- Generated when persons who have pulmonary or laryngeal TB disease cough, sneeze, shout, or sing
- Tiny particles can remain suspended in the air for several hours (depending on the local environment)

Transmission occurs when:

1. a person inhales droplet nuclei containing *M. tuberculosis* AND
2. the droplet nuclei traverse the mouth or nasal passages, upper respiratory tract, and bronchi to reach the alveoli of the lungs

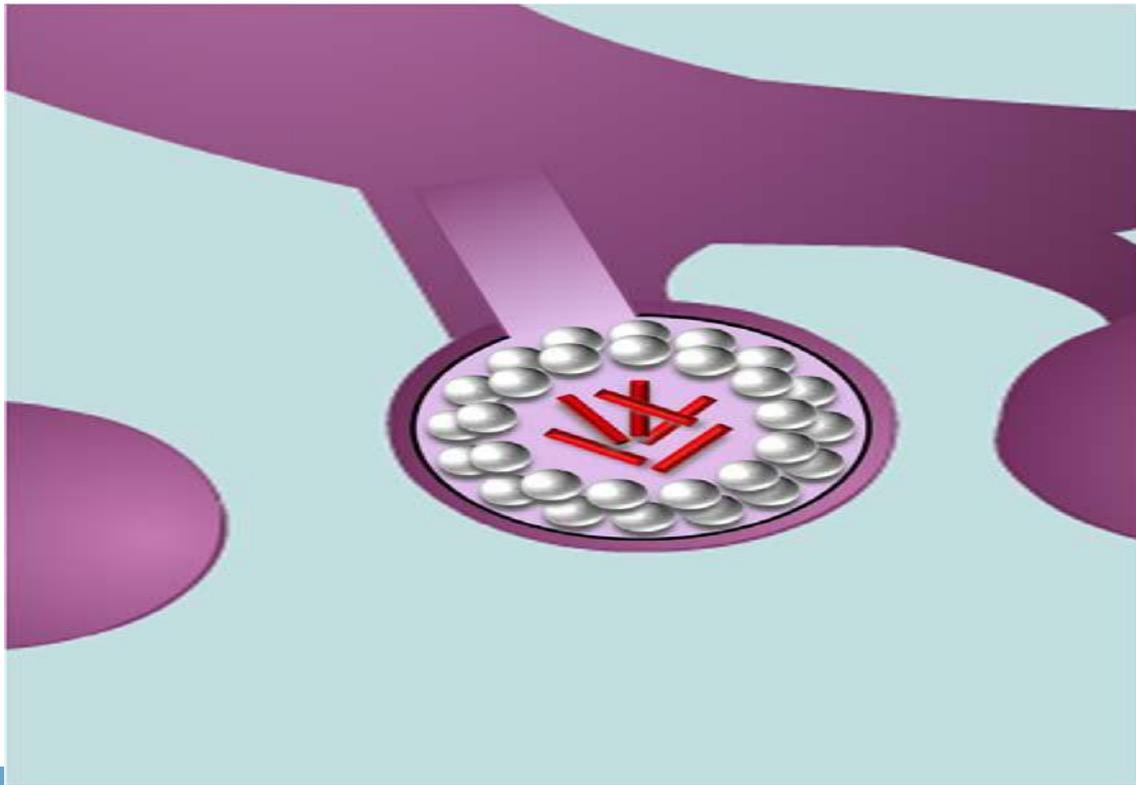
**Tubercle
bacilli
multiply in
the alveoli**



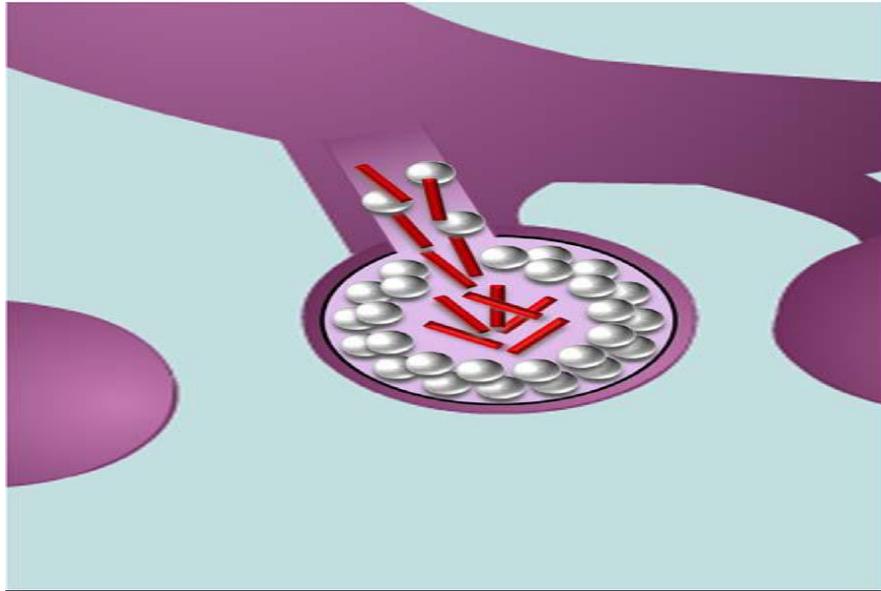


**A small number of
tubercle bacilli enter
the bloodstream and
spread throughout the
body**

Within 2 to 8 weeks, macrophages form granuloma



A weakened immune system may not keep the tubercle bacilli under control, the bacilli begin to multiply rapidly causing TB disease.



Tuberculosis Pathogenesis

- From the alveoli to circulatory system and potential for extrapulmonary
- Window Prophylaxis
- 2-8 weeks for immune system to respond by forming granuloma- latent TB infection
- T-Cell response, antibodies made- respond with INF-gamma
- If the immune system is not strong enough to contain the bacilli in a latent state the bacilli will begin to multiply causing active TB disease.

