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**Expanding Latent Tuberculosis Infection  
Testing and Treatment to Accelerate  
Tuberculosis Elimination**

**Philip LoBue, MD**

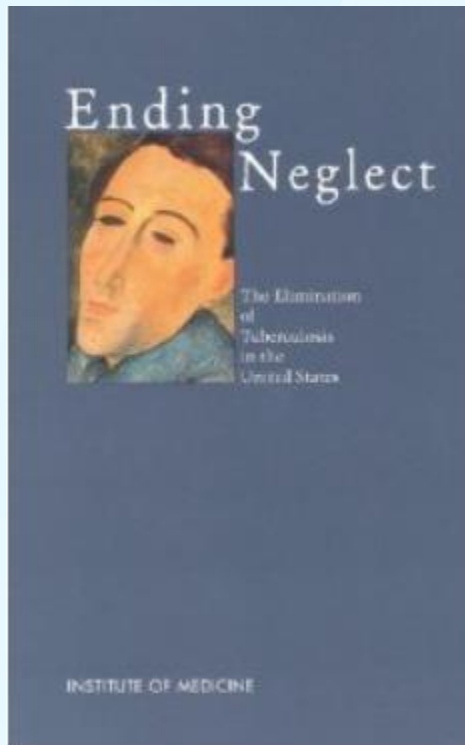
# Disclosure

- I have no relevant financial disclosures

# Outline

- ❑ **Role of latent tuberculosis infection (LTBI) testing and treatment in US TB elimination strategy**
- ❑ **New opportunities**
- ❑ **Challenges**
- ❑ **What is needed to address LTBI**
  - Engagement of private providers and affected communities
  - Role of health department

# Elements of National Elimination Strategy



- ❑ **Ending Neglect: The Elimination of Tuberculosis in the U.S.**
- ❑ **Institute of Medicine Report published in 2000**
- ❑ **CDC response includes 6 goals that are elements of elimination strategy in United States**

## 6 Goals

- ❑ Main control of TB
- ❑ **Accelerate the decline**
- ❑ Develop new tools
- ❑ Reduce the global TB burden
- ❑ Mobilize and sustain support
- ❑ Track Progress



## Goal II: Accelerate the decline

**Advance toward TB elimination through targeted testing and treatment of persons with latent TB infection, appropriate regionalization of TB control activities, rapid recognition of TB transmission using DNA fingerprinting methods, and rapid outbreak response.**



# Why Focus on Latent TB Infection?

- ❑ Data regarding TB arising from recent transmission versus reactivation of LTBI
- ❑ Modeling
- ❑ New Opportunities

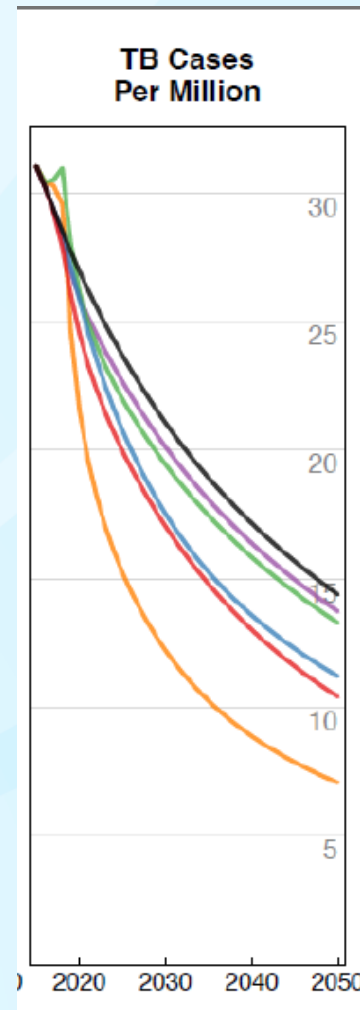
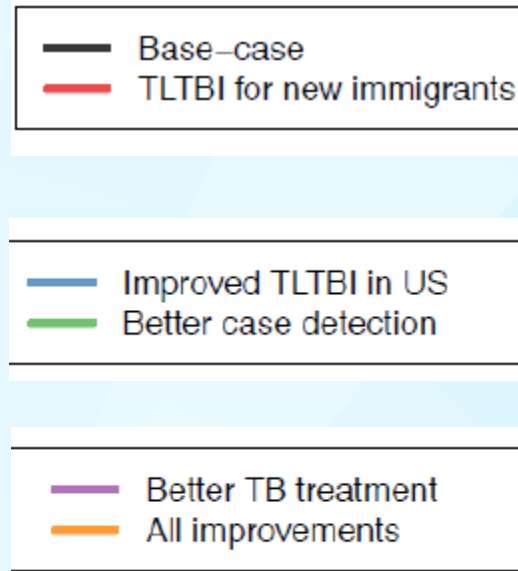
# Updated Estimate of Recent TB Transmission

