

Modelling Diseases: Prevention, Cure and Management

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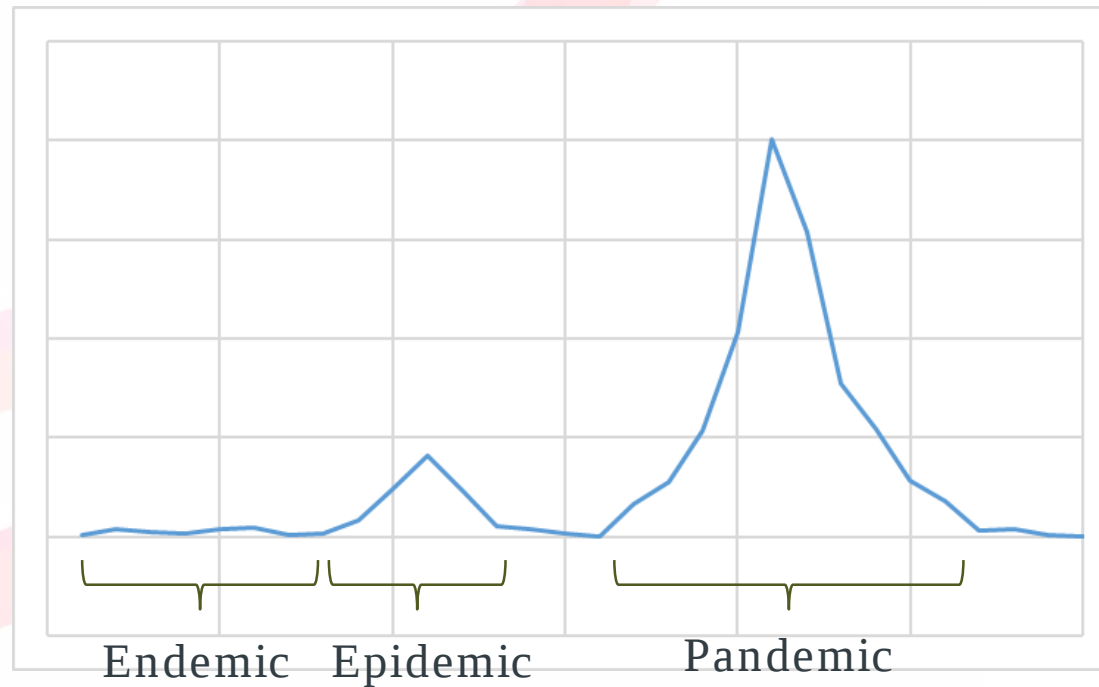
Agenda

- Modelling communicable diseases: Christine
 - Overview
 - Case Study: tuberculosis
- Modelling non-communicable diseases: Tom

COMMUNICABLE DISEASES

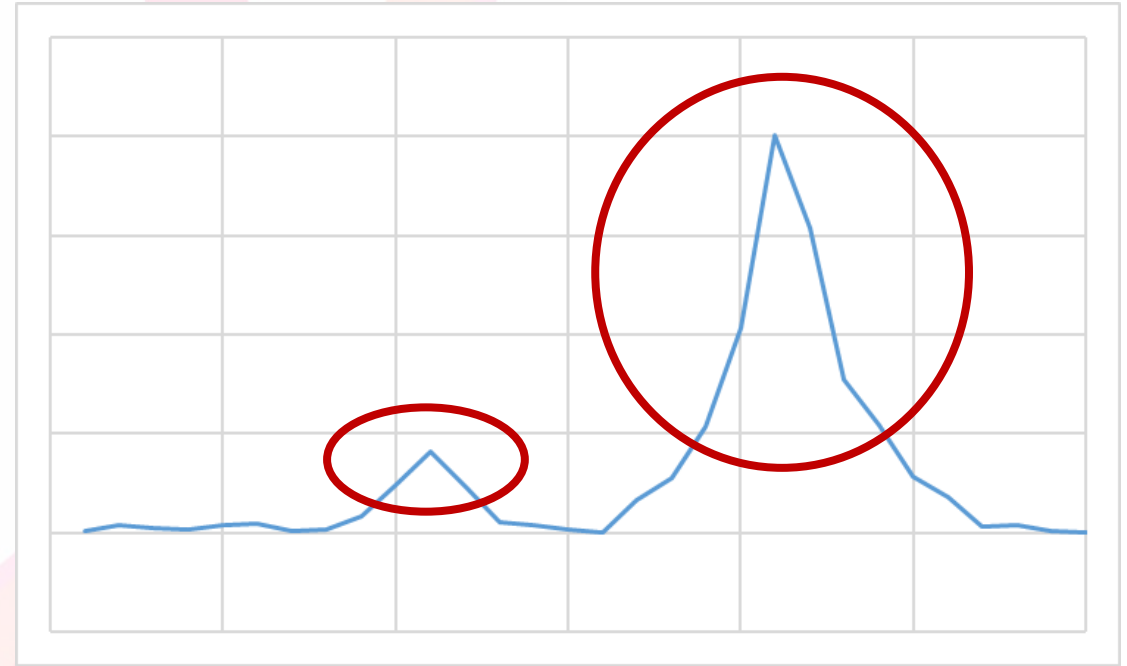
Overview of Communicable Diseases

- The timing and the transmission mechanism are the key differentiators between communicable disease models.
 - Outbreaks
 - Endemic diseases
 - Sexually transmitted diseases
 - Vector-borne diseases
 - Water-borne diseases



Outbreaks

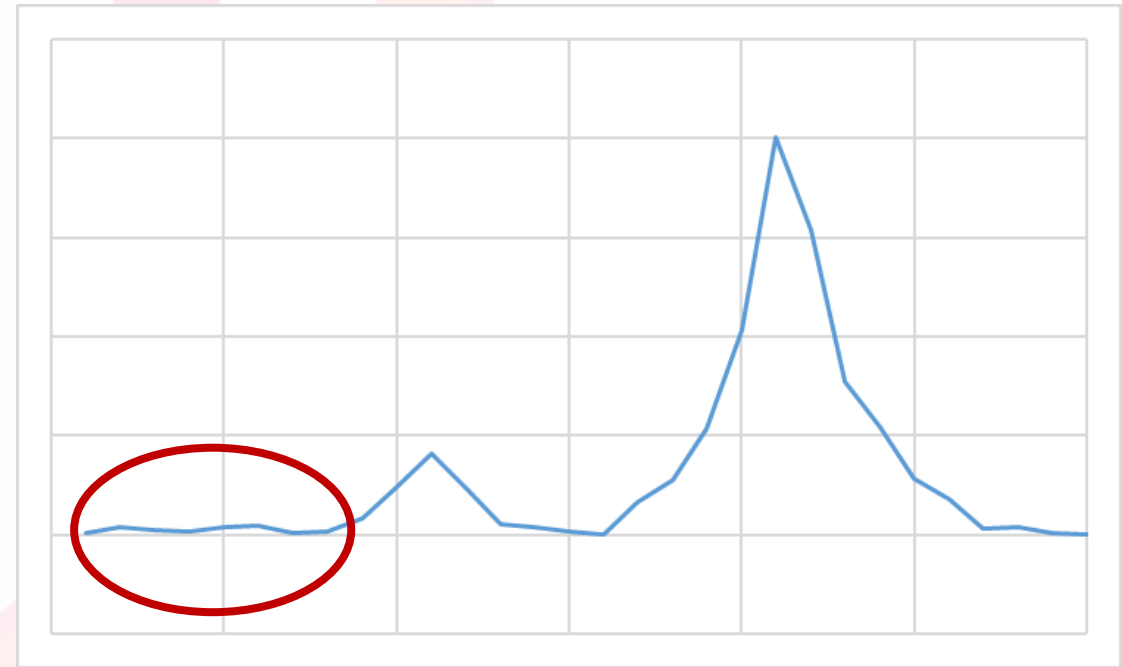
- High probability of transmission
 - Fast disease progression
 - Interventions
 - Vaccination
 - Isolation
- } Disrupting transmission
- Natural history is typically incorporated at a coarse level of detail (e.g. SEIR model)
 - Huge agent based models with millions of individuals
 - Individual heterogeneity dependent on questions being asked



“ABMs can record exact chains of transmission from one individual to another. Perhaps most importantly, agents can be made to behave something like real people: prone to error, bias, fear and other foibles” (Epstein, 2009)

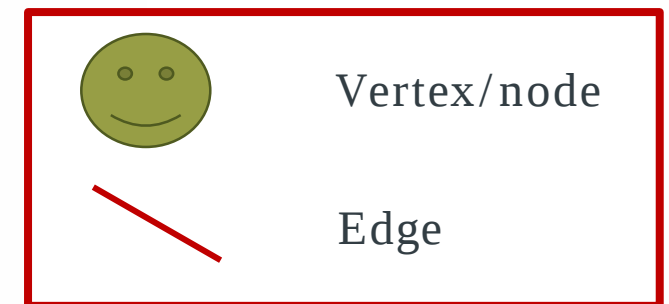
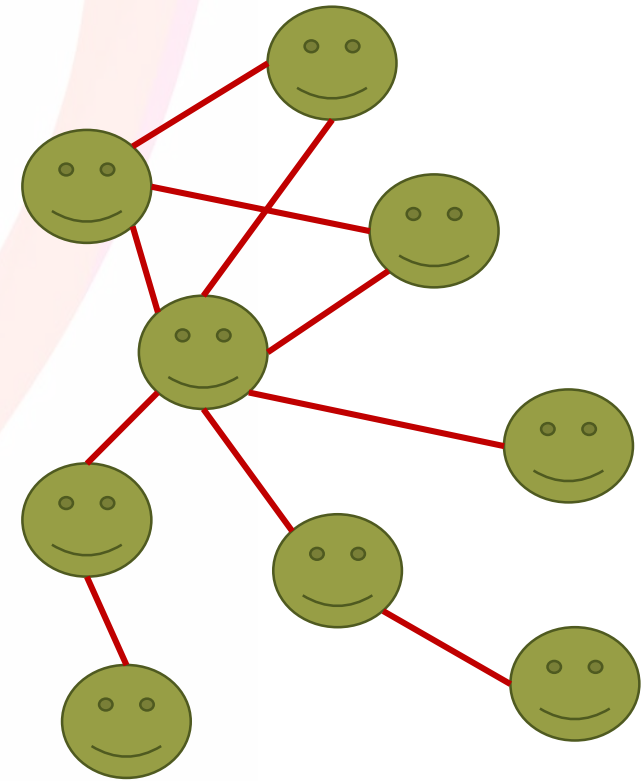
Endemic diseases

- Constant base level of incidence within the population
- May be viewed as being “under control”
- Examples: TB (see later); opioid crisis
- Population-level models often involve deterministic compartmental models or system dynamics models
- Targeting hard-to-reach populations might involve DES or ABM
- See TB-HIV example in a moment



Sexually transmitted diseases

- Key distinguishing feature: rely on a contact network for transmission
- Brings in ideas from networks
 - **Degree distribution:** probability distribution for the number of edges each vertex has
 - **Edge weights:** different edges have different probabilities of transmission
- Models aim to:
 - Test interventions that break transmission connections
 - Investigate behaviour, e.g. determine the effect of super-spreaders
- Other models
 - System dynamics for resource allocation (Kok et al. 2015)