Tuberculosis Infection

- Breathed in the TB bacteria
- No signs or symptoms of TB and is not sick
- Not infectious
- Not a reportable “case” of TB disease
- Can be treated BEFORE active disease occurs

Tuberculosis Disease

- Usually symptomatic and contagious
 - Cough
 - coughing up blood
 - weight loss
 - Fever
 - night sweats
- 20% are asymptomatic
- Abnormal X-ray, positive Sputum culture (usually)
 - Can be extrapulmonary
- Case of TB disease must be reported to County

Care of Patients with TB Disease

- Remain in isolation until non-infectious
- Treated with 4-drugs for a minimum of 6 months
- Directly Observed Therapy (DOT)
- Managed by local health departments
 - Contact Investigations
 - Directly Observed Medication Therapy (if needed)
 - Case Management (if needed)
 - Reporting to WA State DOH
 - Isolation

Global Statistics – 2014¹

9.6 *million* new cases worldwide

1.5 *million* TB-related deaths

- TB surpasses HIV as leading infectious disease killer in 2014

Estimated 300,000 new cases of

- multidrug-resistant TB (MDR-TB)
- Estimated 190,000 MDR-TB deaths

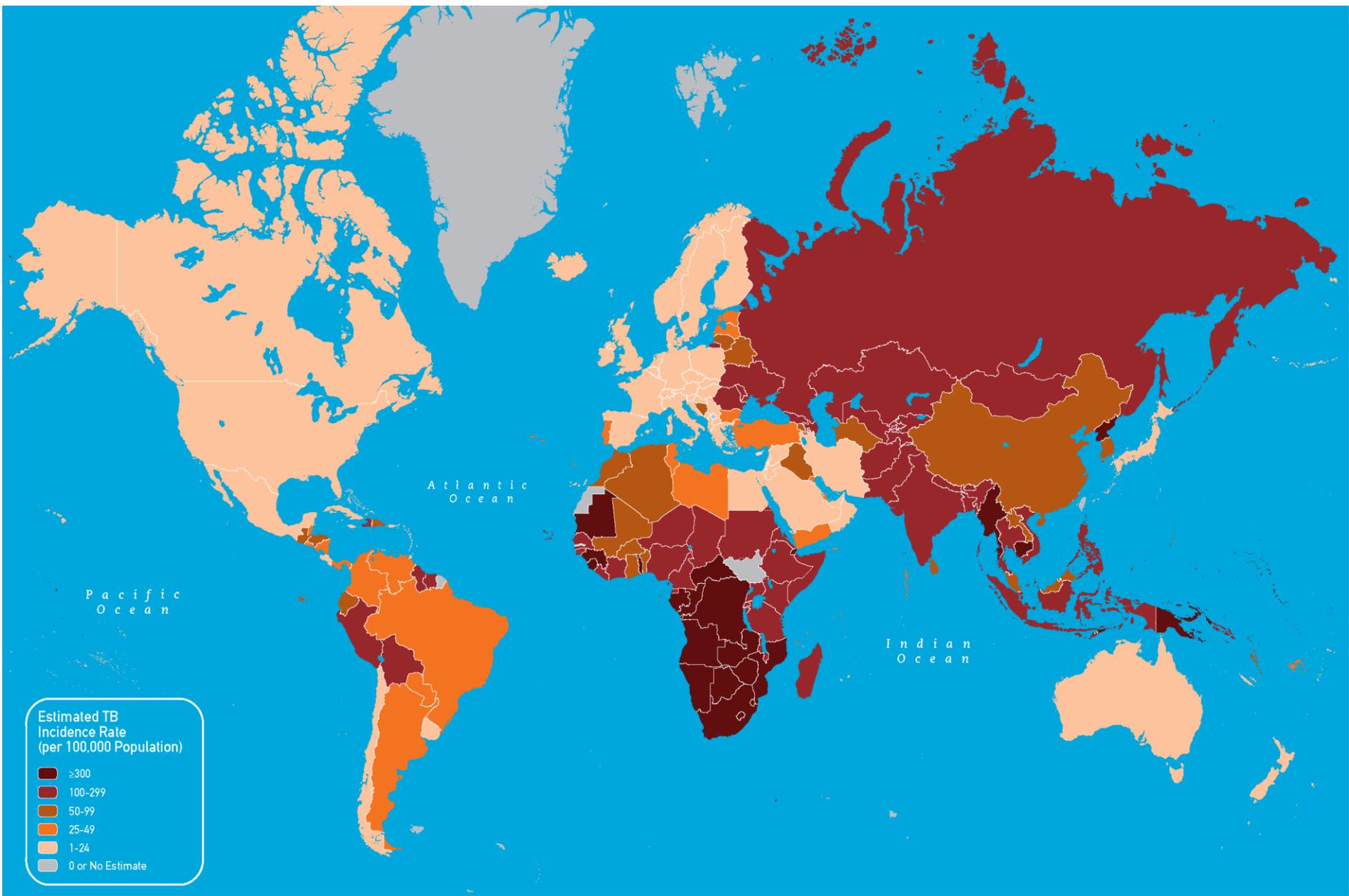
National Statistics – 2015²

9,563 newly-diagnosed cases reported

- 1.7% increase from 9,406 cases in 2014

Incidence rate of 2.98 cases/100,000

- Slight rise from 2014 rate (2.95)
- First National TB rate increase in 23 years



