DH301: Basic Epidemiology

Mathematical Epidemiology

(Lecture 4)

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Concepts we'll cover

- **Boxes and arrows**
  - Building a simple compartmental model
  - Relation between a model diagram and its equations
- **Competing hazards**
  - Modelling different possible outcomes
- **Force of infection**
  - What makes an infectious disease model
  - The basic reproduction number (R_0)
- **Interventions**
  - Vaccination and treatment
- **More complex models**

Recap

When is an infection capable of causing a major epidemic?

- Basic reproduction number, R_0
- **Definition**: average number of secondary cases caused by a single infected case, in an otherwise susceptible population
- An epidemic is possible when $R_0 > 1$
- Otherwise, introductions of the infection go extinct without causing an epidemic

Recap

$$\frac{dS}{dt} = -\beta \frac{I}{N} S \qquad \boldsymbol{\frac{dI}{dt} = \beta \frac{I}{N} S - \gamma I} \qquad \frac{dR}{dt} = \gamma I$$

β = infection rate
γ = removal rate

Infection progresses in population when

$$\beta \frac{I}{N} S > \gamma I \Rightarrow \beta \frac{S}{N} > \gamma \Rightarrow \frac{\beta}{\gamma} \frac{S}{N} > 1$$

In completely susceptible population S = N

$$\Rightarrow \frac{\beta}{\gamma} > 1$$

$$\boldsymbol{R_0 = \frac{\beta}{\gamma}}$$

Basic Reproduction Number (R_0)

Number of secondary infections that is produced by a single infected host during its entire infectious period, in a completely susceptible population

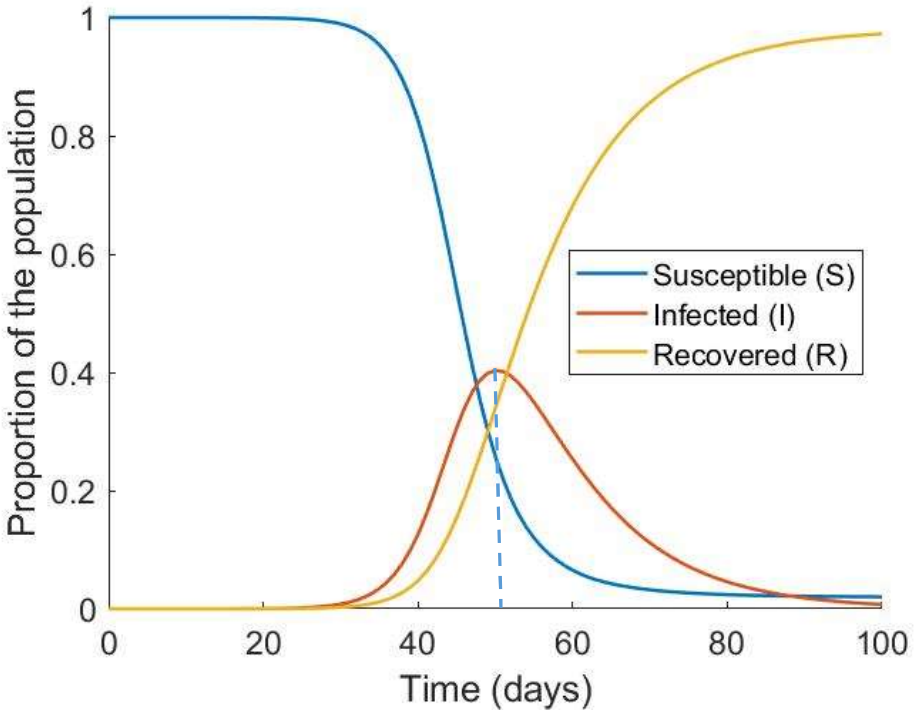
$R_0 > 1$ Epidemic **$R_0 = 1$ Endemic** **$R_0 < 1$ Eradication**

Effective reproduction number

$$\boldsymbol{R_{eff} = R_0 \frac{S}{N}}$$

Question: How does R_{eff} vary over the course of the epidemic? What do you notice about the connection between the change in R_{eff} and the epidemic curve over time? In relation to R_{eff}, when does the epidemic peak and start to decline?

Effective reproduction number

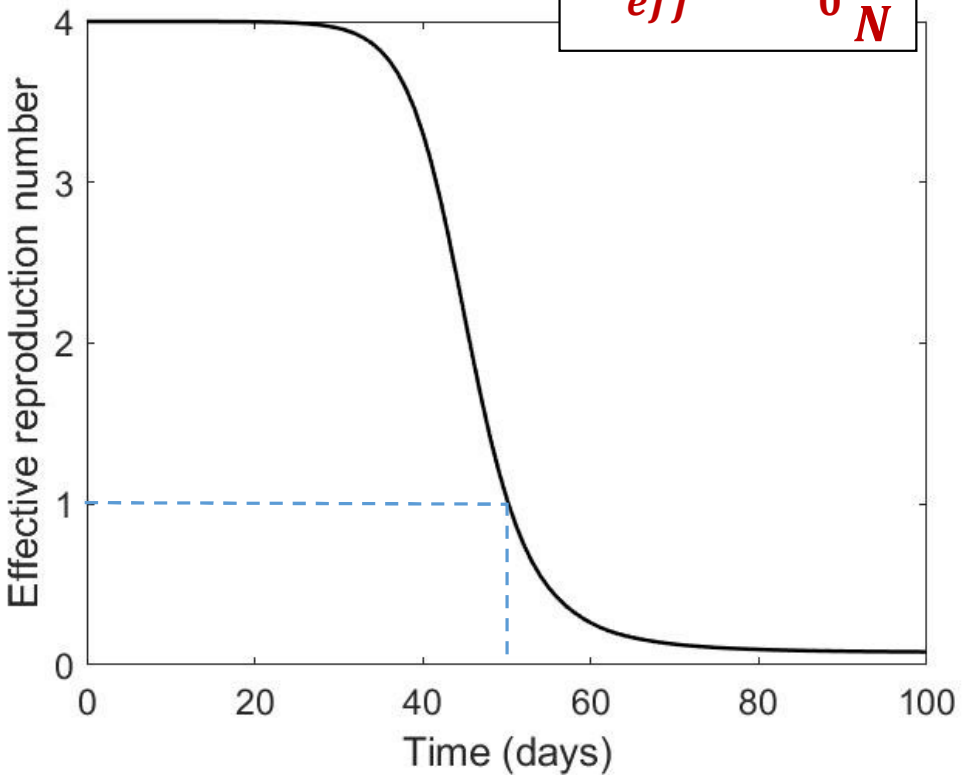


Beta = 0.4; gamma = 0.1

R_0 = Beta /gamma = 4

Effective reproduction number

$$R_{eff} = R_0 \frac{S}{N}$$



Vaccination

What proportion of the population would have to be vaccinated with to prevent an epidemic?

R_0 : Number of secondary infection if all are susceptible

If p proportion of people are vaccinated then
Effective Basic Reproduction number: $R_0 - p\,R_0$

To prevent epidemic: $R_0 - p\,R_0 < 1$ $\qquad$ $R_0\,(1-p\,) < 1$

$(1-p\,) < \frac{1}{R_0}$ $\qquad$ $p > \left(1 - \frac{1}{R_0}\right)$

Here, p is referred as Herd Immunity Threshold (HIT)

Vaccination (perfectly effective)

Question: Assuming *beta* equals 0.25 days-1 and *gamma* equals 0.1 days-1, what proportion of the population would have to be vaccinated with a perfectly effective vaccine to prevent an epidemic?

Using the formula of Herd Immunity Threshold (HIT)

$$HIT = \left(1 - \frac{1}{R_0}\right) \qquad R_0 = \frac{\beta}{\gamma}$$

$$R_0 = \frac{0.25}{0.1} = 2.5$$

$$HIT = \left(1 - \frac{1}{2.5}\right) = 0.6$$

We need a vaccine coverage of 60% to prevent the epidemic

Modelling a leaky vaccine

Question: Given the parameter assumptions above, what proportion of the population would have to be vaccinated with an *all-or-nothing* vaccine with 70% efficacy to prevent an epidemic?

This means that vaccinated people can still become infected, but at a reduced rate (i.e. with reduced force of infection)

Modelling a leaky vaccine

In the previous example, we need a vaccinate 60% to prevent the epidemic when the efficacy of the vaccine is 100%

$$\boldsymbol{HIT = \left(1 - \frac{1}{2.5}\right) = 0.6}$$

When the efficacy is less than 100%, we need to cover more people to prevent the epidemic. In this case the efficacy of the vaccine is 70%. Therefore,

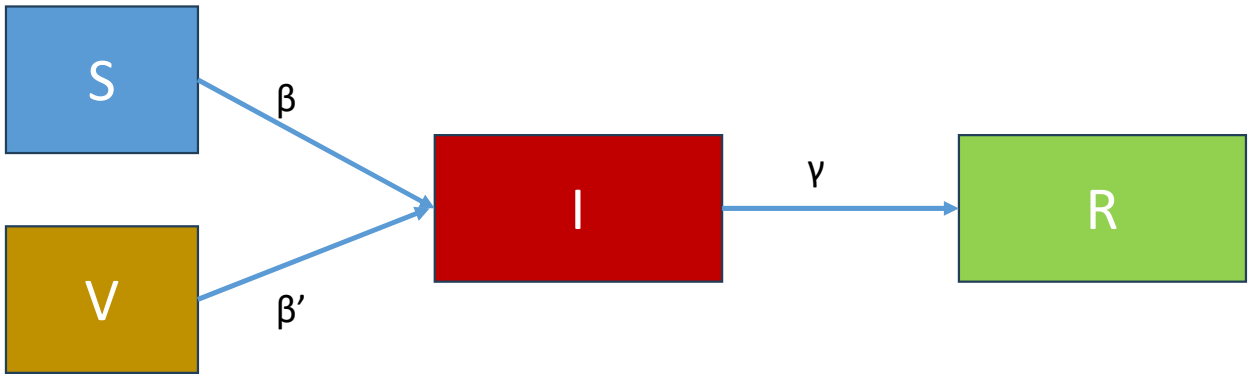
$$\boldsymbol{HIT = \frac{0.6}{0.7} = 0.857}$$

Simplest diagram of a vaccination model

β = infection rate

γ = removal rate

$S + I + R = N$



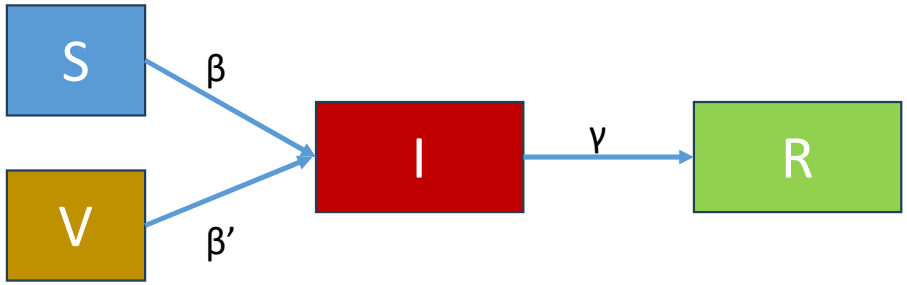
$S + V + I + R = N$

$\beta' = \beta * c_s$ (Infection reducing vaccine)

Question: What is the value of c_s for a leaky vaccine with 70% efficacy?

