



Modelling impact of a new test for incipient TB

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Overall aim

To estimate the health and economic impacts of screening and treatment of high risk groups for Latent Tuberculosis Infection (LTBI) with a **potential new test for incipient TB**

Target Product Profile:

- Predict risk of progression to active TB from TB infection (LTBI) within the next 2 years
- Test result to decrease or revert to negative with treatment
- Sensitivity: 75-90%
- Specificity: 75-90%

What cost for the new incipient TB test would make the use of this test cost-effective?

4 countries: Netherlands, Portugal, Viet Nam, African country

Target Population

- Asymptomatic individuals who have increased exposure to a person with active TB, and
- Individuals with increased risk of progression of LTBI to active disease.

Medium/high incidence countries

- Children < 5 years who are contacts of TB patients
- Other contacts of TB patients
- HIV infected persons

Low incidence countries

- As medium/high, AND
- Other immunocompromised (silicosis, diabetes, immune transplant, TNFalfa blockers)

Action after a positive incipient TB test

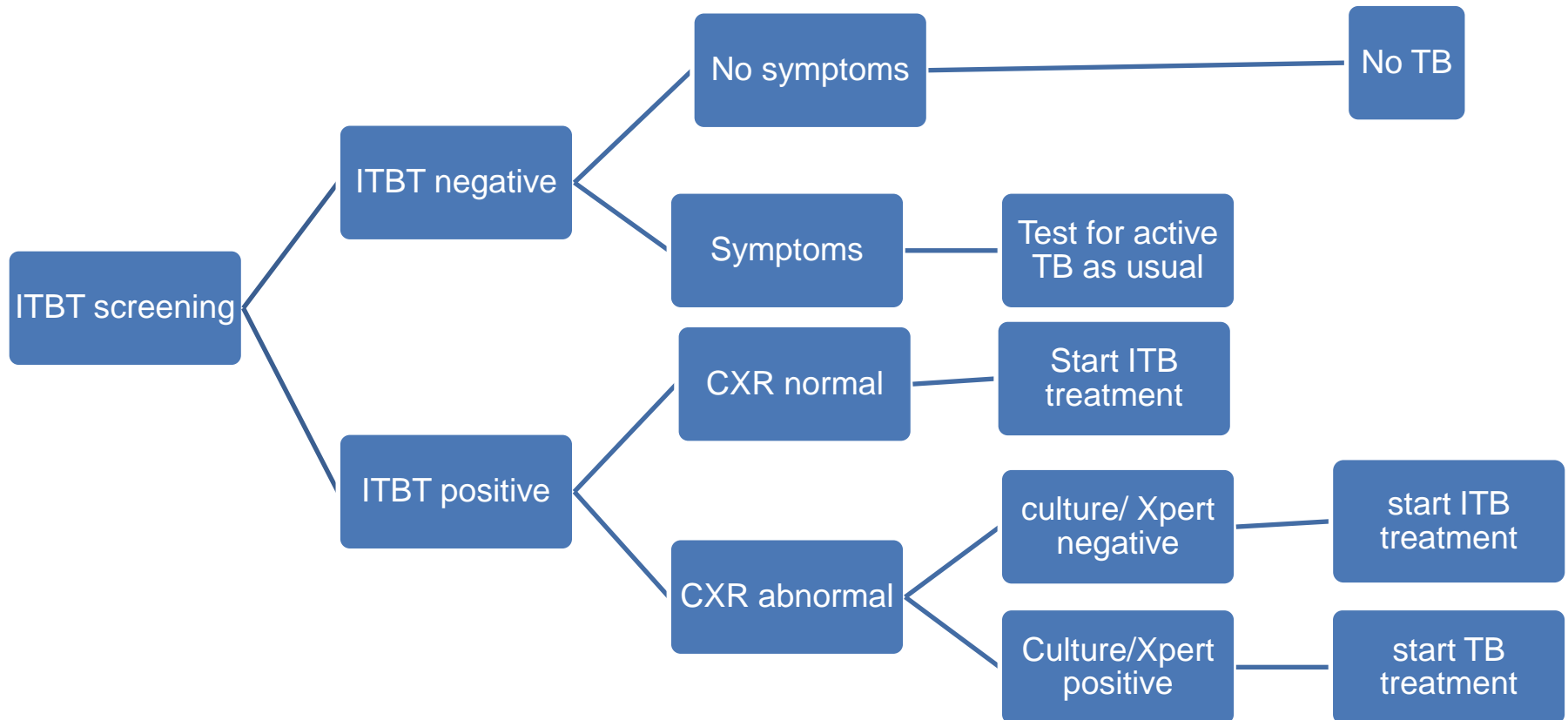
- Exclude active disease by assessing symptoms, CXR, culture or Xpert test (algorithm)

