Tuberculosis modelling – Interventions

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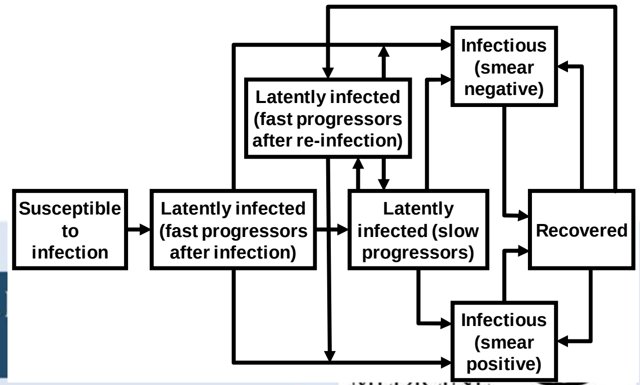
What you've done so far...

- Lecture
  - Seen what a TB model is, and why we might bother setting one up
  - Seen the steps to setting up a TB model
  - 'As simple as possible, but still useful'

- Practical
  - Changing key parameters and evaluate impact on model outcomes

- Dissected a modelling paper



What is coming up?

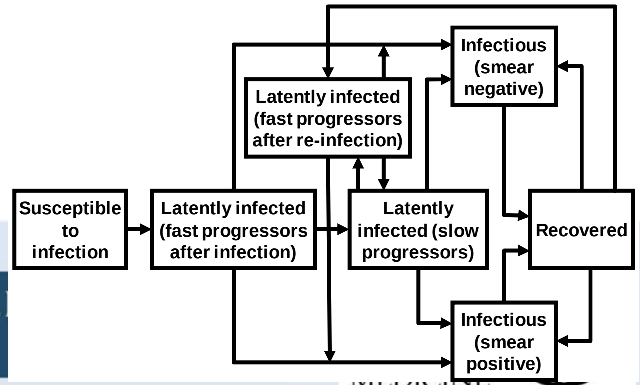
- 2nd half lecture
  - Introduction to cost-effectiveness analysis

- Practical 2
  - Explore impact and cost-effectiveness of intervention in our model

- Summary and close

Objectives of this lecture

1. Why do we model interventions?
2. How do we model interventions?
   – Examples of classic models
3. Give practical example of model intervention
   – Add novel diagnostic tool to our natural history model

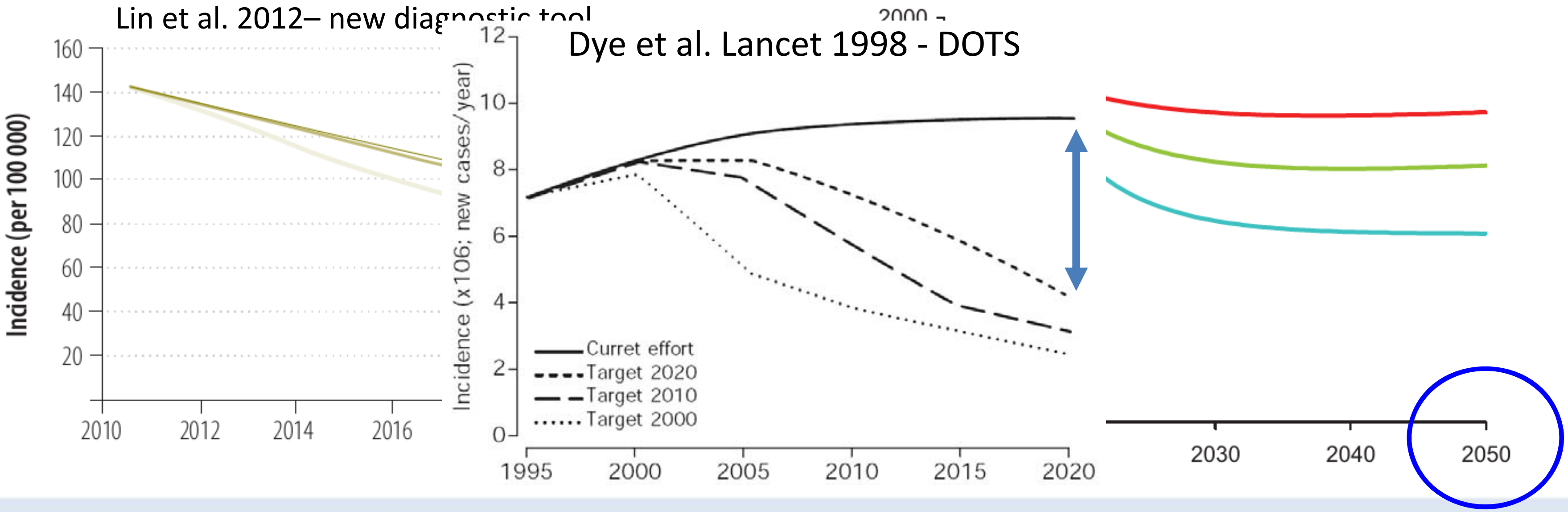


1. Why do we model interventions?

Why model interventions?

