Modeling TB interventions in high burden settings: what are the gaps in evidence?

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13 Sep 2018

TB MAC/WHO Annual Meeting, Washington DC

Session 5: Implementing TB prevention: what aspects of implementation should models improve upon?

The SEARO experience

- 11 countries in the WHO South-East Asian Region

- *What do we need to do*, to achieve the End TB goals in the region by 2035?
  90% reduction in incidence rates relative to 2015
  95% reduction in TB mortality relative to 2015

Team members

- Nimalan Arinaminpathy, (Imperial College, London)
- Swarup Sarkar, Vineet Bhatia, Hyder Alam (WHO/SEARO)
- Ross McLeod (eSYS, Sydney)
- Country programmes in the SEA region

World Health Organization
Regional Office for South-East Asia

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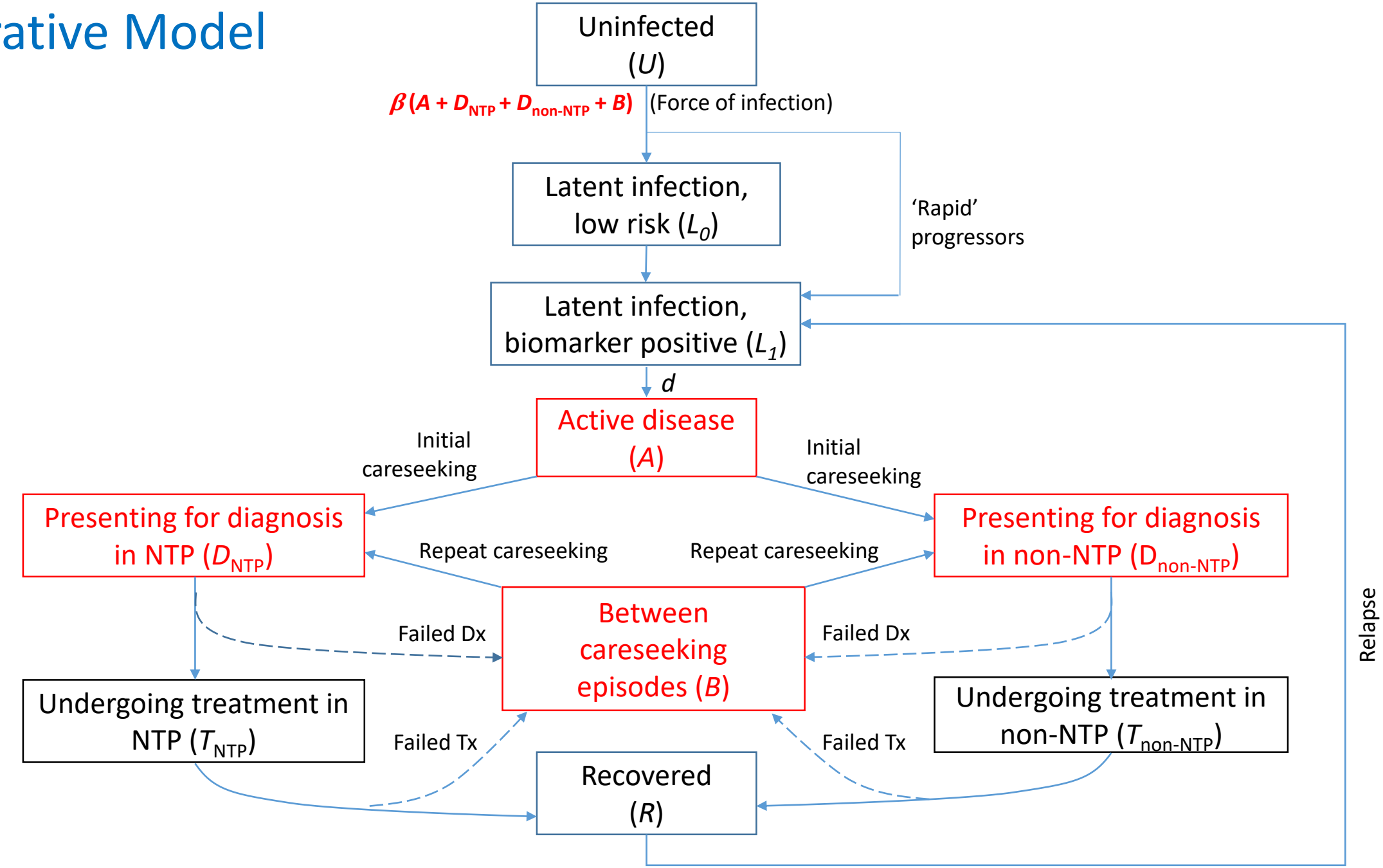
IMPERII DECUS ET TUTAMEN
Imperial College London

Illustrative Model



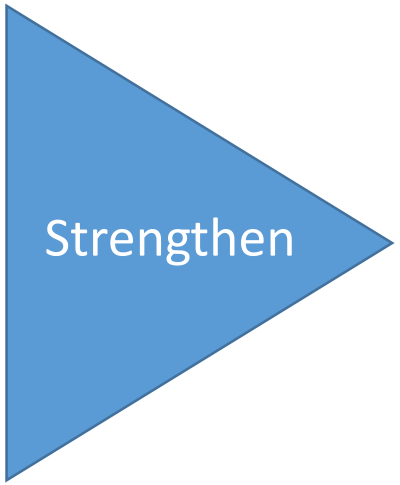
Assumptions

- ❑ This structure is replicated by HIV, drug resistance and risk-group status
  - Current analysis: 10% of the population have 3x prevalence rates of TB *(Consistent with urban slums in India)*

- ❑ Amongst latent infection, we distinguish those who are most at risk of developing disease within the next two years as being ‘incipient TB’.

