Modeling infectious diseases

Modeling infectious diseases using R: Practical Session

Transmission models for HIV/AIDS and HCV

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What do we cover in this practical session ?

- More complicated transmission models in R.
- HIV/AIDS.
- Hepatitis C among injecting drug users.
- Connection with data (without modeling…).

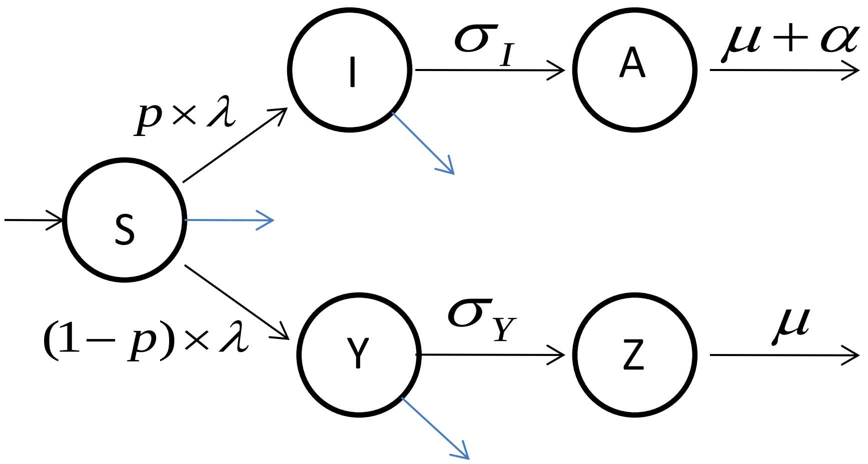
- Software: the deSolve package in R.

R program: ModelingIDinR1_V1_HIV&HCV_Sep2019.R

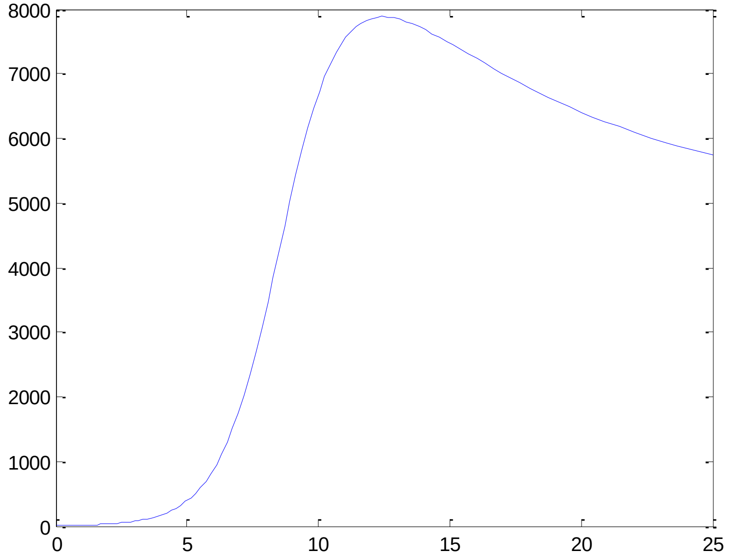
Part 1:
transmission model for HIV/AIDS

Example 1

Transmission model for AIDS



Number of infected individuals



Capasso 2008, Anderson and May 1991, Anderson 1988

Observed data from the initial outbreak AIDS in UK (Healy and Tillett, 1998)