- **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**



# Harvard Projections to 2050 by Intervention

Intervention scenarios 2015-2050



# Opportunities to Better Address LTBI

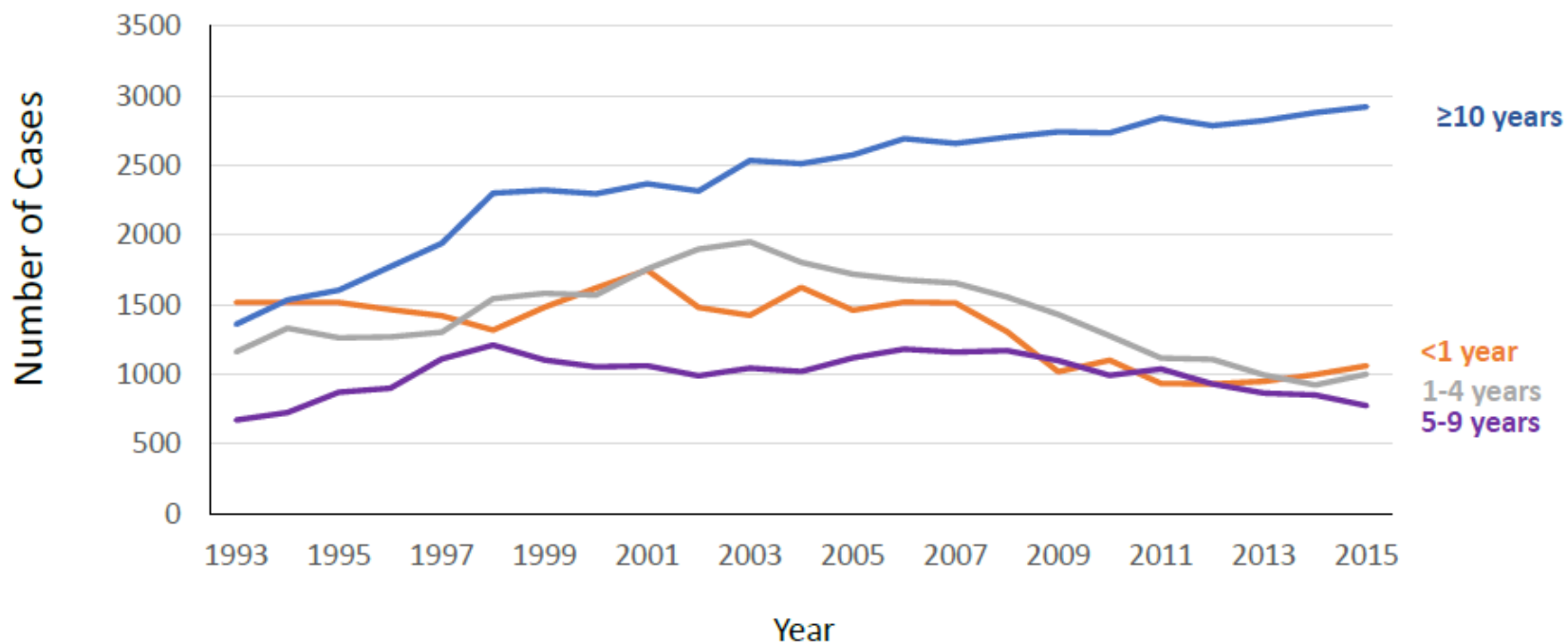
- ❑ **Relatively low burden of TB disease in the US**
- ❑ **Very high treatment completion rates; not much room for improvement**
- ❑ **Can we reduce diagnostic delays?**
  - No easy answer because delays arise from patients not seeking care and providers not consider TB as diagnosis
- ❑ **Newer tests that have advantages in key populations**
- ❑ **Newer and better treatment regimens**
- ❑ **Recommendation by US Preventive Services Task Force**



# Key Risk Groups for TB in the United States

- ❑ **Foreign-born: 67% of cases; case rate 13 times higher than US-born**
  - Mexico, Philippines, Vietnam, China, India top 5 countries
- ❑ **Racial/ethnic minorities: ~85% of cases; case rates 7-28 times higher than whites**
- ❑ **HIV infected: ~ 7% of cases**
- ❑ **Homeless: ~ 6% of cases**
- ❑ **Incarcerated: ~ 4% of cases**
- ❑ **Substance abuse: 7-12% of cases**

## TB case counts among foreign-born persons by time since arrival, 1993–2015



# LTBI Testing: Advantages of Interferon-gamma Release Assays (IGRAs) in Key Populations

- ❑ **Foreign-born persons with BCG vaccination**
  - No cross-reaction with BCG so no false positive tests due to BCG
- ❑ **One visit for blood draw**
  - Do not have to re-test persons who miss TST reading
  - Advantage in groups that are particularly unlikely to follow up for second visit (e.g., homeless)
  - Only have to track down persons with positive test results