- ❑ Age dependency is not considered in the model

The interventions



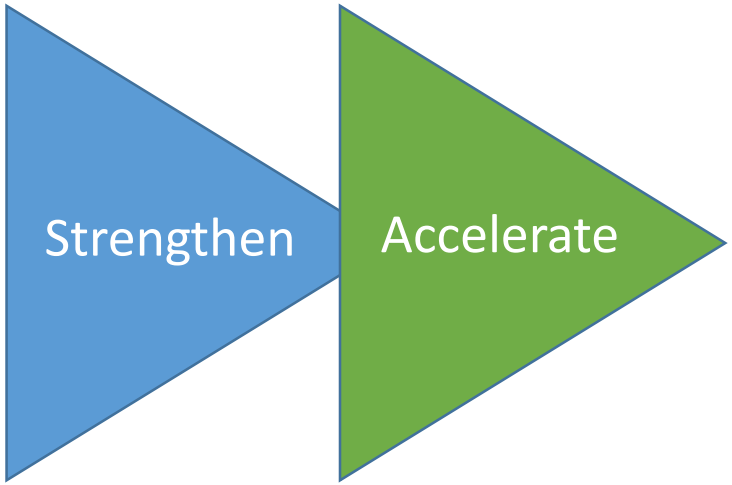
Private Sector Engagement:
Engage with 80% of non-NTP sector to raise quality of TB care, and to increase notifications

Lab expansion:
Expand lab facilities to increase access to public sector facilities by 35%

Better diagnostics:
Substitution of smear by GeneXpert

Treatment cascade:
In NTP and engaged providers, increase treatment initiation and completion to 95%

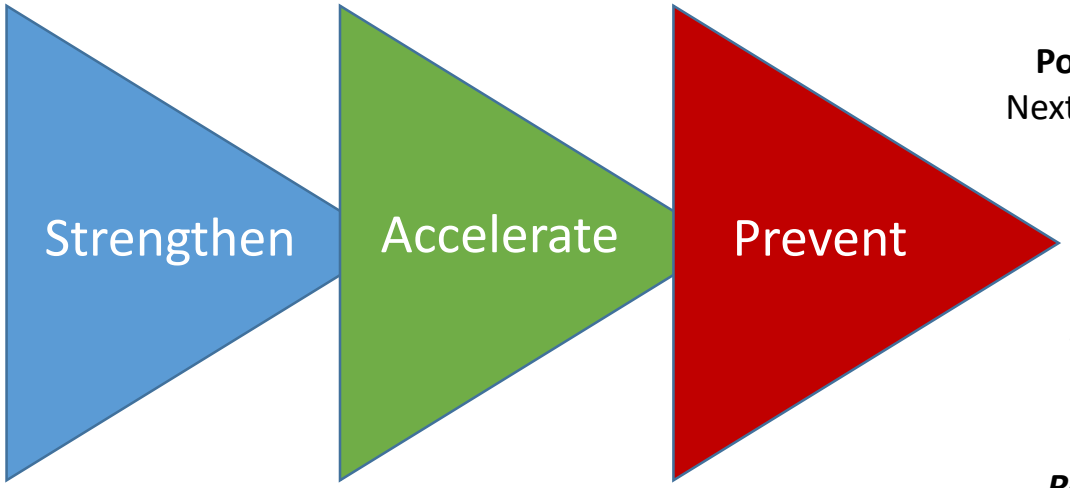
The interventions



Community contact tracing:
For every index case, screening *community contacts*: occupational, social, household. Initially assumed to yield *one additional* TB case for every two index case

Intensified case finding:
Stepped-up, sustained case-finding in populations with concentrated TB burden (e.g. slum populations)