GLM for count data

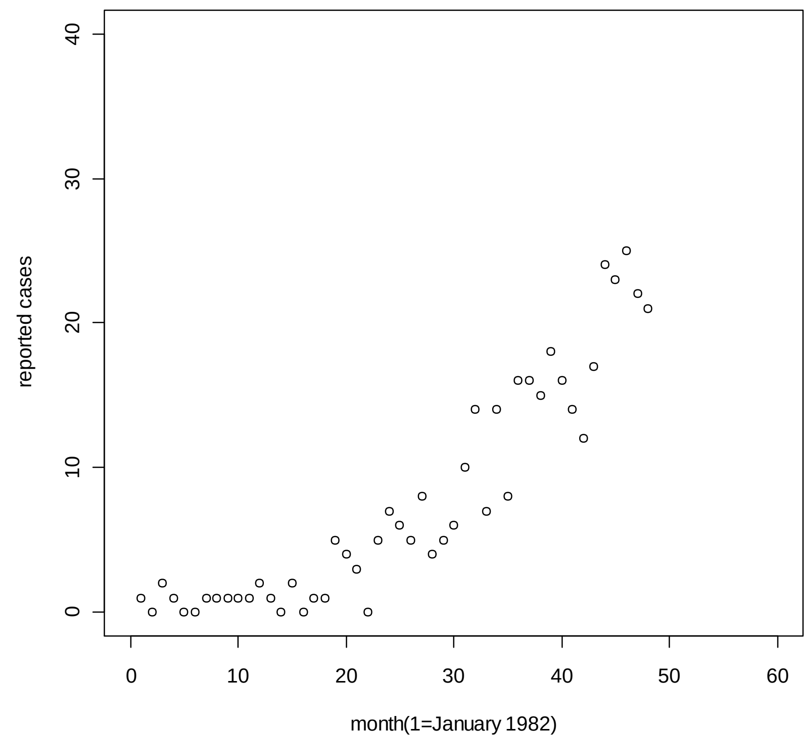
$$I(t) \sim Poisson(\mu(t))$$

$$\mu(t) = I(0)e^{\Lambda t}$$

Initial number of cases at t=0

Exponential growth

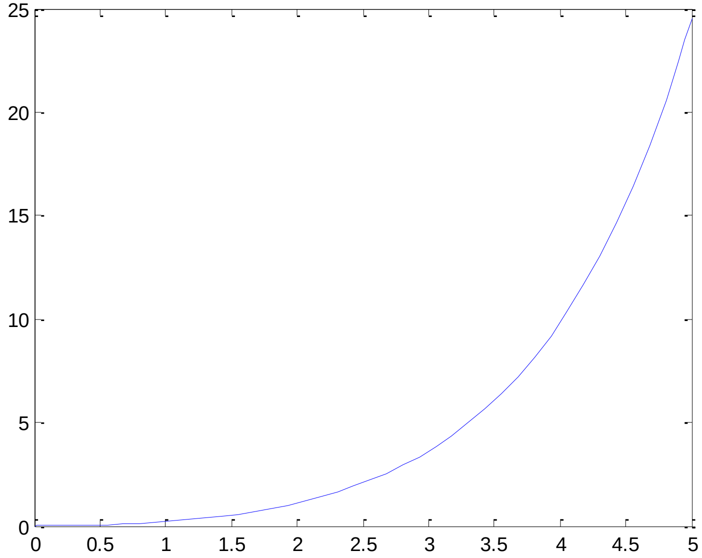
Monthly number of cases (1982-1986)



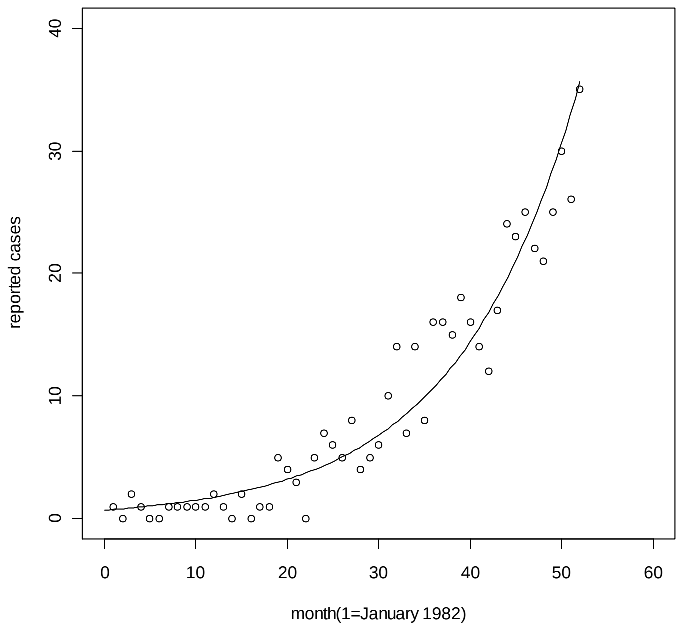
Healy and Tillett (1998)