## Better Treatment for LTBI

- ❑ **12-dose, once-weekly isoniazid and rifapentine (3HP)**
- ❑ **4 months of daily rifampin (4R)**
- ❑ **Both regimens have better completion rates and less hepatotoxicity than 9 months of isoniazid (9H)**

# US Preventive Services Task Force (USPSTF) Recommendation in 2016

Population	Recommendation	Grade (What's This?)
Adults who are at increased risk for tuberculosis	The USPSTF recommends screening for latent tuberculosis infection (LTBI) in populations that are at increased risk.	<b>B</b>

# Main Challenges to TB Elimination

- ❑ **Political commitment**
  - As cases continue to decrease, seems less of a priority to general public and policymakers
  - Resources at risk
- ❑ **Loss of expertise and experience**
  - Clinical, laboratory, program
- ❑ **Drug and biologic shortages because of lack of market**
  - Regulatory requirements limit access to GDF 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 latent tuberculosis infection (LTBI)**
  - <10 thousand TB cases; millions of persons with LTBI





# Tuberculosis (TB) Disease: Only the Tip of the Iceberg

There are **two** types of TB conditions:  
**TB disease** and **latent TB infection**.

People with **TB disease** are sick from active TB germs. They usually have symptoms and may spread TB germs to others.

People with **latent TB infection** do not feel sick, do not have symptoms, and cannot spread TB germs to others.

But, if their TB germs become active, they can develop **TB disease**.

**Millions** of people in the U.S. have **latent TB infection**. Without treatment, they are at risk for developing **TB disease**.



U.S. Department of  
Health and Human Services  
Centers for Disease  
Control and Prevention



To learn more about TB, visit  
[www.cdc.gov/tb](http://www.cdc.gov/tb)

## **Estimating LTBI: NHANES**

- ❑ **NHANES is a series of sequentially run cross-sectional studies, implemented in 2-year cycles that assess the health of the civilian, non-institutionalized U.S. population**
- ❑ **To obtain a nationally representative sample of the civilian, non-institutionalized U.S. population, NHANES employs a complex, stratified, multistage probability cluster sampling design**
- ❑ **Approximately 5,000 persons participate in the survey in approximately 15 counties per year**
- ❑ **In 2011-2012, NHANES included a TB component with TST and Quantiferon testing**

## How Much LTBI Is There in the United States?

	Prevalence	Number of people
TST positive	4.7%	13.1 million
Quantiferon positive	5.0%	13.9 million
Both positive	2.1%	5.9 million

Estimates from National Health and Nutrition Examination Survey, 2011-2012, manuscript submitted

# How Much LTBI Is There in the United States in Foreign-born Persons?

	Prevalence	Number of people
TST positive	20.5%	8.2 million
Quantiferon positive	15.9%	6.4 million
Both positive	9.3%	3.7 million

Estimates from National Health and Nutrition Examination Survey, 2011-2012, manuscript submitted

## **Targeted Testing and Treatment of Latent Tuberculosis**

- ❑ **Primary focus on foreign-born from medium- and high-incidence countries**
- ❑ **Highest priority to foreign-born with conditions that increase risk of progression (e.g., HIV, smoking , diabetes, TNF-a antagonists)**
- ❑ **IGRAs have an advantage in BCG-vaccinated persons**
- ❑ **Short-course regimens can increase completion**
- ❑ **Expansion of testing and treatment beyond health department**

# **LTBI: What Needs to Be Done Using Existing Tools?**

- ❑ **Major initiative with 5 parts**
  - Requires substantial additional resources
- ❑ **1) Registry/surveillance system**
- ❑ **2) Scale up of testing to targeted populations**
- ❑ **3) Scale up of short course LTBI treatment**
- ❑ **4) Communication, outreach**
- ❑ **5) Increased public health staffing for implementation and oversight**

# **Expansion of Testing and Treatment Beyond Health Department**

- ❑ How can we leverage USPSTF draft recommendation for LTBI testing?**
- ❑ Who serves targeted populations in the community and how can we engage them?**
- ❑ Effective engagement of affected communities and their medical providers**

# **Medical Provider and Community Engagement**

- ❑ Provider education**
- ❑ Outreach to primary care professional societies**
- ❑ Toolkits for providers**
  - Easy to use apps and brochures**
- ❑ Integration of clinical decision support tools for LTBI testing and treatment into electronic health records**
- ❑ Outreach to community leaders at all levels**
- ❑ Community education**



## **Role of Health Department**

- ❑ Lead community and provider engagement**
- ❑ Consultation and oversight**
- ❑ Require increased staff and resources**

## What New Tools Are Needed?

- ❑ **A test that is much more predictive of progression from LTBI to TB disease than TST or IGRAs**
  - IGRAs are better in BCG vaccinated persons, but are still poor
- ❑ **Even shorter LTBI treatment**
  - Next aim should be for 4-6 weeks

**Thank You !**

**Questions?**