$C_s = (1 - 0.7) = 0.3$

Based on the diagram, write down the differential equations for this model.



$$\frac{dS}{dt} = -\beta \frac{I}{N} S$$

$$\frac{dV}{dt} = -\beta' \frac{I}{N} V$$

$$\frac{dI}{dt} = \beta \frac{I}{N} S + \beta' \frac{I}{N} V - \gamma I$$

$$\frac{dR}{dt} = \gamma I$$

$\beta' = \beta * Cs = \beta * (1 - \varepsilon)$

ε = Vaccine efficacy

Modelling treatment

A viral epidemic has been reported in a town of 300000 people. A sero-prevalence survey has shown that currently 30% of the population are infected and 10% of the population have become immune and developed antibodies against the virus. The infection rate was estimated at 0.3 day-1 and people stay infected for 10 days on average before recovering. Once recovered, people are immune to reinfection.

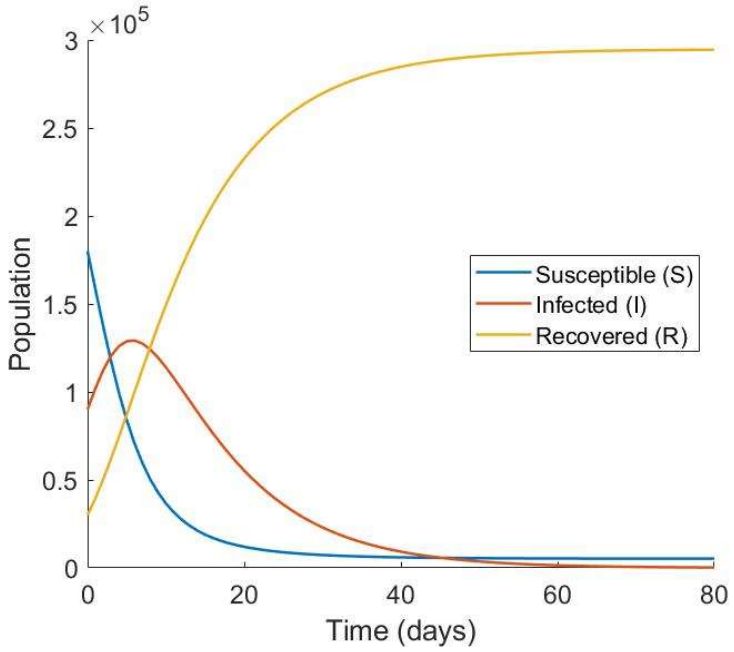
Model the course of this epidemic using your SIR model and plot the number of infected people over time.

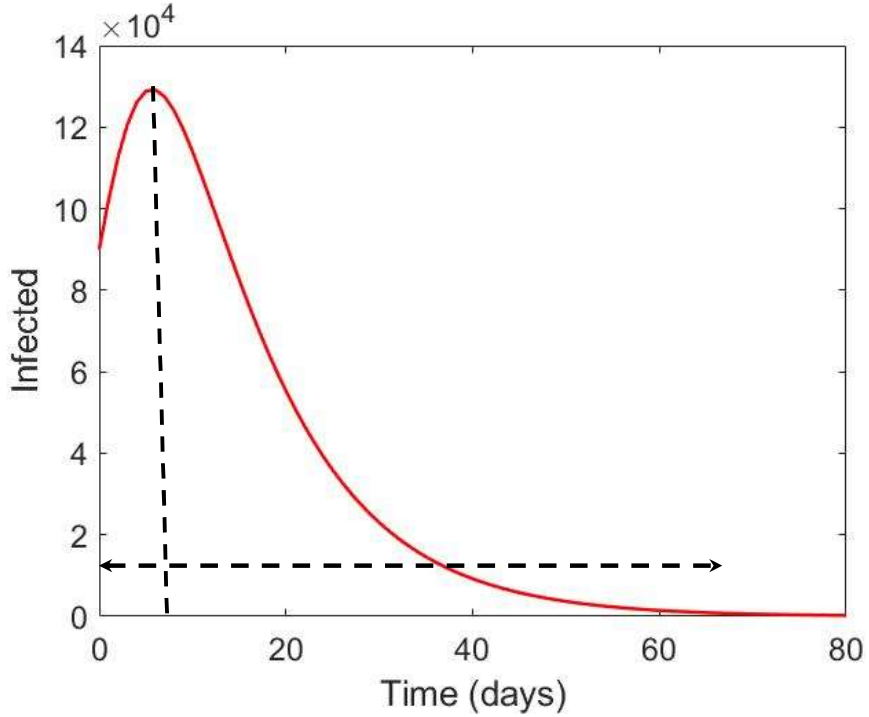
- **Question: Has the epidemic already reached its peak? When does the model predict it will end?**

Initial conditions: N = 300000, Infected = N*0.3, Immune = N*0.1, Susceptible = N*(1-0.4)

β = infection rate = 0.4 day-1

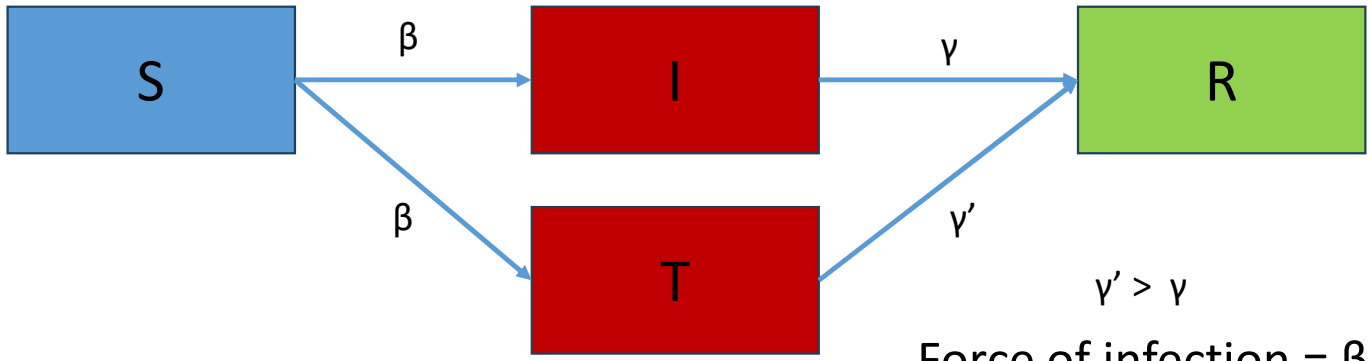
γ = removal rate = 0.1 day-1





Modelling treatment

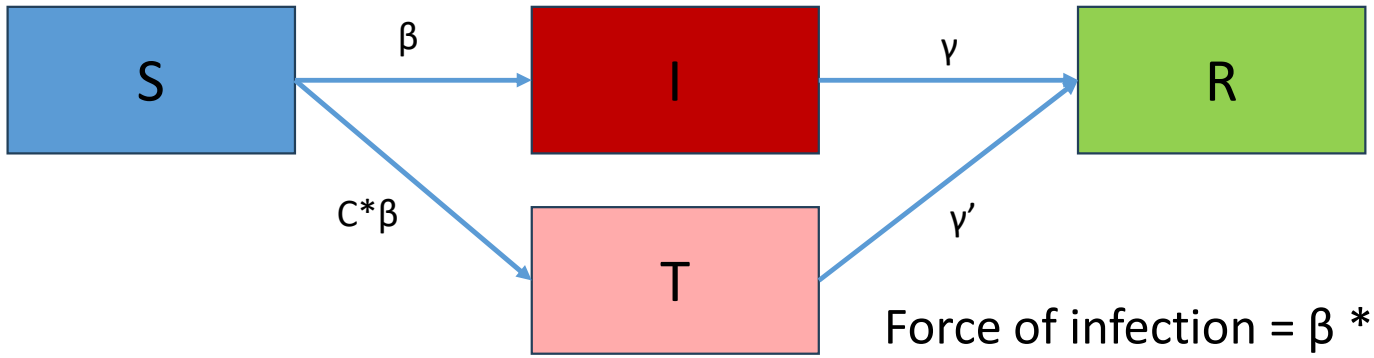
When people are equally infectious during treatment



$\gamma' > \gamma$

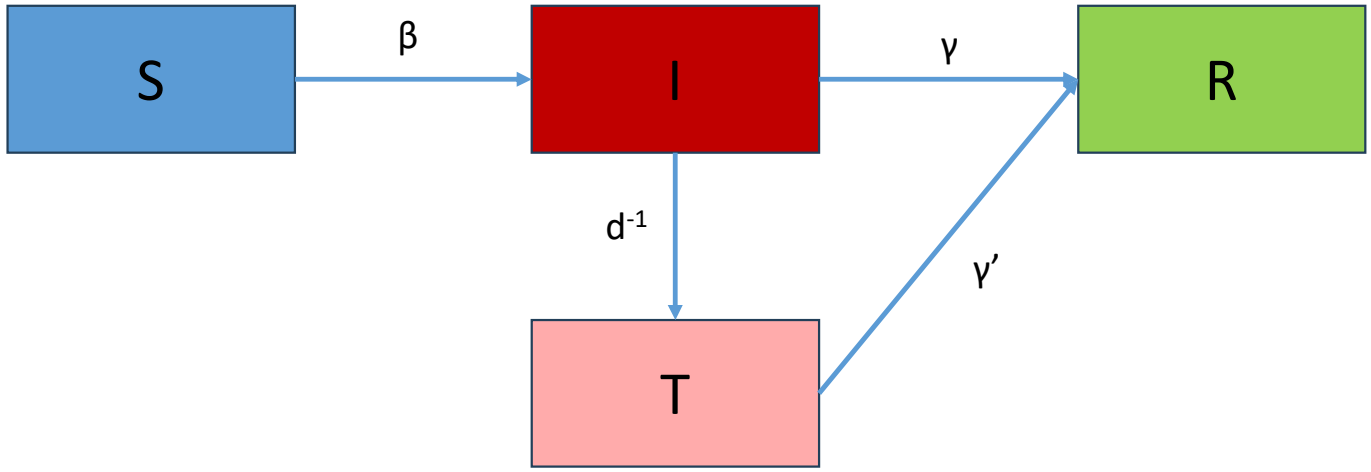
Force of infection = $\beta * (\frac{I}{N} + \frac{T}{N})$