- Look beyond natural course of epidemic
- Ask: what would be achieved if we changed the status quo?
  - New diagnostic tool, vaccine, treatment, etc...
  - Change in policy/health system
  - Near vs more distant future

Abu-Raddad et al. 2009 – new diagnostics



Why model interventions?

Goals of intervention model

- Estimate population impact of intervention (over time)
  - Change in incidence, mortality, risk of infection
  - General population, high risk groups (HIV+, prison, children)
  - Input for costing models (*see next presentation*)
  - Potential negative effects (e.g. false positives/misdiagnoses)

- Understand most influential aspects of the intervention(s)
  - Speed of roll-out, population targeted, etc

- Inform estimates of cost-effectiveness, affordability

--> Support policy decisions, research funding trial design, product pipeline

Advantages of modelling interventions

- Models are flexible
  - Evaluate single or combination of interventions
  - Evaluate alternative roll-out strategies
  - Extrapolate to different epidemiological situations or populations (incidence, existing diagnostic pathway)
- Models capture mechanics of intervention, and can project into future
- Modelling studies are (relatively) cheap and fast

But be aware

- Like any scientific tool, apply rigour in design, analysis and reporting
- Apply best available empirical data and understanding of disease and intervention processes
- Capture and clearly present uncertainty
  - Similar to need for 95% confidence interval in statistical analyses
- Acknowledge that uncertainty increases rapidly when projecting into future