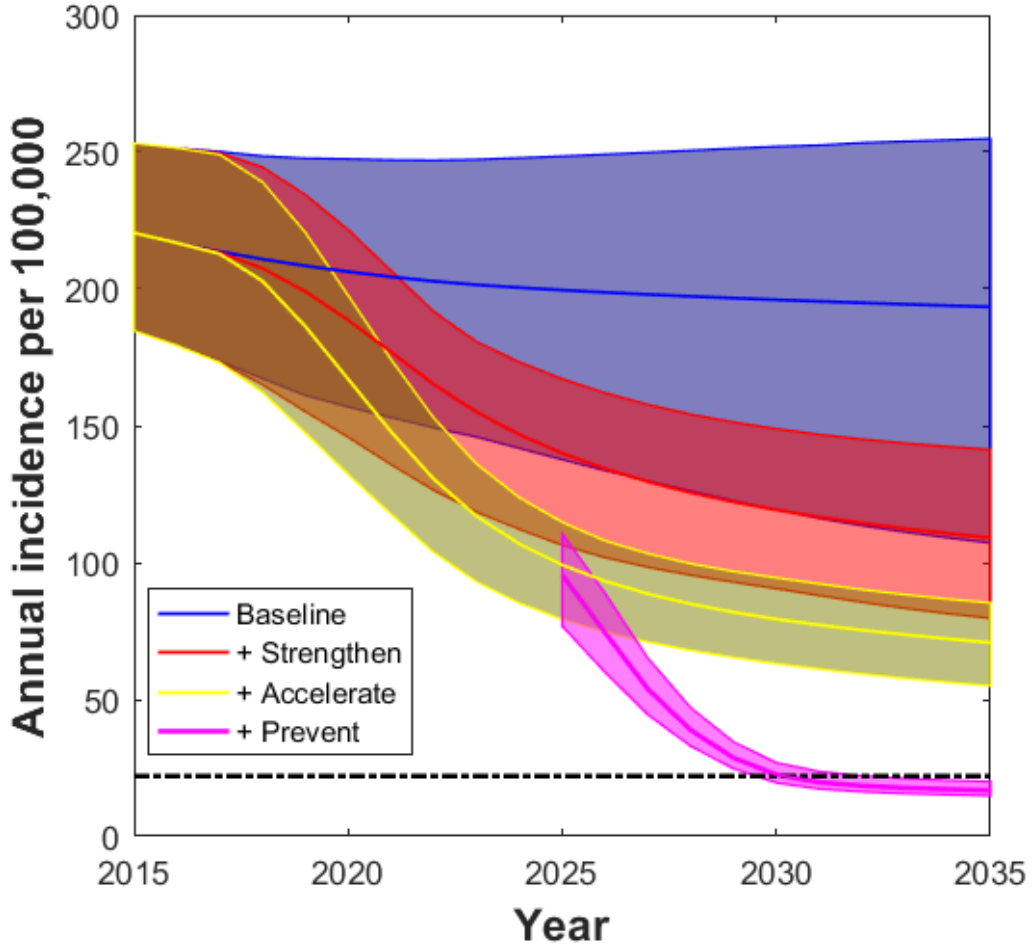
The interventions

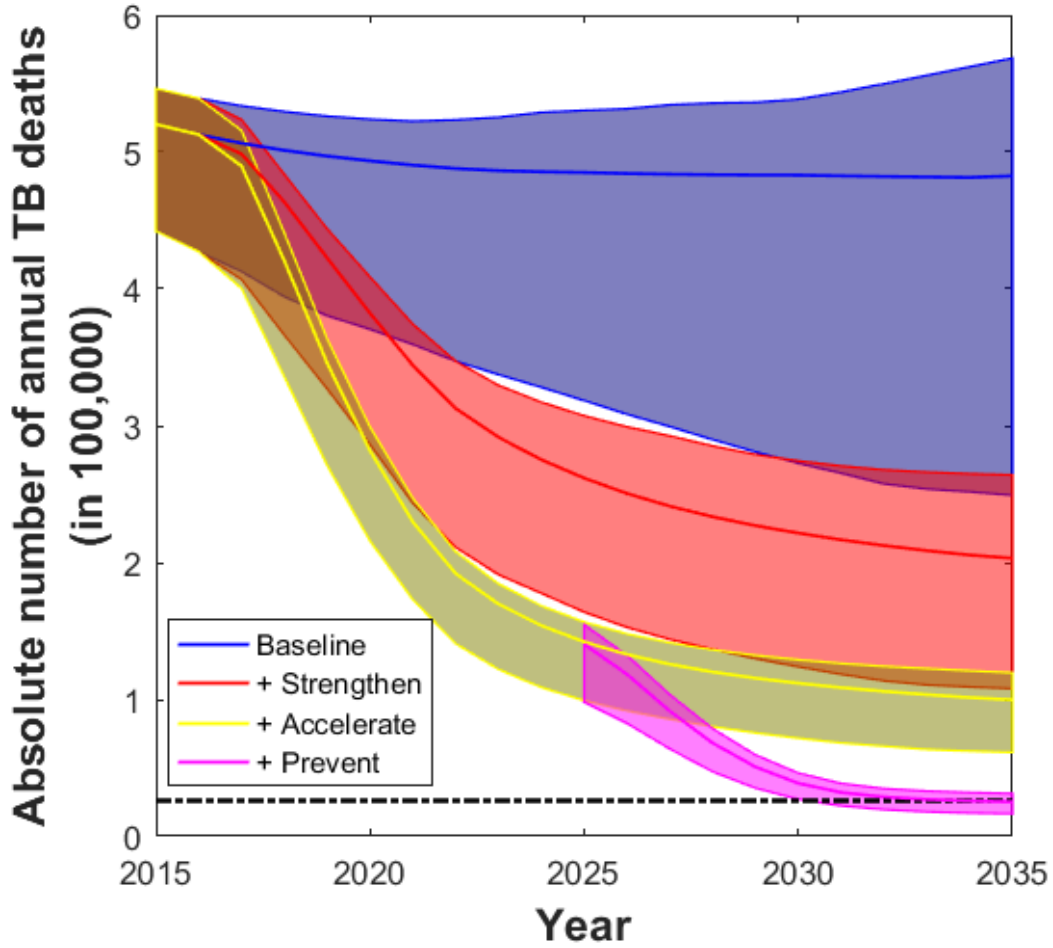


Population Preventive Measures:
Next-generation preventive therapy guided by a biomarker test

But could also involve:
Transmission-blocking vaccines
Primary infection control

Requires investment in research



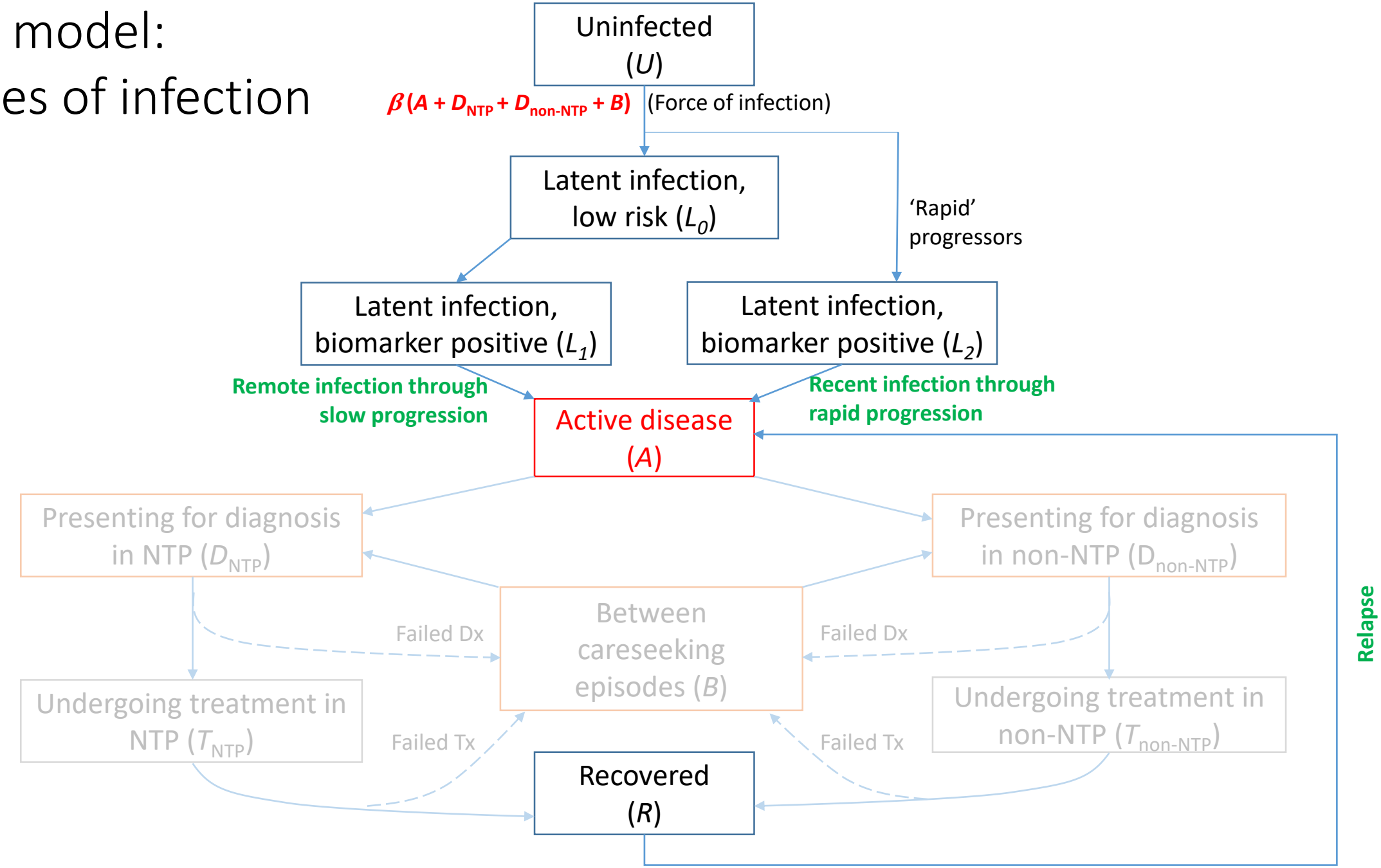


Intervention	Reduction in Incidence rate	Reduction in TB mortality numbers
Strengthen existing systems	50%	56%
Accelerated Case Detection	69%	80.4 %
Mass Preventive Measures	92.3%	95.0%