When people during treatment are less infectious



Force of infection = $\beta * (\frac{I}{N} + c * \frac{T}{N})$

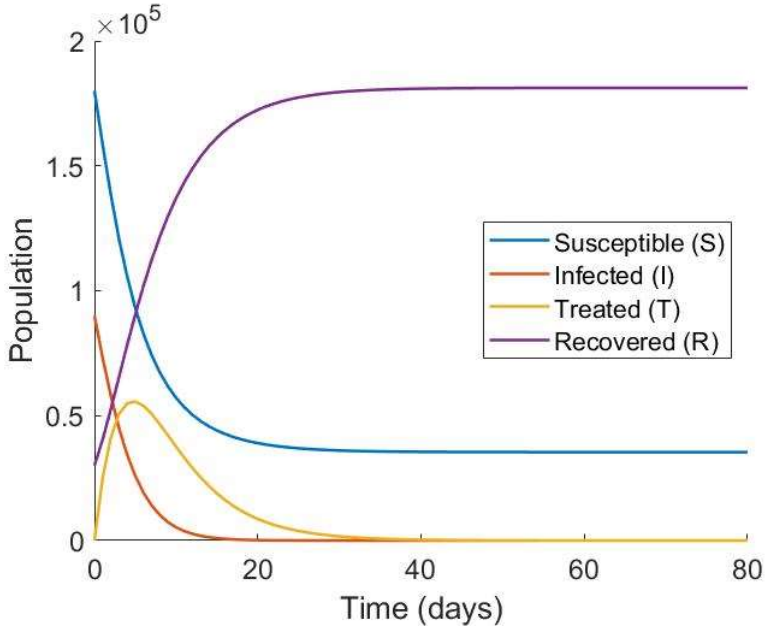
Model when it takes an average '*d*' days to start treatment after getting infection

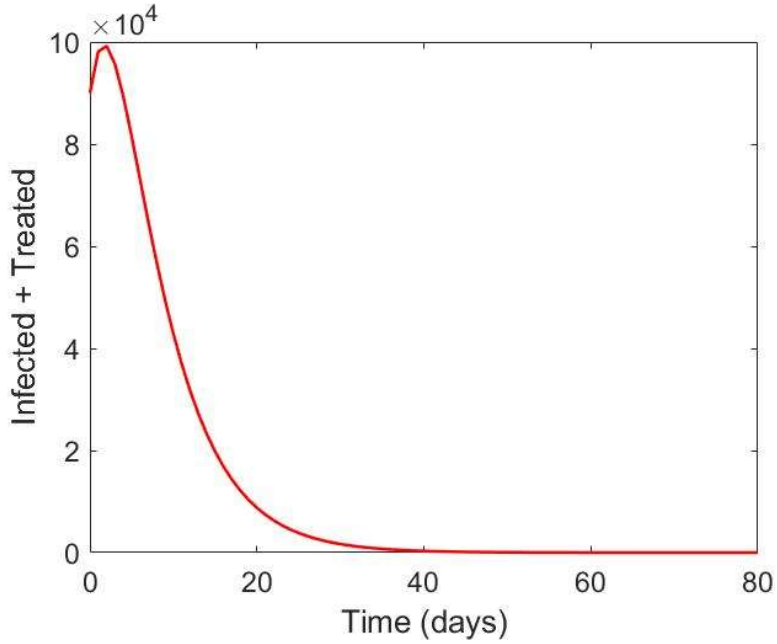


Force of infection = β *$(\frac{I}{N} + c * \frac{T}{N})$

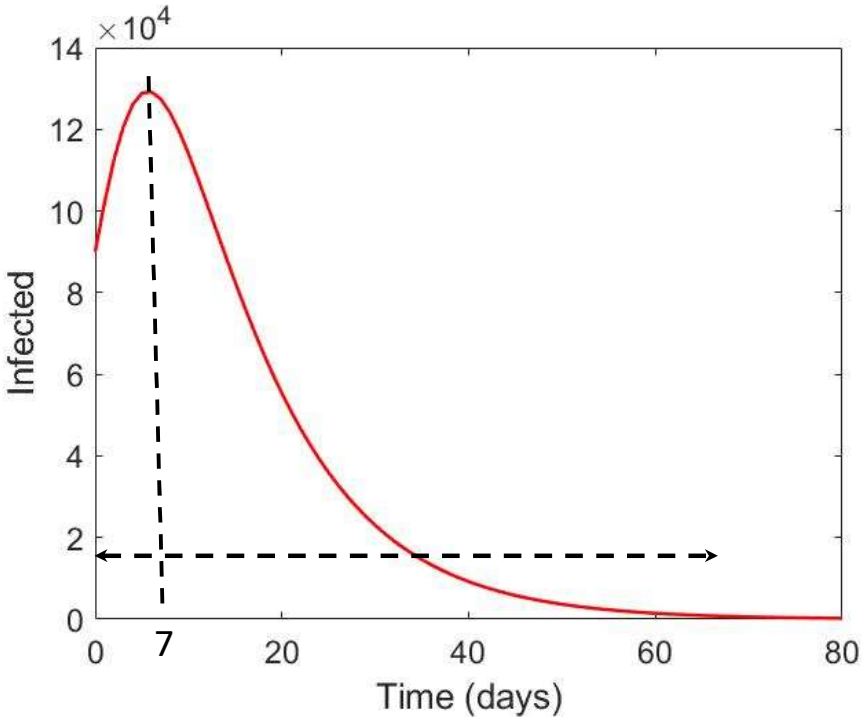
Initial conditions: N = 300000, Infected = N*0.3, Immune = N*0.1, Susceptible = N*(1-0.4), Treated = 0

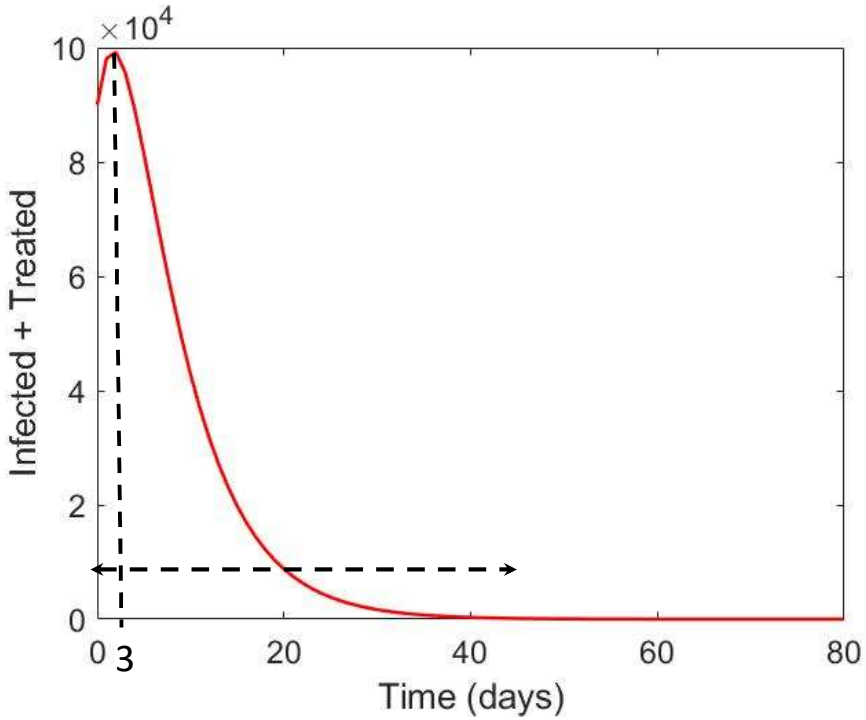
β = infection rate = 0.4 day-1, c = relative infectiousness during Rx = 1
$\gamma 1$ = recovery rate (without treatment) = (1/10) day-1
$\gamma 2$ = recovery rate (with treatment) = (1/6) day-1
d = Average duration of initiating treatment = 3 days





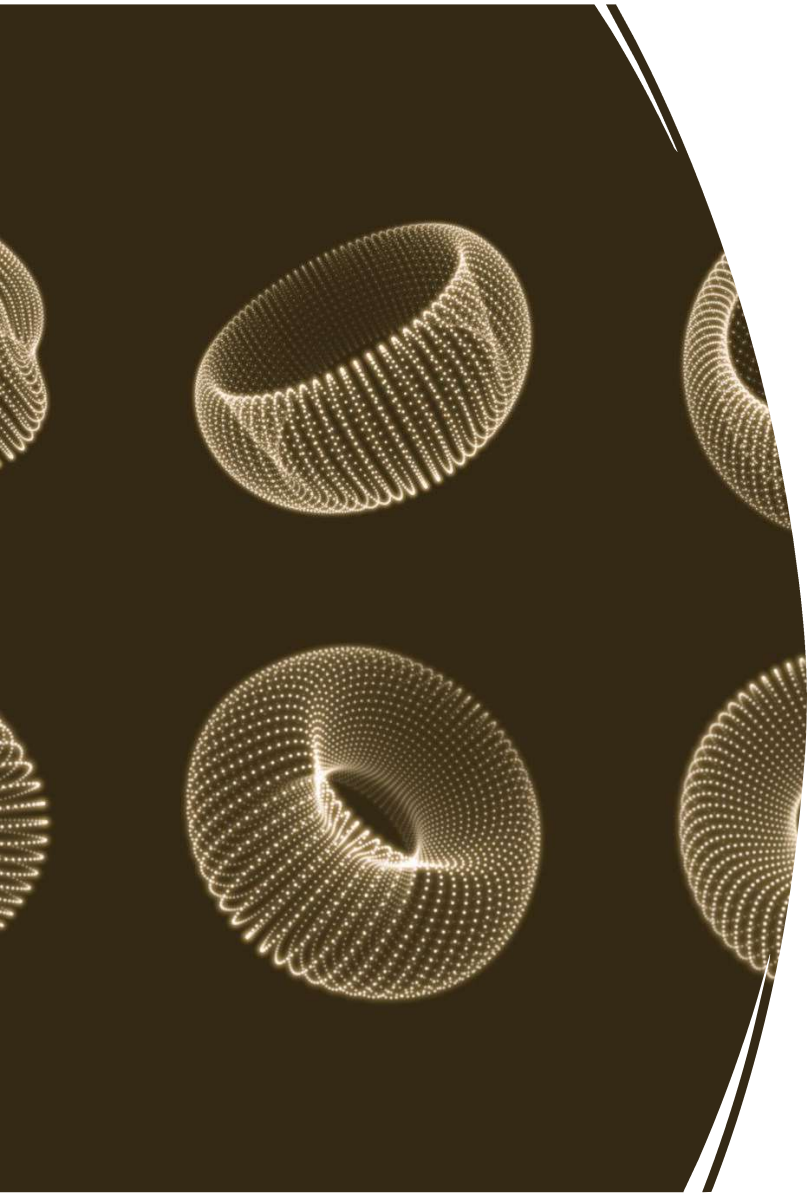
Comparison between with/with-out treatment





- **How does treatment affect the duration of the epidemic?**
- **When does the model predict it will end?**

