

**National Center for HIV/AIDS, Viral Hepatitis, STD,
and TB Prevention**



APHL 10th National Conference on Laboratory Aspects of Tuberculosis

Opening Remarks

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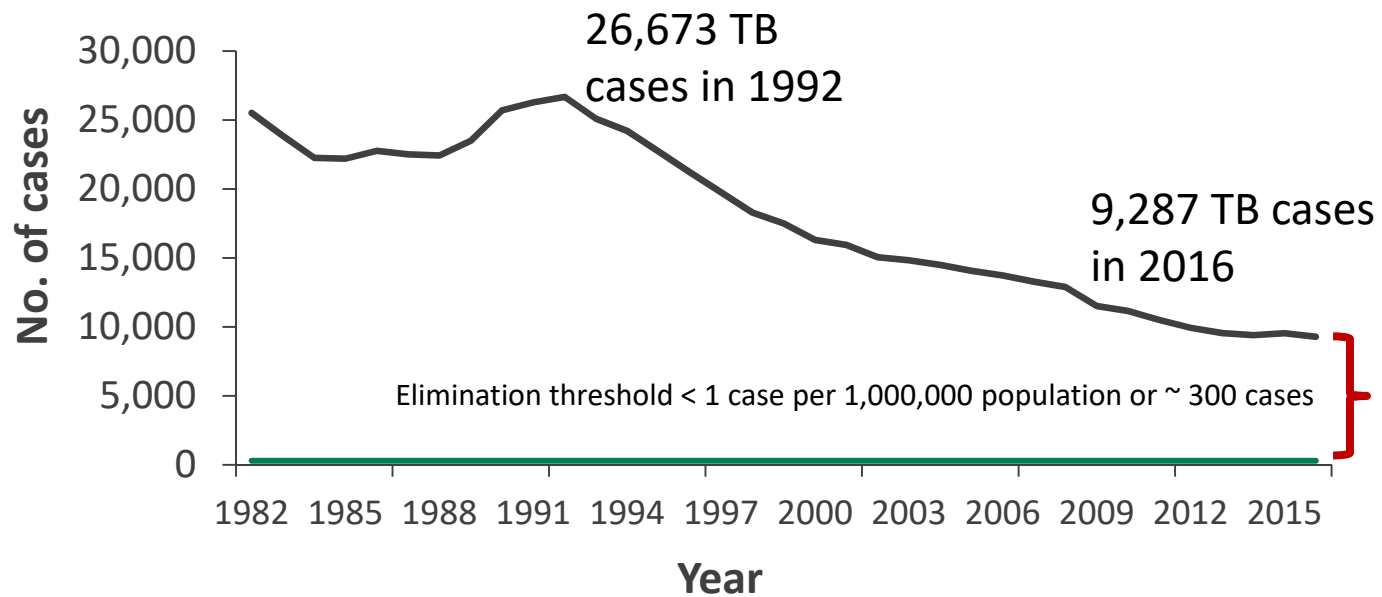
Outline

- **Status of TB Elimination in the United States**
- **Importance of Addressing Latent Tuberculosis Infection (LTBI) for TB Elimination**
- **Laboratory Testing and TB Elimination**
 - TB Disease Diagnosis
 - Detection of Drug Resistance
 - Response to Treatment
 - Molecular Epidemiology
 - LTBI Testing



Status of TB Elimination in the United States

Reported Tuberculosis (TB) Cases United States, 1982–2016*



*Provisional data, as of February 17, 2017.