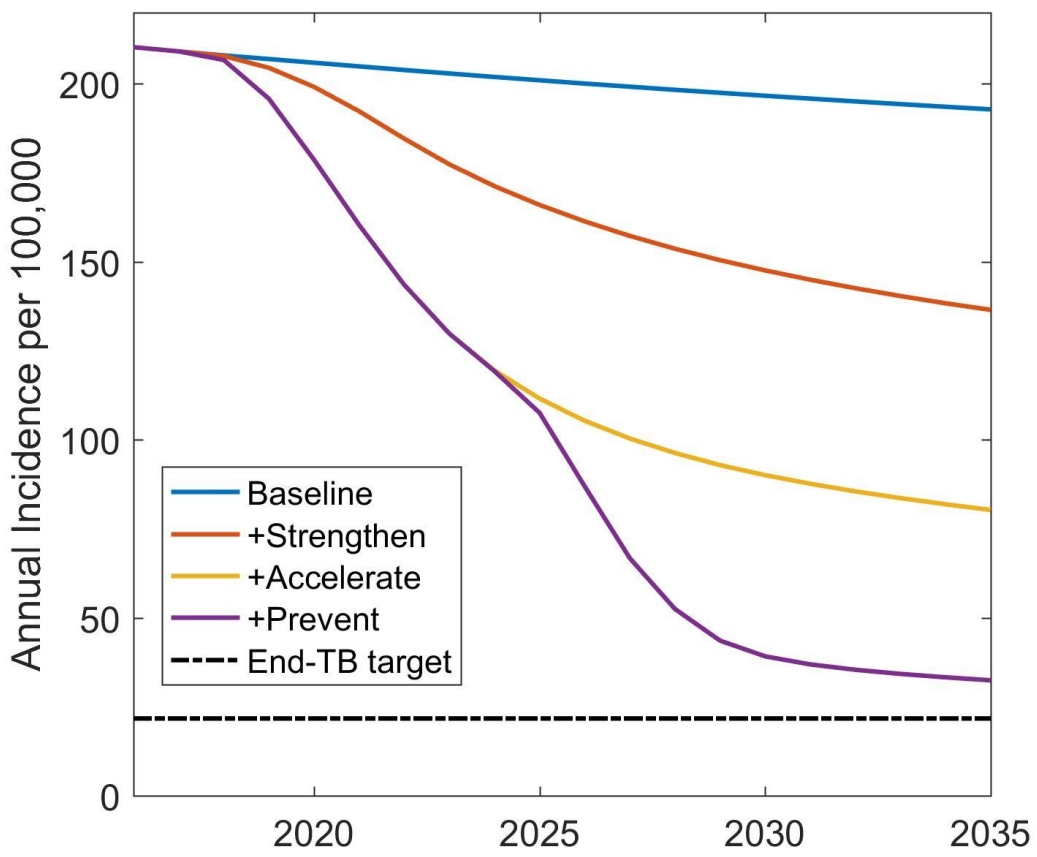
*In review

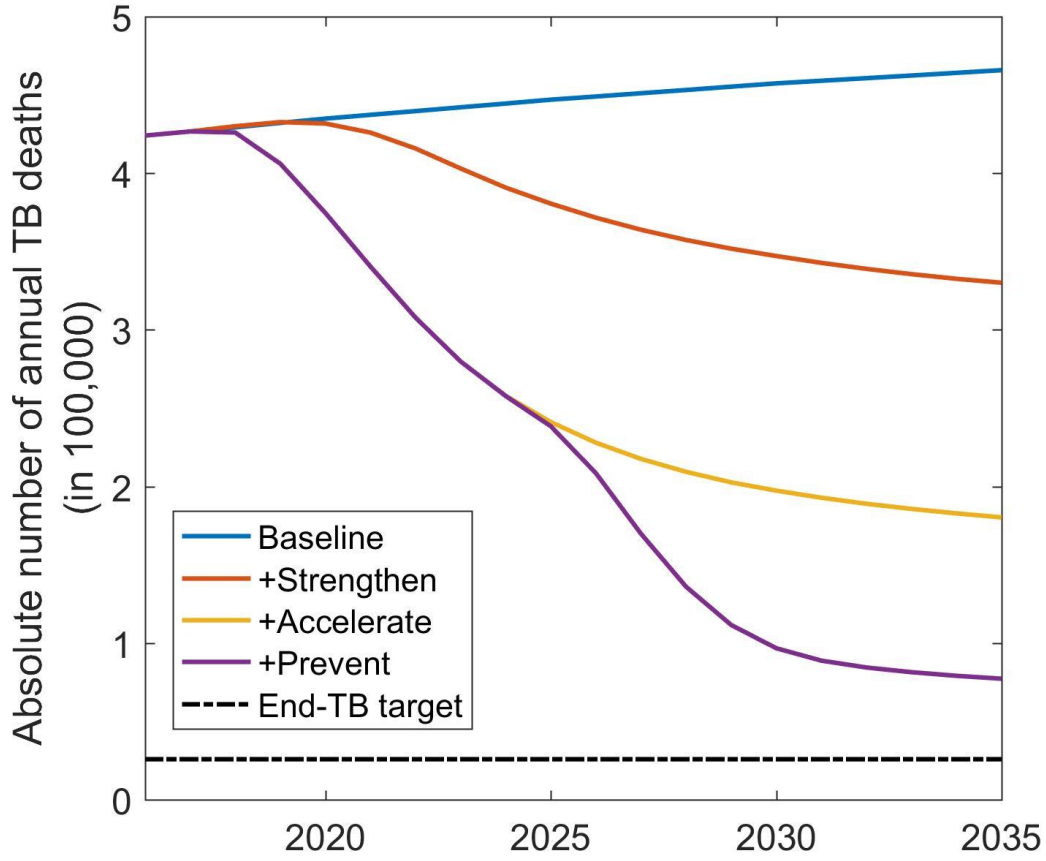
1. Does preventive therapy offer protection against relapse?