WA State Statistics – 2015

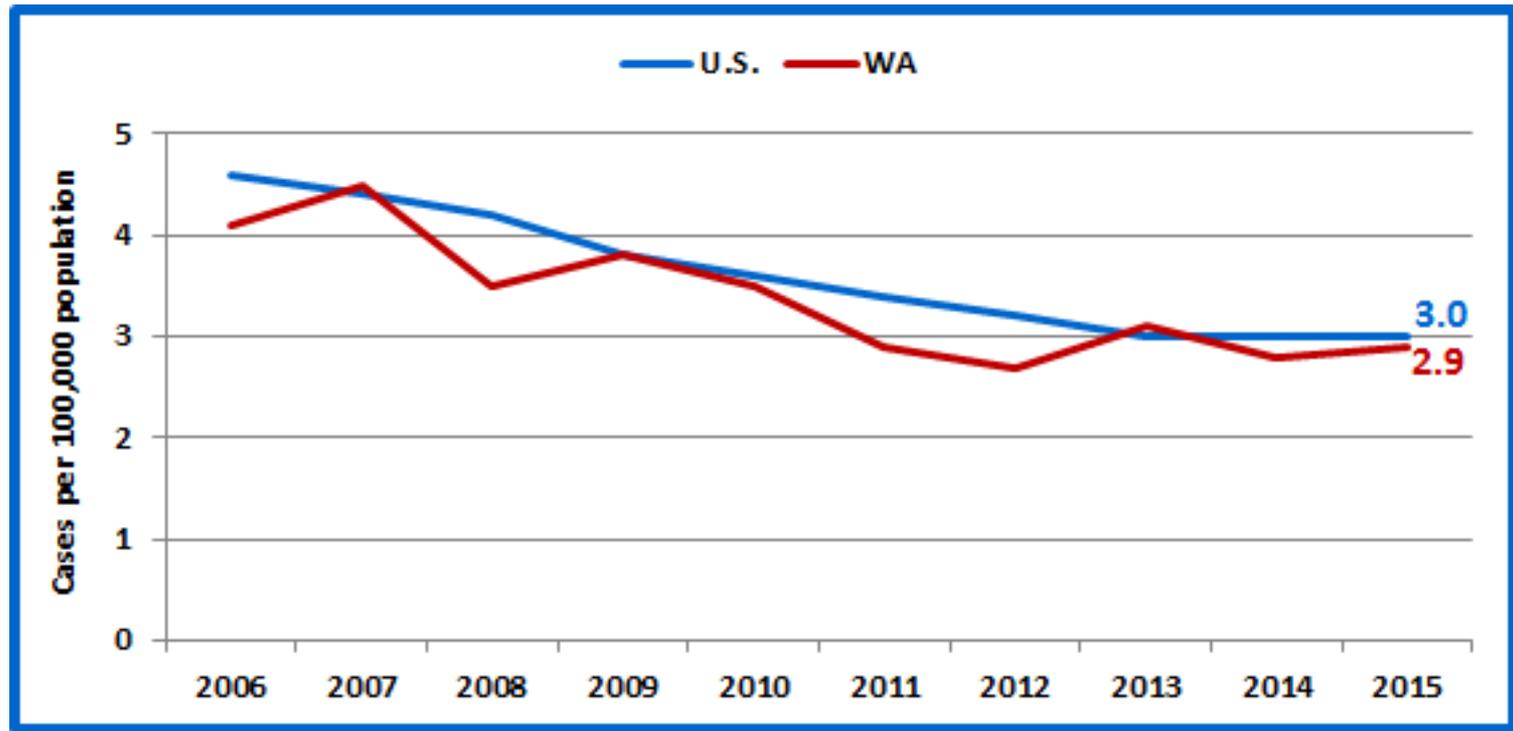
208 newly-diagnosed cases reported

- 7.2% increase from 194 cases in 2014

Incidence rate of 2.9 cases/100,000

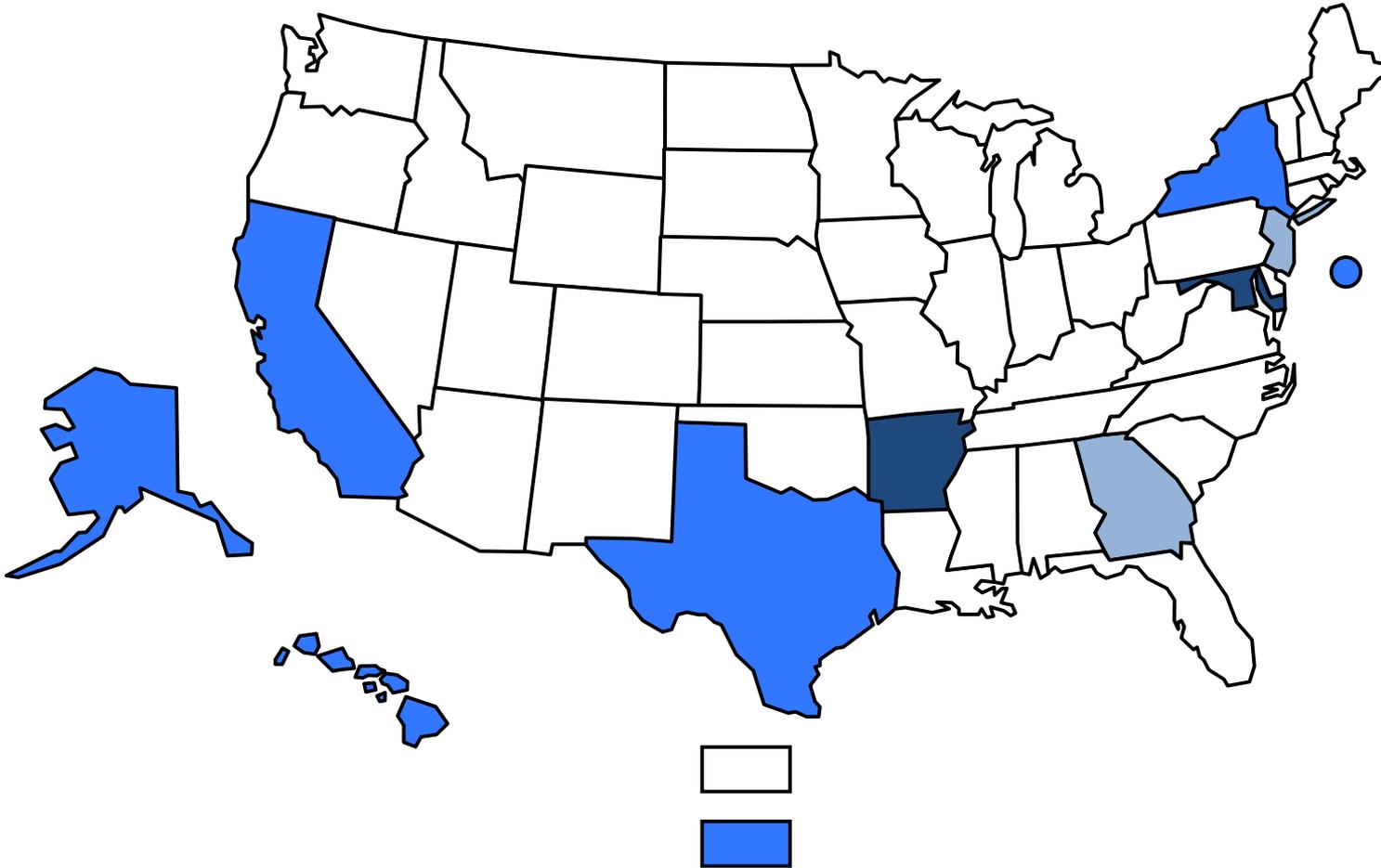
- Slight rise from 2014 rate (2.8)
- 2.4% multidrug-resistant (MDR-TB)