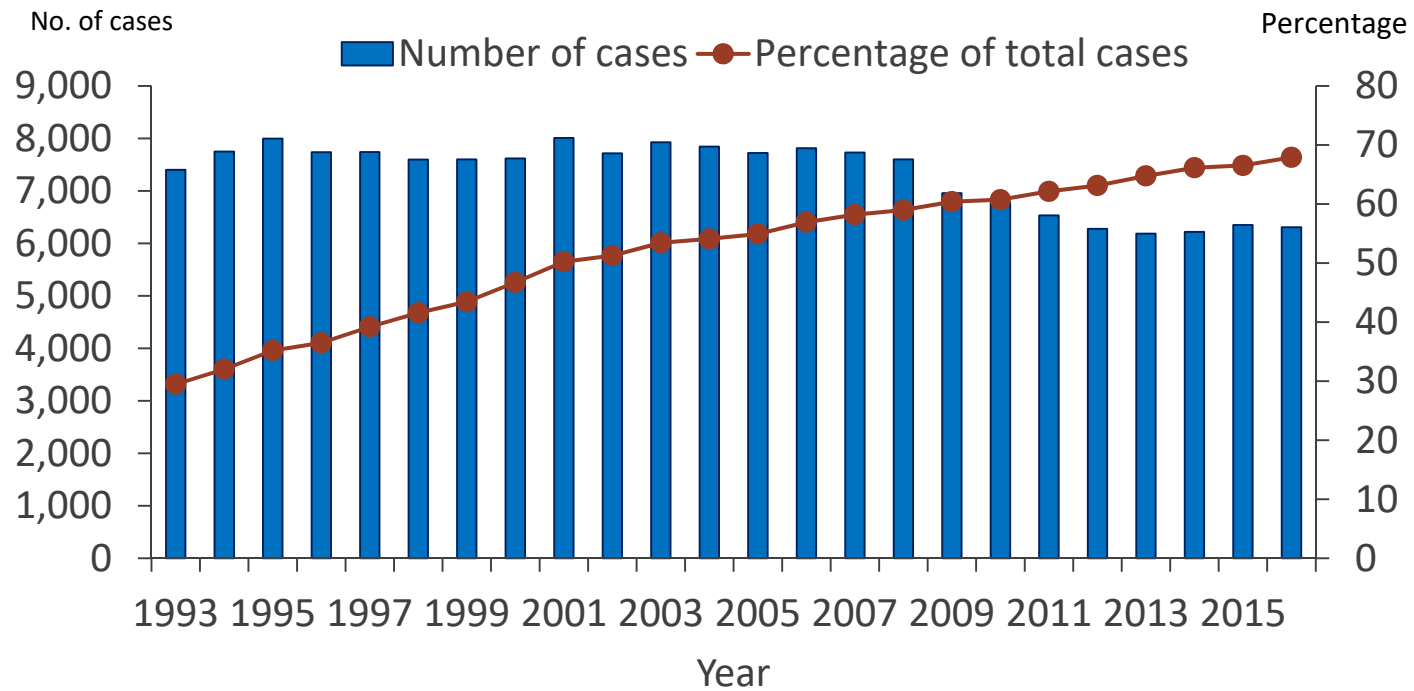
TB Morbidity United States, 2011–2016

Year	No.	Rate*
2011	10,510	3.4
2012	9,941	3.2
2013	9,549	3.0
2014	9,403	3.0
2015	9,546	3.0
2016	9,287	2.9

* Cases per 100,000 population; provisional data as of February 17, 2017.



