Strategies for Elimination of Tuberculosis in the United States

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CURRENT STATE OF TUBERCULOSIS IN THE UNITED STATES
Reported TB Cases
United States, 1982–2013

Fewest cases since systematic recording began in 1953

Elimination threshold ~ 300 cases
### TB Morbidity
United States, 2008–2013

<table>
<thead>
<tr>
<th>Year</th>
<th>No.</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td>11,520</td>
<td>3.8</td>
</tr>
<tr>
<td>2010</td>
<td>11,163</td>
<td>3.6</td>
</tr>
<tr>
<td>2011</td>
<td>10,517</td>
<td>3.4</td>
</tr>
<tr>
<td>2012</td>
<td>9,945</td>
<td>3.2</td>
</tr>
<tr>
<td>2013</td>
<td>9,582</td>
<td>3.0</td>
</tr>
<tr>
<td>2014 (provisional)</td>
<td>9,412</td>
<td>3.0</td>
</tr>
<tr>
<td>Elimination</td>
<td>~ 300</td>
<td>&lt; 0.1</td>
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</tbody>
</table>
Key Risk Groups

- 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
Main Challenges

- **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; 11 million persons with LTBI
STRATEGIES TO ELIMINATE TUBERCULOSIS IN THE UNITED STATES
Reaching TB Elimination (<1 case per 1 million population)
Hill et al. Modelling tuberculosis trends in the USA

2 x = doubling rate of LTBI treatment; 4 x = quadrupling rate of LTBI treatment
Decrease LTBI Among Foreign-Born Persons to 25% of Current Level

2 x = doubling rate of LTBI treatment; 4 x = quadrupling rate of LTBI treatment
Two Key Themes for TB Elimination

- Address TB in foreign-born persons
  - Domestic strategies
  - Global strategies
- Address latent tuberculosis infection (LTBI)
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
TB Controllers Consultation

- February 10-11, 2015
- Purpose: to obtain input from 62 CDC TB Prevention and Control cooperative agreement recipients on implementing strategies for TB elimination
- Used framework of 6 IOM report goals
- Captured input to elicit themes that can lead to specific actions and activities
- Work through NTCA to follow up on potential action items
Goal I: Maintain control of TB

Maintain the decline in TB incidence through timely diagnosis of active TB disease, appropriate treatment and management of persons with active disease, investigation and appropriate evaluation and treatment of contacts of infectious cases, and prevention of transmission through infection control.
Diagnose and Treat All Persons with TB

- **Complete and rapid detection of persons with TB**
  - Almost all persons with TB are ultimately found, but sometimes delays occur
  - New technologies can help, e.g., Gene Xpert
  - Main challenge will be making providers “Think TB”; diagnostic tests are useless if they are not ordered
  - Be persistent in educational efforts; think about use of clinical decision support tools for primary providers
  - Multiplex respiratory infection test that includes TB; does not require provider to order specific TB test

- **Maintain high treatment completion rates**
  - Can be done with current treatment
  - Shorter course regimens (4 months as being studied by TBTC) would help, especially with cost
  - Use of video and wireless technologies to decrease cost of DOT
Contact Investigation

- Secondary case finding: up to 1-2% of contacts have TB disease
- Detect and treat LTBI
  - Limited by tests (tuberculin skin test [TST] and interferon-gamma release assays [IGRAs]) that poorly predict who will get TB in the future
  - IGRAs have advantages in foreign-born population who received BCG; IGRAs only require visit
  - Greater opportunities for improving treatment completion with short-course regimens: 3 months isoniazid and rifapentine (3HP) or 4 months rifampin (4R)
Prevent Transmission Through Infection Control

- US has generally done well in preventing transmission in health care settings
  - Have not seen healthcare-associated outbreaks seen in 1990s
- More focus is needed on infection control and prevention in homeless shelters and correctional facilities
  - Recent outbreaks tend to be associated with these populations
  - DTBE homeless workgroup collaboration with federal interagency council on homelessness
Goal I: TB Controllers Input

- 5 components: detection/diagnosis of TB cases; treatment of TB cases; investigation of contacts; treatment of infected contacts; infection control