Initial model: Sources of infection



Screening in the risk group 3 times a year, and in general population 0.8 times a year



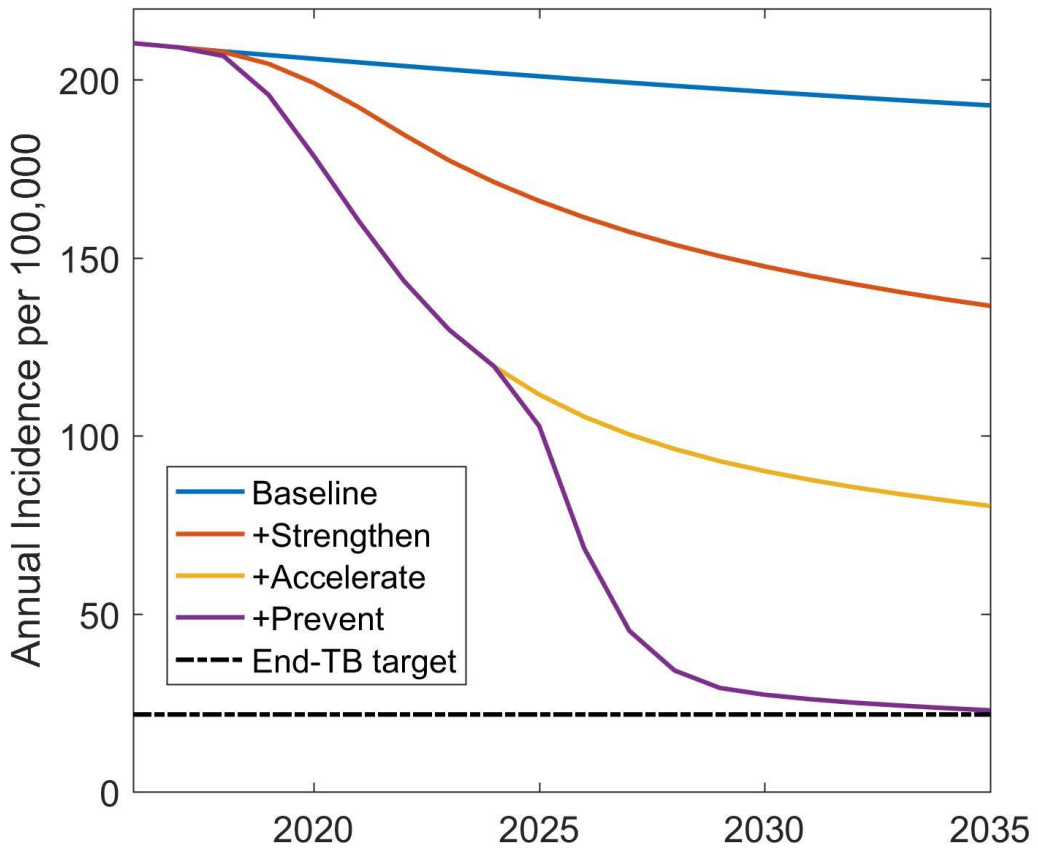


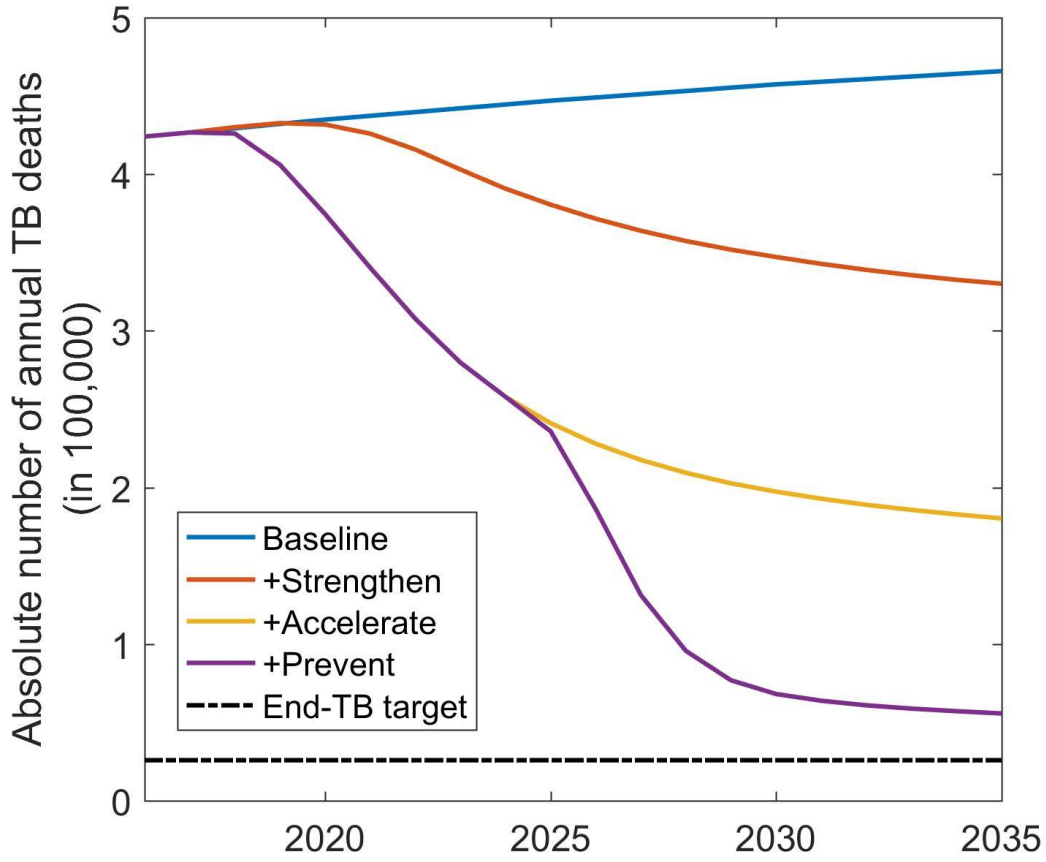
Reduction in incidence = 85%
Reduction in mortality = 87%

*In review

Increasing the coverage level further…

Screening in the risk group 8 times a year and in general population 2 times a year