--> Designing a good (intervention) model requires a lot of thought

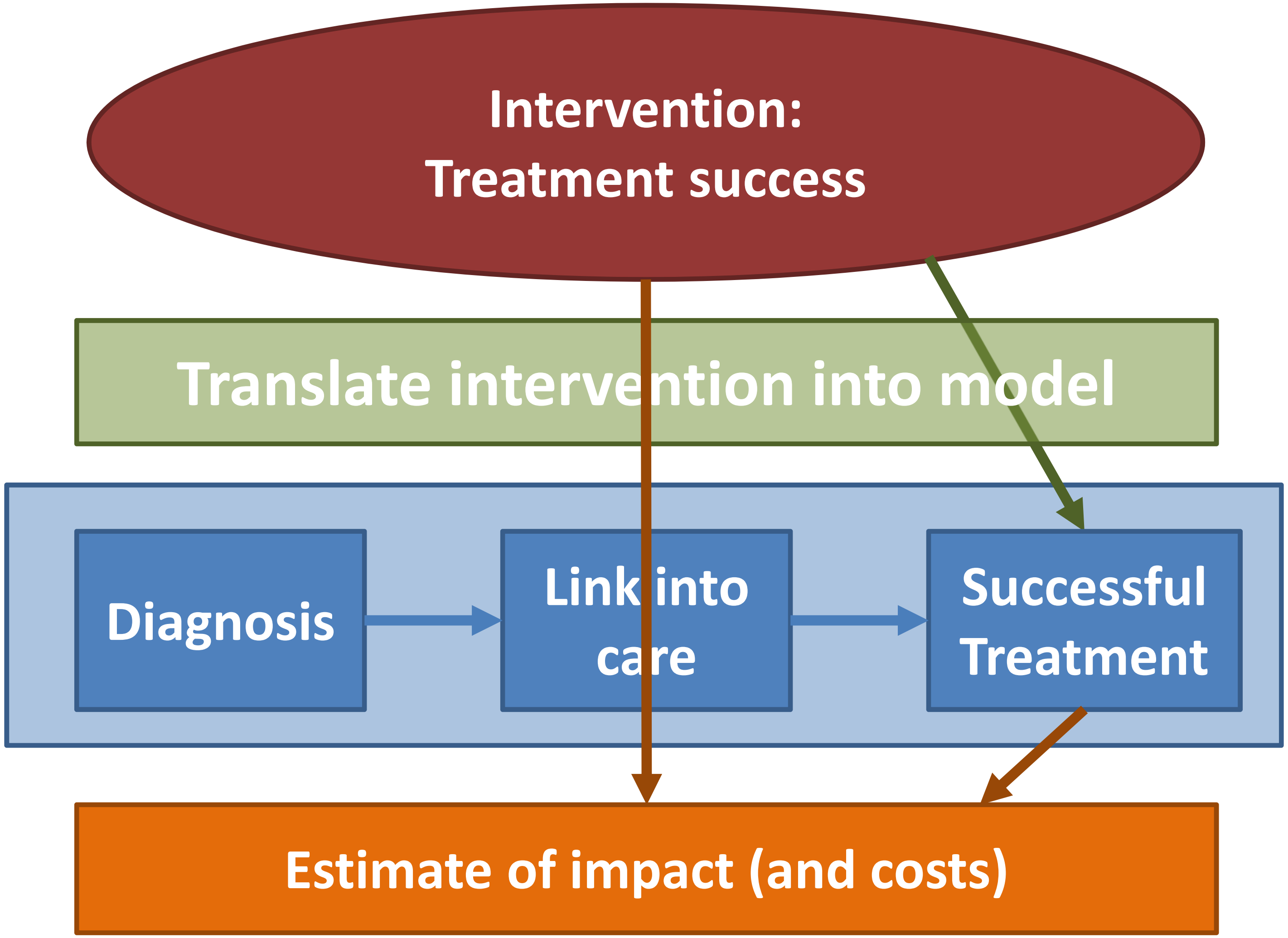
2. How to model interventions

How to model intervention

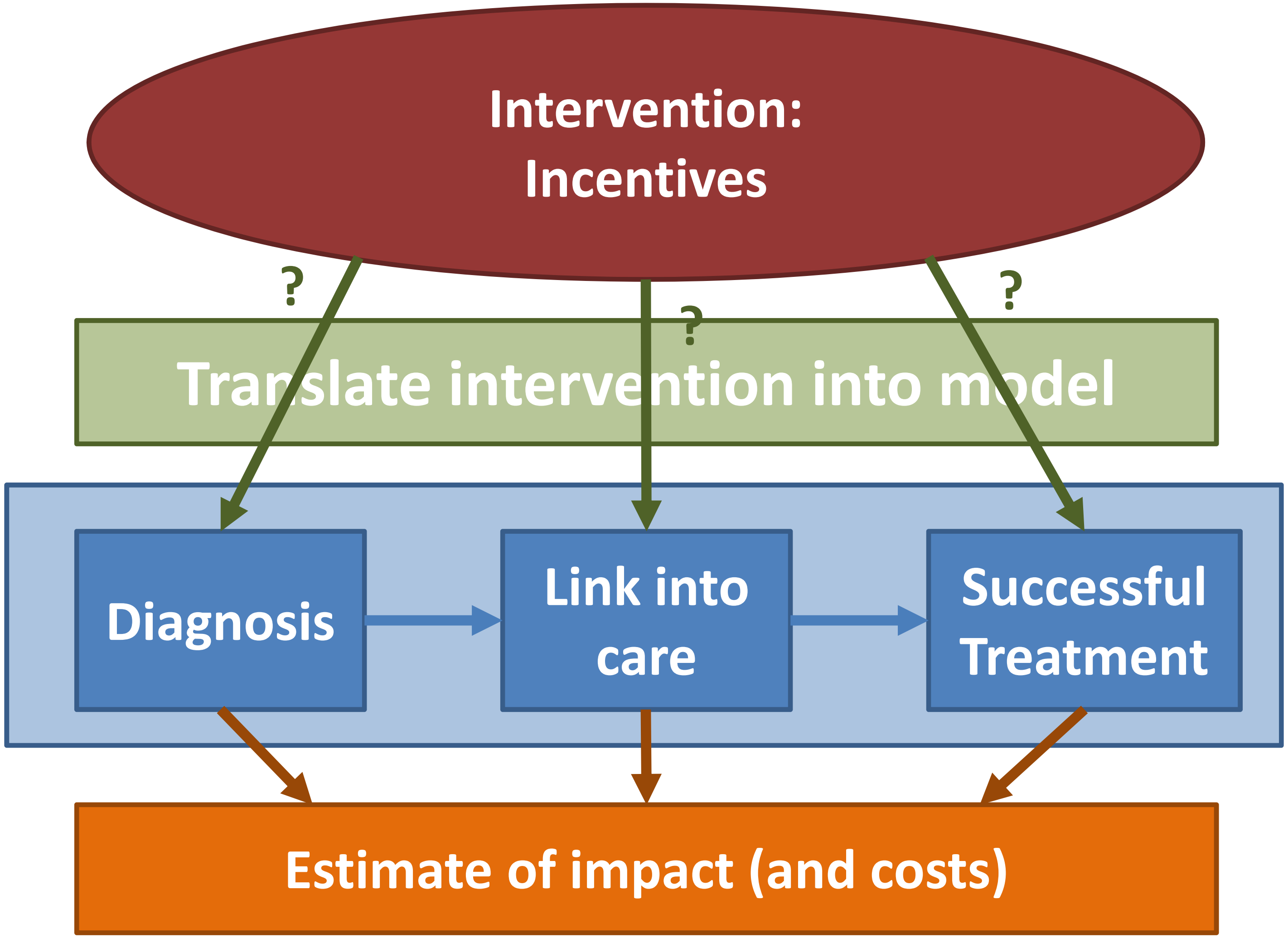
Just like building a natural history model...

