Modelling cost-effectiveness of testing and treating for incipient TB

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Background

Incipient TB (ITB) = the asymptomatic phase of early disease during which pathology evolves, prior to clinical presentation as active disease. Targeting ITB may be a better strategy than targeting latent TB infection (LTBI).

Objective

To estimate the public health impact and cost-effectiveness of screening for and treating ITB, assuming an ITB test meeting the WHO Target Product Profile performance targets.

Methods

- We adapted a published deterministic dynamic transmission model, to include an ITB stage and 4 age groups, and included extra-pulmonary TB.
- A **cohort model variant** was applied for screening
  - close contacts of TB patients,
  - HIV infected and other immunocompromised persons
- **Fitted** model to literature and country specific values.
- Model **applied** to the Netherlands, Portugal, Viet Nam and South Africa.
- **Data** on TB, demography and costing from WHO, literature, country informants and other experts

Scenarios

- Patients with a positive ITB test were assumed to be treated with **preventive therapy** of 6 months isoniazid.
- The model allowed for **repeating** the ITB test at specified intervals.
- **Comparison** to baseline doing nothing or following WHO recommended strategy, including Chest x-ray (CXR), tuberculin skin test (TST), interferon gamma release assay (IGRA)
- We assumed each prevented case prevented 0.5 **secondary cases**

Cost-effectiveness

- **Effectiveness** of the screening included averted TB disease (0.331 Quality Adjusted Life Year [QALY] loss) and life years lost (1 QALY loss)
- For cost-effectiveness a **willingness-to-pay threshold** of 2x average income was applied.

Unit cost

- Health care costs
  - Screening: Chest X-ray, culture, TST, IGRA
  - Treatment: LTBI and TB treatment (allowing for multidrug-resistant TB and Directly Observed Treatment)
  - Other: contact tracing and hospitalization
- Estimates for Netherlands, converted to Portugal using purchase power parity (PPP) approach, allowing for country-specific quantities.
- Costs and effects are discounted at 3% annually

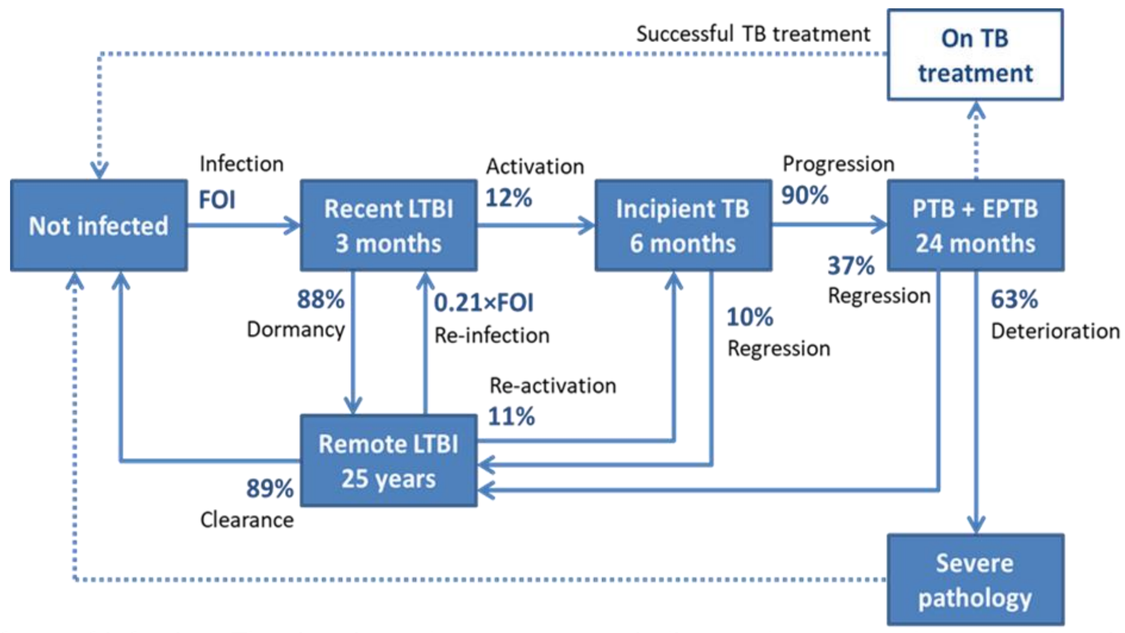
Results

The model fitted reasonably well to age specific TB incidence and LTBI prevalence data and contact tracing studies in the 4 countries.