Vector-borne diseases

- Account for >17% of all infectious diseases
- Transmission is via a vector – blood-sucking insect
- Two entity types in the model
 - Hosts
 - Vectors
- Ross (1911) – early model of malaria using differential equations
- Interventions can be aimed at either the host or the vector
 - Chemical vector control(vector)
 - Public health/environmental control (host/vector)
 - Paediatric vaccination (host)
 - *Wolbachia*: naturally occurring bacteria that render *Aedes aegypti* mosquitoes less able to transmit viruses to people (vector)

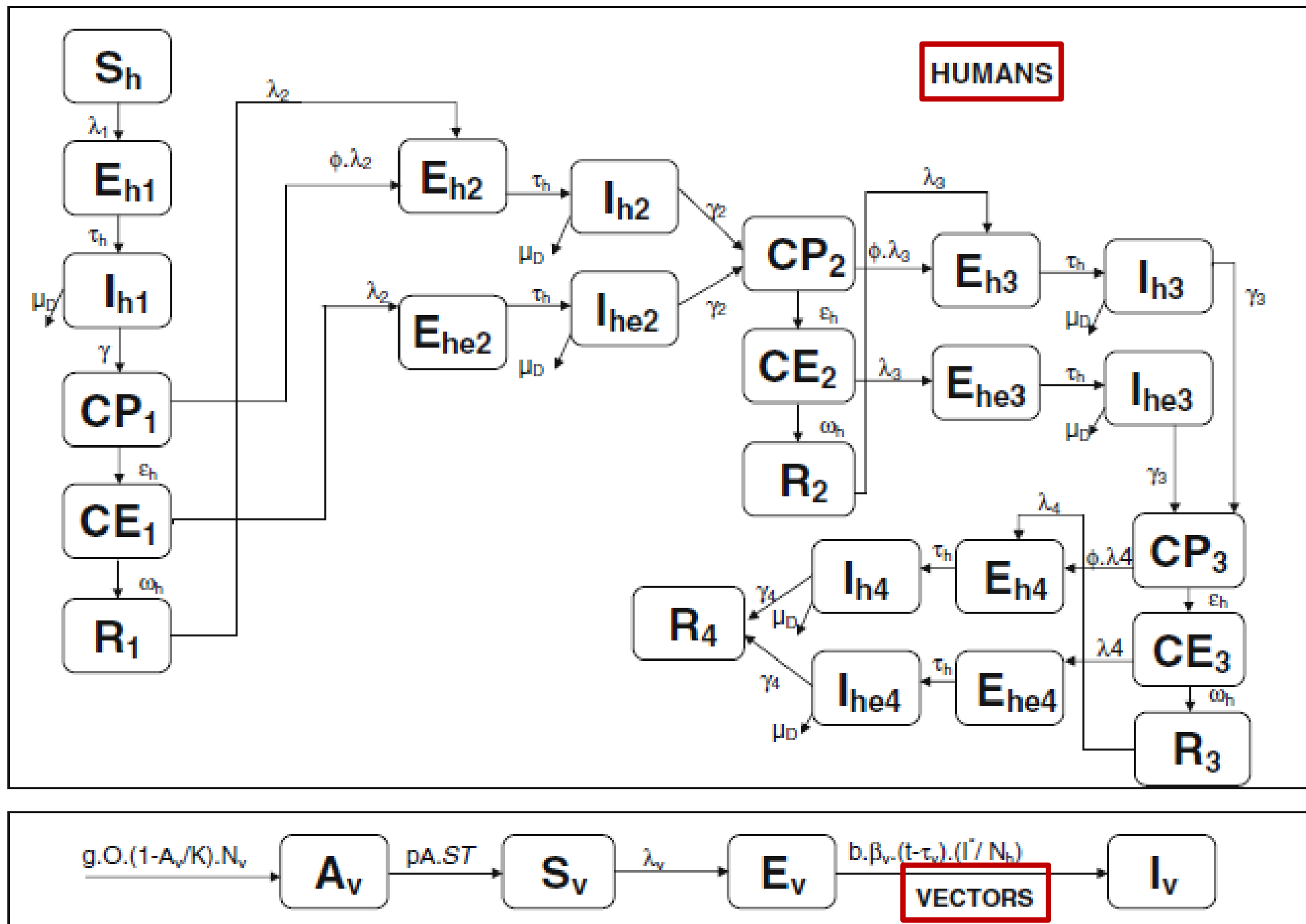


Mini Case Study: Dengue Fever

- Mosquito-borne viral disease that occurs in >100 countries in tropical/sub-tropical regions of the world
- Well-understood but not always well-managed
- > 3 billion people at risk
 - Increase in part due to rapid population growth, non-biodegradable packaging, increased air travel, deteriorations in public health infrastructure
- Comparing interventions
 - Calculate costs per DALY (Disability Adjusted Life Year)

Flows

- Diff eqns
- Homogeneous
- Human flows
- Vector flows
- Link by infection
- Age included



Alternative models: Agent based modelling

- Geographical features can be incorporated into the model
- Allows for heterogeneous mixing
- Allows for geographically-distinct vector control policies
- E.g. see de Lima et al. (2016), Isidoro et al. (2011)

Water-borne diseases

- Most common examples: cholera, dysentery
- Relatively little simulation modelling work in the area
- Incorporating the spatial environment can be important
 - E.g. Modelling the spread of cholera in a refugee camp: geography allows targeted interventions
 - Often important to incorporate hydrology
- Models often require a range of different expertise



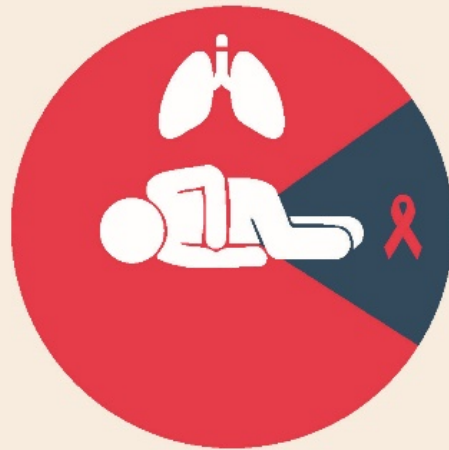
Georgina Mellor, Christine Currie, Liz Corbett (2011) Incorporating Household Structure into a Discrete-Event Simulation Model of Tuberculosis and HIV. *TOMACS*, Vol. 21, Article 26

CASE STUDY: TB/HIV

TB IS THE TOP INFECTIOUS KILLER IN THE WORLD



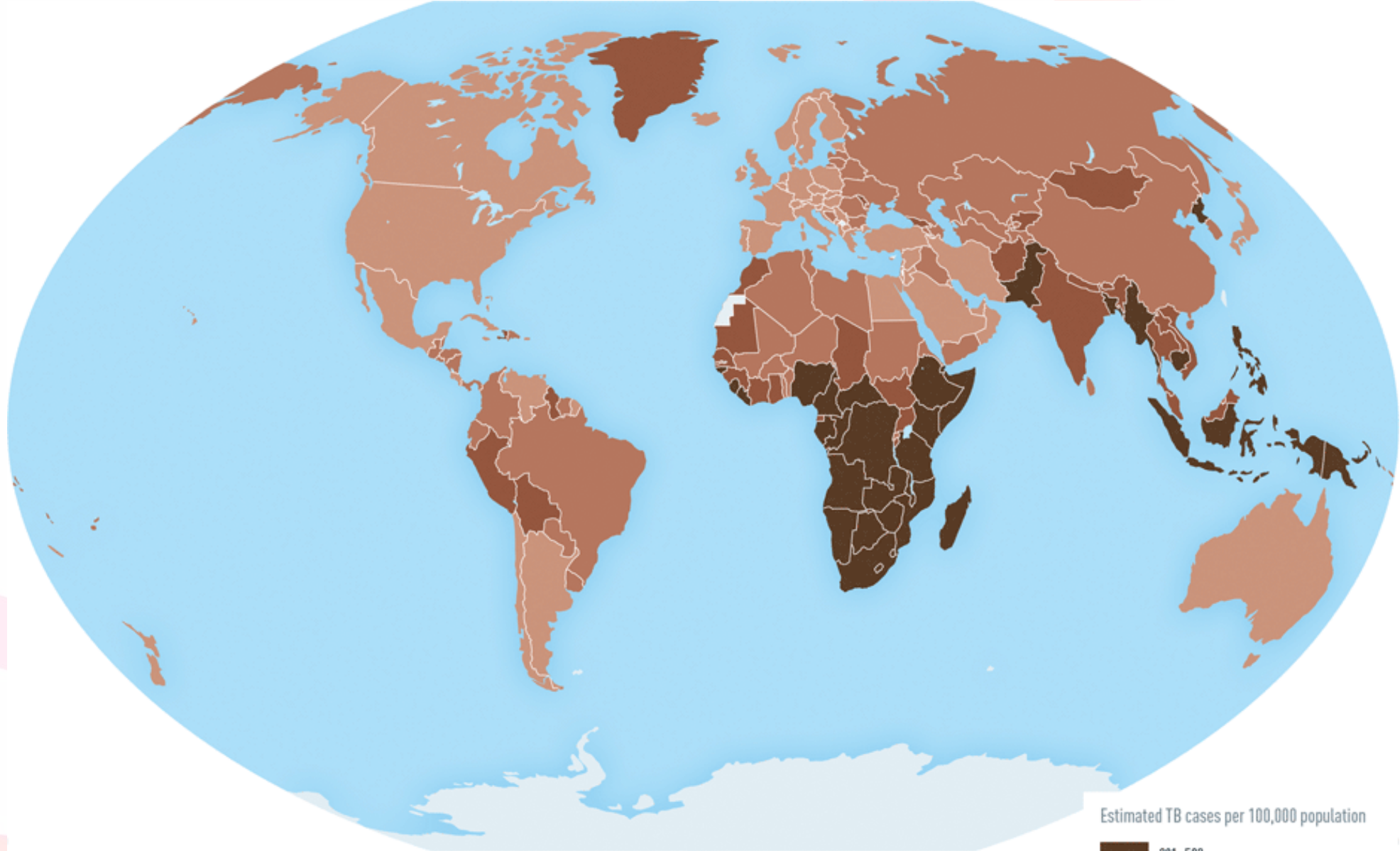
IN 2017



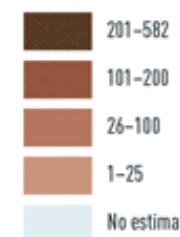
**1.6 MILLION
PEOPLE DIED
FROM TB**

INCLUDING
**300 000 PEOPLE
WITH HIV**

TB is the leading killer of people with HIV and a major cause
of deaths related to antimicrobial resistance



Estimated TB cases per 100,000 population



TB Incidence (CDC, using WHO Data)

