MODELING AGE-TARGETED INTERVENTIONS FOR TUBERCULOSIS IN INDIA

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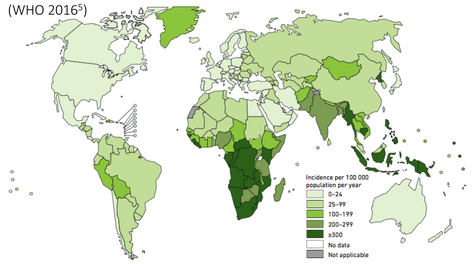
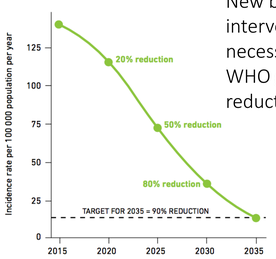
INTERVENTION STRATEGIES FOR *MYCOBACTERIUM TUBERCULOSIS*

- Tuberculosis disease (TB) is a globally distributed infectious disease.
- Anti-TB drugs have been available since the 1940s and the Bacillus-Calmette Guerin (BCG) Vaccine is the most widely distributed vaccine in the world. *Both are problematic.*
- The WHO emphasizes the importance of research on optimizing currently available treatment but some studies suggest…

Global Incidence of TB (WHO 2016[5])



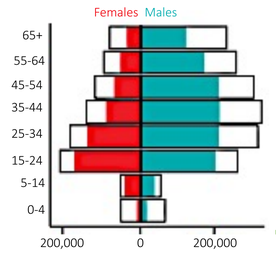


New biomedical interventions may be necessary to achieve WHO goals of 90% reduction by 2035[1]

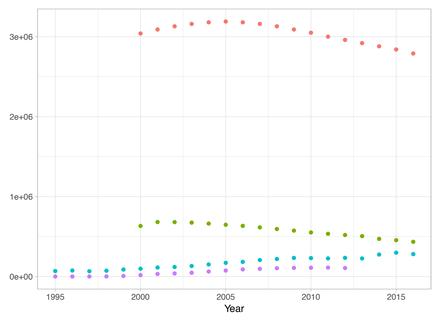
Can age-targeted interventions enhance progress towards elimination of *Mycobacterium tuberculosis*?

MODELING TB IN INDIA

- In 2016, 26% of all new cases were in India[5].
- Co-infections with HIV are relatively rare (compared with similar incidence countries in Africa)[5].
- In the past three years, spending on TB programs more than tripled in India, indicating increased capacity to control the epidemic[5].



TB is primarily a disease of adults (90% of cases occur among adults) and more prevalent in men than in women[5].



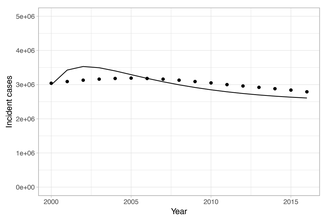
After running the model from 2000 to 2016 (the latest available data from the WHO) we tested **18 different intervention scenarios**:

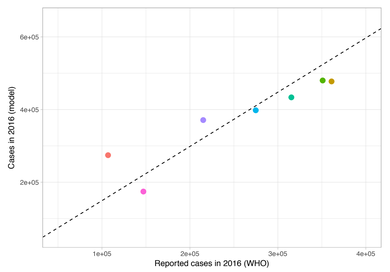
- We increased treatment rates in **each age class separately (n=16)**
- We compared targeted interventions to **blanket** strategies where we increased treatment rates overall
- We also predicted the **baseline** level of TB in which no complementary strategies were undertaken

MODEL PERFORMANCE

Estimated # of cases (all forms) from 2000 through 2016 in India were obtained from a publicly available WHO TB Report[5]. We optimized the initial number of susceptible, infectious, and non-infectious individuals as well as the progression rate from latent to infectious TB using the sum of square errors (SSE) deviation from WHO data.