Comparative Incidence – US and WA



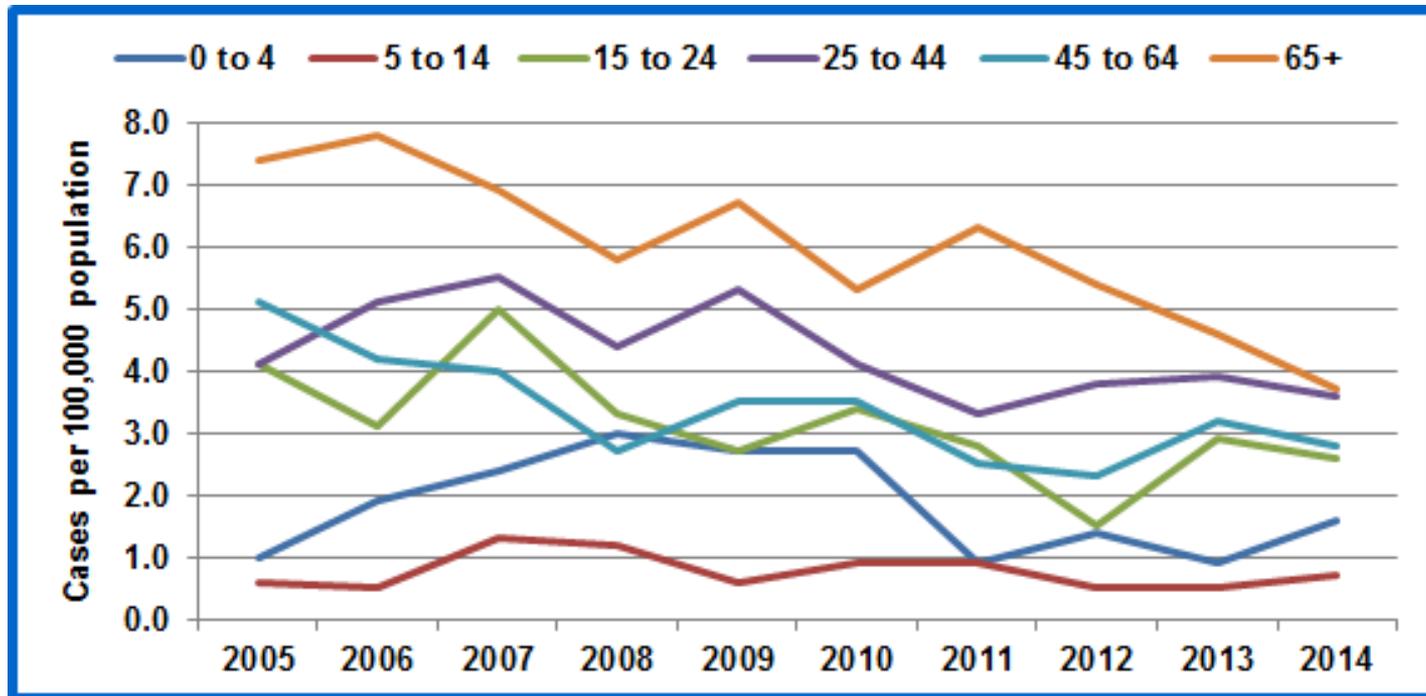
*Overall decline in WA rate over past decade
Tracking at or below U.S. rate.*

TB Case Rates,* United States, 2014²



*Cases per 100,000.