Background

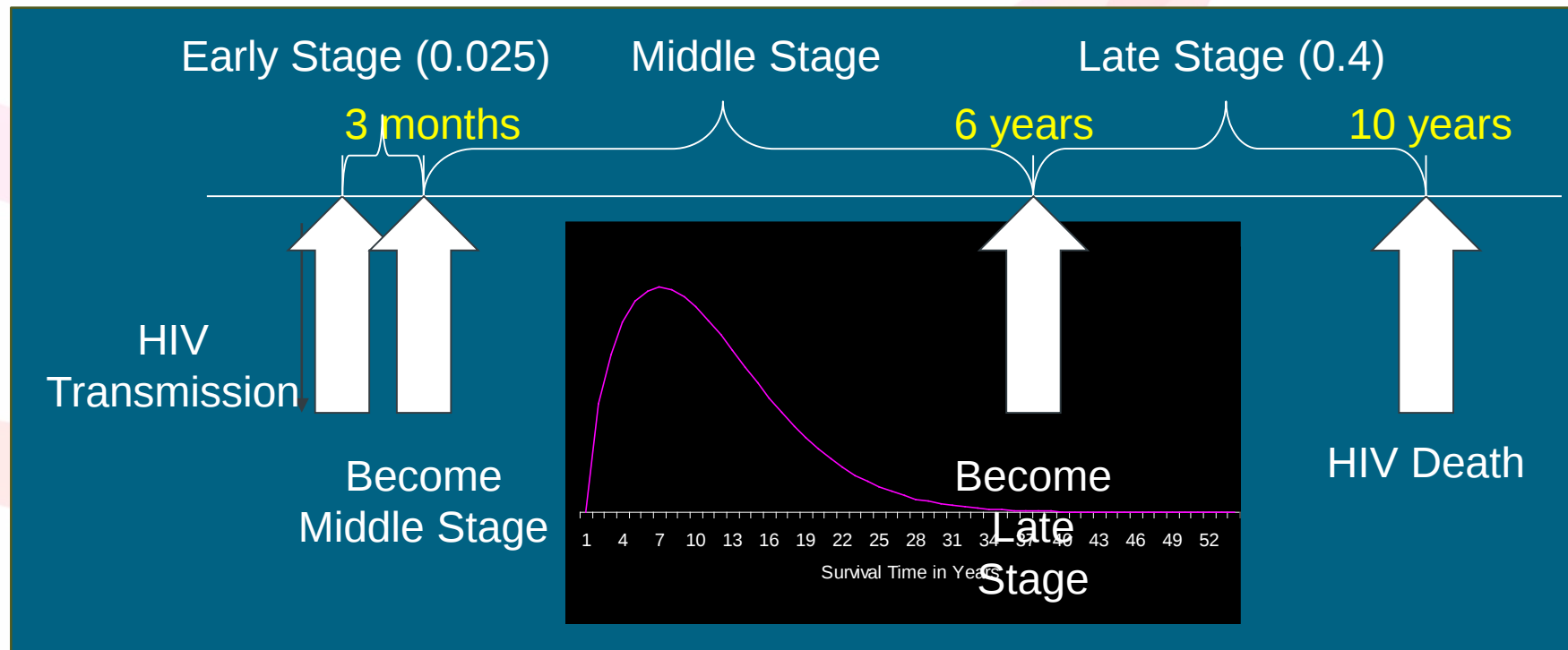
1. TB is the leading infectious disease killer worldwide today, and among the top ten causes of death
2. In 2017, 10 million people fell ill with TB, and 1.6 million died from the disease (including 0.3 million among people with HIV)
3. TB is a leading killer of HIV-positive people
 - People living with HIV are 20 to 30 times more likely to develop active TB disease than people without HIV
 - In 2017, there were an estimated 0.9 million new cases of TB amongst people who were HIV-positive, 72% of whom were living in Africa
4. Globally, TB incidence is falling at about 2% per year
5. Ending the TB epidemic by 2030 is a key health target of the UN Sustainable Development Goals and the WHO end TB Strategy

What is TB?

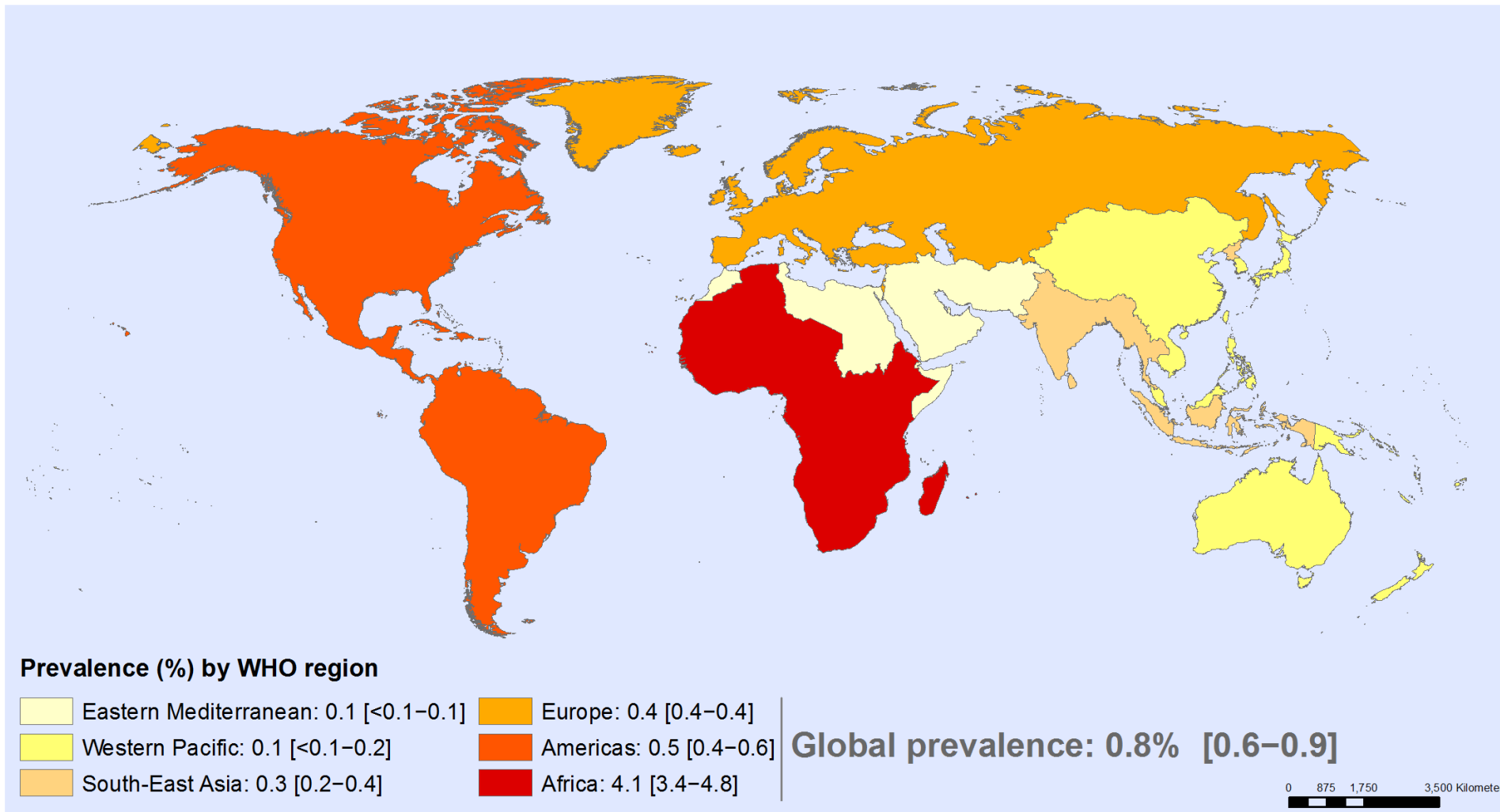
- Tuberculosis or TB is a bacterial infection that typically affects the lungs (~75%) but can also affect other parts of the body when it is typically non-infectious
- TB is transmitted when mycobacterium Tuberculosis (mTB) are exhaled by an infectious person (coughing, sneezing, spitting, singing!) and breathed in by a susceptible person
- Symptoms include persistent coughing, night sweats, weight loss, high temperature, fatigue
- Treatment is a 6-month course of antibiotics (chemotherapy)
- Preventive treatment (prophylaxis) is available

What is HIV?

- Human Immunodeficiency Virus (HIV) reduces the body's ability to fight infections
- Without treatment a person infected with HIV will progress to AIDS after around 10 years
- HIV transmission is principally through sexual intercourse, needle-sharing or mother-to-child transmission
- Treatment exists in the form of antiretroviral therapy



Prevalence of HIV among adults aged 15 to 49, 2017 By WHO region



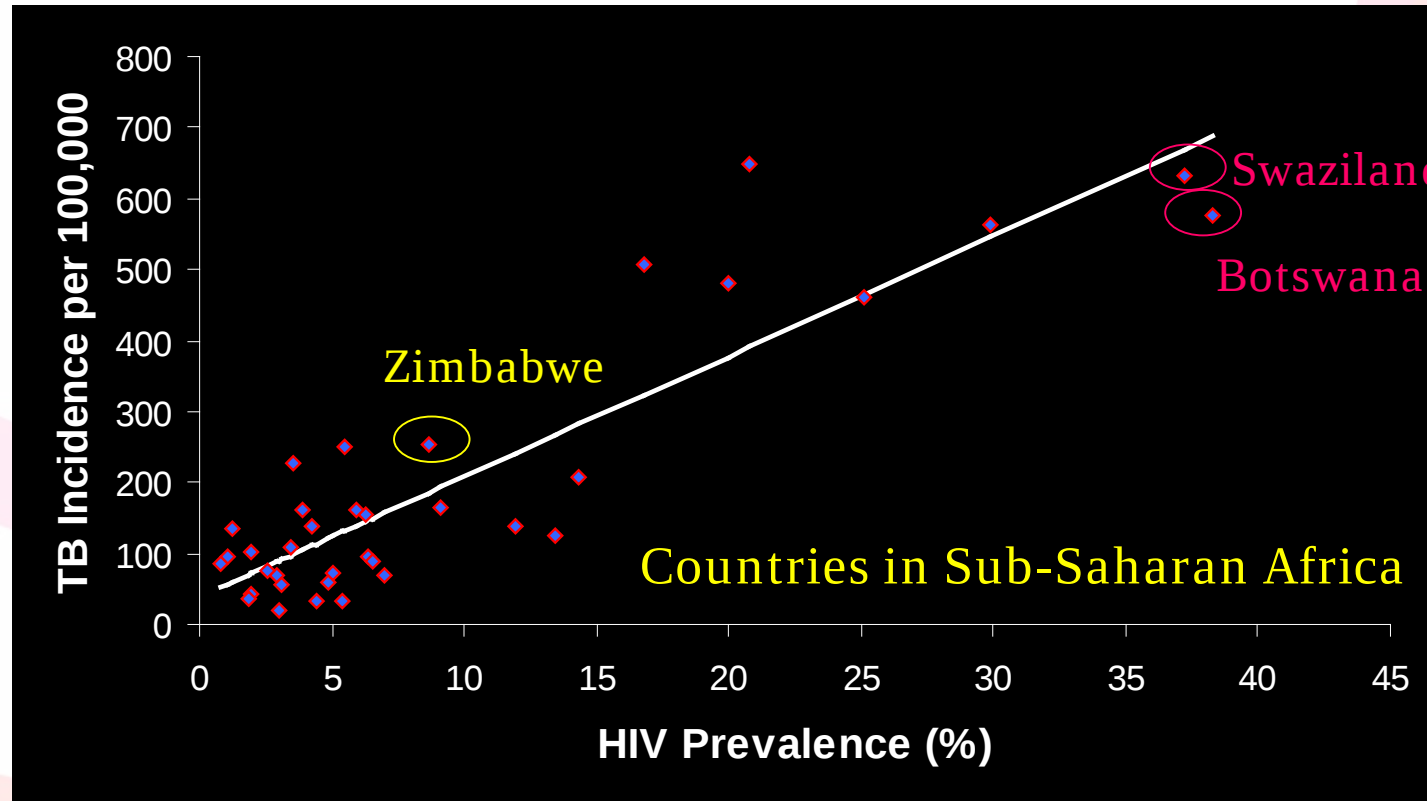
The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: World Health Organization
Map Production: Information Evidence and Research (IER)
World Health Organization