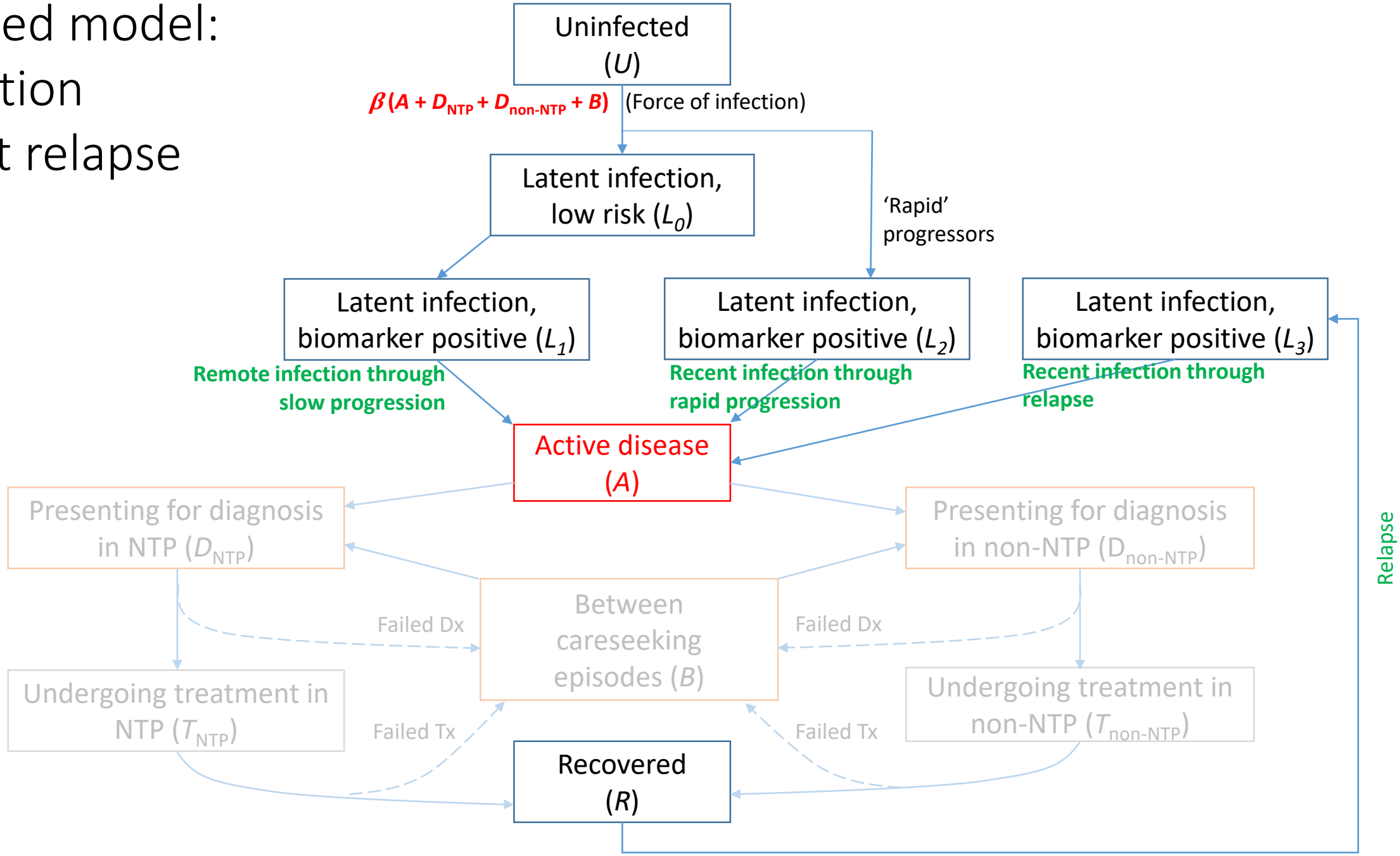




Reduction in incidence = 89%
Reduction in mortality = 91%

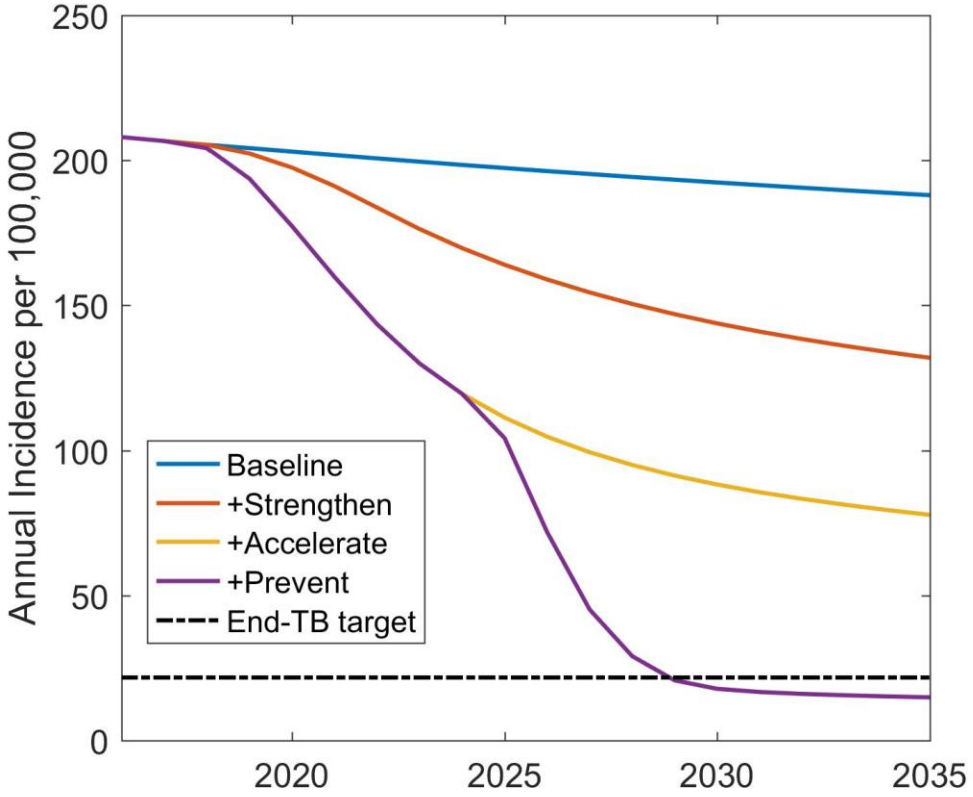
*In review

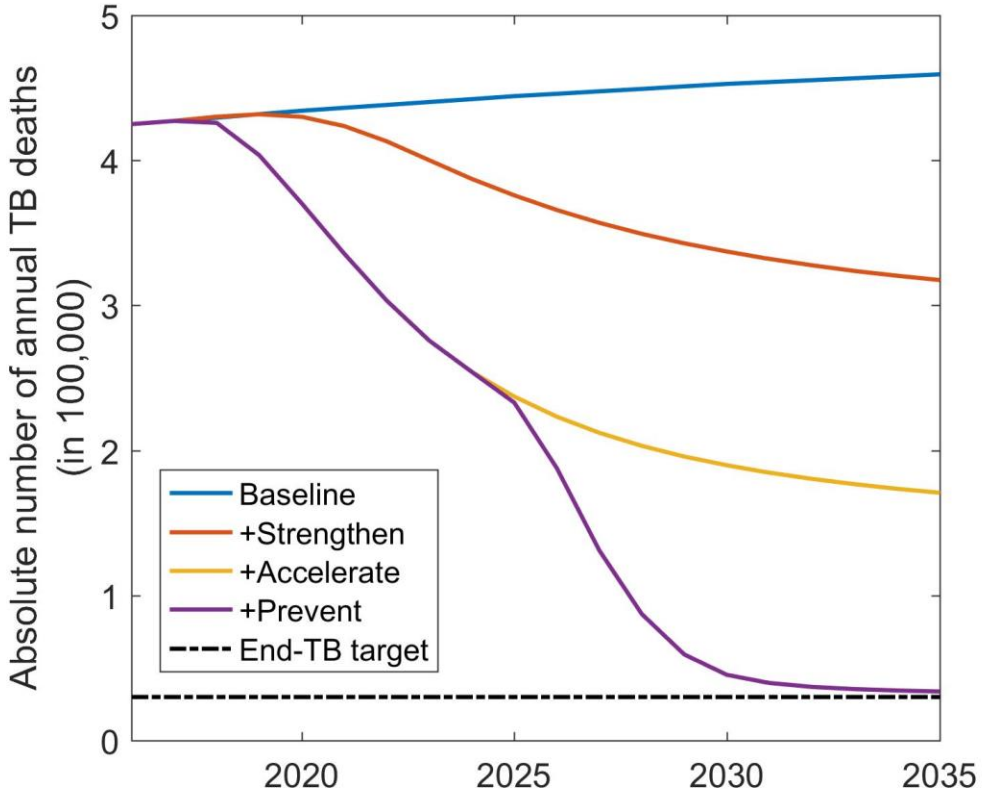
Modified model: Protection against relapse



Preventive intervention

Screening in the risk group 3 times a year and in general population 0.8 times a year