1. Identify the question
2. Identify relevant data
3. Choose model methods
4. Choose model structure
5. Specify model inputs/ outputs
6. Set up and check model
7. Calibrate model
8. Prediction, sensitivity analysis and communication

From intervention to model to impact



From intervention to model to impact

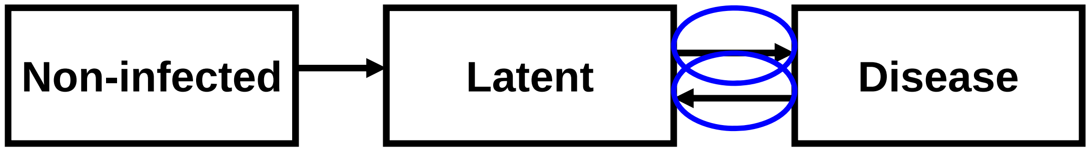


Structure of intervention models

- Broadly 2 approaches:
  - Single intervention – specific model
    - Extra structure to capture the specific intervention context
  - Multiple interventions – general model
    - Relatively simple model of natural history
  - Note: most models in grey area in between
- In common: model must have a 'hooks' that can capture the impact of the intervention

Example 1 – Waaler (1962)

– First model of interventions (case finding or BCG) in South India
– Very simple model
1. BCG intervention = 70% coverage, 70% protection
→ Hook: reduced parameter progression from infection to disease by 50% (0.7*0.7=0.49)
2. Case finding: Two-thirds of cases detected and successfully treated
→ Hook: assume out 2/3 of all cases at start are immediately cured



Waaler et al. 1962
Am J Public Health Nat Health

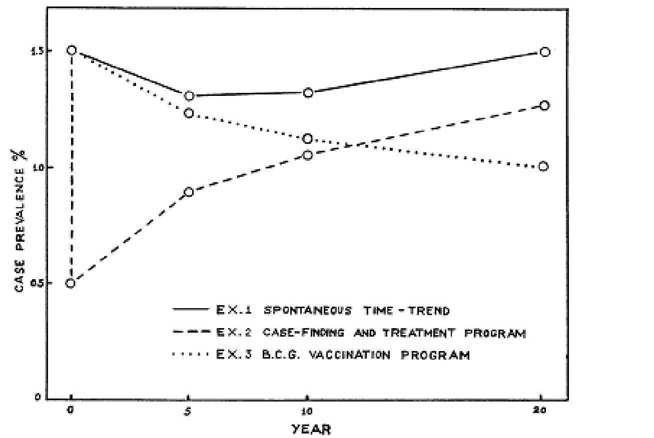
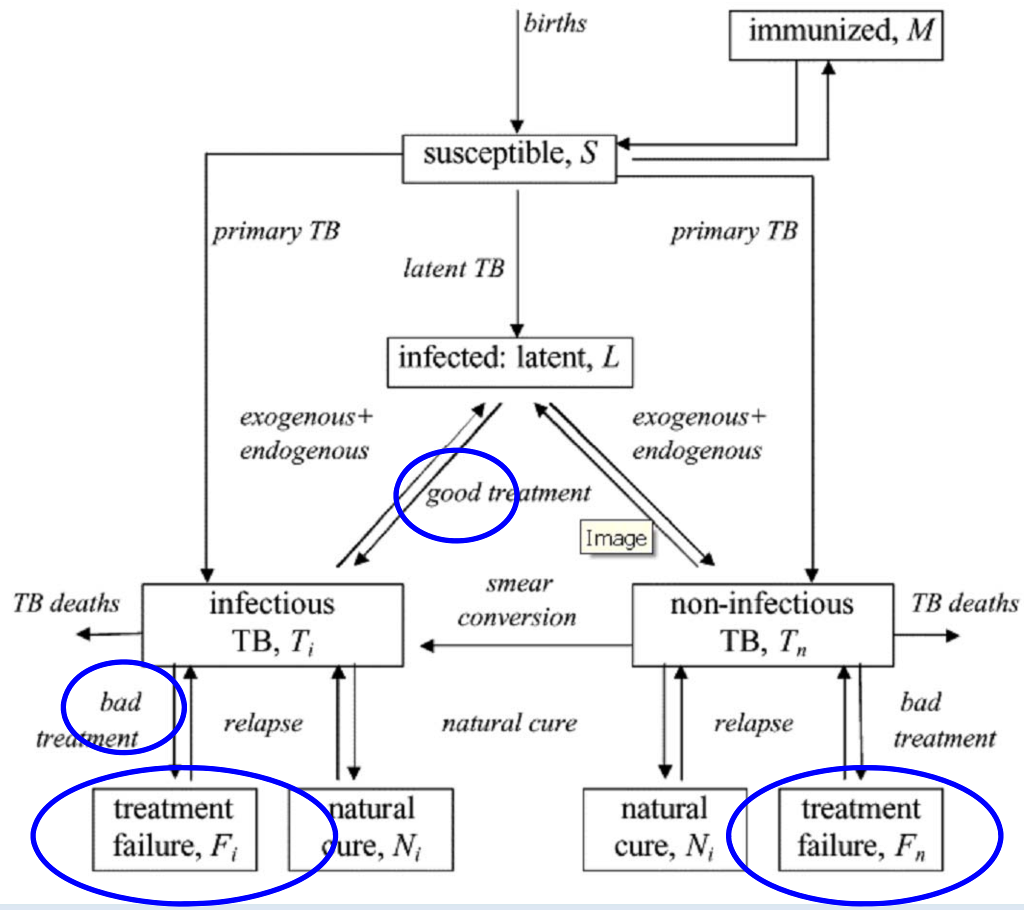