More complex models

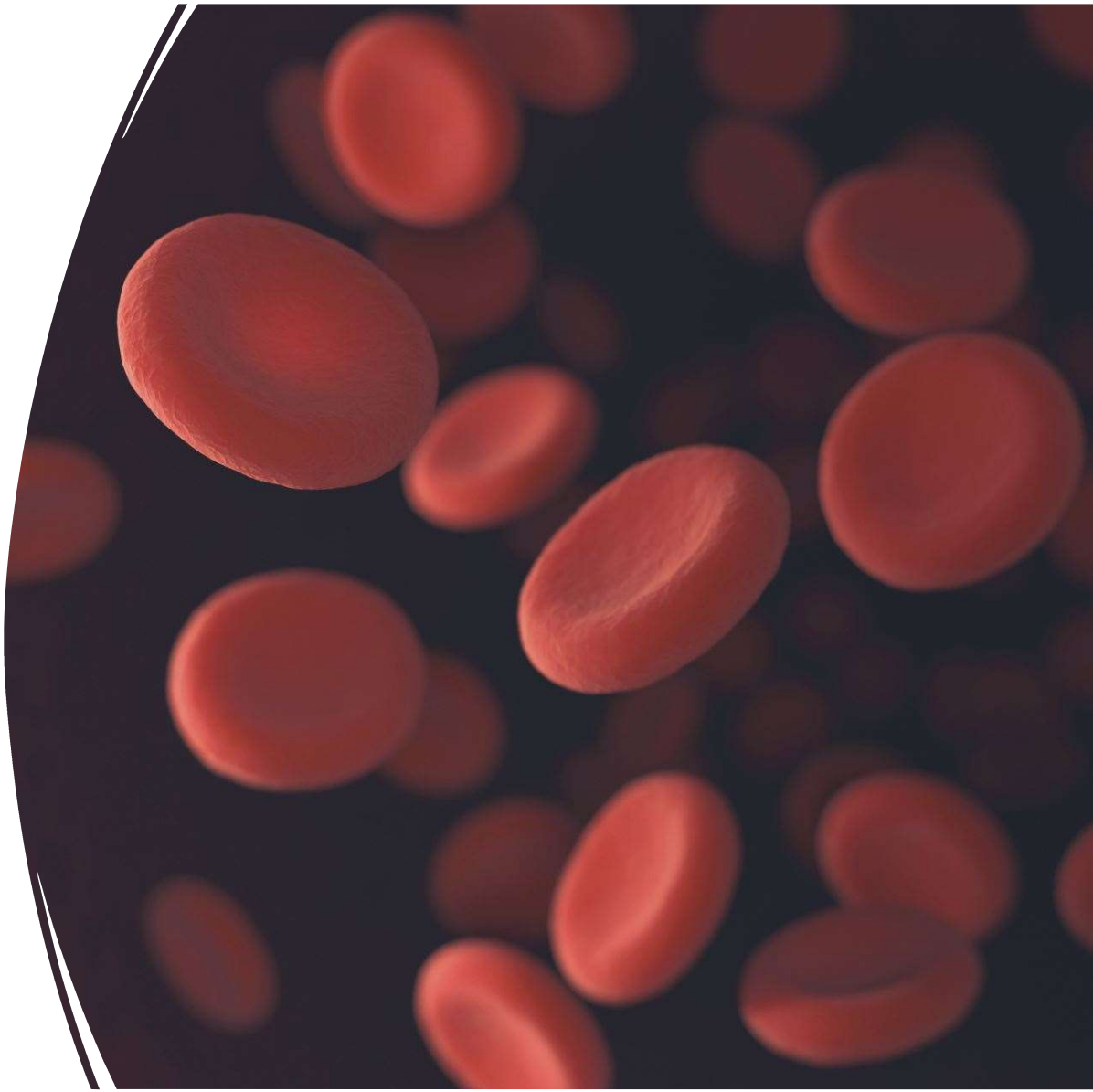


Complex models

- Vector borne diseases
- Multiple hosts/ multiple strains
- Loss of immunity
- ‘Carriers’ who are infectious but asymptomatic
- A symptomatic but un-infectious category
- More realistic mixing

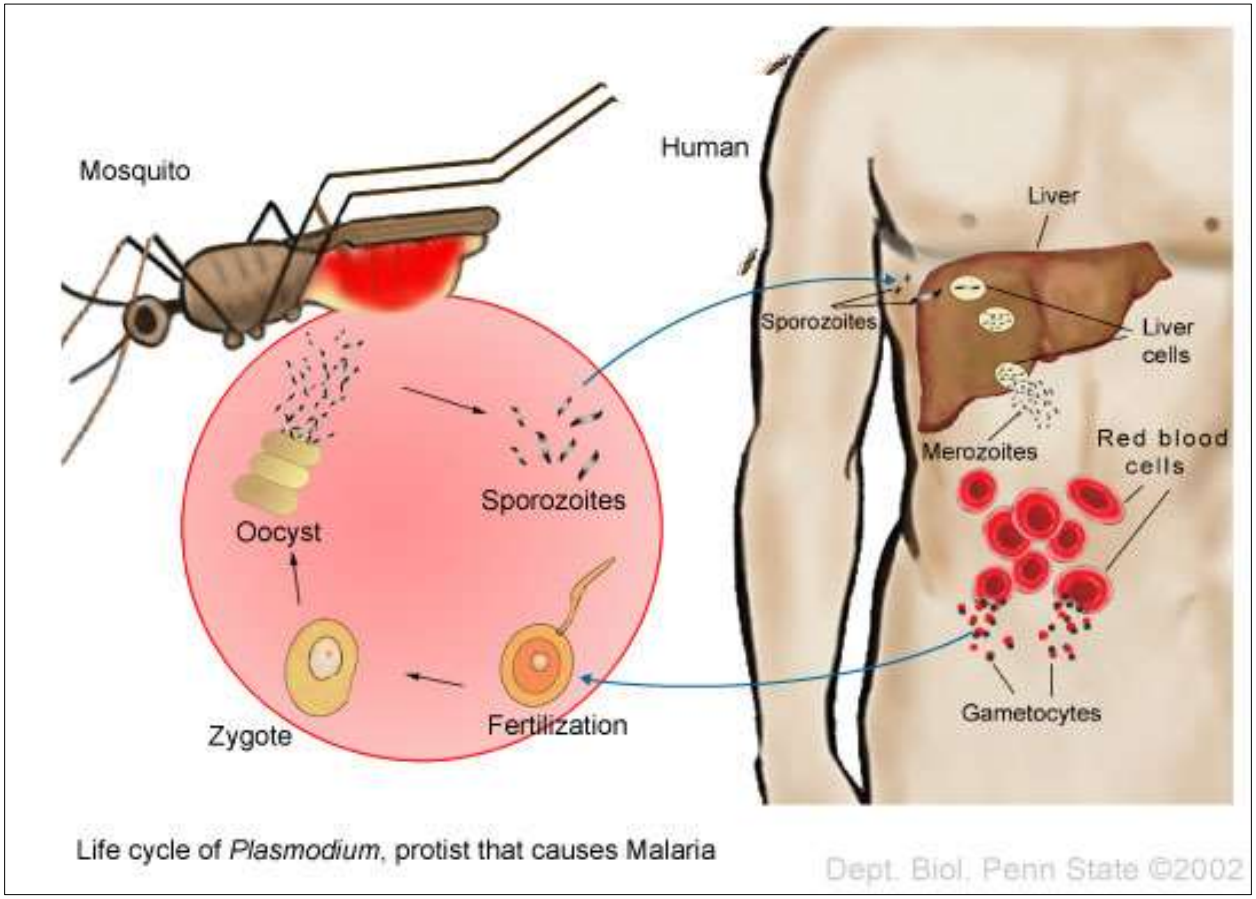
Modelling malaria

a vector-borne parasitic infection



MALARIA: Life cycle of Plasmodium parasite

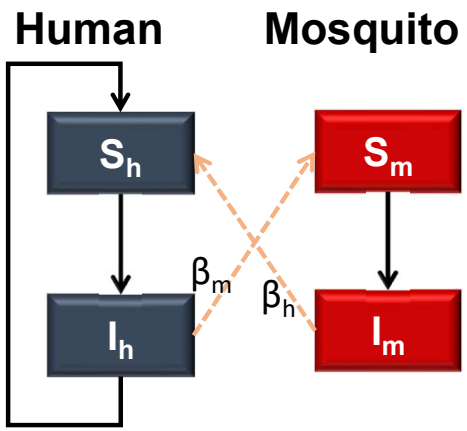
Human host, Mosquito vector, Malaria parasite



Assumptions

- Homogeneously distributed population
- Each population is divided into two compartments
- No disease induced death in human
- Mosquitoes do not recover from the disease

Ross model (1911)



Model equations

$$\frac{dI_h}{dt} = \beta_h a b m I_m S_h - \gamma I_h$$

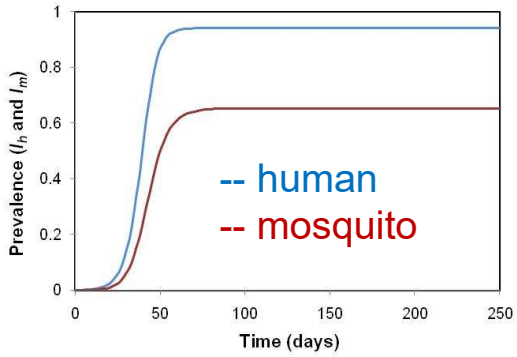
$$\frac{dI_m}{dt} = \beta_m a c I_h S_m - \mu I_m$$

$$S_h + I_h = 1$$

$$S_m + I_m = 1$$

a: biting rate (day-1)
b: infection probability of human
m: mosquito to human ratio
γ: recovery rate of human (day-1)
c: infection probability of mosquito
μ: mosquito mortality rate (day-1)

Human and mosquito prevalence

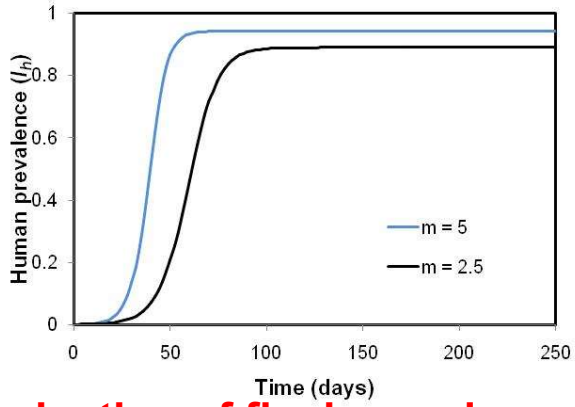


a=0.2, b=0.5, m=5 , γ=0.02, c=0.5, μ =0.05

Effect of parameter variation for Ross Model

Changing mosquito to human ratio (m)