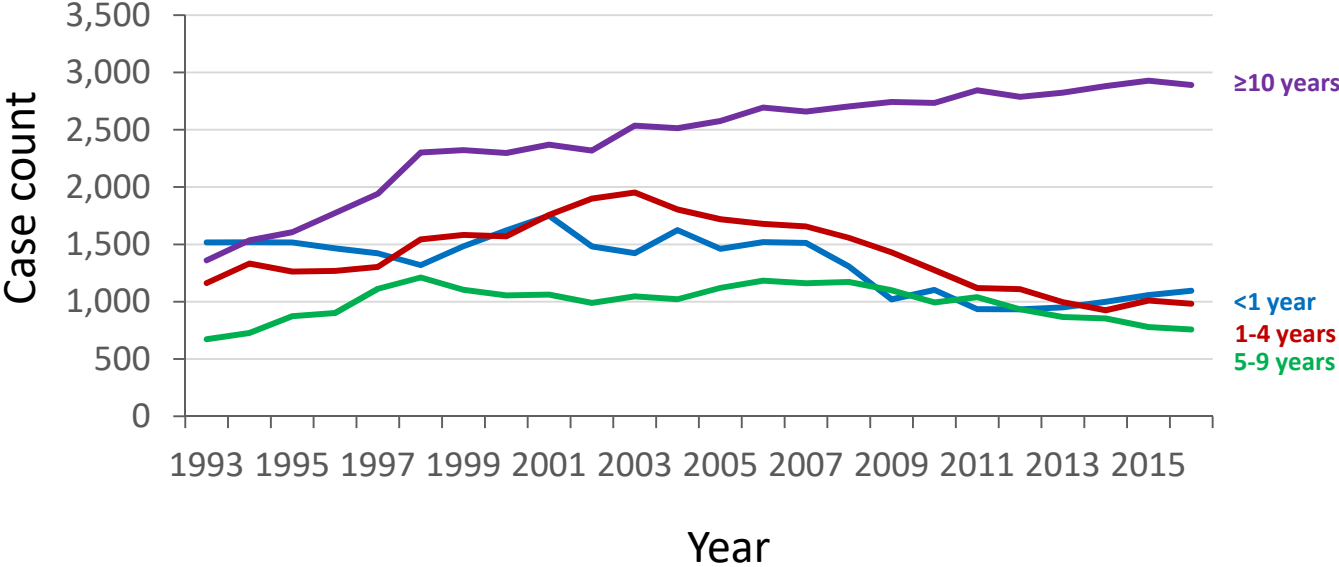
TB Cases Among Foreign-Born Persons, United States, 1993–2016*



*Provisional data, as of February 17, 2017.



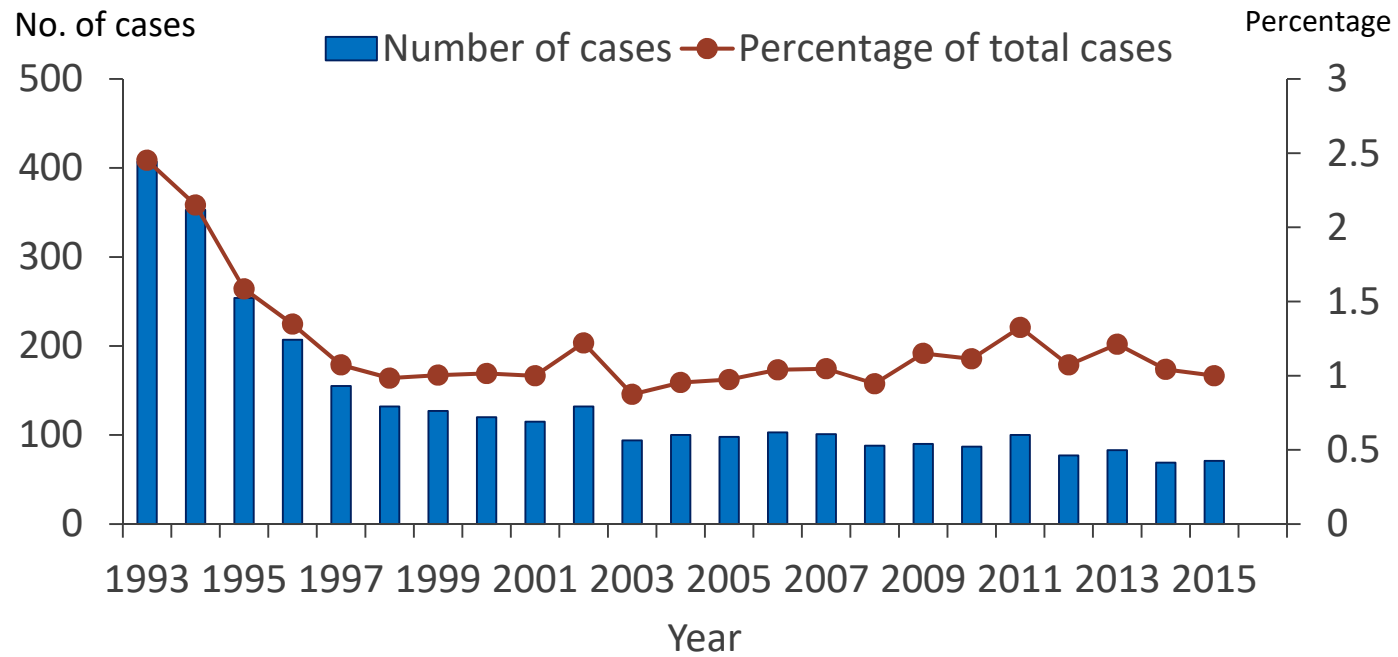
TB Case Counts Among Foreign-born Persons by Time Since Arrival, 1993–2016