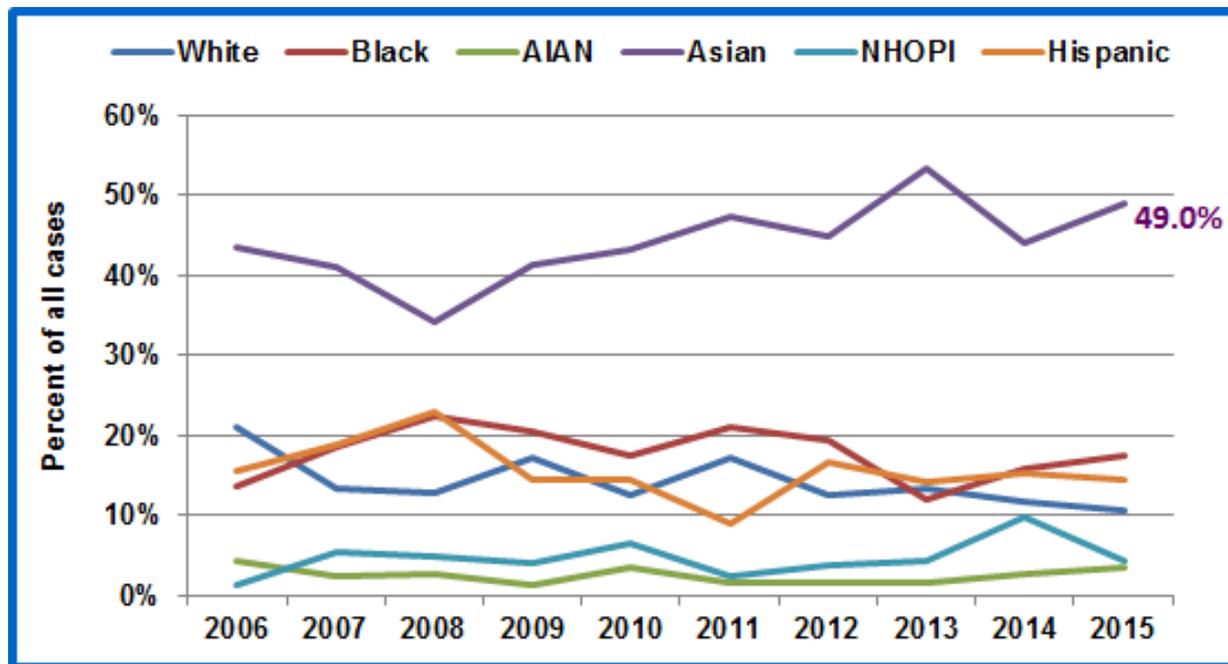
Crude Incidence by Select Age Groups – WA



Persons 65+ years of age at greater risk of TB compared to most other age groups.

Notes: Age calculated in years from DOB to date of case report (2008 and before), and to date of TB diagnosis (2009 and after). Date of TB diagnosis defined as earliest collection among positive clinical specimen(s) supporting final case verification – else report date if verified as provider diagnosed.

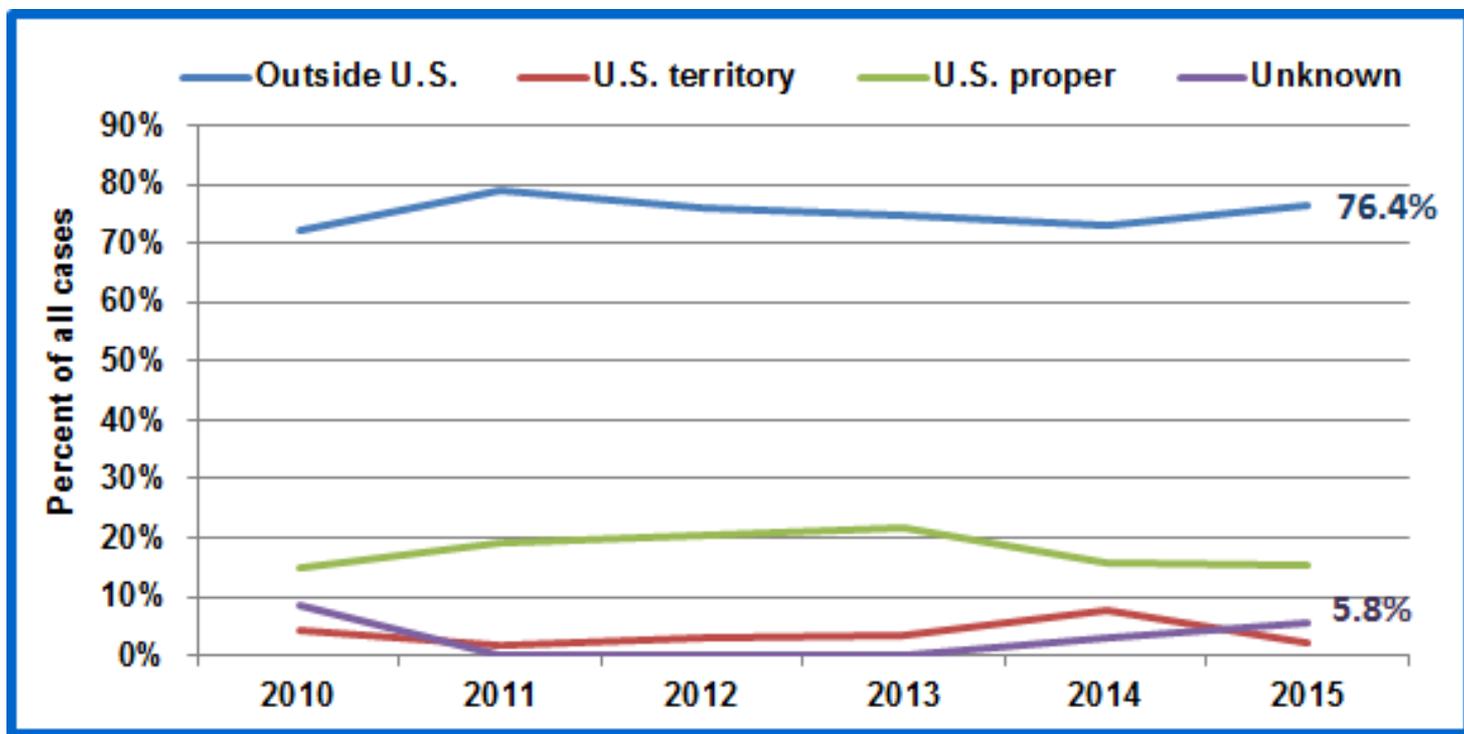
Proportional Disease Burden by Race/ Ethnicity – WA



Asian communities suffer greatest TB disease burden among all race-ethnic groups.