Initial outbreak AIDS in UK – data and predicted means

Predicted by the transmission model

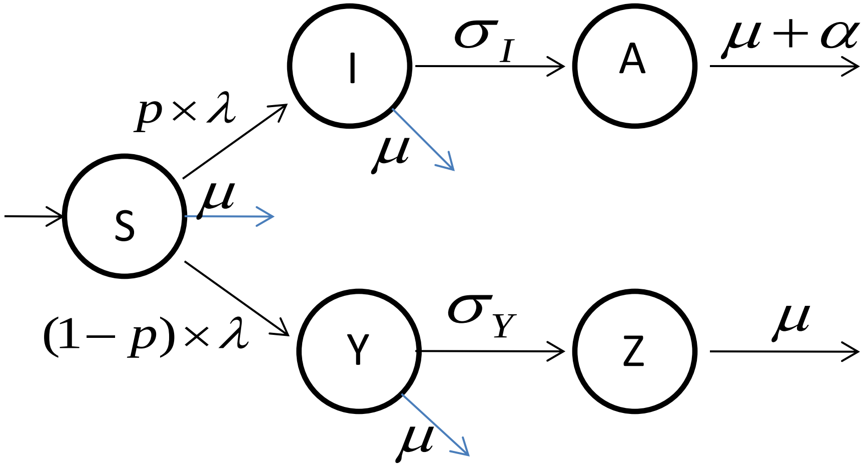


Predicted by the data



Transmission model for HIV/AIDS

Transmission model for AIDS



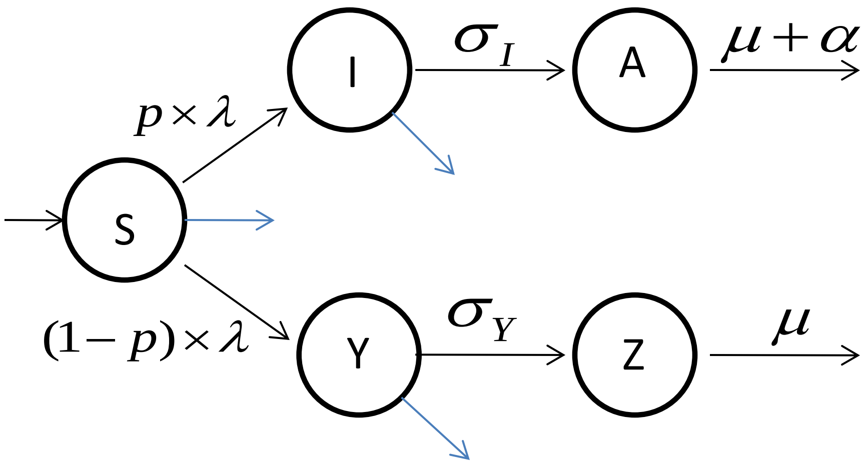
A: Clinical AIDS

Z: infected but do not develop Clinical AIDS

Capasso 2008, Anderson and May 1991, Anderson 1988

Transmission model for HIV/AIDS

Transmission model for AIDS



THE ODE system

$$\frac{dS(t)}{dt} = B\mu - \lambda S(t) - \mu S(t)$$

$$\frac{dI(t)}{dt} = P\lambda S(t) - (\sigma_I + \mu) I(t)$$

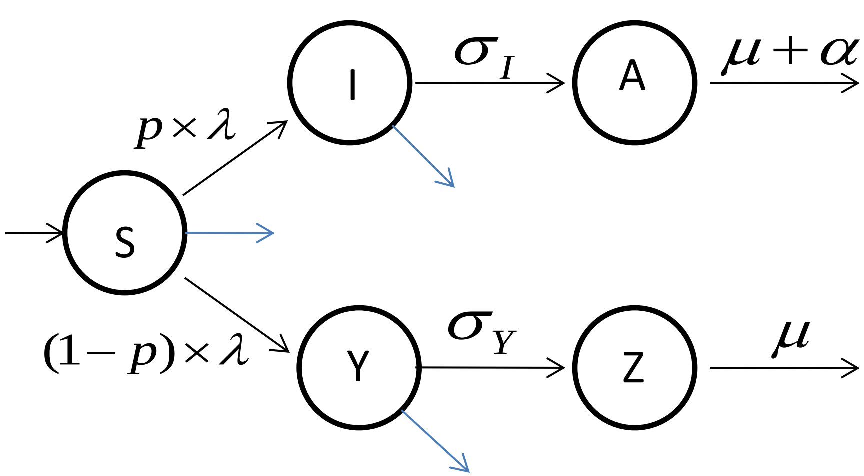
$$\frac{dY(t)}{dt} = (1-P)\lambda S(t) - (\sigma_Y + \mu) Y(t)$$

$$\frac{dA(t)}{dt} = \sigma_I I(t) - (\mu + \alpha) A(t)$$

$$\frac{dZ(t)}{dt} = \sigma_Y Y(t) - \mu Z(t)$$

Capasso 2008, Anderson and May 1991, Anderson 1988

Model parameters



λ	Force of infection
σ_I	Incubation period
σ_Y	Incubation period
μ	Death rate
α	Death rate from AIDS