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Relationship between TB and HIV



- Clear relationship between HIV prevalence and TB incidence
- Countries in Sub-Saharan Africa are particularly hard hit

Deterministic Compartmental Models

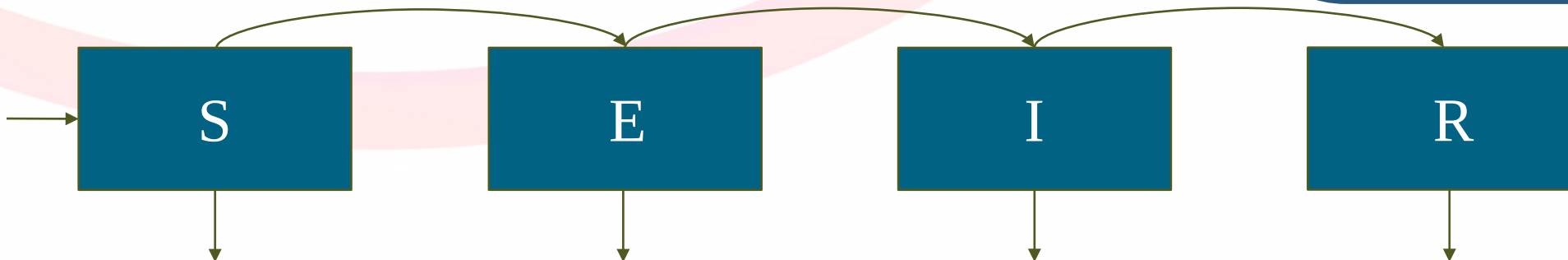
- A complex system of differential equations
- Flows are deterministic
- Good for determining population-level dynamics
- Not good when numbers are small and stochastic effects dominate

$$\frac{dS}{dt} = \beta(t) - \gamma S(t)I(t) - \mu S(t)$$

$$\frac{dE}{dt} = \gamma S(t)I(t) - \nu E(t) - \mu E(t)$$

$$\frac{dI}{dt} = \nu E(t) - \mu_{TB}I(t) - \alpha I(t)$$

$$\frac{dR}{dt} = \alpha I(t) - \mu R(t)$$

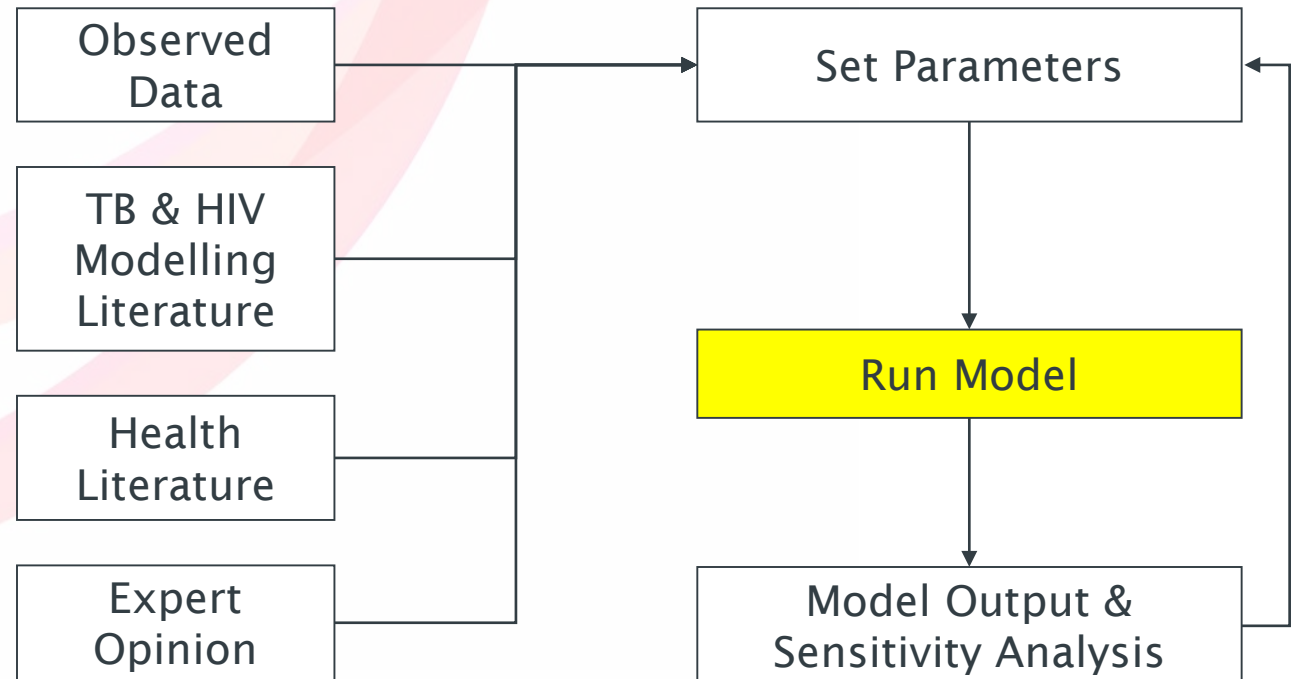


Why was more modelling needed?

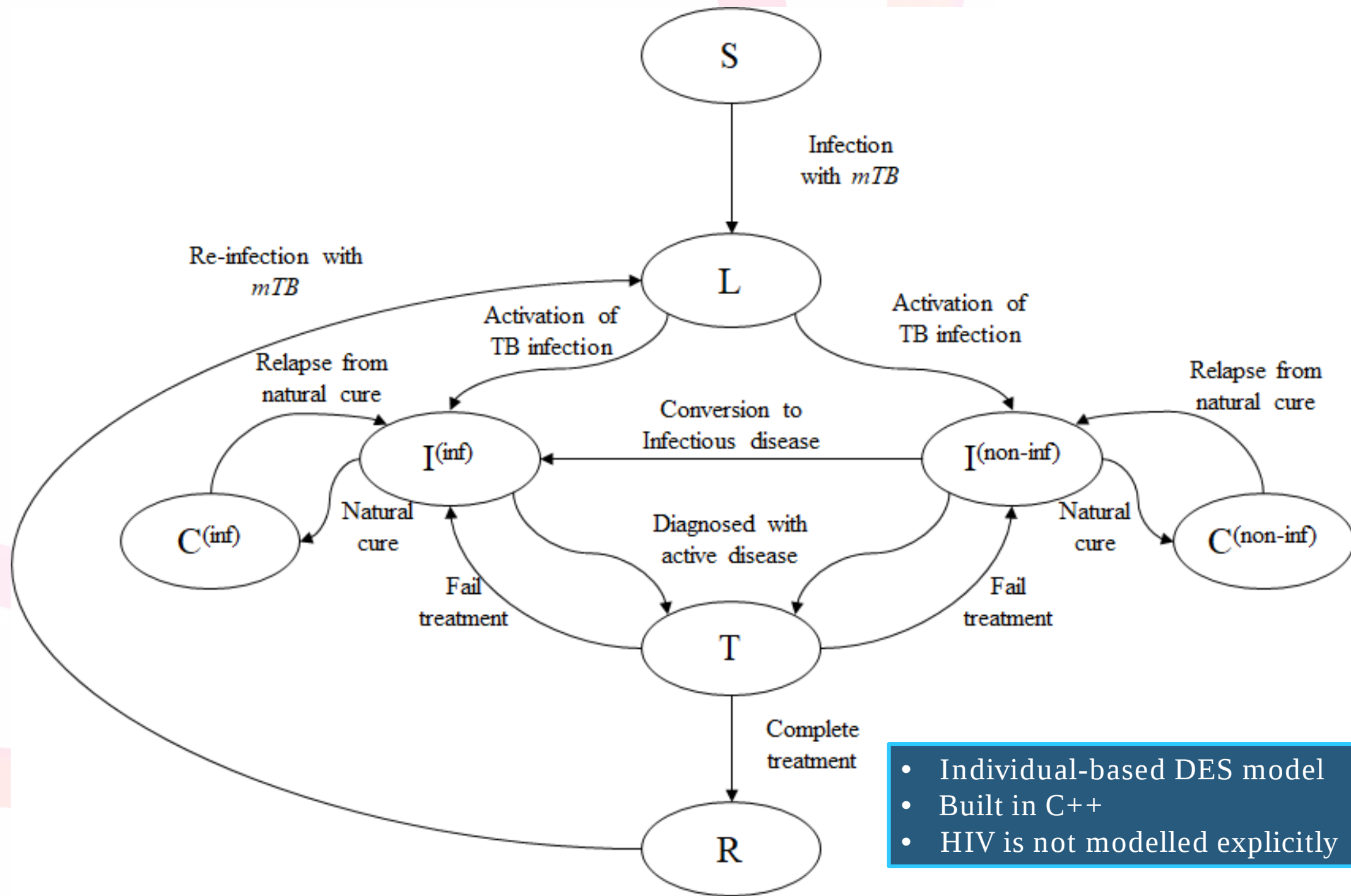
- Identify TB control strategies that are effective in high HIV prevalent settings
- Update the current policy which was developed in an era of low HIV prevalence
- Estimate the impact of the HIV epidemic on the relative importance of household versus community transmission
- DCMs are an unsuitable method for investigating interventions at the household level
- DCMs don't allow the mechanics of transmission to be explored

Developing a DES household transmission model

- AIM: to understand the role of household versus community transmission of both TB and HIV
 - This helps determine which aspects to model in more detail
- Data-driven model:
 - Harare: household size
 - Zimbabwe: HIV prevalence
 - Zimbabwe: TB incidence