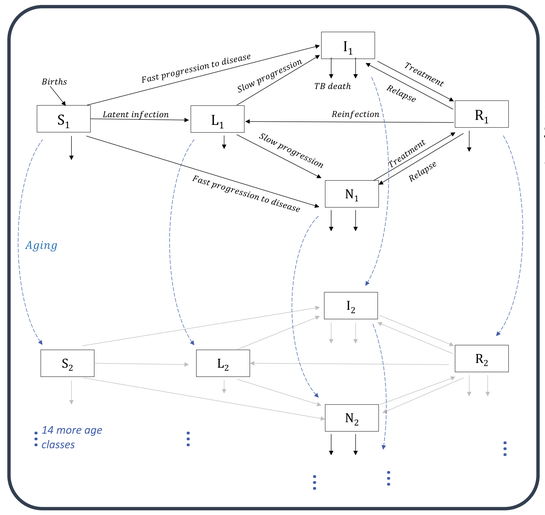
The best-fit model (line) from 2000 to 2017 using WHO estimated incident case data (points).

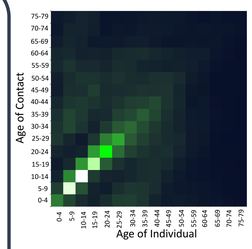




Predicted age distribution of cases in 2016 by the best-fit model compared with *actual reported* cases per age class in 2016 (R^2=0.916).
Dashed line shows 67% reporting probability in 2016[5].

MODEL



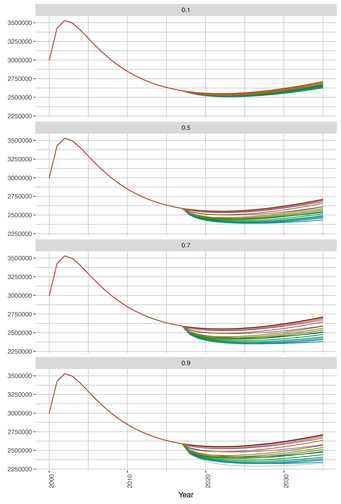


Major model assumptions:

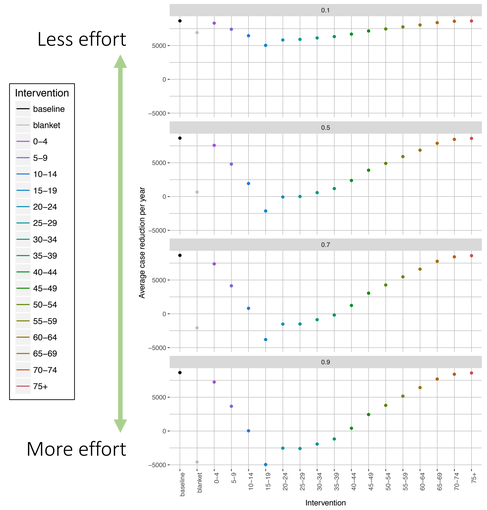
- Constant demography (no change in pop. size over time or age distribution, and all have constant lifespan of 75 years)
- Simplified life history of TB not accounting for smear progression
- No change in parameters since 2000 (e.g., cure rates)

We analyzed an age-structured, ODE model for transmission of TB based on previous models[2,3]. The model stratifies the population into 16 different age classes and 5 infection states: Susceptible (never infected), Latent (lasts for a period of 1-10 years on average), Infectious (contagious, pulmonary TB), Noninfectious (non-contagious, extrapulmonary TB), and Removed (treated or recovered). We used projected data to inform contact among ages[4].

RESULTS



As expected, higher effort strategies which increase cure rates for infectious individuals more than low effort strategies, result in more case reductions.



Age group 15-19 resulted in the most cases reduced regardless of effort level followed by younger adults (20-29) if the effort is low, and the blanket strategy if the effort is high.

CONCLUSIONS

While the age-dependence of TB is widely known, age-targeted interventions have never been considered. This is in contrast to many other respiratory transmitted infections (e.g., measles) where age-targeted interventions such as school-closings have been tested.

Our model roughly characterizes the age distribution of TB cases seen in India in 2016.

We found that similar to other respiratory transmitted infections, target age classes could include teenagers and young adults. But blanket strategies may work just as well depending on effort.

The WHO emphasizes research to optimize currently available interventions. Age-targeted interventions may complement current efforts.

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Looking for parameter values & model equations? Scan this code! Or visit…

https://github.com/paigemiller/paigemiller.github.io/tree/master/docs

[1] Dye et al. *Annual Review of Public Health*. **2013**, 34, 271. [2] Blower et al. *Nature Medicine*. **1995**, 1, 815. [3] Arregui et al. *PNAS*. **2018**, 115, 3238. [4] Prem et al. PLOS Computational Biology. 2017, 13. [5] WHO TB Report. **2016**.

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