How can TB elimination models inform program strategies today?

Modeling by the CDC and the NCHHSTP Epidemiologic and Economic Modeling Agreement (NEEMA) Grantees

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What is a model?

• A system of mathematical equations that describes or projects the past, present, or future

• Answers questions that cannot otherwise be addressed (for practical, ethical, or financial reasons), by making sense of incomplete data from disparate sources (ref. 1)

• Lists inputs and assumptions explicitly (ref. 1)
What do we need to know?

• What is the current trend in TB cases, given existing activities and resources?

• What would happen if we changed resources and activities?

• Projected outcomes, overall and by population:
  – TB and latent TB infection (LTBI) cases and rates
  – Time to TB elimination
  – Intervention costs
  – Cost effectiveness: costs per TB case averted or per quality-adjusted life year
What have we learned so far from CDC and NEEMA modeling?
Estimated 145,000 to 319,000 TB Cases Averted During 1995–2014 (ref. 2)
Estimated societal benefits of averted TB cases 1995–2014 were $3.1 to $6.7 billion, excluding deaths; $6.7 to $14.5 billion, including deaths (ref. 2).
If TB Elimination had occurred in 1994, estimated societal benefits of averted TB cases 1995–2014 would have been $9.3 billion to $27.7 billion (ref. 3).
NCHHSTP Epidemic and Economic Modeling Agreement (NEEMA)

• 5 year cooperative agreement, beginning in FY2014, with CDC/NCHHSTP

• To model epidemiologic and economic outputs and outcomes of HIV, hepatitis, STDs, TB, and for school-age populations

• 3 grantees (Emory/Johns Hopkins, Harvard, UCSF) funded through awards each year
## TB NEEMA Principal Investigators and Collaborating Organizations

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With current resources and activities, TB elimination is not projected to occur before 2100

- In 2020, Yelk-Woodruff (ref. 4) projects:
  - 78% of cases will be foreign-born (FB), with 22% of FB from Mexico, 11% from Philippines, 9% from India, 7% from Vietnam, and 5% from China
  - Combined with projected 2020 US population (ref. 5), implies a TB case rate of 24/M

- In 2025, Shrestha (ref. 6) projects TB case rates at:
  - 52/M in California
  - 36/M in New York
  - 29/M in Texas
  - 25/M in Florida

- In 2050, Menzies (ref. 7) projects a TB case rate of 14/M, or ~ 5,600 cases

- In 2050, Goodell (ref. 8) projects:
  - ~ 1100 TB cases in California in 2050

- Barry (ref. 9) estimates that TB elimination in California would require a 14% annual rate of decline, compared with the 4% current rate
What would be the impact on TB elimination of interventions to improve TB disease control?

• Increased use of rapid TB diagnostics
  – Menzies (ref. 7) projected impact: reduces TB transmission and consequently TB case rate by 1.1/M compared with current trends, from 14.4/M in 2050 to 13.3/M
  – Medicare allowable fee: nucleic acid amplification (NAA) testing or Xpert MTB/RIF is ~ $59 per test (ref. 10)
  – Estimated cost effectiveness:
    • NAA testing was found cost saving in persons with HIV, homelessness, or substance abuse (ref. 11)
    • Modeling of the Xpert MTB/RIF test found it cost effective (ref. 12)

• Better TB treatment (increased completion)
  – Menzies (ref. 7) projected impact: decreases TB case rate by 0.7/M, from 14.4/M to 13.7/M in 2050

• More accurate and effective outbreak detection and response
  – Impact: Mindra (ref. 13) found that 76% of TB outbreaks from 2009-2015 were first identified through genotype data
TB elimination will require LTBI testing and treatment to prevent reactivation to TB

- NHANES 2011-2012 Estimated LTBI prevalence by IGRA: ~5% of the US population aged ≥ 6 years (ref. 14):
  - 3% of US-born (USB) (ref. 14)
  - 16% of FB (ref. 14)
    - 27% of Indian-born (ref. 15)
    - 26% of Chinese-born (ref. 15)
    - 24% of Filipino-born (ref. 15)
    - 19% of Vietnamese-born (ref. 15)
    - 15% of Mexican-born (ref. 15)
  - Shrestha (ref. 6) estimates FB LTBI prevalence at 20%-45% in CA, 15%-40% in NY, 10%-30% in both TX and FL