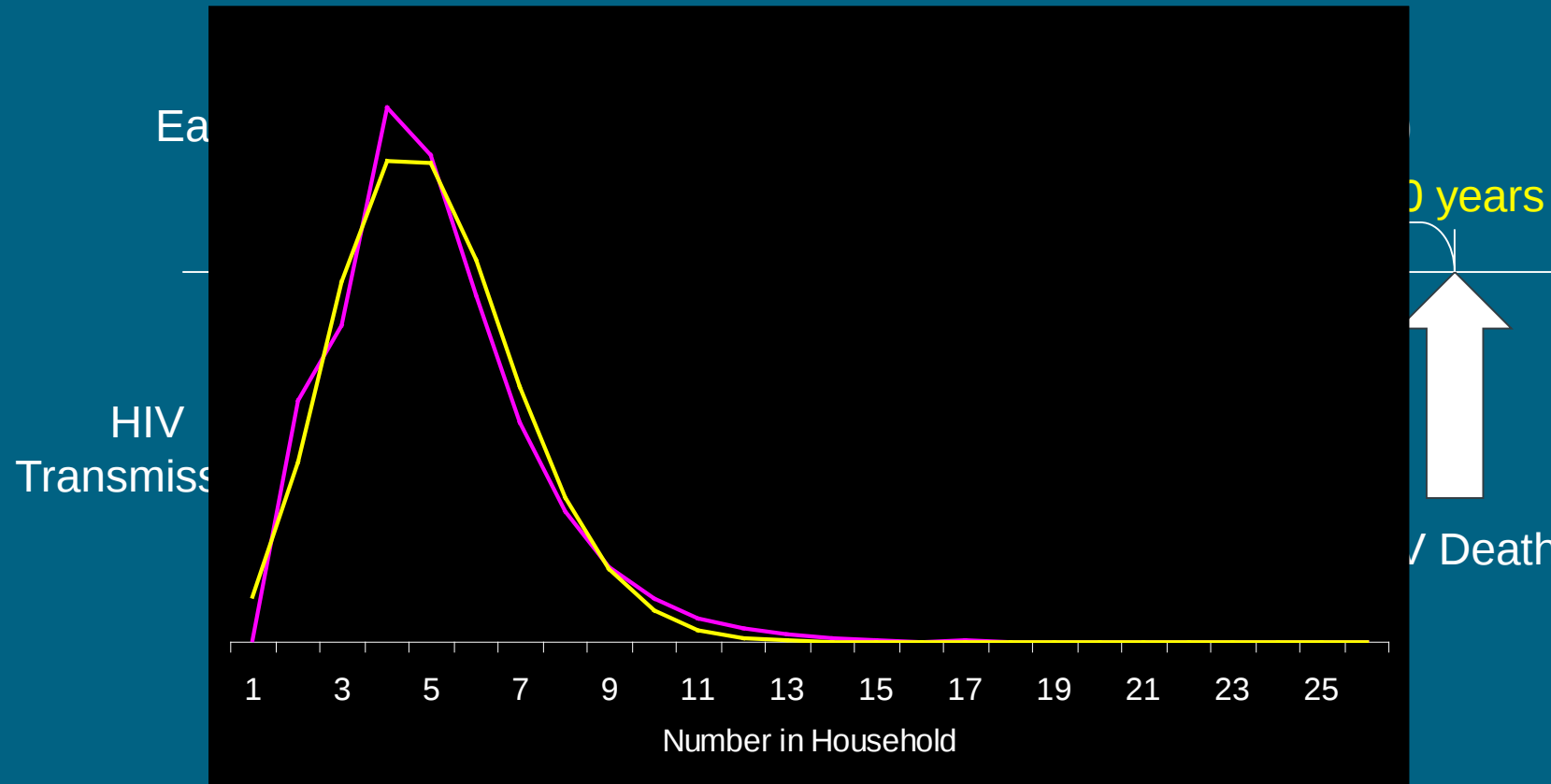


Model

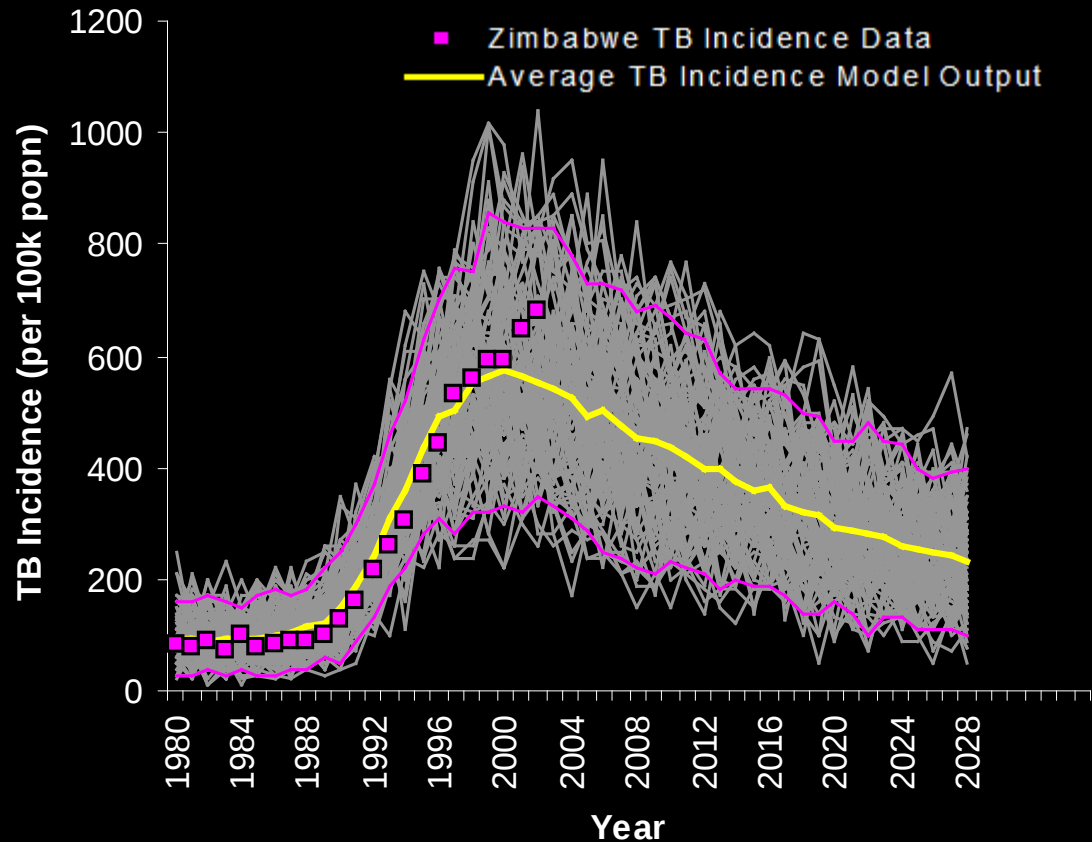


Key features

- Setting up the households
 - Poisson(4)
- Transmission
 - Random: Poisson(9)
 - Household: Poisson(1)
- HIV



Validation



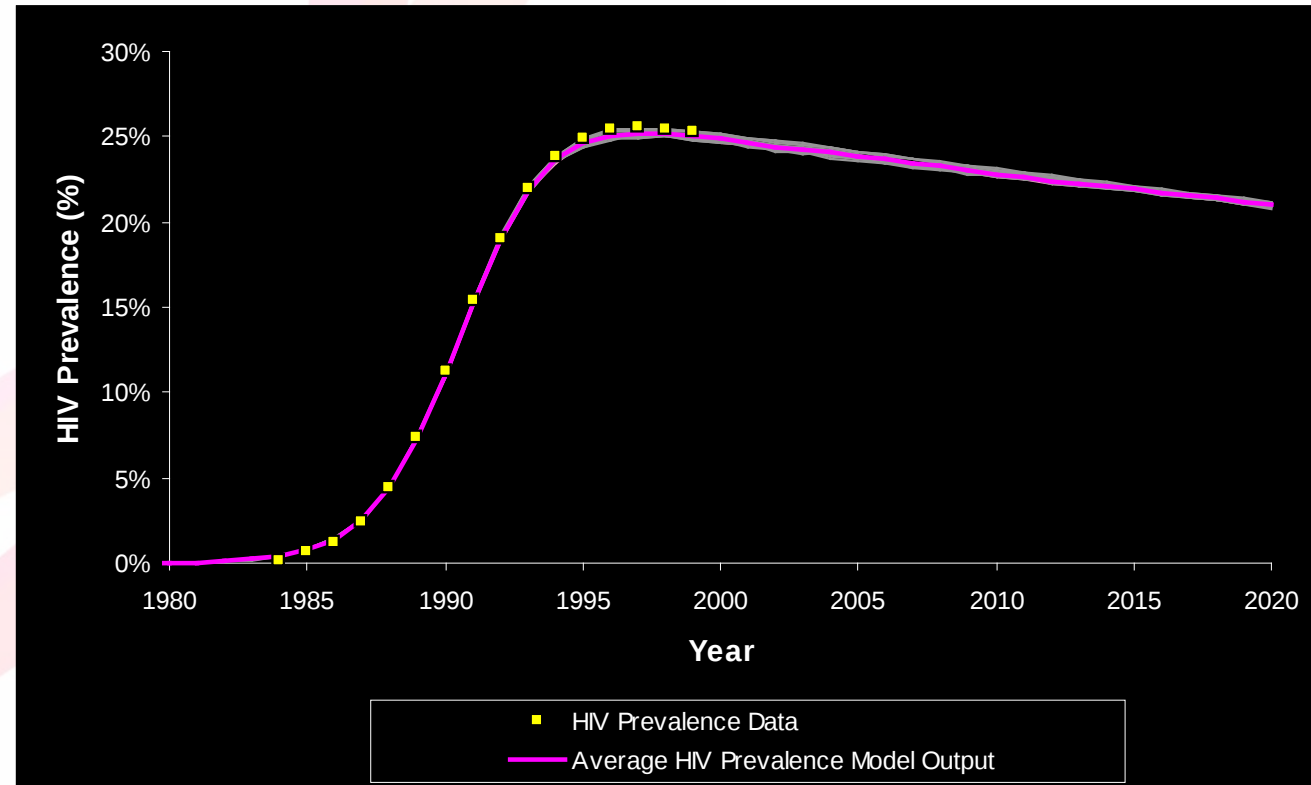
- Key model output: TB incidence
 - Output from 100 runs
- Mean TB incidence in yellow
- 95% confidence intervals in pink
- Model consistently underestimates TB incidence
 - Incorrect assumptions about case detection rates?
 - Underestimation of the impact of HIV on TB cases?