- If no active disease, treat as TB or LTBI:
 - LTBI: 6H or 3HP
 - TB: 2HRZE/4HR

- Actions after a negative incipient TB test: repeat test
 - For contacts: at 0, and at 3, 6 and/or 12 months after exposure
 - For HIV infected persons and other immunocompromised: annual or every 3 years

Flowchart for screening risk groups for incipient TB

(ITBT = incipient TB test)



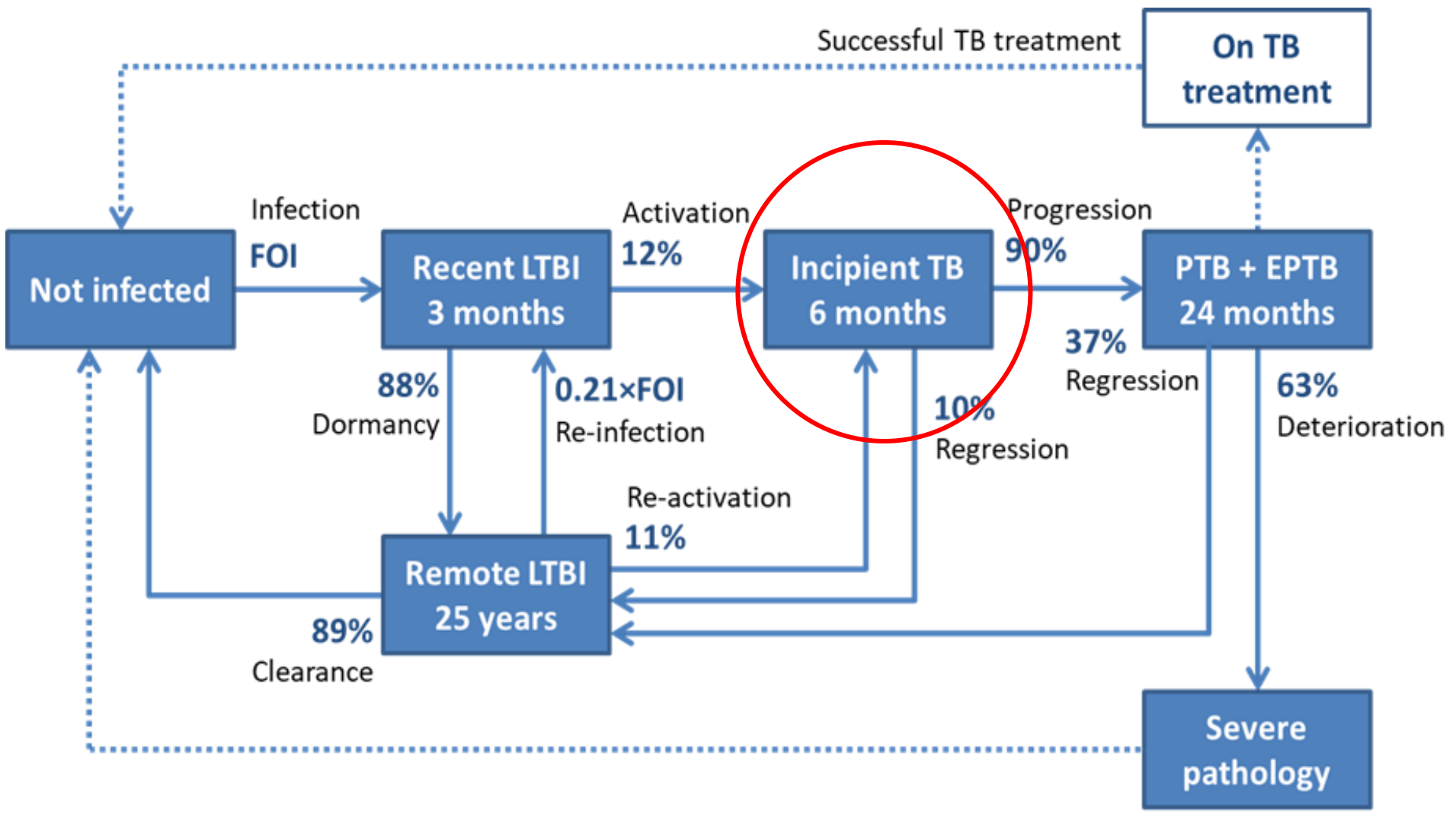
Model steps

- Start with transmission and cohort model developed for ECDC to estimate impact of screening and treatment for Latent TB Infection (LTBI)

(Poster Friday: LTBI-the last frontier (PD758-13) row 24)

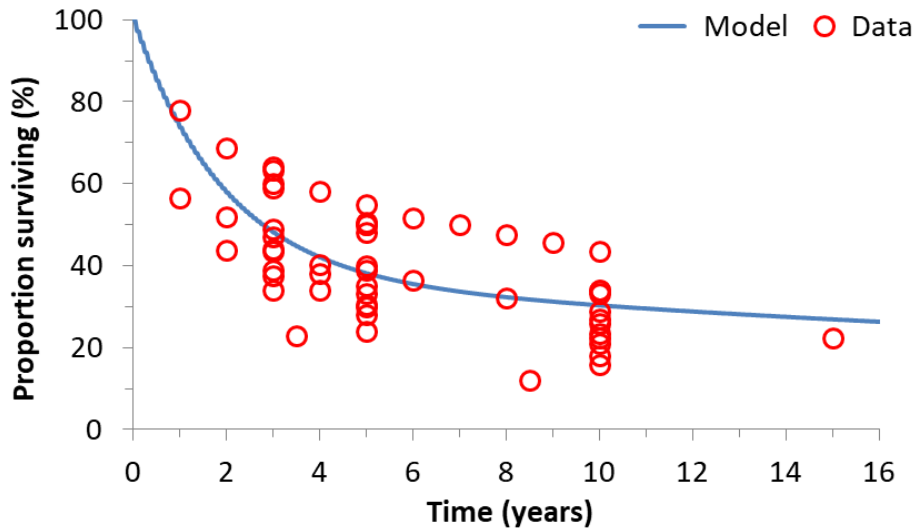
- Adapt model for incipient TB test
- Feed and fit cohort model for risk groups with country data from NTP, WHO, literature & expert opinion
- Estimate health impact: TB disease and death
- Estimate cost for health system