Figure 1—Examples of Model Solutions in Terms of Case Prevalence over 20 Years

Example 2 – Dye 1998

Prospects for worldwide tuberculosis control under the WHO DOTS strategy



<u>Expanded model</u>

- Compartment for individuals receiving ineffective ('bad') treatment

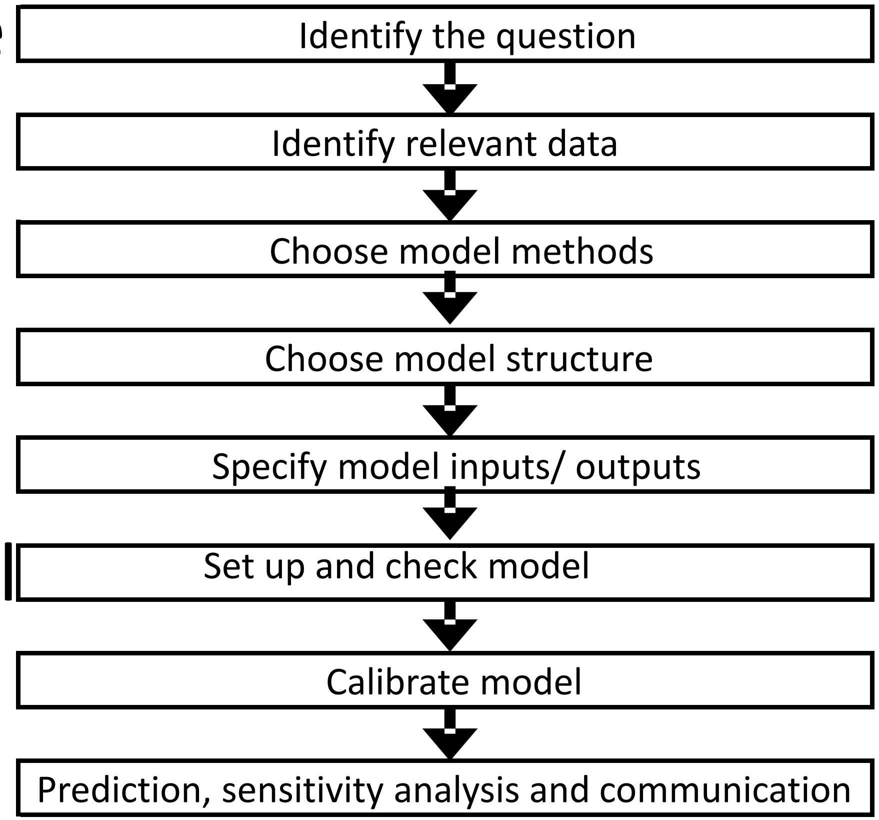
<u>Single intervention</u>

- Expansion of DOTS

Hook: increase proportion receiving 'good treatment'