Validation

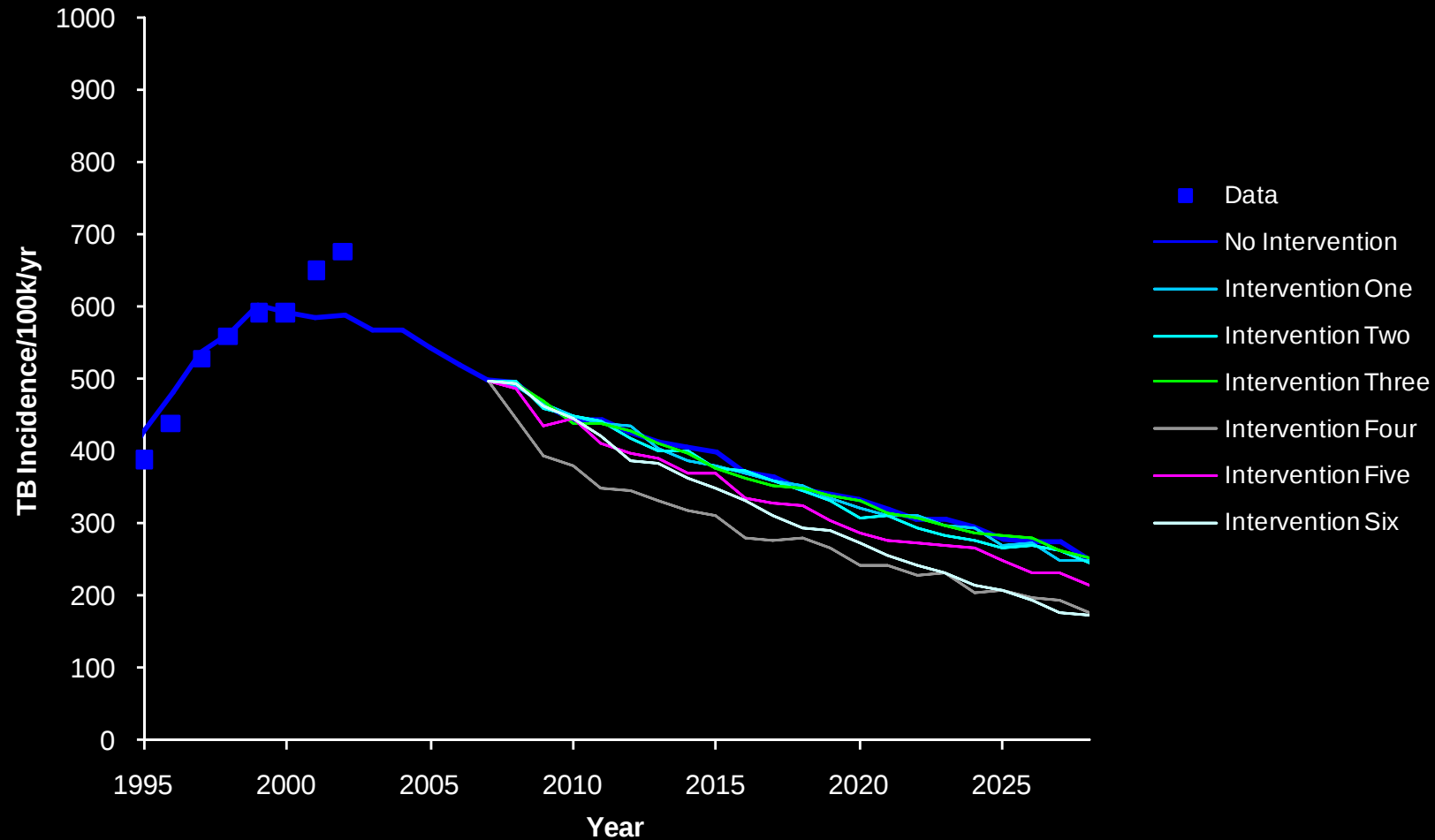
- HIV prevalence in Zimbabwe
- Very low variability in the output
- Good fit

Other outputs to validate:

- Household distribution
- Survival distribution
- Age distribution
- Age-specific HIV rates



Results



Interventions

1. Case-finding in TB households
2. Case-finding in random households
3. Case-finding in HIV households
4. **Case-finding in late-stage HIV households**
5. Same number of households as intervention 4
6. **Double diagnosis rate**

Case Study: Conclusions

- Case-finding among people with late-stage HIV is particularly effective but so too is treating TB
- Interactions between TB and HIV make this an interesting problem
- Focus: transmission mechanisms and potential interventions
 - Helps to guide the model structure
- What next?
 - Use optimal control to find the best mix of interventions for dengue fever
 - Apply methods to other (neglected) diseases
 - Tuberculosis: multi-drug resistance is still a major problem; operationalising recommendations

Modelling non-communicable diseases

Tom Monks.

Director. NIHR CLAHRC Wessex. Data Science Hub.

Turing Fellow. Alan Turing Institute

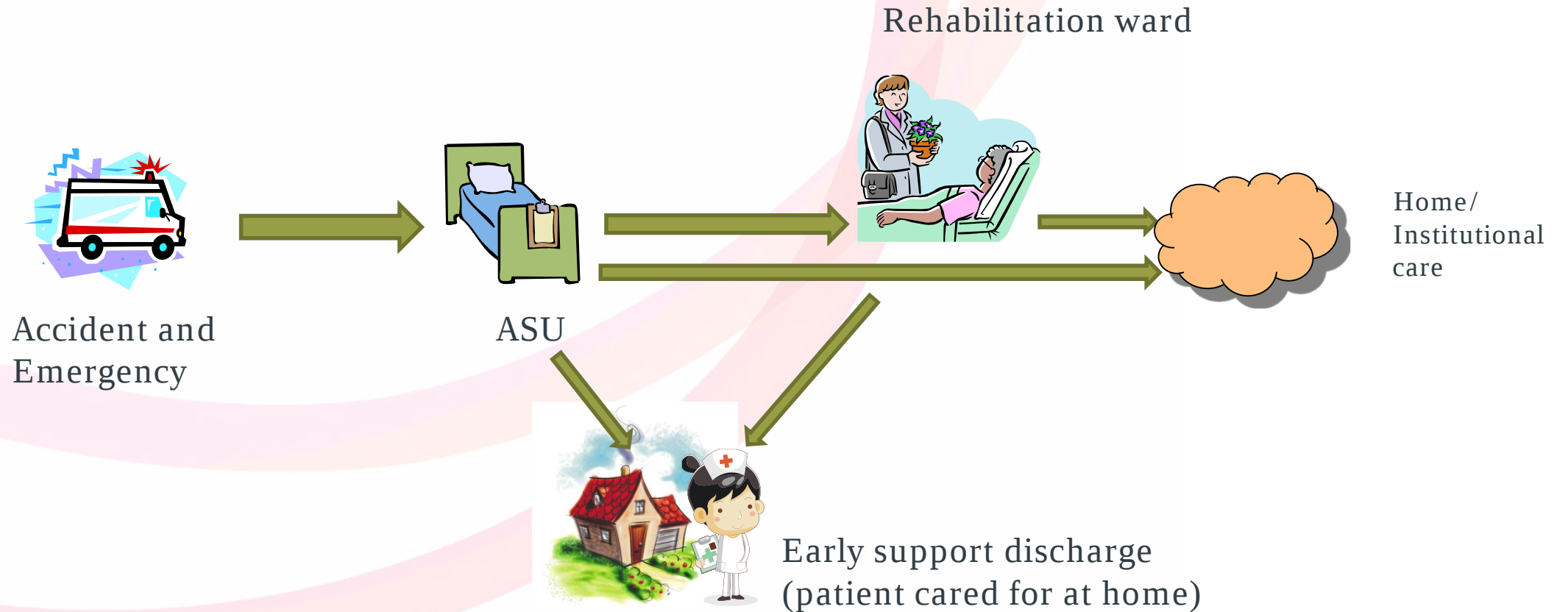
Overview

- A modelling problem for you to think about for 5 minutes
- How we handled the same problem

Problem: How many stroke beds do we need?

- In early 2014 I was asked to help a hospital plan out how many beds their stroke wards needed.
- The hospital was struggling to admit acute stroke patients to the 'acute stroke unit' (ASU) quickly.
- The acute stroke unit is the best place for patients who have recently suffered a stroke.
- I was given a couple of weeks to develop a model and help them plan.

Background to stroke pathways



5 minutes thinking about...

1. How would you begin to solve this problem?
2. What questions would you ask the hospital staff?
3. What are the things you need to model?
4. What data might you need to build a model?
5. What difficulties and issues might you encounter in a project like this?

Pair up and have a think. You will need to be brave and shout out some suggestions in 5 minutes time.

Some suggestions on initial steps

1. Clarify modelling objectives and what the hospital wants to achieve
 - Asking for current performance statistics helps identify objectives for a model
 - E.g. Increase the proportion of patients admitted to the ASU within 4 hours
2. Clarify what patient populations use the wards. E.g. is it just stroke?
3. Get an initial idea of the patient pathway (process) in an early conversation
4. Spend some time on the wards to find out how patient flow and bed logistics are actually managed
5. Meet with the data controller for the disease area

Common types of input data (1)

- **Demand data**
 - E.g. the date and time that a stroke patient was referred to the acute stroke unit (and if possible the time they arrived at the hospital)
- **Process time data**
 - E.g. a sample of data describing acute treatment time, rehabilitation time and length of supported discharge
 - Watch out for the impact of 'bed blocking' that skew length of stay
- **Patient routing data**
 - E.g. the proportion of patients that move from the acute stroke unit to rehabilitation, early supported discharge and discharge with no support.

Common types of input data (2)

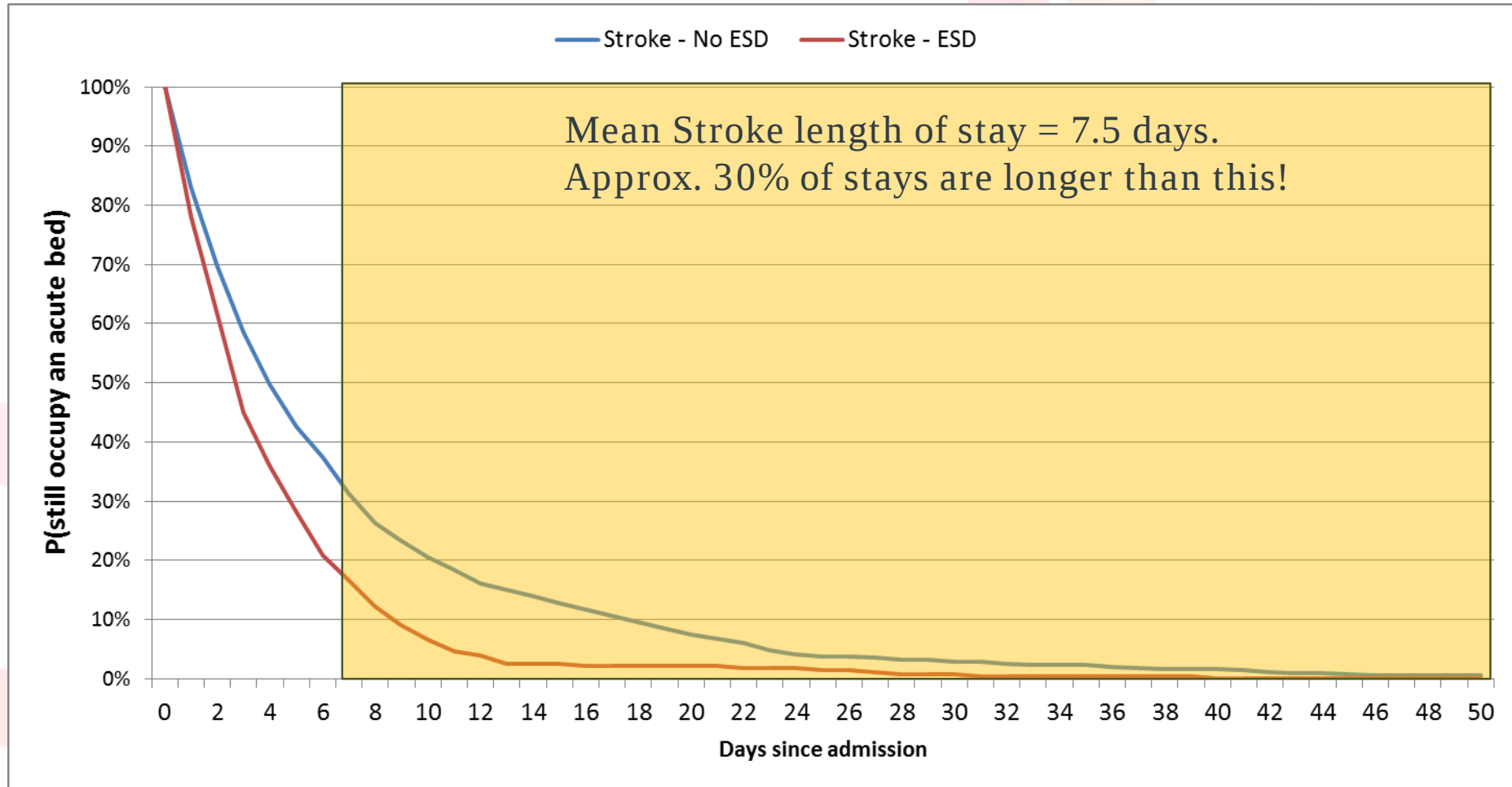
- **Resource data**

- E.g. workforce configuration – nurses, physiotherapists, medics.
- Specialization and pooling – e.g. beds specialized by disease area; age; gender