Erasmus MC model: natural history of TB and LTBI

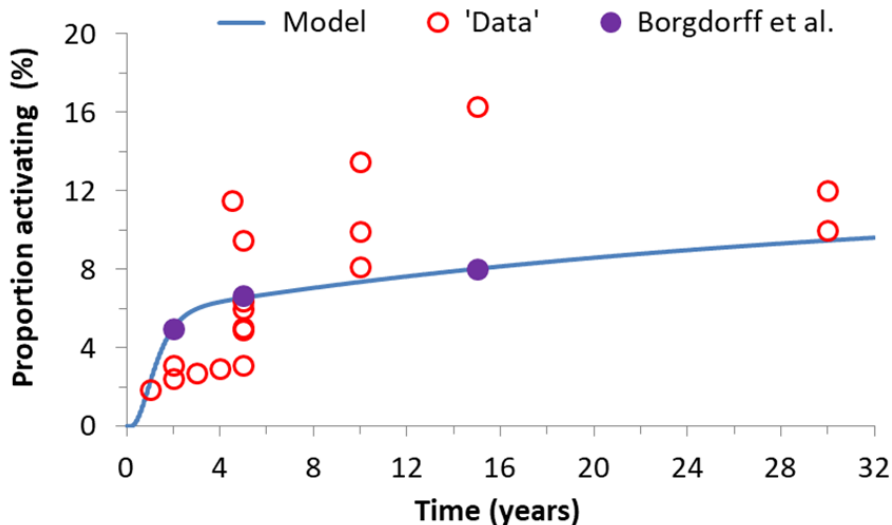


Fitting the model to:

Survival of smear positive cases

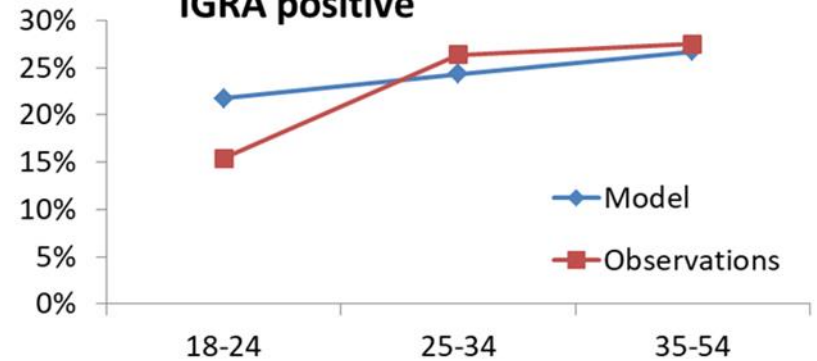


Activation to PTB after recent infection

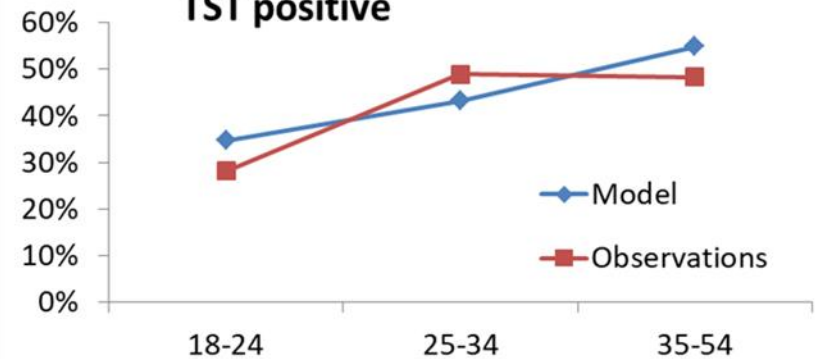


Migrant screening at entry in the Netherlands