- Many ideas about what is and is not effective; not easy to summarize briefly

- Importance of oversight and support by health department to ensure patients complete treatment
  - DOT and incentives/enablers: effective, but resource intensive and difficult to sustain
  - Alternatives, e.g., video or e-DOT

- Loss of expert personnel, especially experienced public health nurses
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.
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
  - How can we leverage Affordable Care Act?
  - USPSTF considering recommendation for LTBI testing
  - Who serves targeted populations in the community and how can we engage them?
Appropriate Regionalization

- Regional Training and Medical Consultation Centers
- Laboratory Center of Excellence for drug-susceptibility testing
- Genotyping (national)
- When case numbers become very low, can and should regional approach be expanded?
  - Legal and practical challenges
Outbreak Response: Interrupting Transmission

- Outbreaks generally concentrated in homeless, persons who abuse substances and have spent time in correctional facilities
- Earlier (not necessarily rapid) recognition of transmission through universal genotyping
  - Alerts built in to genotyping database
  - Allows earlier response
- Beginning to understand some predictors of cluster growth
  - Allows us to prioritize clusters and respond more rapidly
- Focus on better implementation of infection control and prevention measures in homeless and correctional settings
Goal II: TB Controllers Input

- 3 components: address LTBI; regionalization; genotyping/outbreak detection and response
- Genotyping was useful, but different applications based on incidence
  - Low incidence not as valuable for outbreak detection, may be more useful for detecting false positives
  - Methods with better resolution needed in some situations (WGS)
- Insufficient surge capacity to respond to outbreaks
- No clear themes on regionalization other than support for RTMCCs
LTBI: TB Controllers Input

- Problem is vast, and a major initiative with funding is needed to address: 5 parts
  - Registry/surveillance system
  - Scale up of testing to targeted populations
    - More focused guidance on who to target
    - Eliminate wasteful testing of low-risk persons
    - Specific funding for IGRAs, especially for foreign-born
  - Scale up of short course LTBI treatment
  - Communication, outreach
    - Engagement of affected communities and their medical providers
  - Staffing
Goal III: Develop new tools

Develop and assess new tools for the diagnosis, treatment, and prevention of TB.
Available Now and the Near Future

- Implement new tools in the most effective manner
  - IGRAs
  - Gene Xpert
  - 3HP – can it be self administered? TBTC Study 33
  - Genotyping – what is role of whole genome sequencing?
  - Molecular detection of drug resistance (beyond Gene Xpert)
  - Bedaquiline and delamanid for MDR TB

- Under development
  - New drugs and regimens in various stages
  - Shorter course regimens for drug-susceptible (4 months) and MDR (9 months) TB
  - New tests for diagnosis and detection of drug resistance
Dream Big

- Encourage basic research funded by partners such as NIH and Gates Foundation that will lead to breakthroughs

- Game changers
  - LTBI test that is highly predictive of who will progress to TB disease
  - Inexpensive, simple point-of-care tests to diagnosis TB disease and detect drug resistance
  - Ultra-short (e.g., 4 weeks) TB and LTBI treatment
  - Highly effective vaccine
Goal III: TB Controllers Input

- Research priorities for the next 5 years were discussed
- Shorter treatment regimens for TB and LTBI
- Point of care diagnostics
- LTBI test that is better at predicting who will progress to TB disease
- Vaccine
Goal IV: Reduce the global burden of TB

Increase U.S. involvement in international TB control activities.
Address Global TB in Context of Limited Resources

- Support global organizations, e.g., WHO, in developing evidence-based policy
- Work with individual countries in a strategic way
- Drug resistance and HIV play greater role
Overseas Screening of Persons Entering United States

- Current program very effective at detecting and treating TB disease in permanent immigrants and refugees
- Most foreign-born TB cases occur from reactivation of LTBI after person is in US for several years
  - Can LTBI testing and treatment with short-course regimens be incorporated into current screening process?
- Can screening be expanded to other long-term visitors, e.g., students and work-visa recipients?
Goal IV: TB Controllers Input