- **Disease Progression data**

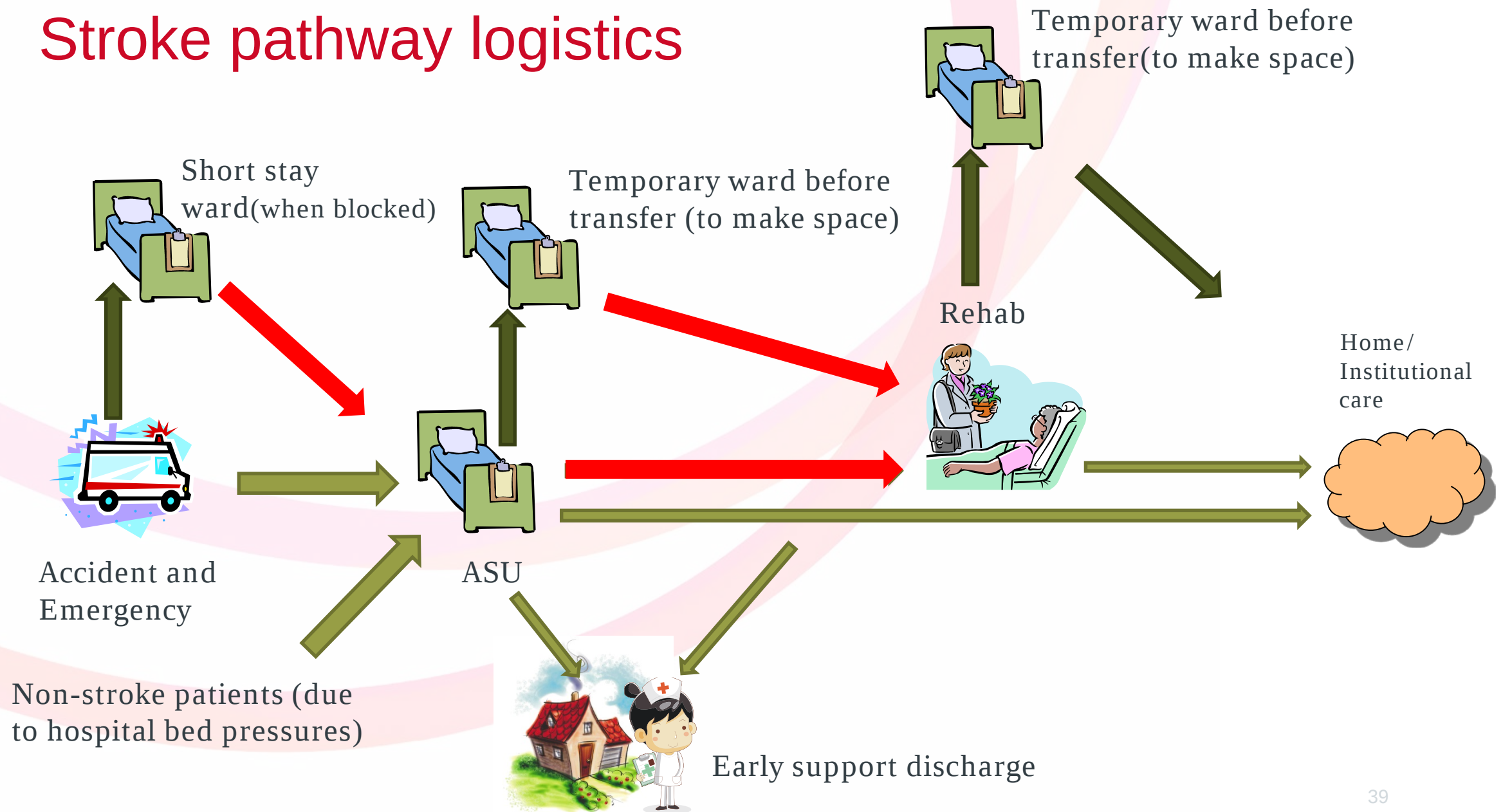
- In some areas patients may be undergoing treatment / monitoring while their disease is progressing
- E.g. A complication of diabetes where people lose their sight (retinopathy).
- Dependent sampling - may need to adjust mortality rates during disease progression and patient aging.

Process time data (ASU)



It is this spread of length of stay that makes capacity planning difficult

Stroke pathway logistics



Questions

1. Do we need to model all of that complexity?
2. Can you think of any ways to simplify the modelling?

Pair up and discuss for 2 minutes.

A simple way to model it?

(1)

- Utley and Worthington (2010) advocate models of 'unfettered demand' (unconstrained)
- These models have infinite bed capacity (sounds odd but can be very useful for planning).
- Patients 'linger' in parts of the model for different time periods and then move to the next ward/treatment when they are ready
- There is no queueing! So we do not model all of the logistics when the system is pressured.
- It can be used to predict the probability that a ward is overloaded for a fixed number of beds.