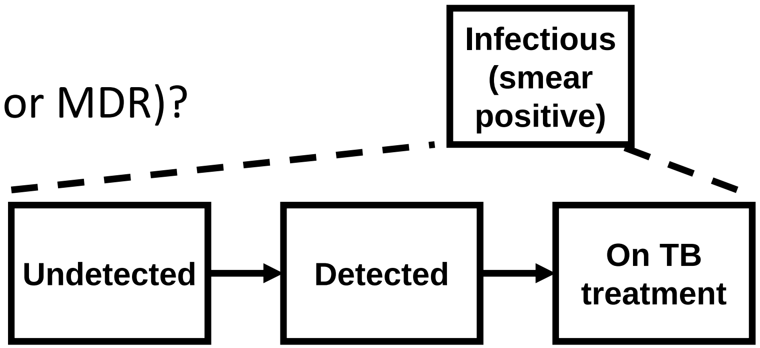
Intervention 'Hook'

- Captures the effect of the intervention
- Quantifies the change in model outcomes
- Has to be built into model during design phase



Some considerations on model design

- Add structure
  - Additional compartments or strata (e.g. HIV or MDR)?
  - Subdivide parameters?



- Advantage of adding compartments
  - Counts individuals in each state
    - Output, or comparison against empirical data
  - Can assign different characteristics to each compartment (e.g. different relative infectiousness, time spent in that compartment)
- How many/what compartments to add?
  - Follows the same principle: as simple as possible, but still useful
  - Depends on available data
- How are these decisions taken?
  - Subjective approach: choose compartments based on your best understanding
  - More objective approach: try out various options, remove or add compartments based on impact on results

3. Practical example of model intervention

Impact of introducing a new diagnostic tool

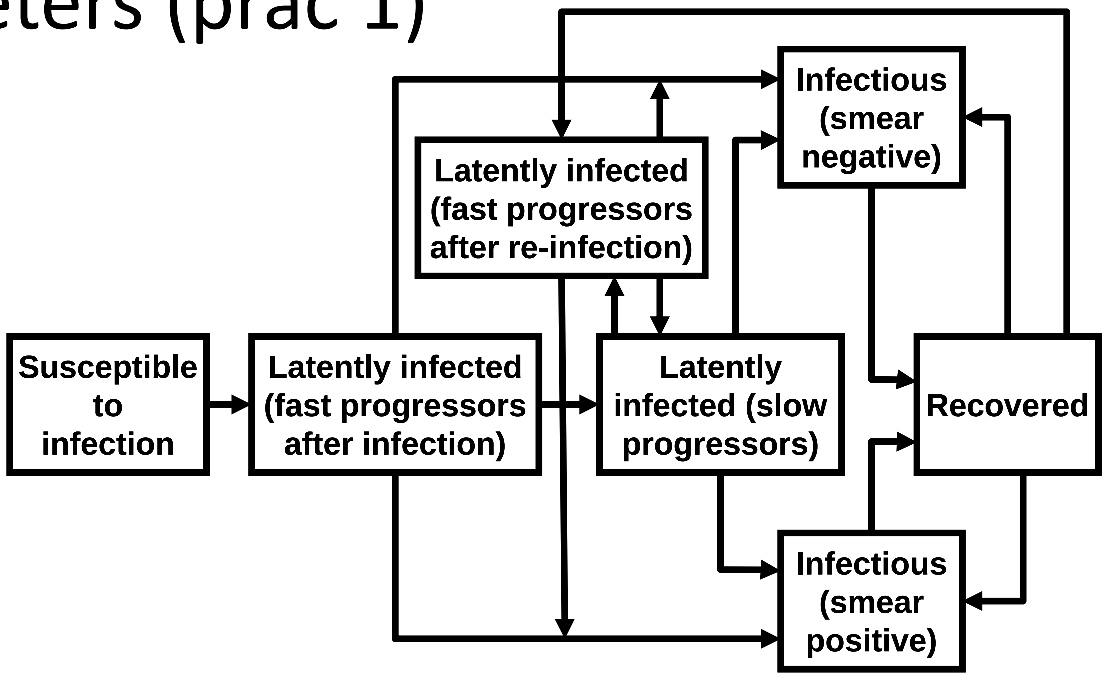
Example (Practical 2)

- Question: what is the impact of introducing a new diagnostic tool for smear-negative TB cases on TB incidence and mortality?

