**Age-structured model for Tuberculosis intervention planning**

**Goal**
The goal of this project was to determine whether age-based interventions could enhance current public health interventions by reducing Tuberculosis prevalence compared with non-age-based interventions, which are currently implemented.

**Background Information**
- Tuberculosis (TB) represents a widespread public health concern: an estimated one fourth of the world’s population is infected with TB.
- The World Health Organization’s “End TB Strategy” has set the goal for Tuberculosis eradication by 2050.
- Studies have shown that current public health intervention strategies may not achieve this goal in many parts of the world that experience high rates of Tuberculosis.
- In high incidence countries, interventions include passive and active forms of TB surveillance.
- We hypothesized that current surveillance and intervention systems might be enhanced by age class specific targeting in an overall aim to reduce TB burden further.

**Modeling Tuberculosis**
- We adapted a standard TB model which included 5 state variables: Susceptible (S: never infected with TB), Latent (L: long term, asymptomatic, non-contagious TB), Infectious (N: active, contagious, respiratory TB), Non-infectious (N: non-infectious, typically extrapulmonary TB), and Recovered (R: treated TB).
- Since the project goal involves age-based interventions, the population was modeled as 16 different age classes, for which contact data was utilized.

**Main Conclusions and Future Directions**
- In India, targeting 15-19 year olds is predicted to result in greatest overall decline in incidence of latent and active TB at all intervention levels (Figs. 3A and 4A).
- In South Africa, targeting 10-14 year olds is predicted to result in greatest overall decline of latent TB at all intervention levels (Figs. 3B and 4B).
- With greater levels of intervention in South Africa, the blanket strategy was more effective at reducing overall infectious TB burden.
- With limited resources, at the 10% intervention level, targeting 10-14 year olds was more effective (Figs. 3B and 4B).
- Model validation analysis revealed that actual reports from WHO vary widely from model predictions for India, yet there was substantial correlation between model predictions for South Africa and WHO actual case reports (Fig. 5).
- Age-based interventions may complement current public health interventions by further reducing TB burden to reach WHO eradication goals.
- Future studies should use a more detailed model for TB dynamics to generate a more realistic depiction.

**Mathematical Model**
- Run for 500 years until equilibrium was reached.

**Model Parameters**
- For India and South Africa, initial conditions for each compartment were determined through use of WHO data pertaining to number of cases.
- Interactions between age classes were informed by contact matrix projections for each country.
- Parameterization of β, c, and r values was determined through systematic variation of parameters with values from literature.

**Model Interventions**
- The infections period was reduced by 10, 70, and 90% independently for each age class.
- Targeted interventions were compared to a “blanket” strategy in which overall. Age = 0.998, 0.76, 0.95.
- Transmission coefficient for TB years), 20*2 = 25 years), 5 * 25 years), 5 * 25 years, 2010, 2018, 2030, 2050.
- Mathematical Model: The mathematical model utilized to test strength of the model in predicting prevalence of Tuberculosis in both India (a) and South Africa (b). Prevalence values determined through model projections against prevalence data contained within the World Health Organization’s Annual Tuberculosis Report.

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**References**

**Table 1. Parameter definitions and values for age-structured TB model.**

<table>
<thead>
<tr>
<th>Biological Interpretation</th>
<th>Units</th>
<th>Value</th>
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<tbody>
<tr>
<td>Birth rate into age class</td>
<td>person/year</td>
<td>India (0-2), 0.0001, South Africa (0-2) 0.00109*</td>
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<tr>
<td>Transmission coefficient</td>
<td>person/year</td>
<td>1.629, 7.418*</td>
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<td>Probability of infection that develops TB within a year</td>
<td>0.4685, 0.4685 (10 years)</td>
<td>0.4685, 0.4685 (15 years)</td>
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<tr>
<td>Progression rate to TB</td>
<td>person/year</td>
<td>0.0355 (10 years), 0.0355 (15 years)</td>
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<tr>
<td>Probability of developing infectious TB (if one develops TB)</td>
<td>person/year</td>
<td>0.0001 (10 years), 0.0001 (15 years)</td>
</tr>
<tr>
<td>Probability of developing extrapulmonary TB (if one develops TB)</td>
<td>person/year</td>
<td>0.0001 (10 years), 0.0001 (15 years)</td>
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<tr>
<td>Weight loss for active TB</td>
<td>person/year</td>
<td>0.011</td>
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<td>Rate of reversion to active TB</td>
<td>person/year</td>
<td>0.0005, 0.0005</td>
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<tr>
<td>Age of diagnosis</td>
<td>person/year</td>
<td>0.0005, 0.0005 (15 years)</td>
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<tr>
<td>Mortality rate</td>
<td>person/year</td>
<td>0.0005, 0.0005</td>
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<tr>
<td>Age class - specific rates</td>
<td>person/year</td>
<td>0.0005</td>
</tr>
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**Figure 1. Projected contact matrix for India (a) and South Africa (b) from Prem et al. High rates of contact are dominant while low rates of contact are indicated by color.**

**Figure 2. Stable age-distribution of TB prevalence in India (a) and South Africa (b).**

**Figure 3. Number of individuals in Latent (L), Infectious, and Non-Infectious (N) classes at 50%, 70%, and 90% treatment intervention benchmarks after model was run to equilibrium for India (a) and South Africa (b). The clusters different age classes tested, baseline, and blanket intervention strategies are represented.**

**Figure 4. Slopes of linear models for 18 different intervention scenarios and 5 different levels of intervention intensity in India (a) and South Africa (b). A greater negative slope value indicates a greater estimated impact of the specific intervention in reducing overall Tuberculosis burden.**

**Figure 5. Model validation plots utilized to test strength of the model in predicting prevalence of Tuberculosis in both India (a) and South Africa (b). Prevalence values determined through model projections against prevalence data contained within the World Health Organization’s Annual Tuberculosis Report.**