Reduction in incidence = 93%

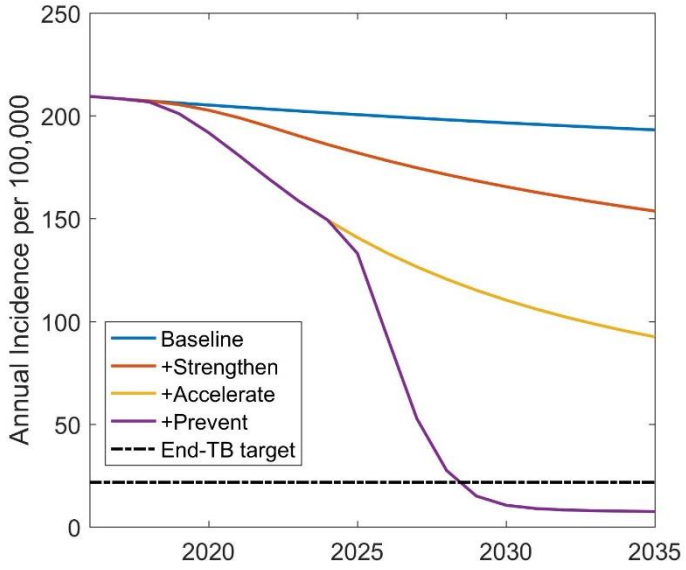
Reduction in mortality = 95%

*In review

2. How do these projections depend on the duration of incipient disease?

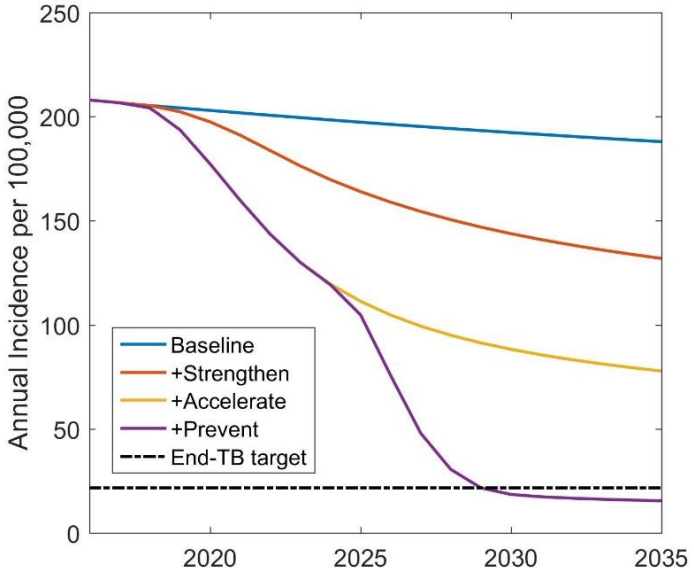
Screening in the risk group 3 times a year and in general population 0.8 times a year