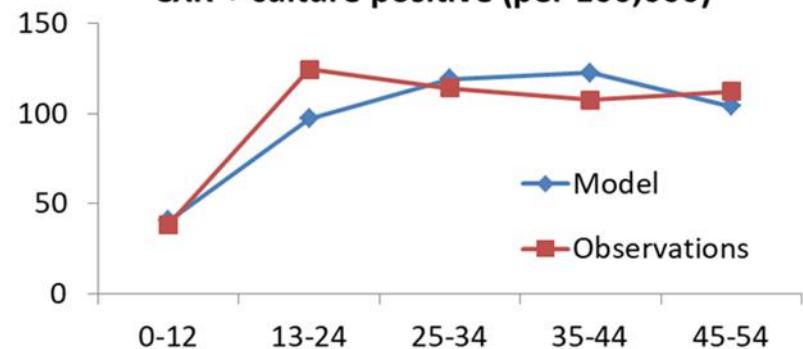
IGRA positive



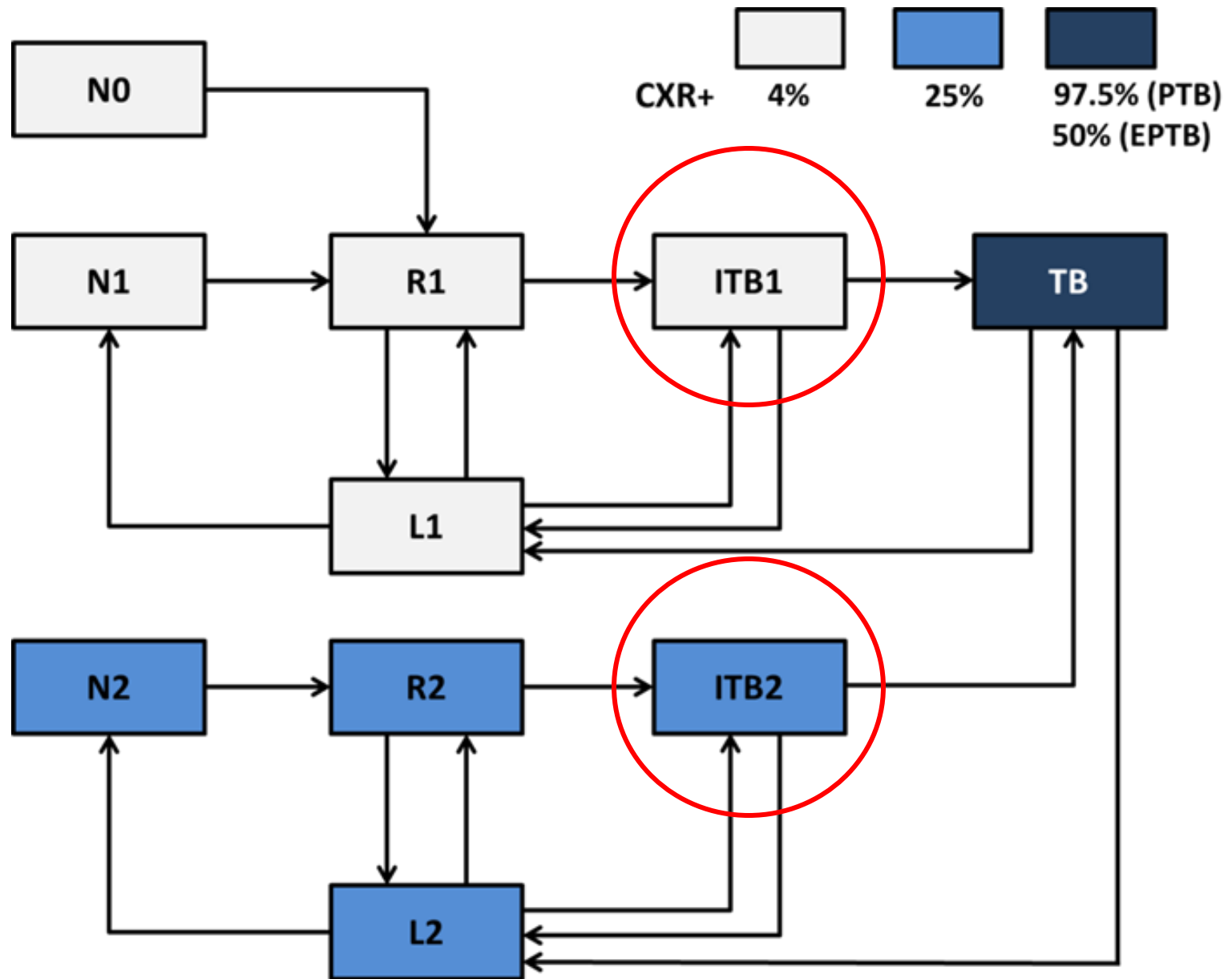
TST positive



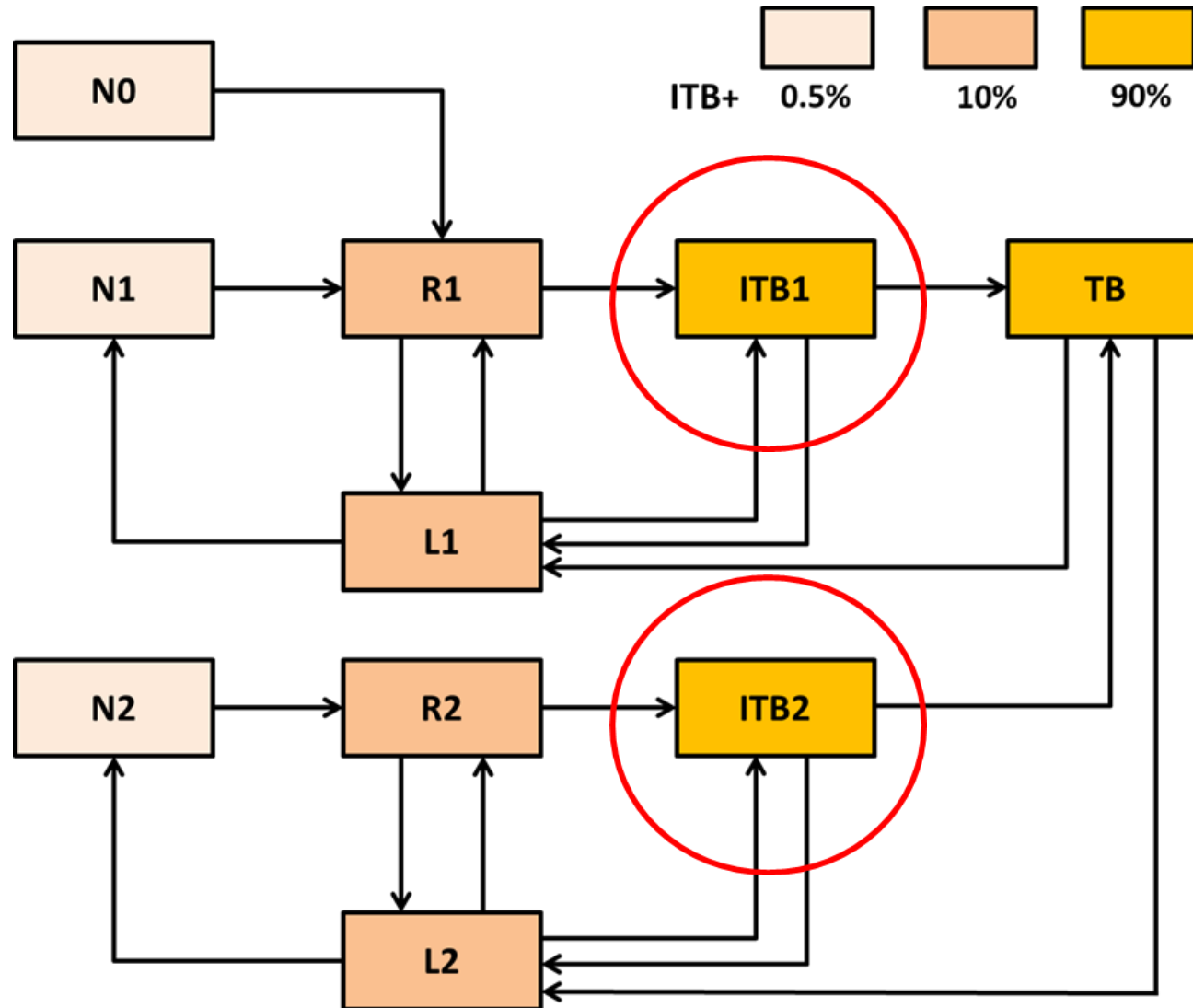
CXR + culture positive (per 100,000)



Testing positive for CXR



Testing positive with incipient TB test



We assume ITB treatment with 6H results in 100% cure for those with LTBI, 80% for those with ITB, and 10% for those with active TB