- In 2015 based on NHANES prevalence and Census Bureau US population (ref. 16) estimates, LTBI prevalence = 14M using TST positivity (6M using positivity by both TST and IGRA and 15M using IGRA alone)
  - LTBI case rate of 47,000/M (21,000/M to 50,000/M)

- In 2050, Menzies (ref. 7) projects LTBI prevalence at 1.9% overall, 0.4% in USB, 7.2% in FB, and annual LTBI incidence of 12,900 cases
What would be the impact on TB elimination of interventions for LTBI testing and treatment?
LTBI Tests and Treatments

- LTBI tests: interferon gamma release assay (IGRA) vs. tuberculin skin test (TST)
  - Projected impact: varies by test and population
  - Medicare allowable fee: $9 for TST, $85 for QuantiFERON Gold-in-tube (QFT-GIT), and $102 for T-spot (ref. 10)
  - Linas estimated cost-effectiveness:
    • In persons having close contact to TB, persons with HIV, and FB, QFT (ref. 17)
    • In FB with no medical risks, IGRA (ref. 18)

- LTBI treatments: 3 months of isoniazid (H) and rifapentine (P) by directly observed therapy (DOT) or self-administered (SAT)
  - Projected impact: 3HP/DOT equal efficacy to 9H/SAT (ref. 19), and higher adherence: 80%-90% vs. 60%-70% for 9H (ref. 20)
  - Holland and Shepardson estimated cost-effectiveness:
    • 3HP/SAT, 3HP/DOT, and 4R are cost effective vs. 9H/SAT (ref. 21, 22)
Populations for LTBI Testing and Treatment

• Linas projected impact: Number Needed to Test (NNT) and treat with isoniazid to prevent one TB case (ref. 17):
  – persons with HIV (67-71),
  – persons with close contact to infectious TB (69-110),
  – recent (within 5 years) immigrants (104-110),
  – FB (301-450),
  – persons with homelessness (411-436),
  – injection drug users (525-555),
  – prisoners (618-655)

• Linas estimated cost effectiveness: greatest in persons with close contact, persons with HIV, and FB (ref. 18)
Targeted LTBI Testing and Treatment (TTT) of Legal Immigrants and Refugees Prior to Arrival

- Menzies projected impact: reduces TB case rate by 4/M compared with current activities, from 14.4/M to 10.4/M in 2050 (ref. 7)

- Wingate estimated cost: ~ $2.8 million annually (in 2011 $) to conduct TTT of Chinese student-visa applicants and ~ $440,000 for Indian student-visa applicants (ref. 23)

- Wingate estimated cost effectiveness: above student-visa intervention is cost-effective and cost saving to the US, but imposes additional costs on students and on public health departments to follow up (ref. 23)
Increasing TTT of US Residents

• Projected impact:
  – Menzies estimates that doubling of TTT of all high risk populations and treatment with 3HP reduces the TB case rate by 3.2/M, from 14.4/M to 11.2/M in 2050 (ref. 7)

  – Goodell estimates that during 2017-2065 (ref. 8):
    • doubling TTT of FB would avert 18,000 cases
    • quadrupling TTT of FB would avert 35,000 cases
    • increasing TTT of FB 10 times would avert 50,000 cases
Harvard Projections to 2050 by Intervention

Intervention scenarios 2015-2050

Menzies estimates (ref. 7)
NEEMAA Ongoing Projects

• Evaluation of the impact and cost of interventions:
  – Expansion of TTT of FB persons in the US
  – Modeling TB interventions in Mexico, Philippines, Vietnam, India, China

• Modeling the impact of US Preventive Services Task Force (USPSTF) recommendations for primary care clinicians to conduct TTT

• Comparing and contrasting models to create a single unified model for US TB elimination
Summary (1)

• With current resources and activities, TB elimination is not projected to occur before 2100

• Additional interventions to improve TB control are projected to have minimal impact on achieving TB elimination

• Achieving TB elimination will require improvements in LTBI testing and treatment

• TTT for LTBI in persons with medical risks, TB contact, or who are FB are estimated to be most cost effective

• IGRA LTBI diagnostics, combined with 3HP, are estimated to be most cost effective vs. TST with 9H
Summary (2)

• TTT of legal immigrants and refugees prior to US arrival is projected to have moderate impact and is cost effective for student-visa applicants

• TTT of all FB US residents is projected to have moderate impact

• Combining interventions has the greatest potential to accelerate TB elimination, but will require large increases in resources to implement them
References

1. CDC Draft White paper on Infectious Disease Modeling at CDC, March 7, 2017
References


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