Screening risk groups in cohort based approach

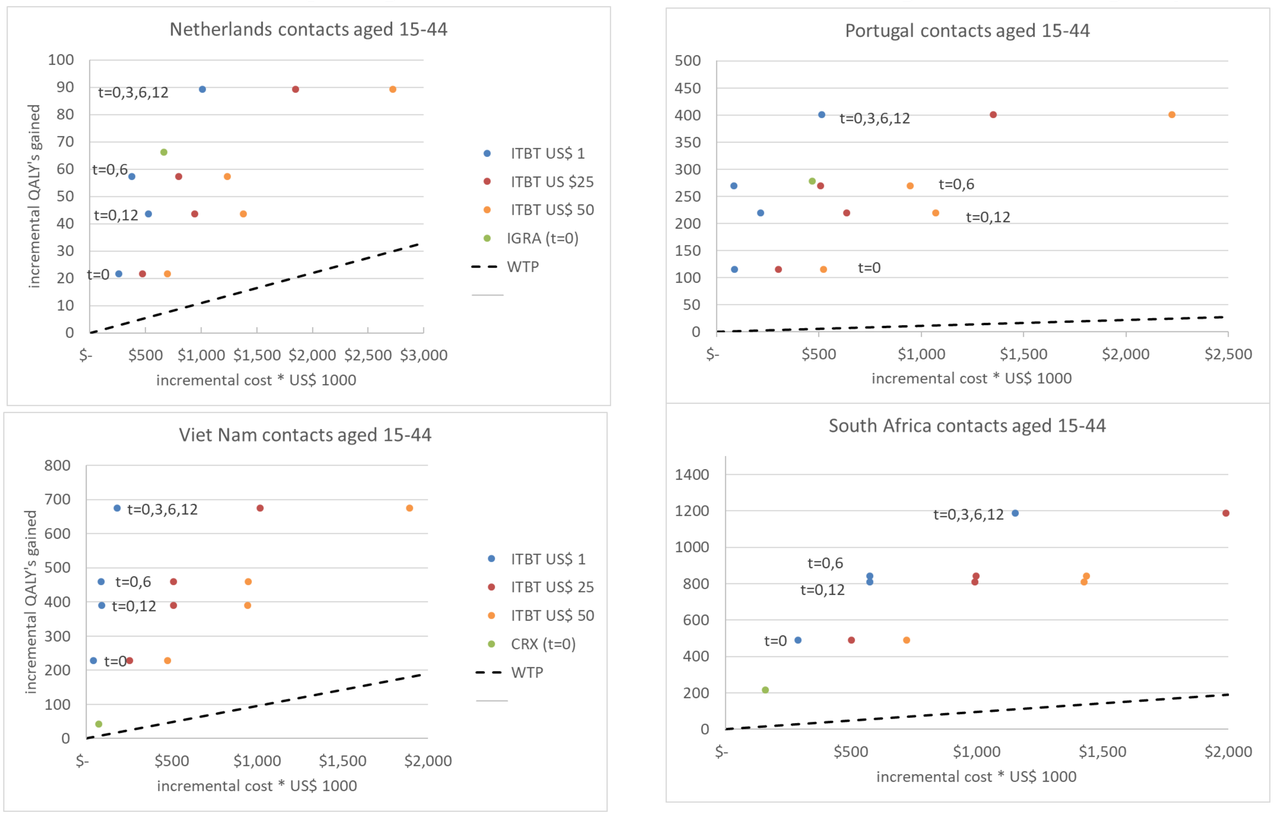
- Testing and treating for ITB among **close contacts** is cost-effective in low incidence countries when testing costs US$20-40, and is highly cost-effective in high incidence countries. In contacts in NL and PT, the health impact of the WHO recommended strategy of one-time testing with IGRA is comparable to 2-3 times ITB testing, and overall costs are similar if ITB testing can be done for US$ 100. In VN and SA, ITB testing strongly outperforms the use of CXR for contacts, by resulting in a much higher health impact.
- Testing and treating of **PLHIV and other immunocompromised persons** is not cost-effective in low incidence settings but highly cost-effective in middle and high incidence settings. For HIV patients, screening every 3 years for ITB results in roughly the same health impact as the WHO recommended strategy of one time using IGRA and CXR combined for NL, PT, VN. The costs are comparable if ITB testing is in the order of magnitude of 25 US$.
- **Sensitivity analysis:** Cost-effectiveness was
  - strongly dependent on assumptions on mortality and prevention of secondary cases
  - robust for comparison with no LTBI screening or with recommended LTBI policies, and for assumptions on LTBI treatment or full treatment.