*Provisional data, as of February 17, 2017.



Primary MDR-TB, United States, 1993–2015*

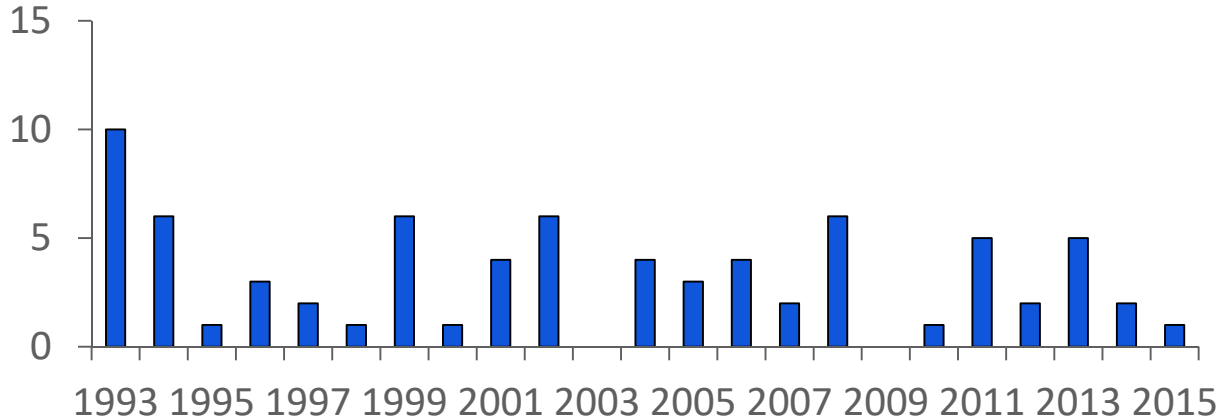


*Provisional data, as of February 17, 2017.

Note: Based on initial isolates from persons with no prior history of TB; multidrug resistant TB (MDR-TB) defined as resistance to at least isoniazid and rifampin.



XDR-TB* Case Count, Defined on Initial DST,† by Year, 1993–2015‡



* XDR-TB , extensively drug-resistant TB.

† DST, drug susceptibility test.

‡ Provisional data ,as of February 17, 2017.

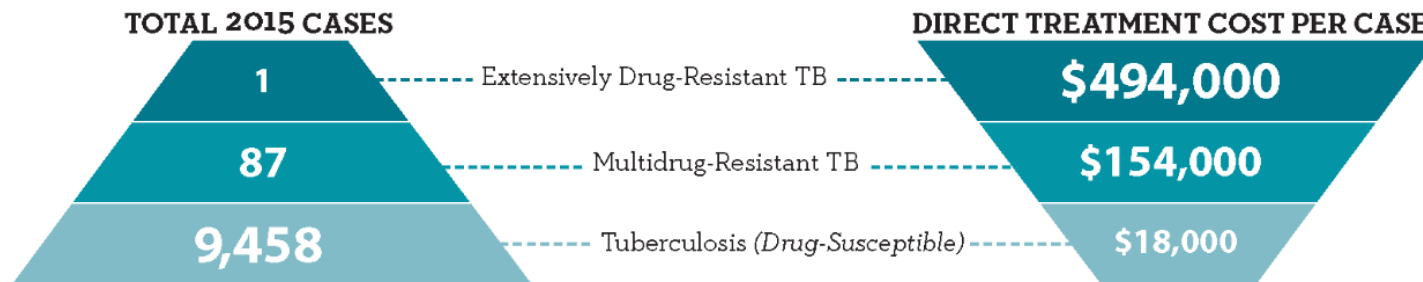
Note: XDR-TB is defined as resistance to isoniazid and rifampin, plus resistance to any fluoroquinolone and at least one of three injectable second-line anti-TB drugs.