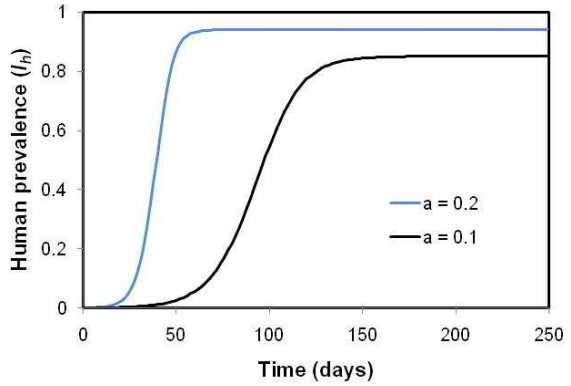
a=0.2, b=0.5, m=5 , γ=0.02, c=0.5, μ =0.05



$$R_0 = \frac{ma^2 bc}{\gamma \mu}$$

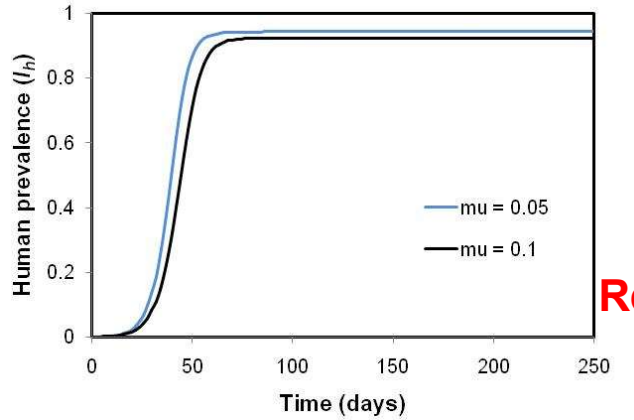
Reduction of final prevalence by 5.6%

Changing biting rate (a)



Reduction of final prevalence by 9.6%

Changing mosquito mortality rate (mu)



Reduction of final prevalence by 2%

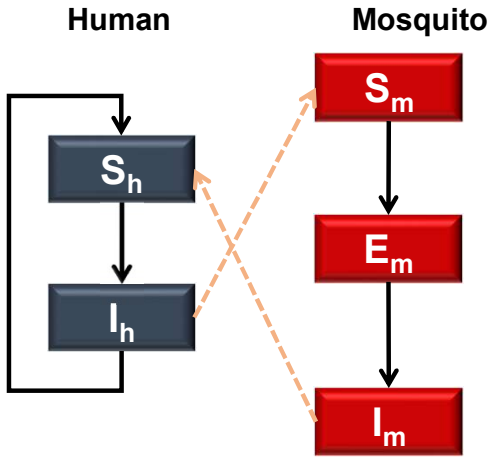
Reduction effects: a > m > mu

Macdonald model (1950s)

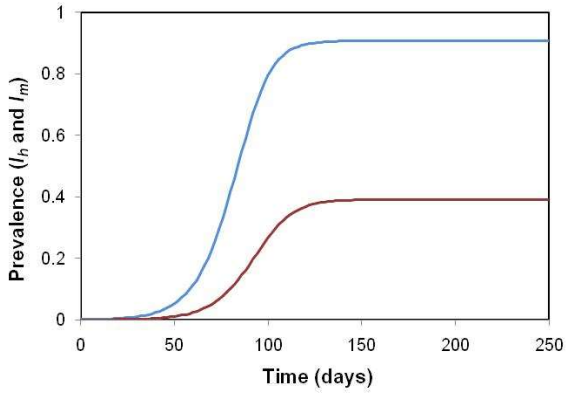
Assumptions

1. Introduced latent period (τ ~ 10 days) of parasite development in the mosquito gut
2. Other assumptions are same as Ross model

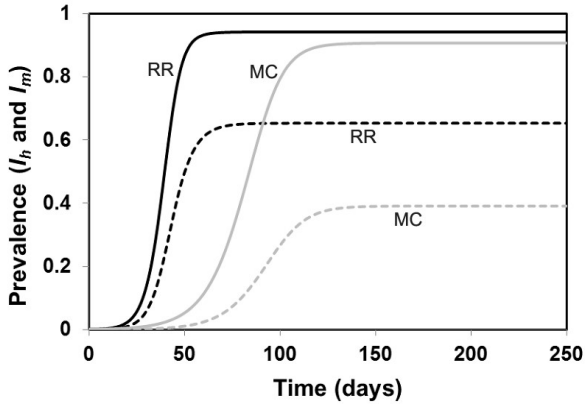
$$S_h + I_h = 1$$
$$S_m + E_m + I_m = 1$$