A quick look at the simulation model

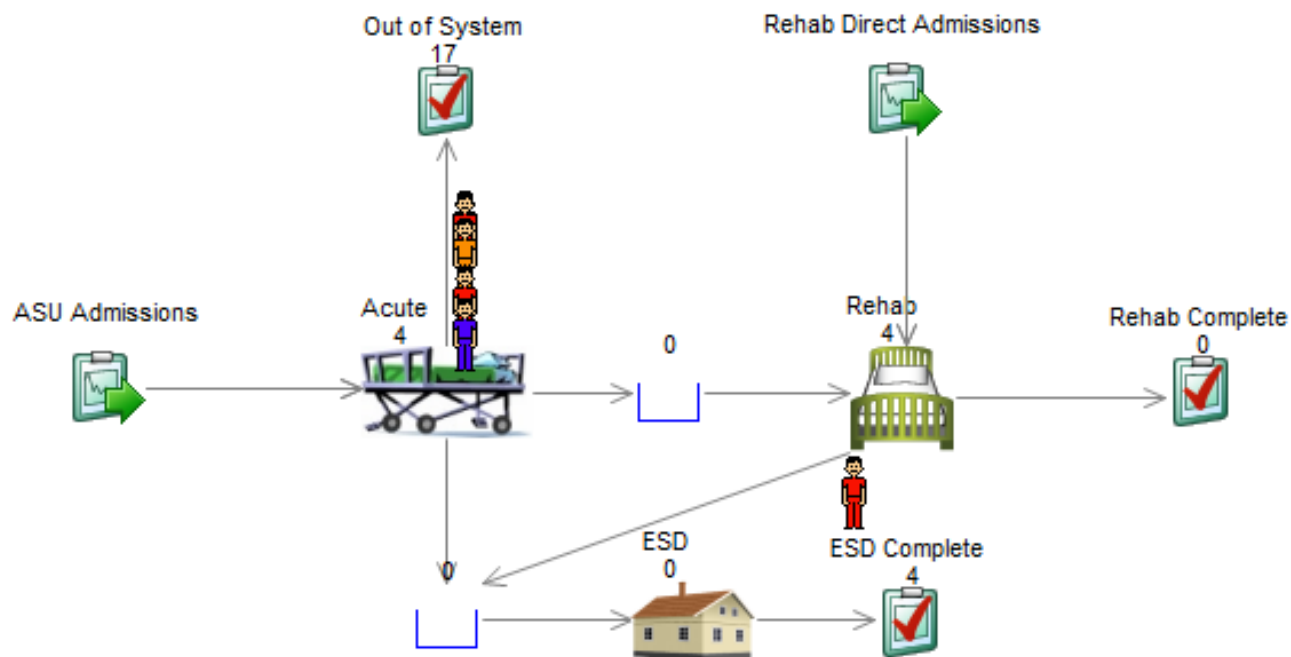
Pen CLAHRC

The NIHR CLAHRC for the South West Peninsula

Stroke Pathway Capacity Planning Model v1.0

1:16

Thu Week 4



Acute Bed Usage



Rehab Bed Usage



ESD Usage

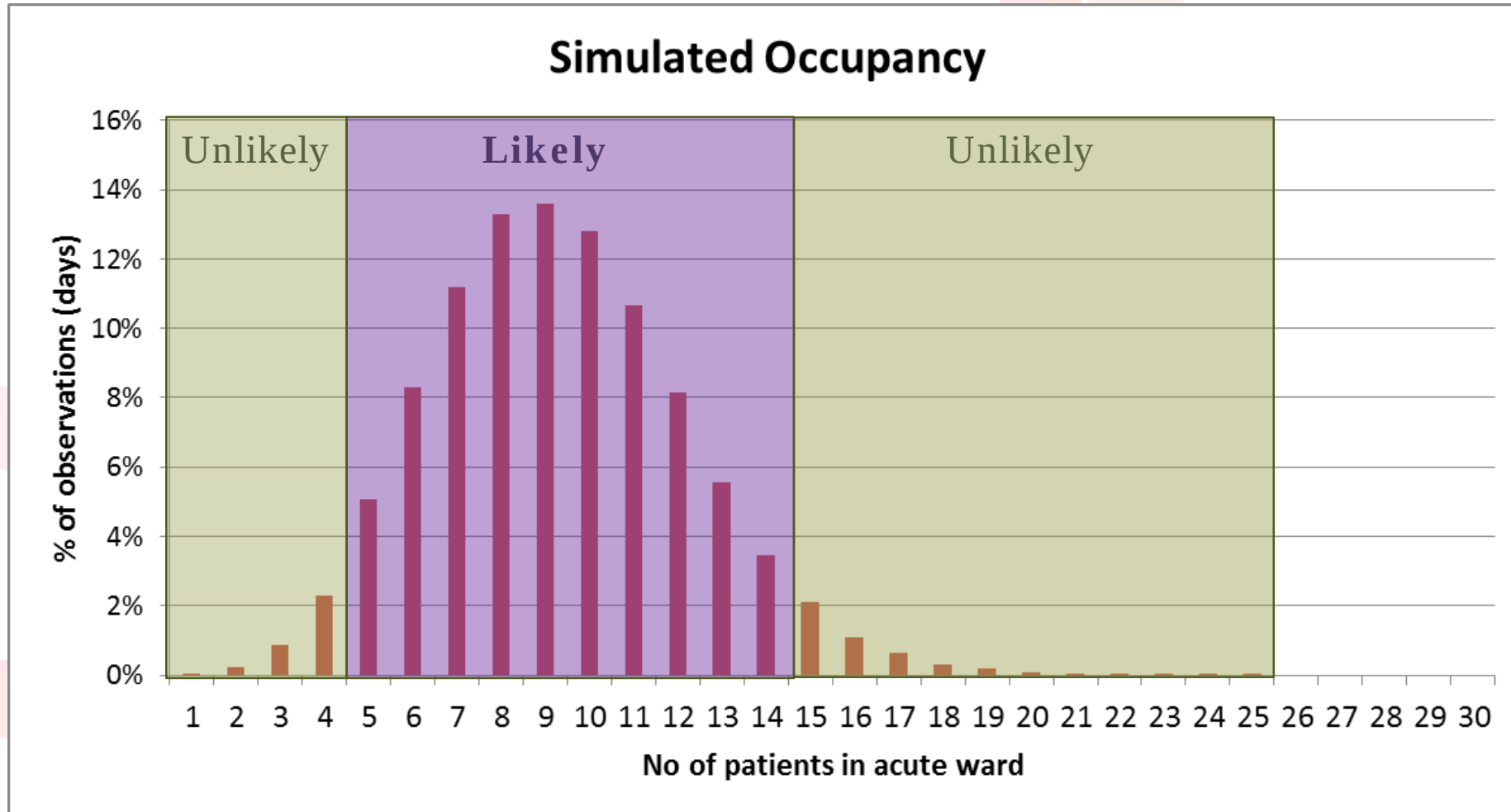
Routing

Distributions

Arrivals

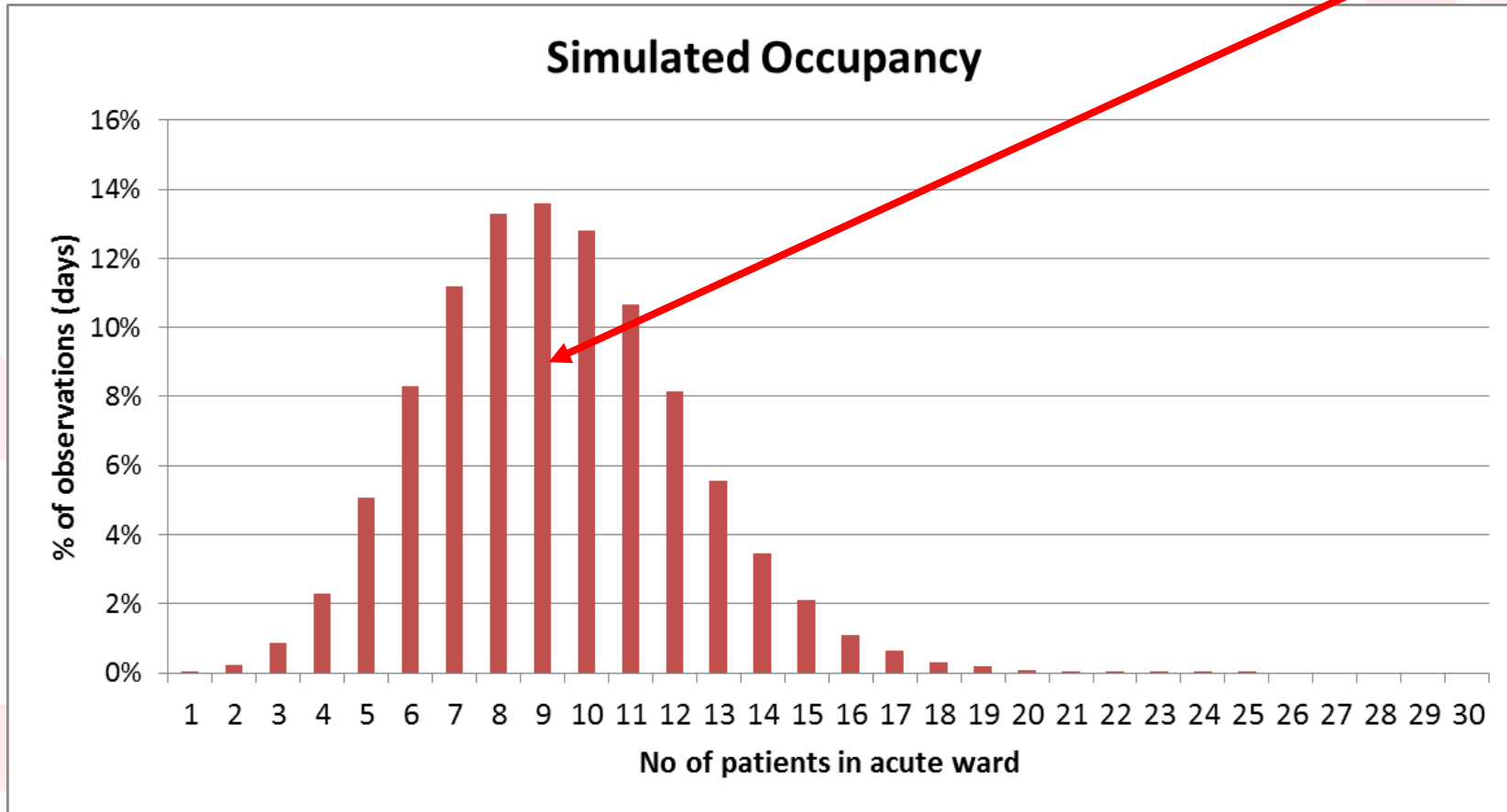
Results

Unconstrained results for ASU



Observations?

Average occupancy of the ward is 9 patients.

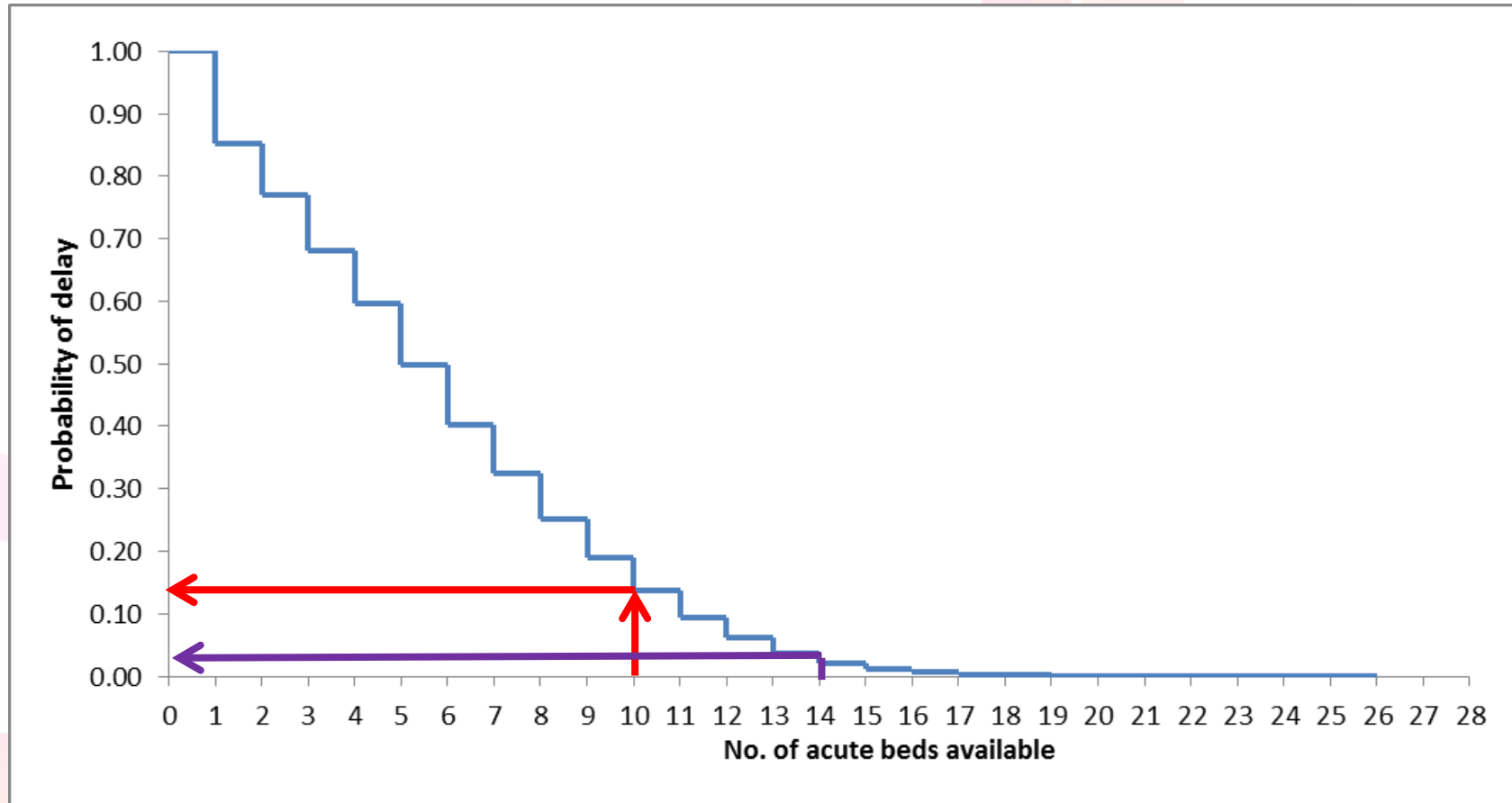


If you had planned capacity by average you would have been unable to cope with demand

Predicting when the ward will be 'overloaded'

- The model estimates the probability that a new patient cannot be immediately admitted to the acute ward or transferred to rehab
- We call this the probability of delay: $p(\text{delay})$
- $P(\text{delay})$ is estimated across a large range of bed numbers to illustrate the trade-off

P(delay)



The original system had 10 beds!

Summary

- Modelling non-communicable diseases is often dominated by the logistics and service delivery of care.
- It is often complicated due to a number of interacting factors
 - Variability in patient arrival rates and length of stay in particular;
 - Understanding current operations, the disease and health professionals knowledge of modelling
 - Time available to conduct the modelling can be short (days, weeks or a few months).
- A critical first step is to try to understand what good performance should look like;
- Observation of the real system often illustrates how the organisation copes under pressure;
- However, we do not necessarily need to model all of that complexity to help with redesign decisions.

Thanks for listening



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Monks, T., Worthington, D., Allen, M., Pitt, M., Stein, K., & James, M. A. (2016). [A modelling tool for capacity planning in acute and community stroke services](#). *BMC Health Services Research*, 16, 1-19.

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