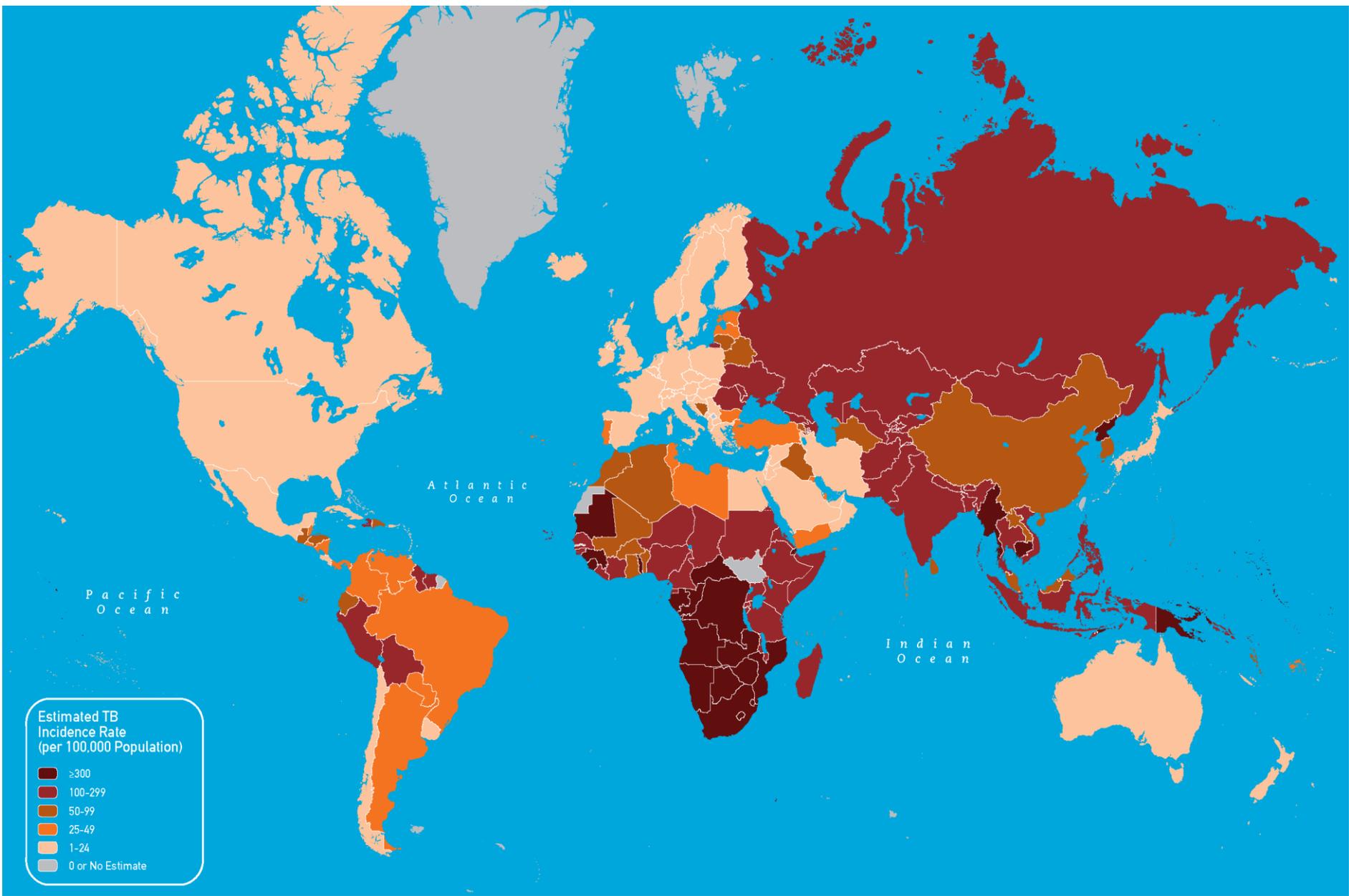
Notes: AIAN - American Indian or Alaskan Native; NHOPI - Native Hawaiian or Other Pacific Islander.