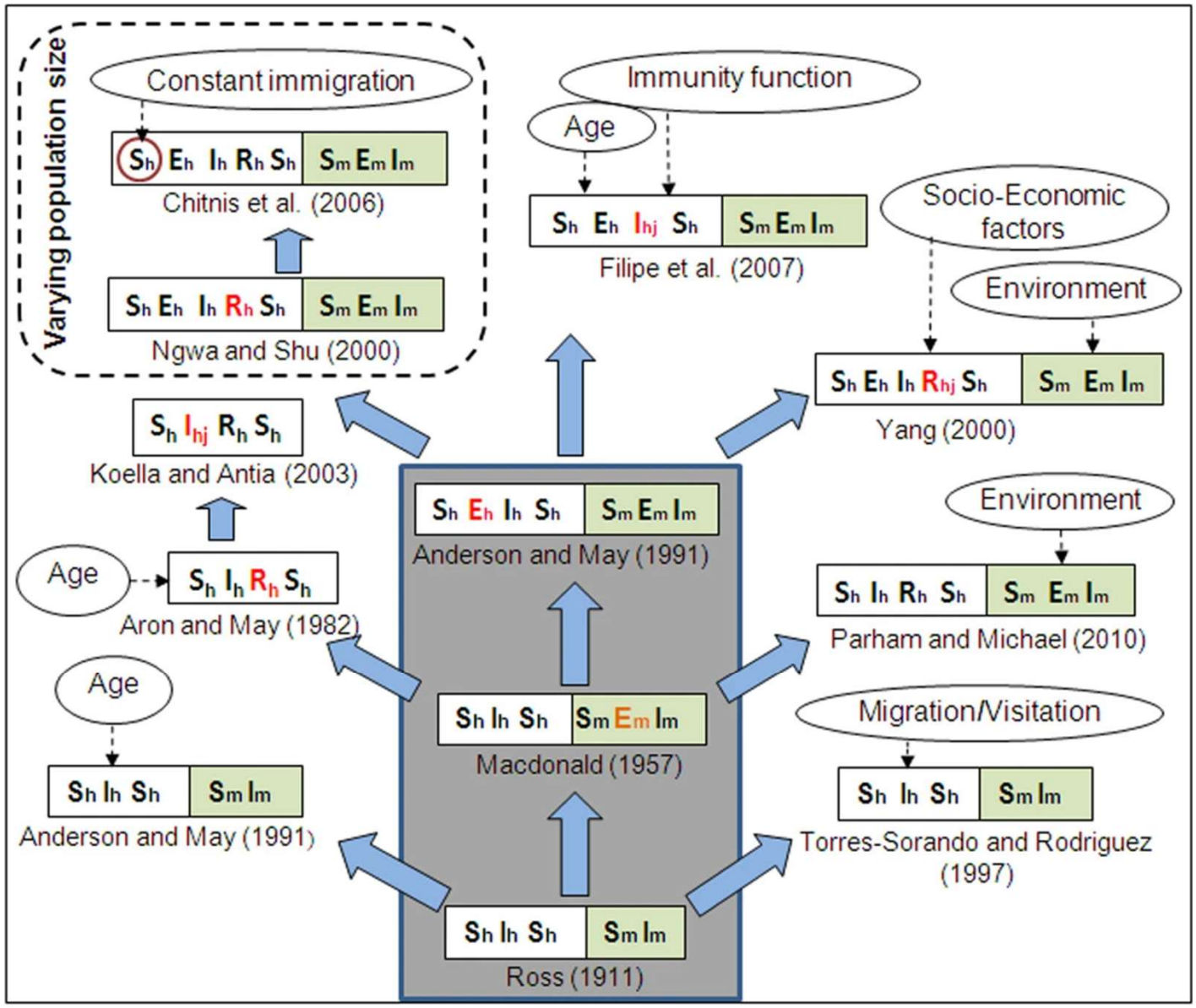
Human and mosquito prevalence



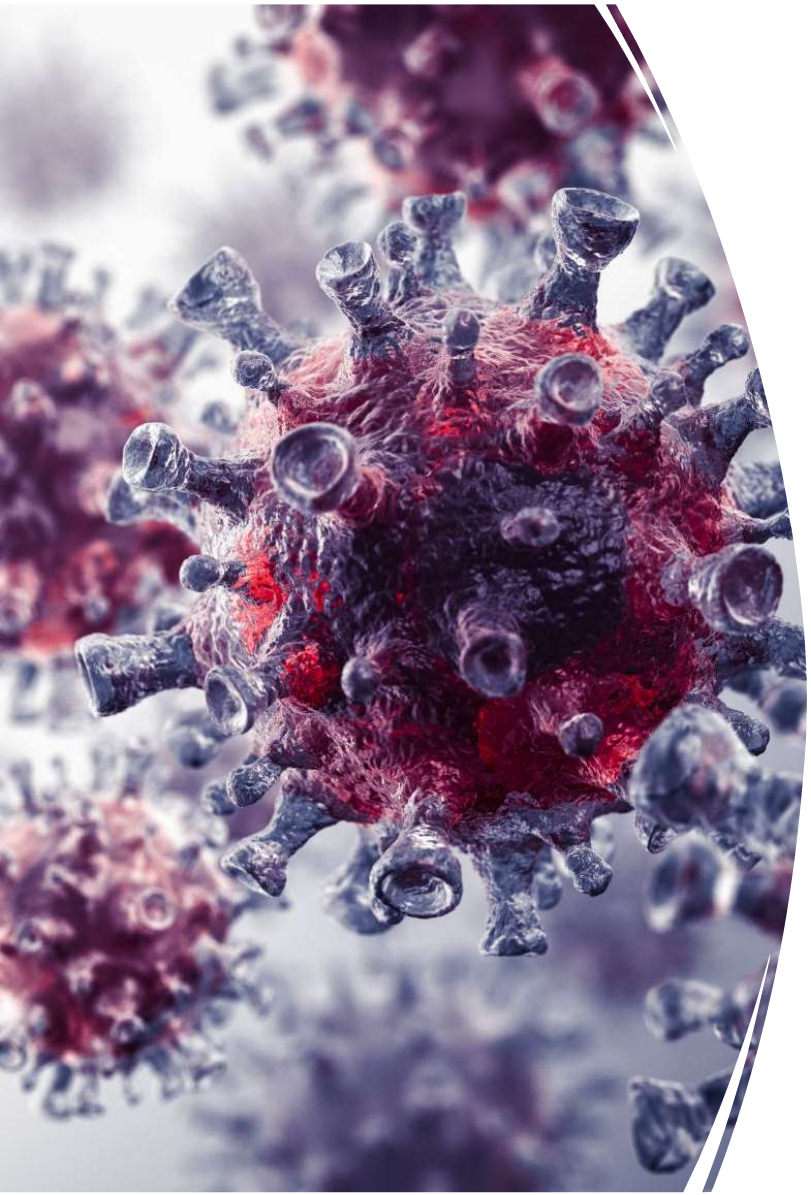
Comparison with Ross model



a=0.2, b=0.5, m=5 , γ=0.02, c=0.5, μ =0.05, τ= 10



Ref. Mandal et al, Malaria Journal, 2011

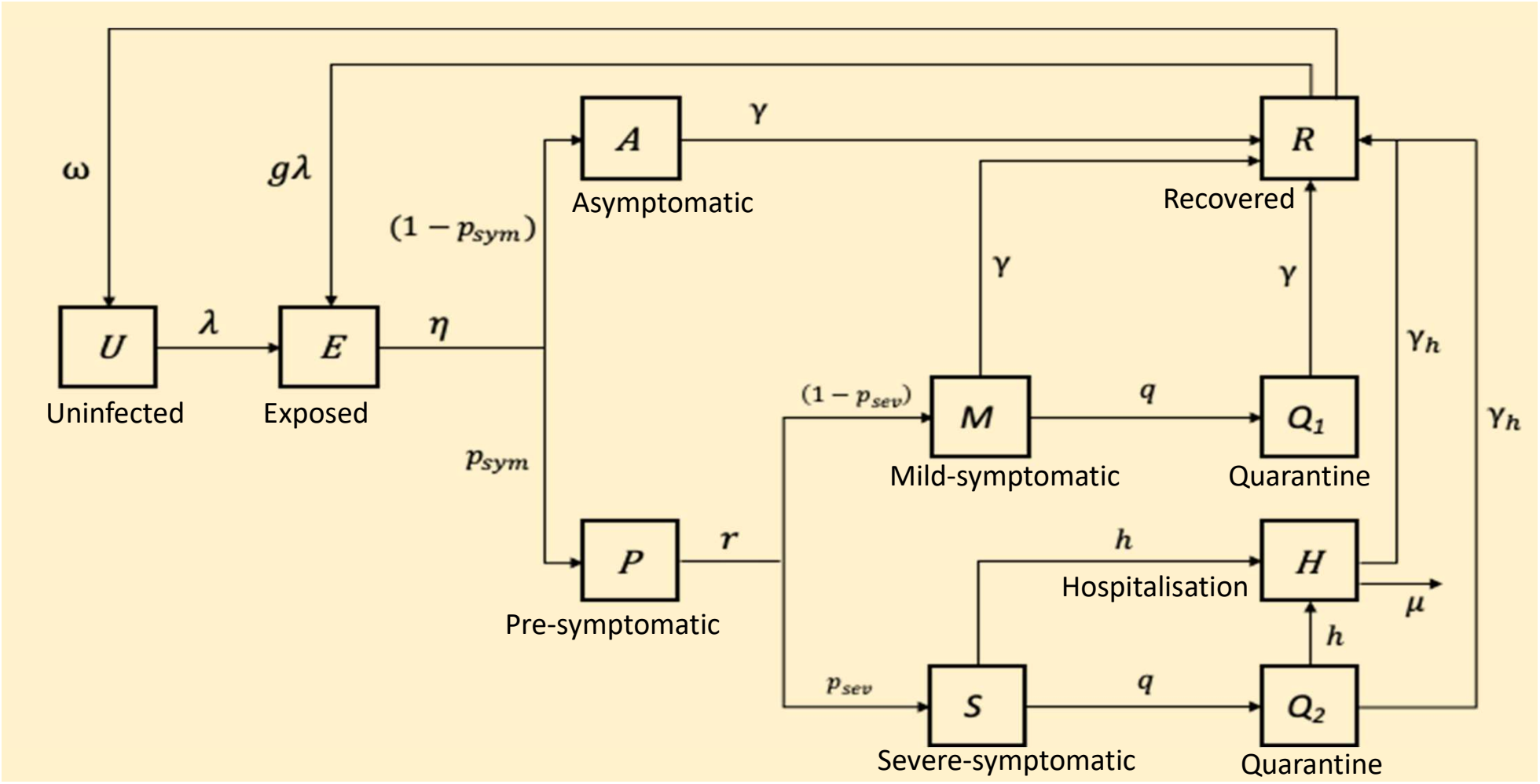


Modelling COVID-19

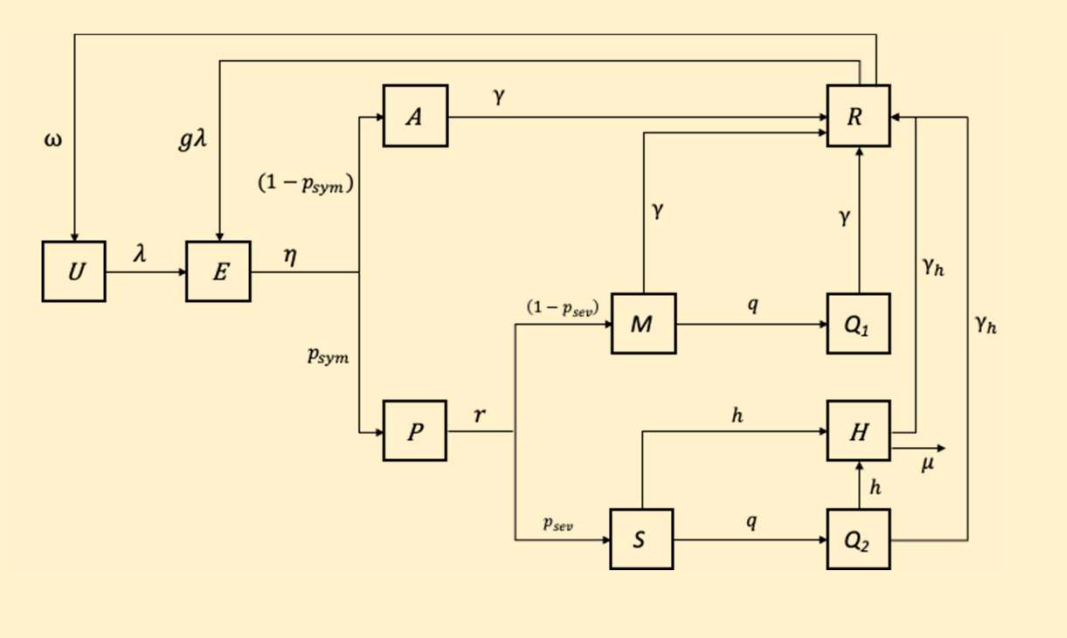
An air-borne viral infection

(mainly transmitted through droplets)

A simple COVID-19 model



A simple COVID-19 model



$$\frac{dU_i}{dt} = -\lambda_i U_i + \omega R_i$$

$$\frac{dE_i}{dt} = \lambda_i U_i + g\lambda_i R_i - \eta E_i$$

$$\frac{dA_i}{dt} = \eta\,(1 - p^{(sym)})E_i - \gamma A_i$$

$$\frac{dP_i}{dt} = \eta\, p^{(sym)}\, E_i - r\, P_i$$

$$\frac{dM_i}{dt} = r\,\left(1 - p_i^{(sev)}\right)\, P_i - (\gamma + q)\, M_i$$

$$\frac{dS_i}{dt} = r\;\, p_i^{(sev)} P_i - (h + q)\, S_{i,2}$$

$$\frac{dQ_{i,1}}{dt} = q\, M_i - \gamma\, Q_{i,1}$$

$$\frac{dQ_{i,2}}{dt} = q\, S_i - \left(h + \gamma_i^h\right) Q_{i,2}$$

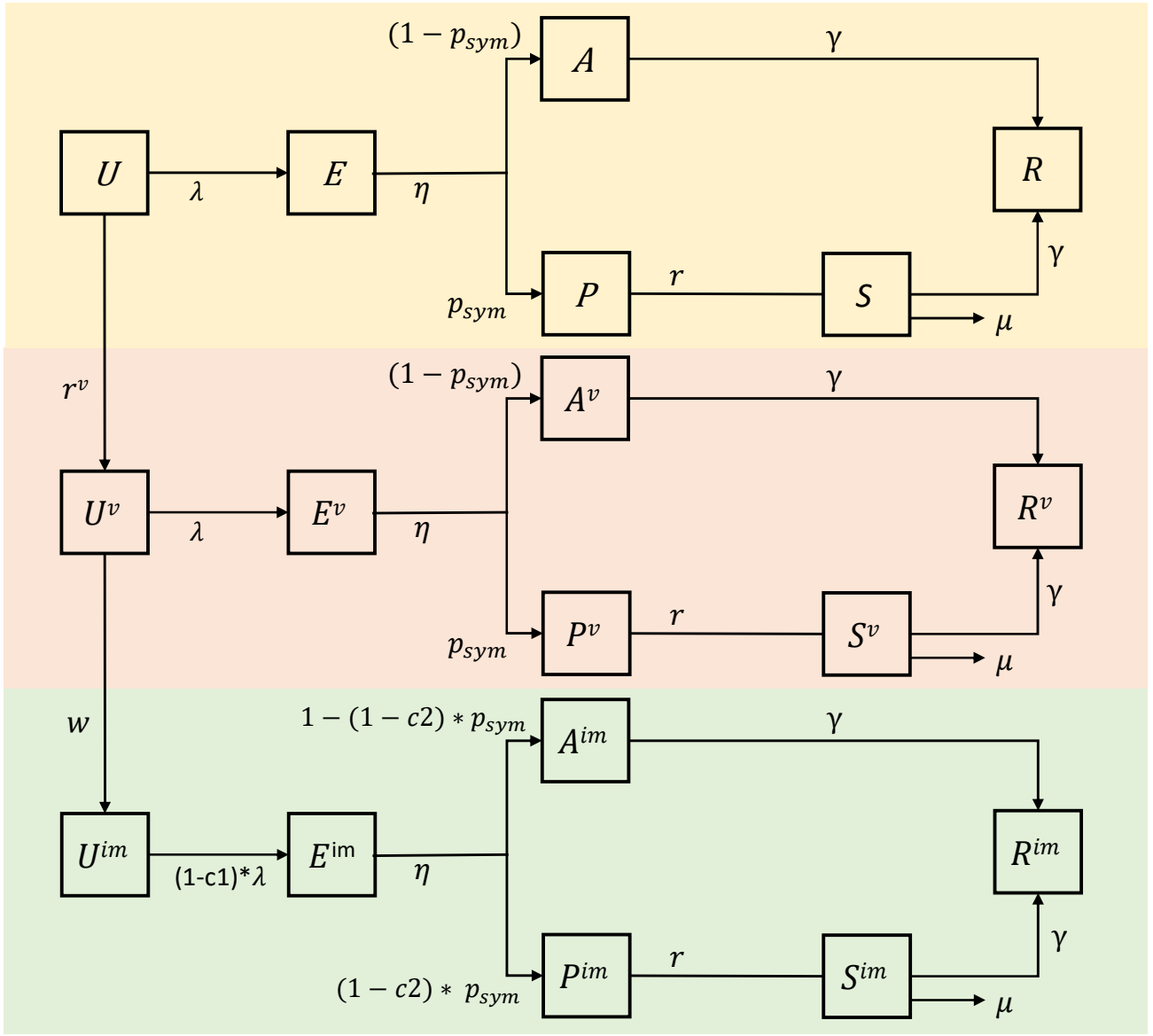
$$\frac{dH_i}{dt} = h\, S_i + h\, Q_{i,2} - (\mu_i + \gamma_i^h) H_i$$

$$\frac{dR_i}{dt} = \gamma A_i + \gamma M_i + \gamma\, Q_{i,1} + \gamma_i^h\, H_i + \gamma_i^h\, Q_{i,2} - (\omega + g) R_i$$