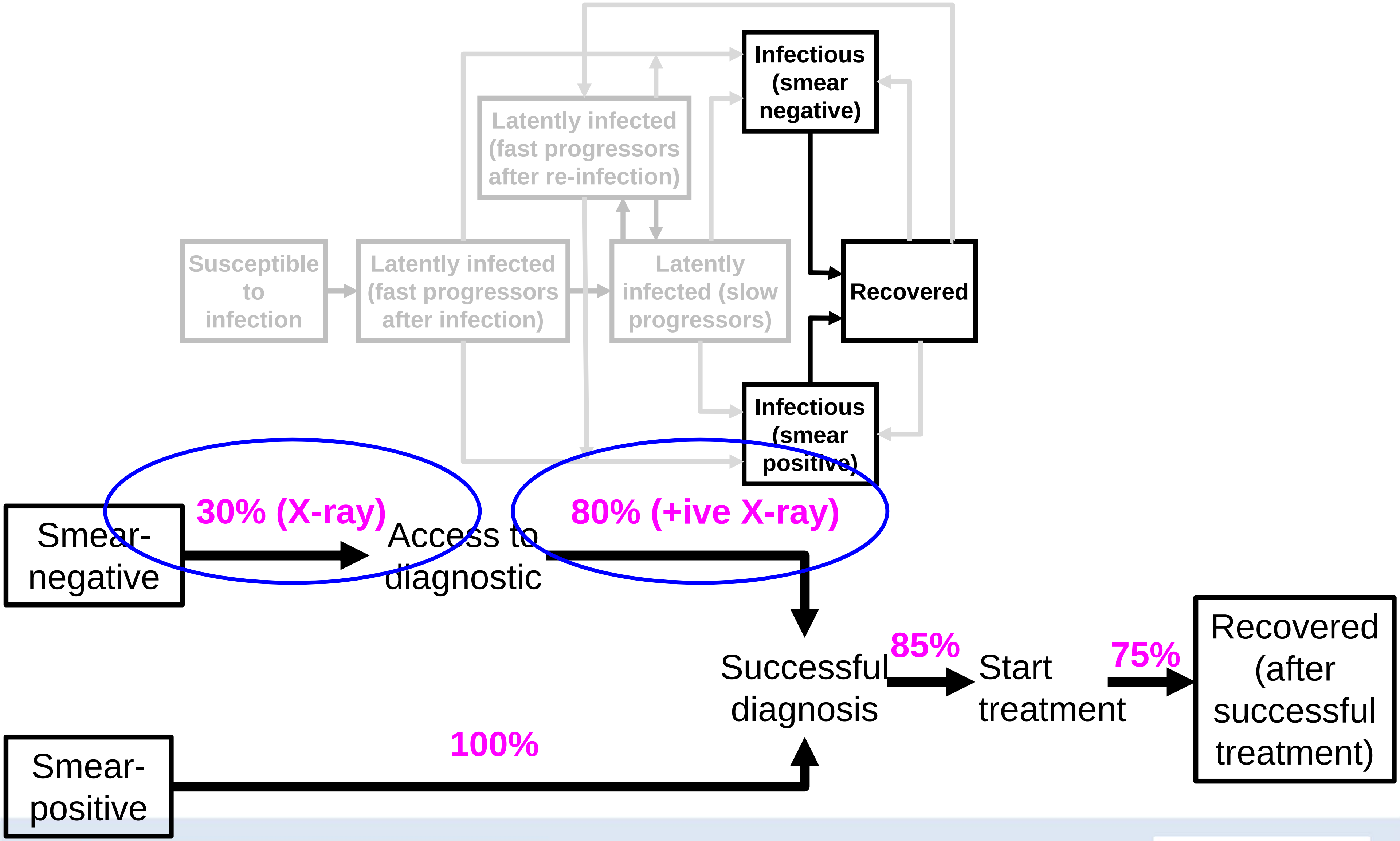
--> What is our intervention hook?