Costing approach

- WHO-CHOICE method: www.who.int/choice/en/
- Healthcare perspective costs of TB control (MoH, MoF, KNVCV)
 - screening
 - LTBI treatment
 - TB treatment & proportion MDR-TB and including contact tracing, directly observed treatment (DOT) and hospitalisation
- Ingredient approach: price x number of items needed (p x q) per patient
- Direct medical costs (consumables & staff time)
- For burden use QALY = quality adjusted life years
 - Disease due to PTB and EPTB: 0.331 QALY-loss (GBD estimate)
 - Death: 1.0 QALY-loss per year of life lost (YLL)
- Incremental Cost Effectiveness Ratio = ICER = $(C1-C0)/(E1-E0)$
- Willingness to pay threshold = 2x national income (NL €80,000/QALY)

Summary health care cost 3 countries

Activity	Netherlands	Portugal	Viet Nam
PPP *	1.00	0.75	N/A
Screening			
IGRA	€ 91.41	€ 68.22	
CXR	€ 62.66	€ 43.00	€ 2.55
Sputum smear			€ 2.34
Culture	€ 52.05	€ 38.84	€ 8.07
GeneXpert			€ 81.4
LTBI treatment			
3HR	€ 461.60	€ 319.16	
6H	€ 520.37	€ 405.94	2.62
TB treatment (DS)	€ 1,414.16	€ 981.68	€ 88.32
TB treatment (MDR)	€ 18,273.11	€ 17,840.63	€ 1045.01
Contact tracing	€ 4,048.00	€ 2,515.03	
DOT			
DS TB treatment	€ 330.00	€ 246.27	€ 4.85
MDR/XDR treatment	€ 1,647.00	€ 1,229.10	€37.00
Hospitalization			
DS TB patient	€ 6,341.50	€ 7,887.43	€ 96.18
MDR/XDR TB patient	€ 39,491.96	€ 30,227.30	€ 40.48

Results have been removed since they were preliminary

Preliminary conclusions

- Substantial QALY gained by screening and treating contacts with ITB test
- **Next steps:**
 - Model screening contacts of all age groups, screening of immunocompromised in 4 countries
 - Calculate: Number Needed to Screen, correct for prevention of secondary cases, sensitivity analysis

Discussion

- Strength: this model allows different sensitivity and specificity of diagnostic test in different stages of disease
- Weakness: model assumes equilibrium (constant) in TB transmission before intervention rather than decreasing trend in incidence
- Data challenges:
 - Unknown characteristics of ITB test
 - Little data on diagnostic test specifics of EPTB
 - Costing differs between national/provincial/district level
 - For high incidence countries:
 - Equilibrium based on migrants at entry less suitable
 - No detailed information for patients who are smear-negative
- Patient perspective not included

Collaborators

- **Research team at Erasmus MC**

Sake de Vlas, Suzanne Verver, Ana Krsteska, Jan Hendrik Richardus, many others

- **Stop TB partnership: New Diagnostic Working Group (NDWG)**

- Chairs: Daniela Cirillo and Catharina Boehme
- Coordinator LTBI task force Alberto Matteelli, University of Brescia
- Member LTBI task force: Samuel Schumacher, FIND
- Secretariat: Alessandra Varga, FIND

- **FIND Viet Nam:** Yen Nguyen

- **Country experts NTP:**

- Netherlands: Gerard de Vries, Connie Erkens, Henriek Schimmel
- Portugal: Raquel Duarte, Marta Gomes
- Viet Nam: Nguyen Viet Nhung, Nguyen Binh Hoa, Vu Cam Thanh, Truong Thanh Huyen, Nguyen Thi Huong Trang, Nguyen Van Hung, Chu Manh Dung, Luong Anh Binh, Le Thi Van, Vu Quynh Hoa

- **Earlier versions of model:** ECDC, KNCV Tuberculosis Foundation, Radboud University Nijmegen (Netherlands), LSHTM

- Starting collaboration with other model teams in TB-MAC