$$\lambda_i = \sum_{ij} \beta c_{ij} [(M_i + S_i) + k(A_i + P_i)]\, /N_i$$

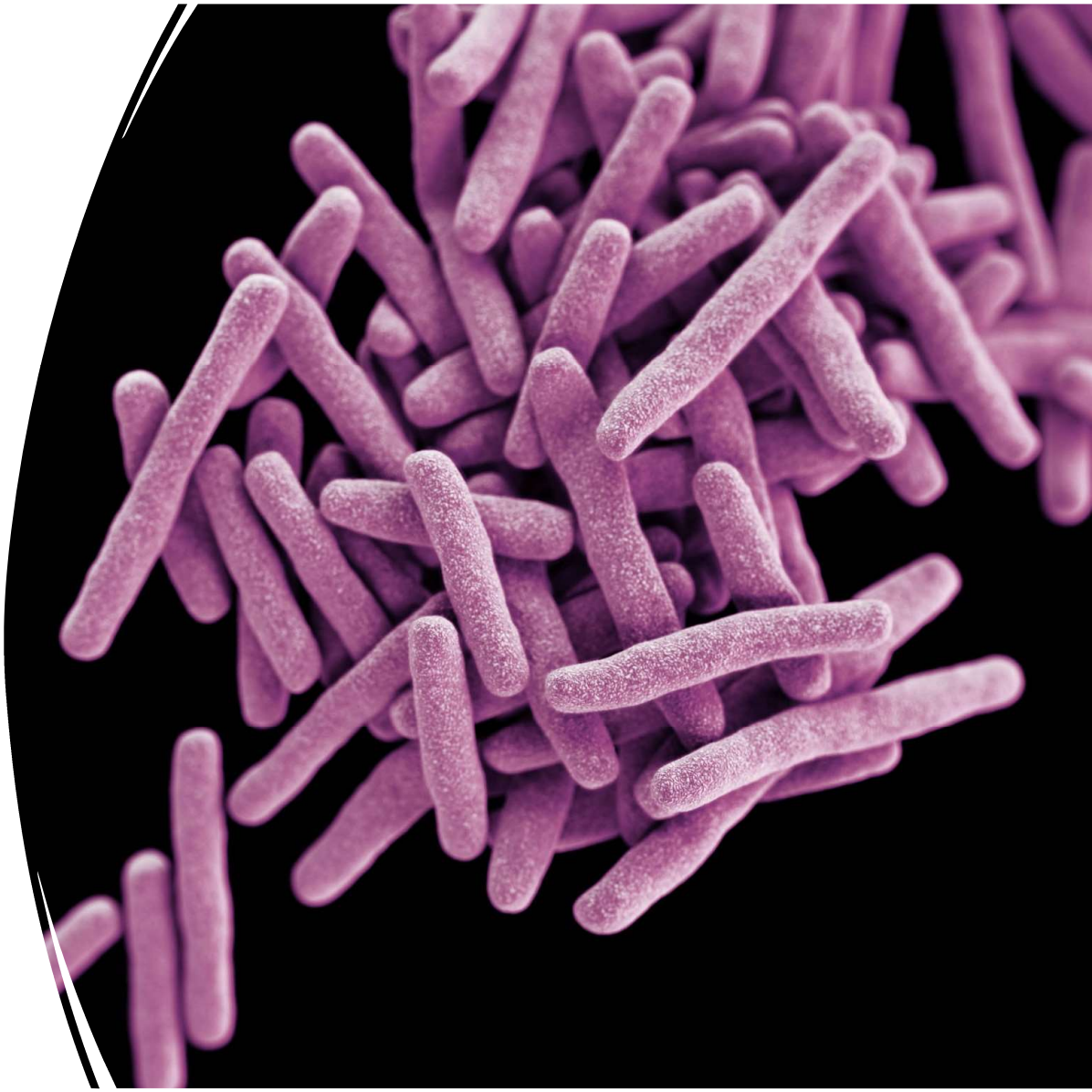
c_{ij}: Mixing between different age groups