Natural history of TB and LTBI



FOI = force of infection. The time in each compartment indicates the assumed average duration that an individual spends in a certain health state. The % indicates the proportion that moves to another health state, when leaving a compartment. Individuals with remote LTBI can get re-infected, but at 21% of the rate for not infected susceptible individuals, due to some degree of immunity. Durations and proportions given for TB are assuming no treatment will take place.

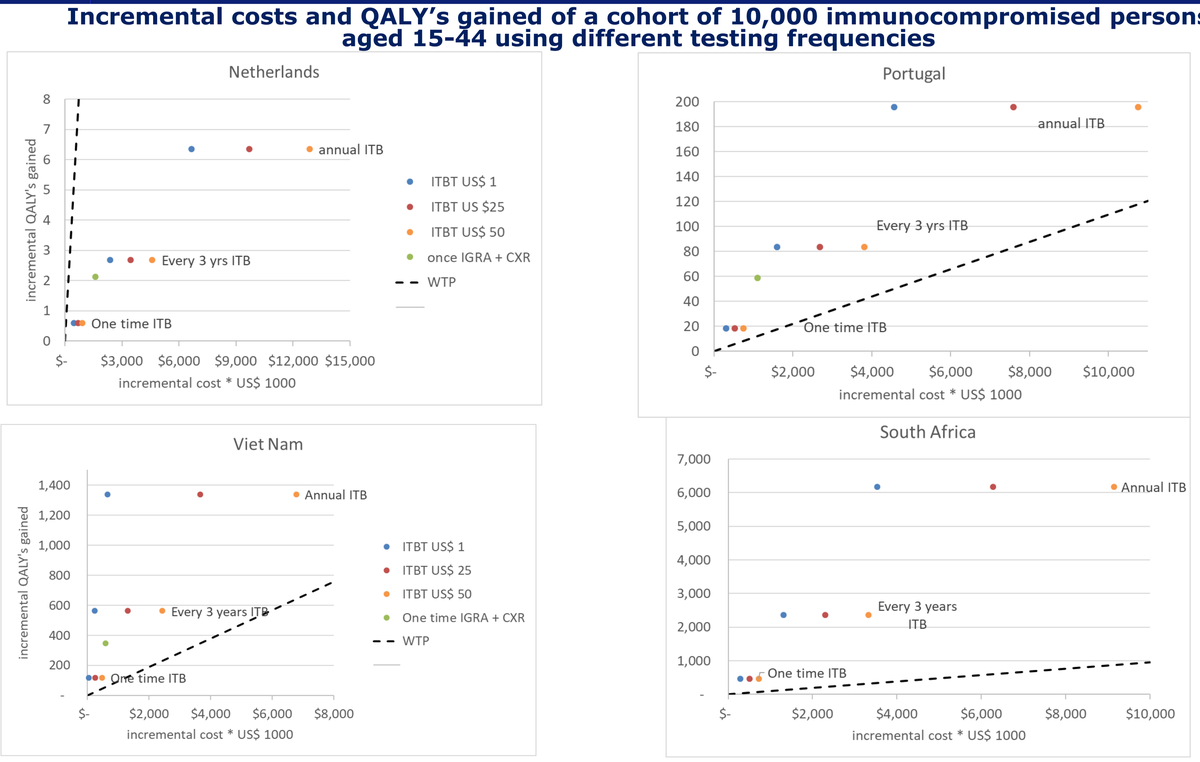
Incremental costs and QALYs gained of a cohort of 10,000 contacts using different testing frequencies



Results are cumulative incremental costs and QALYs gains over a 20-year period by doing ITB testing and treatment (ITBT) in 10,000 contacts immediately after exposure, compared to the baseline of doing nothing.

- Y-axis represents ICER=zero.
- WTP = willingness to pay threshold of 2 x GDP.
- Blue, red and yellow bullets on the same horizontal line are different costing options for the same frequency and time points of doing the ITB test (testing cost = test-cost plus two consultations).
- The alternative baseline is using IGRA screening for NL and PT or CRX screening for VN and SA (green bullet).

Incremental costs and QALY's gained of a cohort of 10,000 immunocompromised persons aged 15-44 using different testing frequencies



Explanation as above. Risk of TB activation (RR) = 4, as in adults with HIV. NL and PT include only natives. Blue, red and yellow dots on a horizontal line represent the same testing frequency at different costing options.

Conclusions

- Testing and treating for ITB among contacts is cost-effective for all countries at reasonable ITB testing cost. For high incidence countries substantial QALYs are gained.
- Testing and treating of PLHIV and other immunocompromised persons is also cost-effective, except for groups with very low TB incidence.
- We encountered many gaps in knowledge. Most policy relevant outcomes require more data. Qualitative insights will likely remain valid.

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