Proportional Disease Burden by Origin – WA

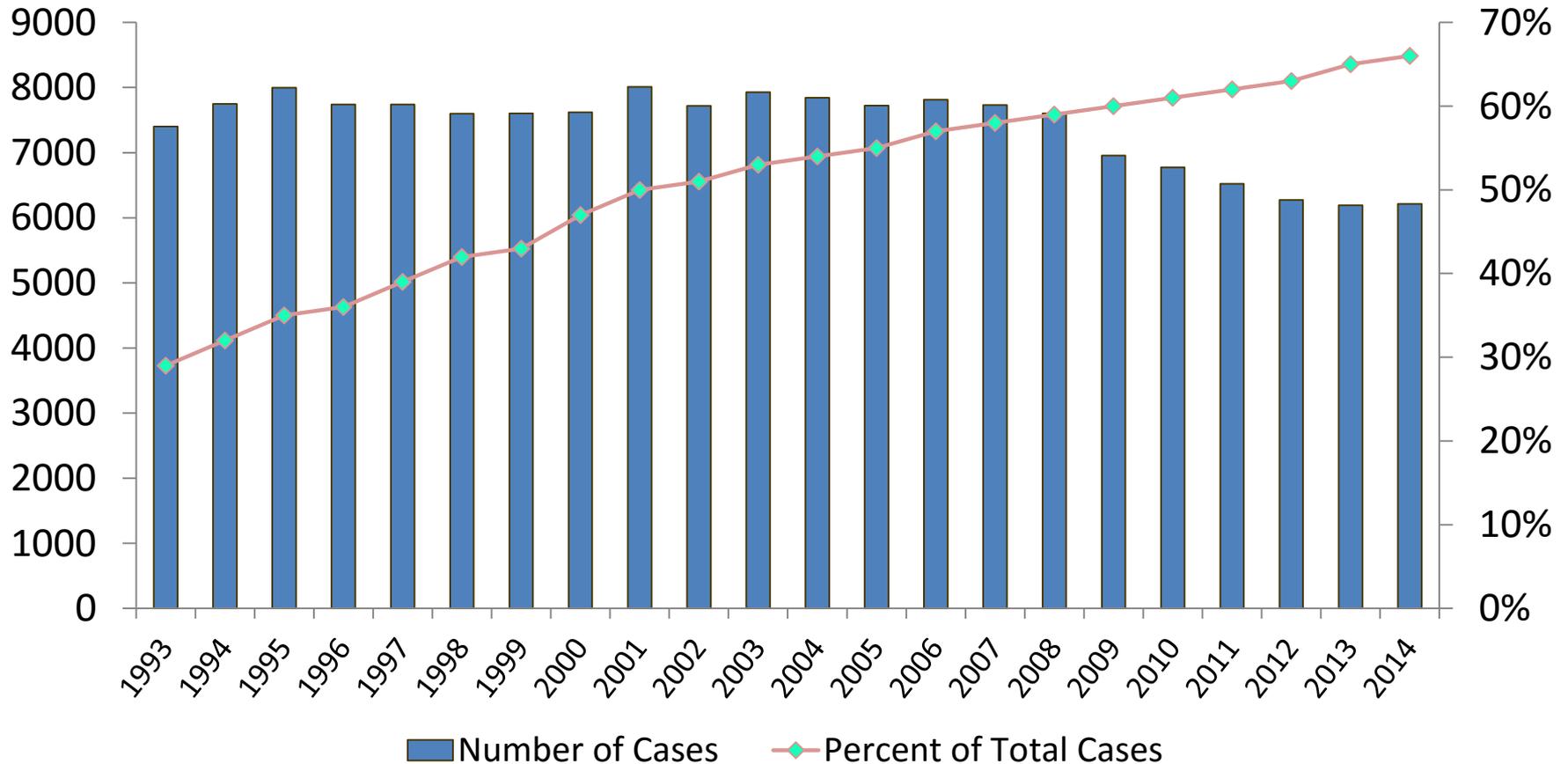


Foreign-born residents carry greatest TB disease burden overall.

Notes: U.S. territories include: American Samoa, Fed. States of Micronesia, Guam, Marshall Islands, Midway Island, Northern Mariana Islands, Puerto Rico, Palau, U.S. Virgin Islands, and U.S. Minor and Outlying Pacific Islands.



Trends in TB Cases in Foreign-born Persons, United States, 1993 – 2014*

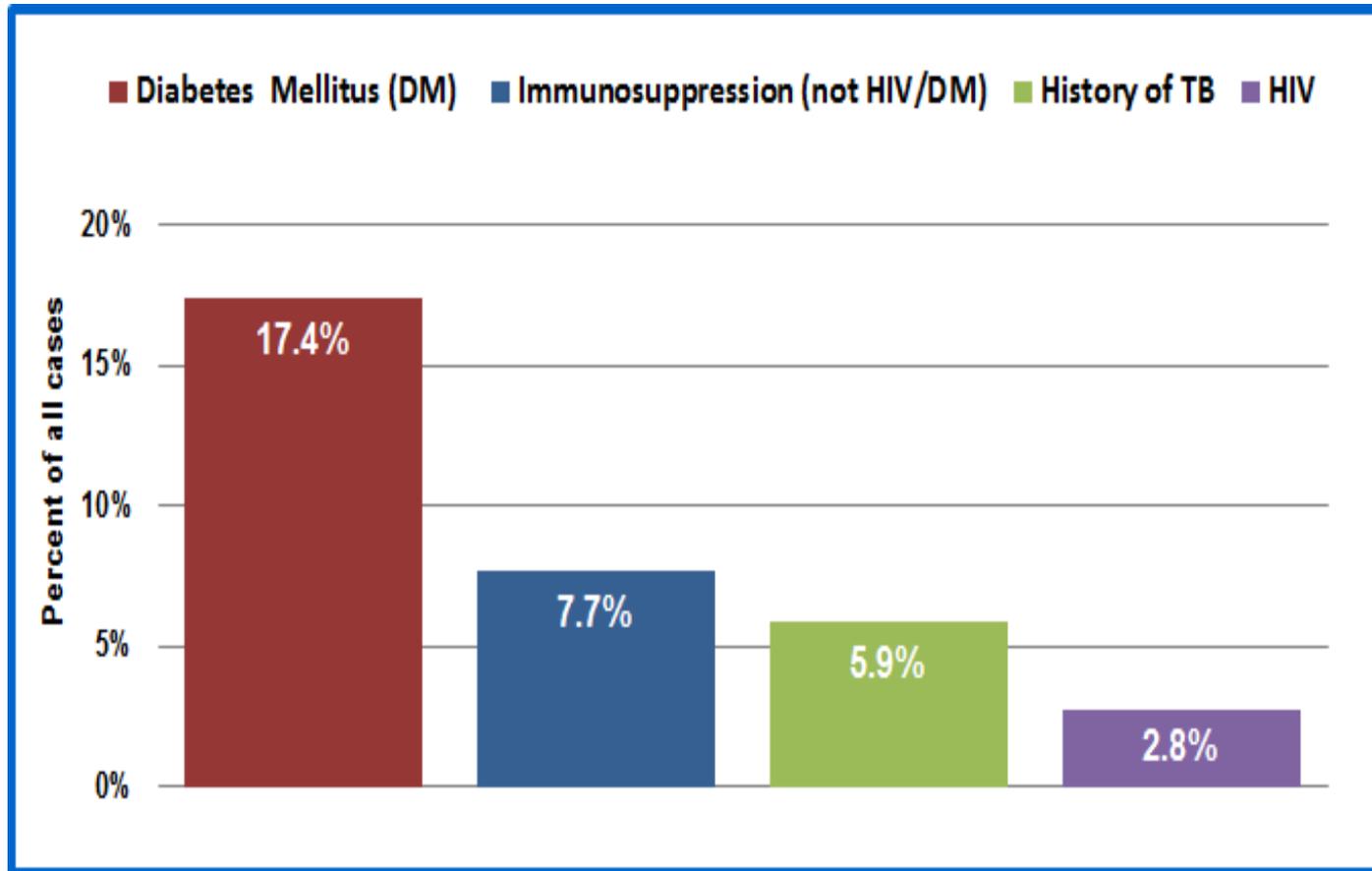


*Updated as of June 5, 2015.