Duration of incipient disease = 5 year



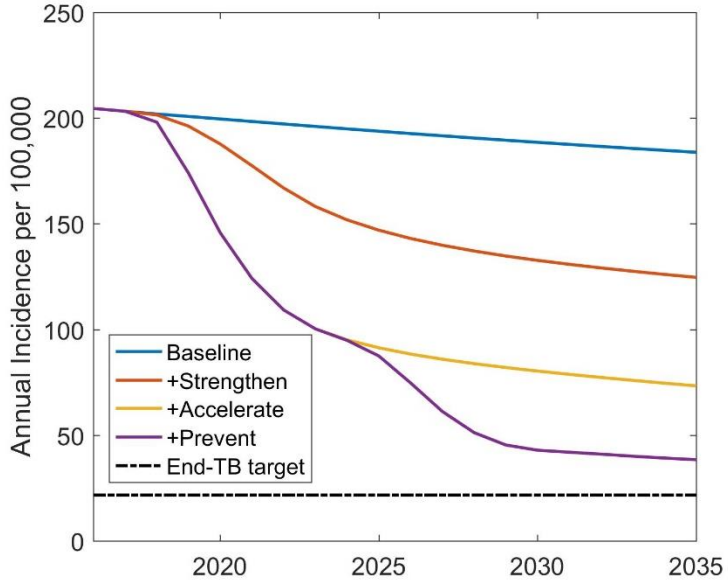
Reduction in incidence = 97%

Duration of incipient disease = 2 year



Reduction in incidence = 93%

Duration of incipient disease = 6 months



Reduction in incidence = 82%

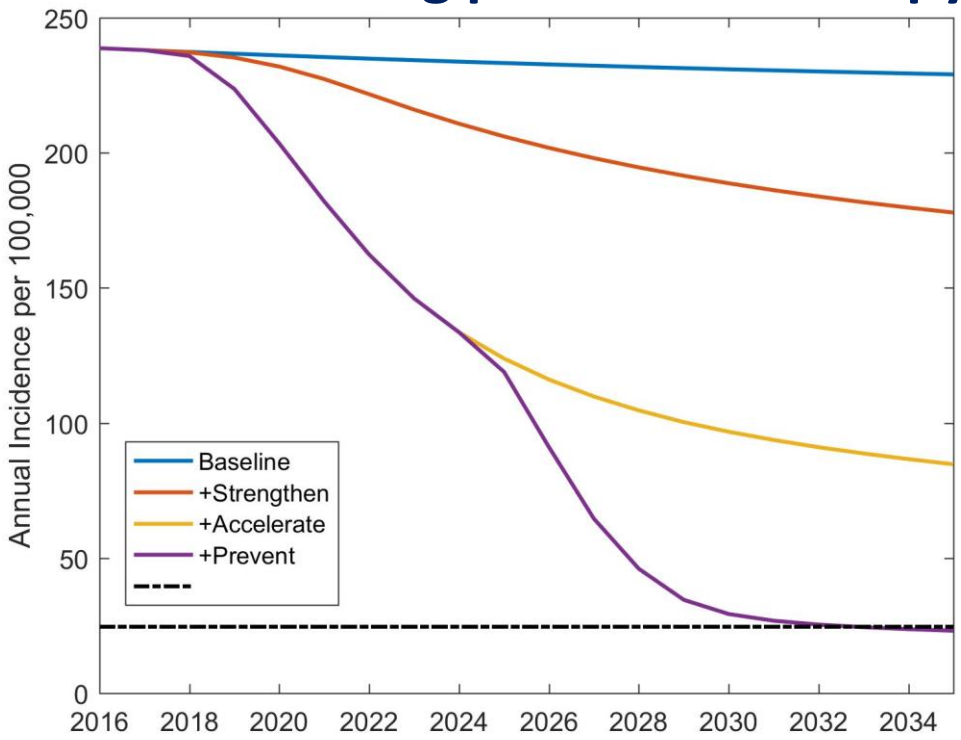
*In review

How does the coverage pattern changes to achieve the End-TB goal depending on the incipient disease duration

Average Duration of incipient disease	Coverage level of preventive therapy
5 year	Screening in the risk group once a year and in general population 0.5 times a year
2 year	Screening in the risk group 3 times a year and in general population 0.8 a year
6 months	Screening in the risk group 8 times a year and in general population 5 a year

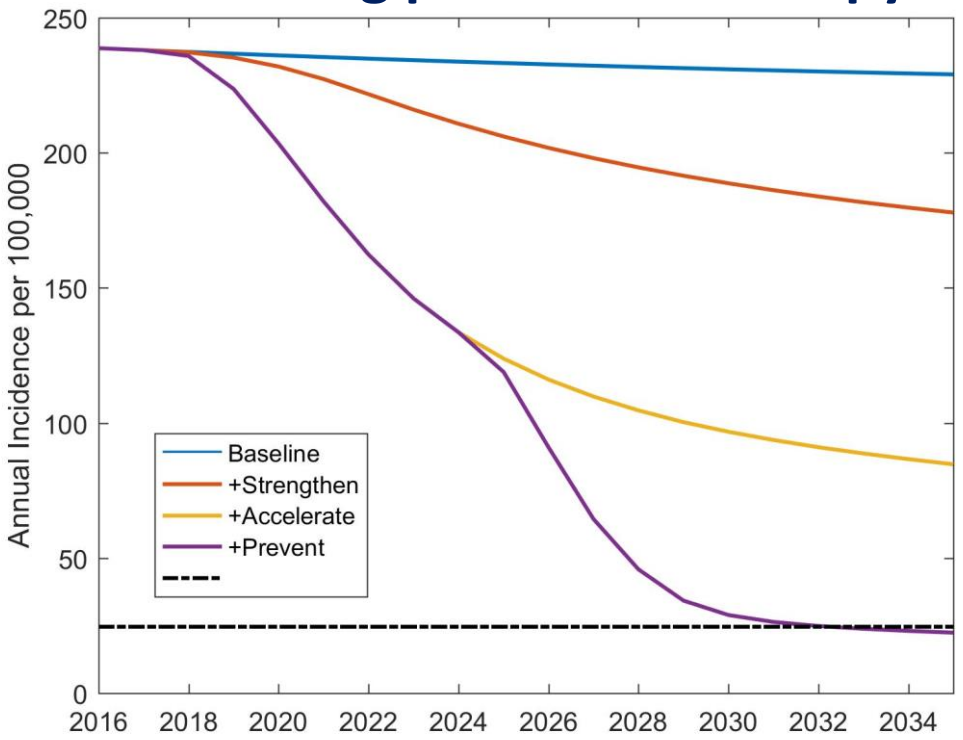
3. Sterilizing vs non-sterilizing protection: does it matter?

Non-sterilizing preventive therapy



Reduction of incidence = 90.6%

Sterilizing preventive therapy



Reduction of incidence = 90.9%

Sterilizing preventive therapy does not make any difference with non-sterilizing preventive therapy for high burden setting if annual risk of infection is low.

An example of the opposite conclusion: "Rein M G J Houben et al., Ability of preventive therapy to cure latent Mycobacterium tuberculosis infection in HIV-infected individuals in high burden settings, *PNAS* 2014".

*In review

Questions arising from this work

1. To what extent does preventive therapy offer protection against relapse? Can the biomarkers associated with incipient disease also detect relapse risk?

2. What is the mean duration of incipient disease in HIV-negative populations? How much variation is there around this average?

3. In which transmission settings is there an important distinction between sterilising and non-sterilising preventive therapy?

Thank you