Incorporating vaccination



Modelling Tuberculosis

An air-borne bacterial infection

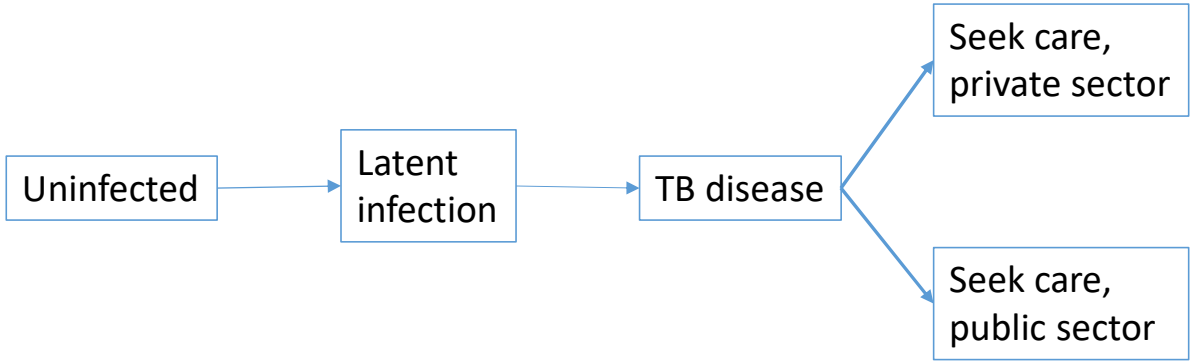


What a TB patient sees

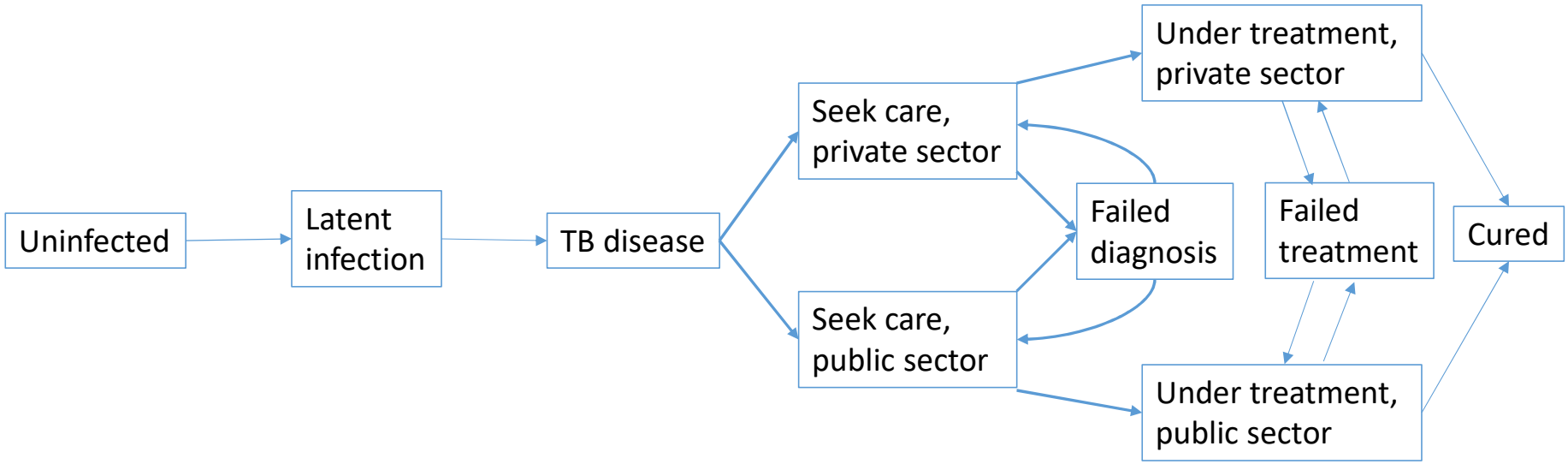
Uninfected

What a TB patient sees

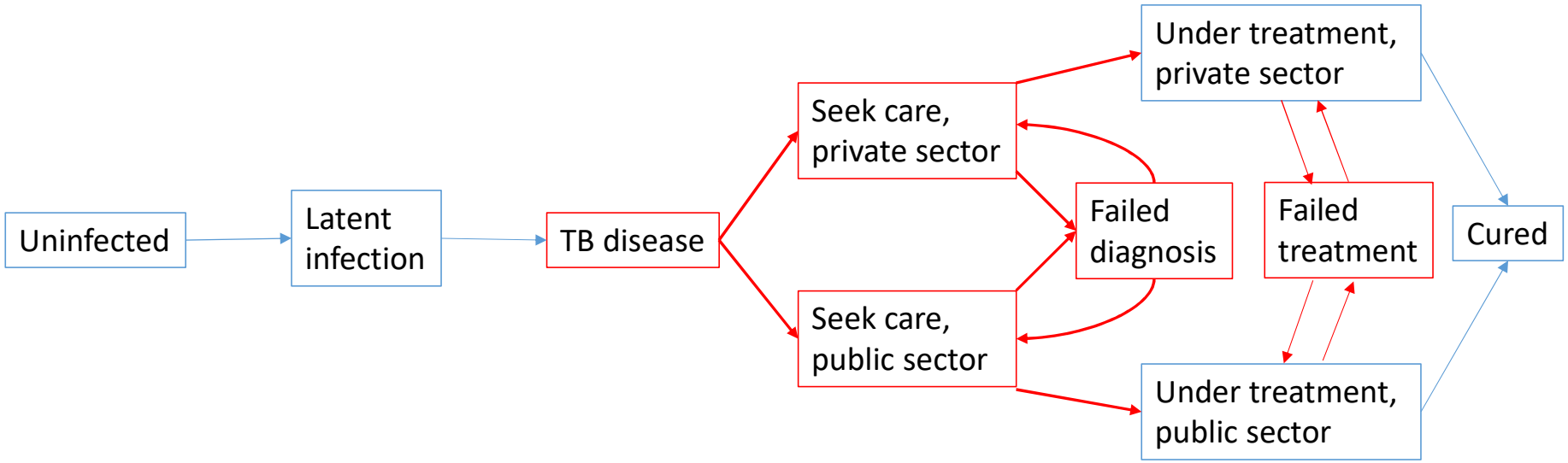
What a TB patient sees



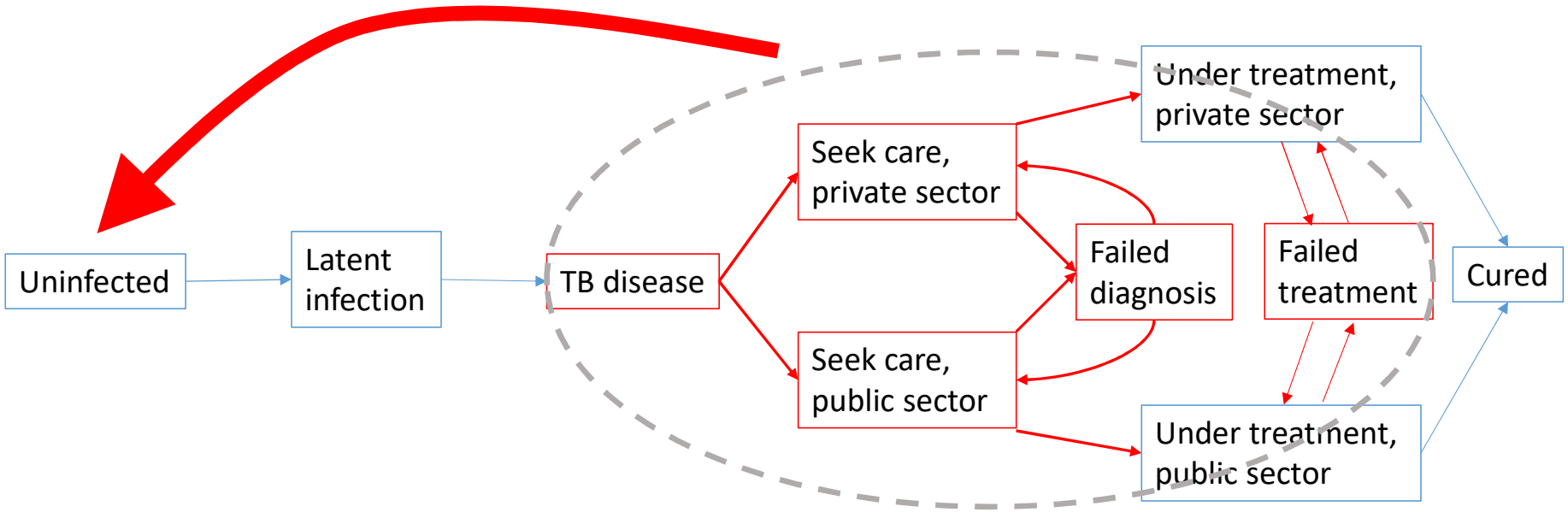
What a TB patient sees



What a TB patient sees

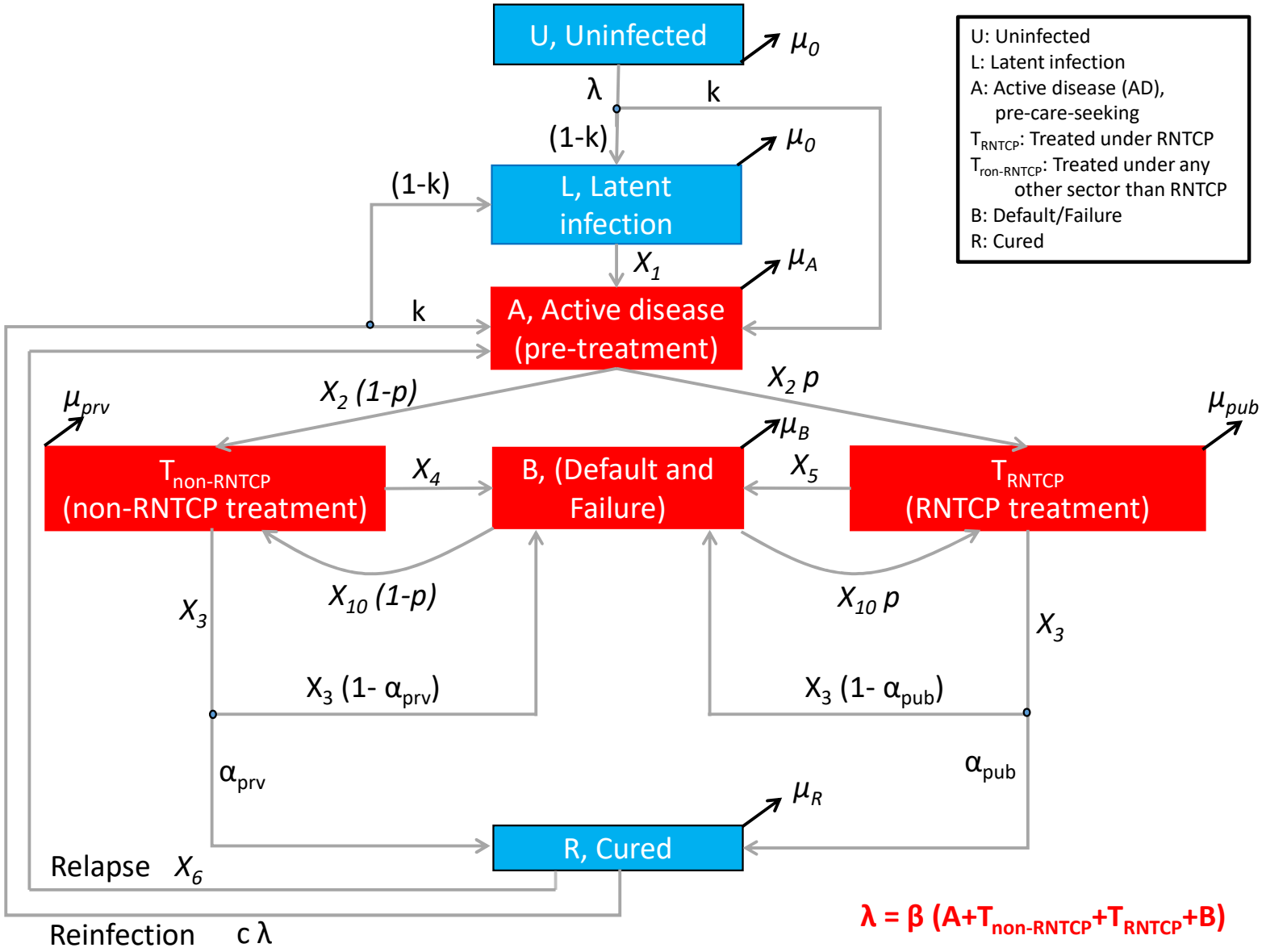


How a TB patient affects others

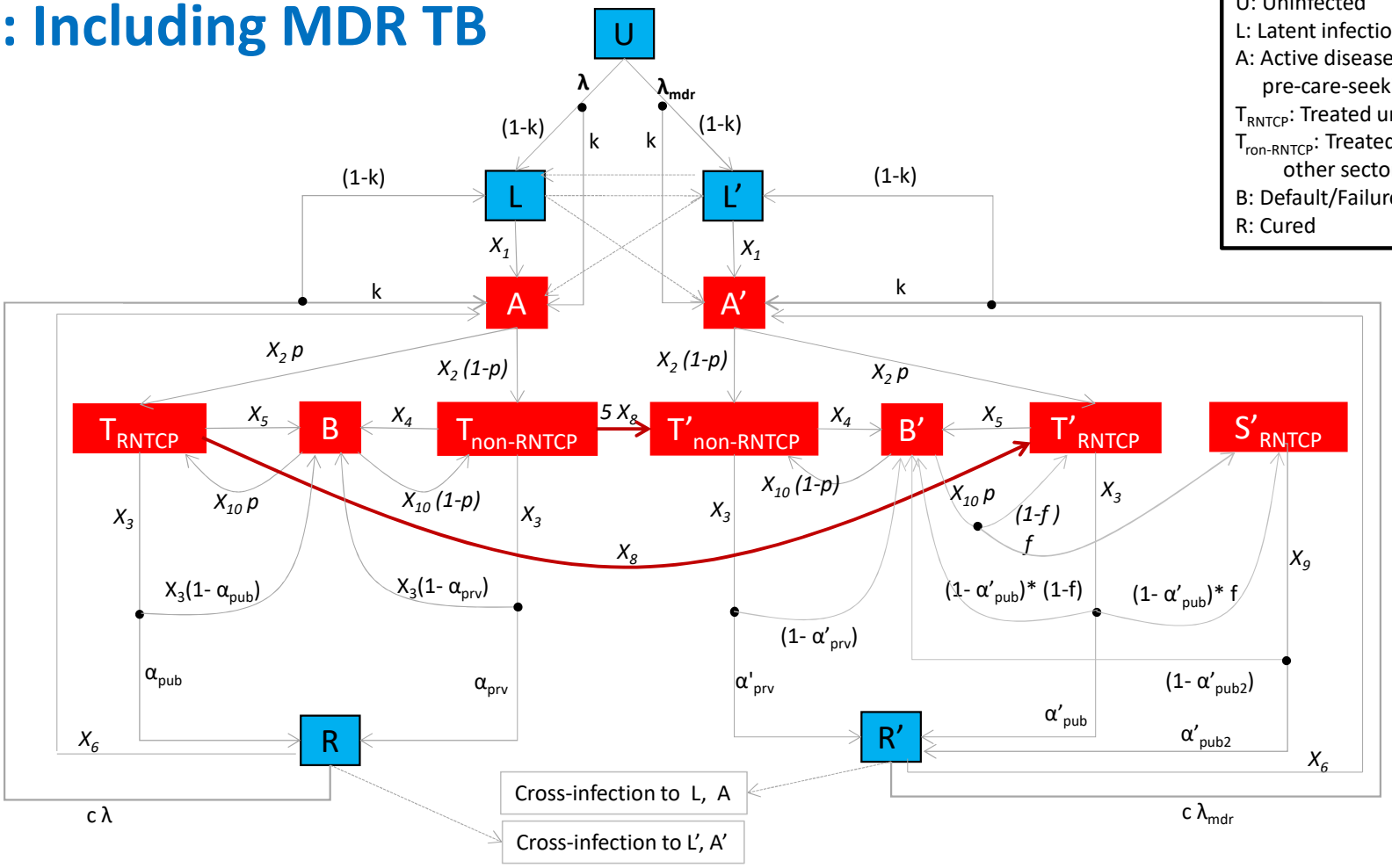


On a population level: *Annual Risk of TB Infection*

Model


U, Uninfected
μ_0
λ
k
(1-k)
μ_0
(1-k)
L, Latent infection
X_1
μ_A
k
A, Active disease (pre-treatment)
X_2 (1-p)
X_2 p
μ_{prv}
μ_{pub}
μ_B
$T_{non-RNTCP}$ (non-RNTCP treatment)
X_4
B, (Default and Failure)
X_5
T_{RNTCP} (RNTCP treatment)
X_3
X_{10} (1-p)
X_{10} p
X_3
X_3 (1- α_{prv})
X_3 (1- α_{pub})
α_{prv}
α_{pub}
μ_R
R, Cured
Relapse X_6
Reinfection c λ
U: Uninfected
L: Latent infection
A: Active disease (AD), pre-care-seeking
T_{RNTCP}: Treated under RNTCP
$T_{ron-RNTCP}$: Treated under any other sector than RNTCP
B: Default/Failure
R: Cured
$\lambda = \beta (A+T_{non-RNTCP}+T_{RNTCP}+B)$

Model: Including MDR TB



U: Uninfected
L: Latent infection
A: Active disease (AD), pre-care-seeking
T_{RNTCP}: Treated under RNTCP
$T_{ron\text{-}RNTCP}$: Treated under any other sector than RNTCP
B: Default/Failure
R: Cured

$$\lambda = \beta (A+T_{non\text{-}RNTCP}+T_{RNTCP}+B)$$

$$\lambda_{mdr} = \beta_{mdr} (A'+T'_{non\text{-}RNTCP}+T'_{RNTCP}+S'_{RNTCP}+B')$$

MDR-TB is also generated at a constant per-capita rate by patients undergoing treatment

Thank you

Questions?