TB Exposure & Disease Risk ^{3, 7}

- Approximately 30% of persons exposed to *Mycobacterium tuberculosis* will develop LTBI,
- If untreated, approximately 5% to 10% of these persons will progress to active tuberculosis disease or reactivation of tuberculosis. ^{3, 7}
- Highest risk in the first 2 years (about 5% of exposed)
- Overall risk increases with immunosuppressive conditions
 - Uncontrolled Diabetes 30% lifetime risk
 - HIV 10% additional risk per year

Select Medical Risk Factors^{1,2,3} – WA Cases, 2009-2015



¹ Medical risks recorded at diagnosis, as documented in medical record or otherwise reported by healthcare provider.

² Frequencies represent medical risks as reported alone or along with other risk factors.

³ Immunosuppressing conditions include: TNF alpha-antagonist therapy, post-organ transplantation, end-stage renal disease, and other immunosuppression.

The Relationship Between TB & DM⁵

- Increased Susceptibility
 - Hyperglycemia- impairs interferon-gamma production
 - Macrophage and lymphocyte function resulting in reduction in interferon-gamma.
- Diminished ability to contain the organism in infection stage (thus developing disease)
- Poorly controlled DM might augment the severity of infections.

Impact of Uncontrolled DM on TB⁵

- Increased difficulty to diagnose TB in DM patients
 - Atypical radiographic pattern and distribution
 - 20% of patients with DM present with lower lobe involvement
 - Less likely to have positive smear or culture
- Increase disease severity and outcomes
 - Multi-lobular involvement
 - Multiple cavities
 - Cavities lengthen treatment beyond 6 months
 - Potentially higher bacillary burden and increased length of time to sputum conversion

Pharmacological Issues ⁵

- TB medication
 - might worsen glycemic control in patients with DM
 - can change oral absorption of other medication
- Overlapping toxicities must be considered when co-managing TB and DM
 - peripheral neuropathy with INH
 - hyperglycemia with rifampin
- Rifampin concentrations can be too low
 - Can lead to treatment failure or resistance

Importance of Partnership^{4, 6}

- Improved patient case management
- Common public health goals, yet competing interests.
- Make collaboration a program goal
- Motivating change
- Screening efficiency: Who should be tested for TB and who should be tested for DM?

Appropriate TB Screening Strategies⁶

- Where was my patient born?
- What are their current glucose levels? A1C>7
- What TB screening test should I use?
 - History of BCG, IGRA recommended
 - TST- ask if immune compromised
 - Discuss with local TB program
- Make screening routine:
 - All patients with DM and exposure risk factors, especially foreign born from high risk TB countries should be screened and treatment recommended.

What Can I do?

- Ask Questions
- Talking Points:
 - Increased chances of active TB disease in presence of DM
 - Protect family and friends from spread of TB
 - Treat BEFORE active TB disease
- Add screening to intake sheet
- Offer information to patients and medical providers regarding various treatment options:
<http://www.doh.wa.gov/TB>

Case Study A

- 52 year old female born in Mexico, in US for 11 years and travels back yearly.
- Symptoms: 2 months of cough with 2 days of blood in sputum; 40lbs of wt loss in last year; night sweats.
- RBG 252, HgbA1c 12.5
- QFT positive
- Initial AFB smears negative, poor quality specimens
- CT and Chest x-ray: consolidation and LUL cavity
- LUL resection, chest tube, etc
- 4 drug TB treatment started
- Lung tissue culture positive MTB
- In hospital for a total of 26 days

Case Study B

- 63 year old US born AI/AN female
- poorly controlled DM
- Household contact
- Mild, chronic dry cough
- Initial TST 00mm
- Second TST at 8 weeks 00mm

Case Study B Continued... 3 months

- Developed productive cough, night sweats, chills, 30lbs weight loss, tiredness
- Last year HgA1c 5.4%; RBG 200-400 currently
- Now QFT positive!
- Chest radiograph showed RLL infiltrate
- Sputum: AFB negative, but NAAT positive, culture negative.
- What happened?

References

- ¹ World Health Organization. Global Tuberculosis Report 2015. 20th ed. Geneva, Switzerland: World Health Organization; 2015.
- ² Center of Disease Control and Prevention: Tuberculosis case counts are based on provisional National Tuberculosis Surveillance System data as of March 4, 2016. Updated data will be available in CDC's annual TB surveillance report later this year at <http://www.cdc.gov/tb/statistics/>
- ³ World Health Organization, Tuberculosis Control: http://www.who.int/trade/distance_learning/gpgh/gpgh3/en/index4.html
- ⁴ World Health Organization. (2011). Collaborative framework for care and control of tuberculosis and diabetes.
- ⁵ Dooley, K. E., & Chaisson, R. E. (2009). Tuberculosis and diabetes mellitus: convergence of two epidemics. *The Lancet infectious diseases*, 9(12), 737-746.
- ⁶ Brostrom, R ; & Mase, S. (2015, October 27). Double Trouble [Webinar]. From Advancing Prevention Project. Retrieved from <http://www.advancingpreventionproject.org/double-trouble.html>
- ⁷ American Thoracic Society. Targeted tuberculin testing and treatment of latent tuberculosis infection. *Am J Respir Crit Care Med*. 2000;161(4 pt 2):S221-47.

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