Current model structure

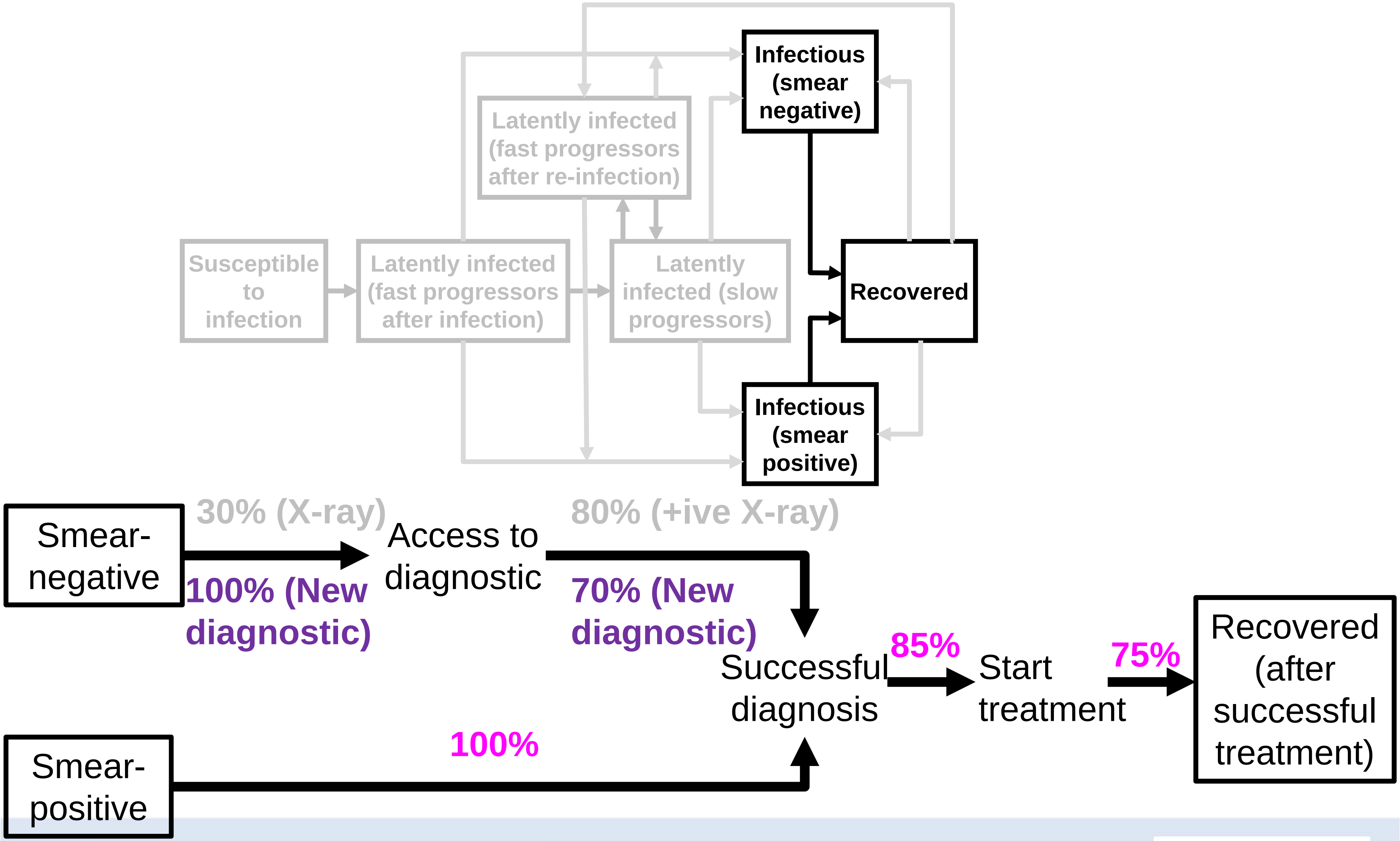
- Diagnosis and treatment – 1 arrow
- Several parameters (prac 1)



Diagnostic Pathway – pre-intervention



Diagnostic Pathway – post-intervention



Should we add more complexity?

What real life processes are not included in our model? Are they important for this question?

What is the potential impact of excluding this complexity? Is effect of new diagnostic tool is under or overestimated? Why?

Example of adding compartments

- As seen during paper discussion
  - Lin et al added various compartments to capture diagnostic pathway in more detail

- Advantage:
  - Understand impact of new tool in health system context

  Paper aim was to evaluate impact of health system context on impact of new TB diagnostic tool

  Note: Different from research question in practical 2

- Disadvantage:
  - More structure = more parameters, probably more uncertainty!
  - More complex structure can made it harder to understand model behaviour

Summary

1. Why do we model interventions?
   – Look beyond status quo, project into future
   – Model can explore variety of scenarios and settings at low costs
   – Important part of policy decision making process
   – But requires careful considerations on design, data and presentation of results

2. How do you model an intervention?
   – Introduce 'hooks' that capture impact of intervention
   – Need to consider whether to introduce more model structure

3. Introduce intervention in our model
   – Evaluated two approaches – change parameter (practical 2), or add structure (Lin et al.)

Next steps

- Lecture Fiammetta Bozzani:
  - Introduce costs and cost-effectiveness
- Practical 2:
  - Model exercise: Explore impact and cost-effectiveness of new diagnostic tool