\$184 Million in 2015 in Treatment Costs Alone

DRUG-RESISTANT TB IS COMPLEX & COSTLY.

Drug-resistance threatens our ability to treat & control TB.



Challenges to TB Elimination

- **Loss of expertise and experience**
 - Clinical, laboratory, program
- **Drug and biologic shortages because of lack of market**
 - Regulatory requirements limit access to Global Drug Facility or other mechanisms that can access larger global market
- **Concentration of remaining cases and outbreaks in more difficult-to-reach populations**
 - Foreign-born, homeless, etc.
- **How to address the large pool of persons with LTBI**
 - <10 thousand TB cases; millions of persons with LTBI



Importance of LTBI

Updated Estimate of Recent TB Transmission

- Publication: *Recent Transmission of Tuberculosis—United States, 2011–2014*. Courtney M. Yuen, J. Steve Kammerer, Kala Marks, Thomas R. Navin, Anne Marie France. PLoS ONE 11(4): e0153728. doi:10.1371/journal.pone.0153728
- Used a field-validated plausible source-case method to estimate cases likely resulting from recent transmission during January 2011–September 2014
- Of 26,586 genotyped cases, 14% were attributable to recent transmission
- Remaining 86% likely result from reactivation of LTBI



Up to 13 Million People in the United States Have Latent TB Infection

ELIMINATING TB REQUIRES A COMPREHENSIVE APPROACH.

CDC is committed to fighting TB whenever & wherever it occurs through:



Vigilant Surveillance



Better Diagnostics
& Treatments



Testing & Treatment of
High-Risk Populations



Education of
Health Care Providers



Laboratory Testing and TB Elimination

Diagnosis of TB Disease

- If the correct tests are ordered, essentially all TB patients should be diagnosed within weeks, with 75% or more diagnosed within days, using currently available technology
- Major delays in diagnosis are due to patients not having access to or seeking care or clinicians not considering TB in differential diagnosis
- Nevertheless, would benefit from an inexpensive, rapid test with sensitivity comparable to culture, especially if point of care



Detection of Drug Resistance

- Substantial advances have been made in molecular testing
 - Allows more rapid detection of drug-resistance
- Xpert TB/RIF has been useful as an initial screen
- Gaps, both for culture-based and molecular testing, for a number of first and second-line drugs
- Discordance between molecular and culture-based tests
- Mutations of unknown significance



Response to Treatment

- **Still dependent on culture conversion**
 - Substantial delay
- **Need new biomarkers to measure response to treatment**
 - Lack of alternative biomarkers is a major obstacle to new drug and regimen development
 - Clinical trials are longer and more costly



Molecular Epidemiology

- **Current national system based on 24 locus MIRU and spoligotyping has been very useful at detecting and responding to transmission events (outbreaks)**
- **In certain situations, discriminatory power has not been adequate**
 - Whole genome sequencing (WGS) has been helpful
- **Challenge will be to transition to universal WGS over next few years**
 - Sequencing capacity
 - Information storage
 - Analysis and integration with conventional surveillance data



Testing for LTBI

- Interferon-gamma release assays (IGRA) have been particularly useful for testing persons with BCG vaccination and those less likely to return for tuberculin skin test (TST) reading
- Incremental improvement
 - For both IGRA and TST, only 5-10% of persons who test positive will progress to TB disease
 - Must treat 10-20 people for LTBI for each one that will progress to TB disease
- A transformational test that is much better at predicting who will progress to TB disease is needed to better address LTBI, which is key to TB elimination



Thank You

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