- Focused on screening of immigrants because TB controllers have the most involvement in this aspect
- About 50/50 split between which should be prioritized
  - Expansion of screening for TB disease to populations beyond permanent immigrants and refugees versus
  - Addition of LTBI testing and treatment to current screening program
- Agreement that to extent possible decisions should be data driven
Goal V: Mobilize and sustain support

Mobilize and sustain support for TB elimination by engaging policy and opinion leaders, health care providers, affected communities, and the public.
Maintain and Ideally Increase Support

- **Partnerships are critical**
  - Domestic: TB controllers, NTCA, STOP TB USA, APHL, ATS, IDSA, TAG
  - International: WHO, IUATLD, Ministries of Health, MSF

- **Make the argument**
  - Example is cases-averted analysis that is underway
  - Over 200,000 TB cases have been averted since the response to the resurgence of TB in the 1980s-1990s
  - Also need to quantify the cost savings and benefits: what is the return on investment?
  - Individual patient stories can also be powerful
Goal V: TB Controllers Input

- Need better messaging – simple, clear and memorable
- Need more active champions and advocates
- Community targeted
Goal VI: Track progress

Monitor progress toward the goal of TB elimination, and regularly report on progress to all target audiences.
Track Progress

- Track progress overall through national indicators (NTIP)
  - Outcome and process measures

- Evaluate individual programs and projects
  - Assess performance of funded TB programs and laboratories on a regular basis
  - Research workgroup has recommended periodic internal and external reviews of research projects

- How do we best harness these evaluation processes to generate improvement?
## National TB Program Objectives and Performance Targets for 2015

<table>
<thead>
<tr>
<th>Objective Categories</th>
<th>Objectives and Performance Targets</th>
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<tbody>
<tr>
<td>1. Completion of Treatment</td>
<td>For patients with newly diagnosed TB for whom 12 months or less of treatment is indicated, increase the proportion of patients who complete treatment within 12 months to 93.0%.</td>
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</tbody>
</table>
| 2. TB Case Rates  | Decrease the TB case rate in U.S.-born persons to less than 0.7 cases per 100,000.  
- Increase the average yearly decline in TB case rate in U.S.-born persons to at least 11.0%.  
- Decrease the TB case rate for foreign-born persons to less than 14.0 cases per 100,000.  
- Increase the average yearly decline in TB case rate in foreign-born persons to at least 4.0%.  
- Decrease the TB case rate in U.S.-born non-Hispanic blacks to less than 1.3 cases per 100,000.  
- Decrease the TB case rate for children younger than 5 years of age to less than 0.4 cases per 100,000. |
| 3. Contact Investigation  | Increase the proportion of TB patients with positive acid-fast bacillus (AFB) sputum-smear results who have contacts elicited to 100.0%.  
- Increase the proportion of contacts to sputum AFB smear-positive TB patients who are evaluated for infection and disease to 93.0%.  
- Increase the proportion of contacts to sputum AFB smear-positive TB patients with newly diagnosed latent TB infection (LTBI) who start treatment to 88.0%.  
- For contacts to sputum AFB smear-positive TB patients who have started treatment for the newly diagnosed LTBI, increase the proportion who complete treatment to 79.0%. |
| Contact Elicitation  |                     |
| Evaluation  |                     |
| Treatment Initiation  |                     |
| Treatment Completion  |                     |
Goal VI: TB Controllers Input

- Standardization with national indicators was good in general, but there are some exceptions
  - Sometimes not as relevant to low-incidence states

- Program evaluation process related to cooperative agreement is too complex and rigid
  - Should be simpler and more flexible
Conclusion: Five Key Strategies for TB Elimination

- **Sustain commitment**
  - Partnerships are critical
  - Make the argument: ROI and stories of persons affected by TB

- **Maintain basic TB control functions**
  - Case finding and treatment, contact investigation, infection control

- **Expand effective LTBI testing and treatment**
  - Expand beyond the health department
  - Foreign-born persons major focus
  - Take advantage of new regimens

- **Strategically engage in global TB efforts**
  - Maximize impact of limited resources

- **Make the job easier**
  - Promote and harness scientific and technological advancement
Thank You!
Questions?