Capasso 2008, Anderson and May 1991, Anderson 1988

The force of infection

Average number of sexual partners

Transmission probability per contact

$$\lambda(t) = \frac{c\left(\beta_1 I + \beta_2 Y\right)}{N}$$

Population size

The force of infection is assumed to be proportional for the number of sexual partners of an individuals

The force of infection

Assumption:

$$c\beta_1 = c\beta_2 = 1$$

$$\lambda(t) = \frac{c\left(\beta_1 I + \beta_2 Y\right)}{N} = \frac{\left(I + Y\right)}{N}$$

Number of infected individuals

Population size

Model parameters in R

Model parameters:

1. Life expectancy: 75 years.
2. Incubation period: 8 years.
3. Proportion of individuals develop clinical AIDS 20%.
4. life expectancy with clinical AIDS: 1 year.

```
> parameters <- c(B=10000,mu=1/75,v1=1/8,v2=1/8,f=0.2,alpha=1)
> parameters
           B           mu           v1           v2            f 
alpha 
1.000000e+04 1.333333e-02 1.250000e-01 1.250000e-01 2.000000e-01 
1.000000e+00
```

State variables

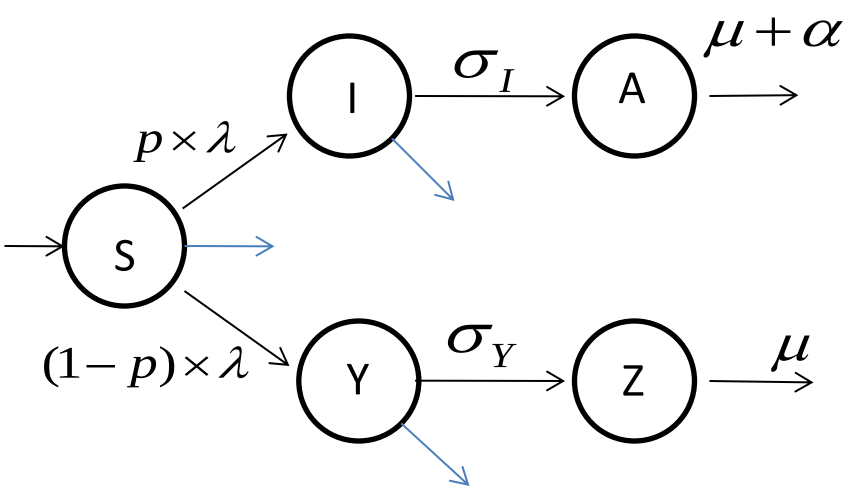
Population size of 10000.

At t=0, 5 individuals are infected.

```
> state <- c(y1=9995,y2=5,y3=0,y4=0,y5=0)
> state
  y1   y2   y3   y4   y5
9995    5    0    0    0
```

Specification of the model in R

The transmission model



The transmission model in R

```
AIDS<-function(t,state,parameters)
{
with(as.list(c(state, parameters)),
{
dy1 = B*mu-(mu+((y2+y3)/10000))*y1
dy2 = f*((y2+y3)/10000)*y1-(mu+v1)*y2
dy3 = (1-f)*((y2+y3)/10000)*y1-(mu+v2)*y3
dy4 = v1*y2-(mu+alpha)*y4
dy5 = v2*y3-mu*y5
list(c(dy1,dy2,dy3,dy4,dy5))
})
}
```

Specification of the model in R

$$\frac{dS(t)}{dt} = B\mu - \lambda S(t) - \mu S(t)$$

$$\frac{dI(t)}{dt} = P\lambda S(t) - (\sigma_I + \mu)I(t)$$

$$\frac{dY(t)}{dt} = (1-P)\lambda S(t) - (\sigma_Y + \mu)I(t)$$

$$\frac{dA(t)}{dt} = \sigma_I I(t) - (\mu + \alpha)A(t)$$

$$\frac{dZ(t)}{dt} = \sigma_Y Y(t) - \mu Z(t)$$

```
AIDS<-function(t,state,parameters)
{
with(as.list(c(state, parameters)),
{
dy1 = B*mu-(mu+((y2+y3)/10000))*y1
dy2 = f*((y2+y3)/10000)*y1-(mu+v1)*y2
dy3 = (1-f)*((y2+y3)/10000)*y1-(mu+v2)*y3
dy4 = v1*y2-(mu+alpha)*y4
dy5 = v2*y3-mu*y5
list(c(dy1,dy2,dy3,dy4,dy5))
})
}
```

Running the model in R

Time range for integration

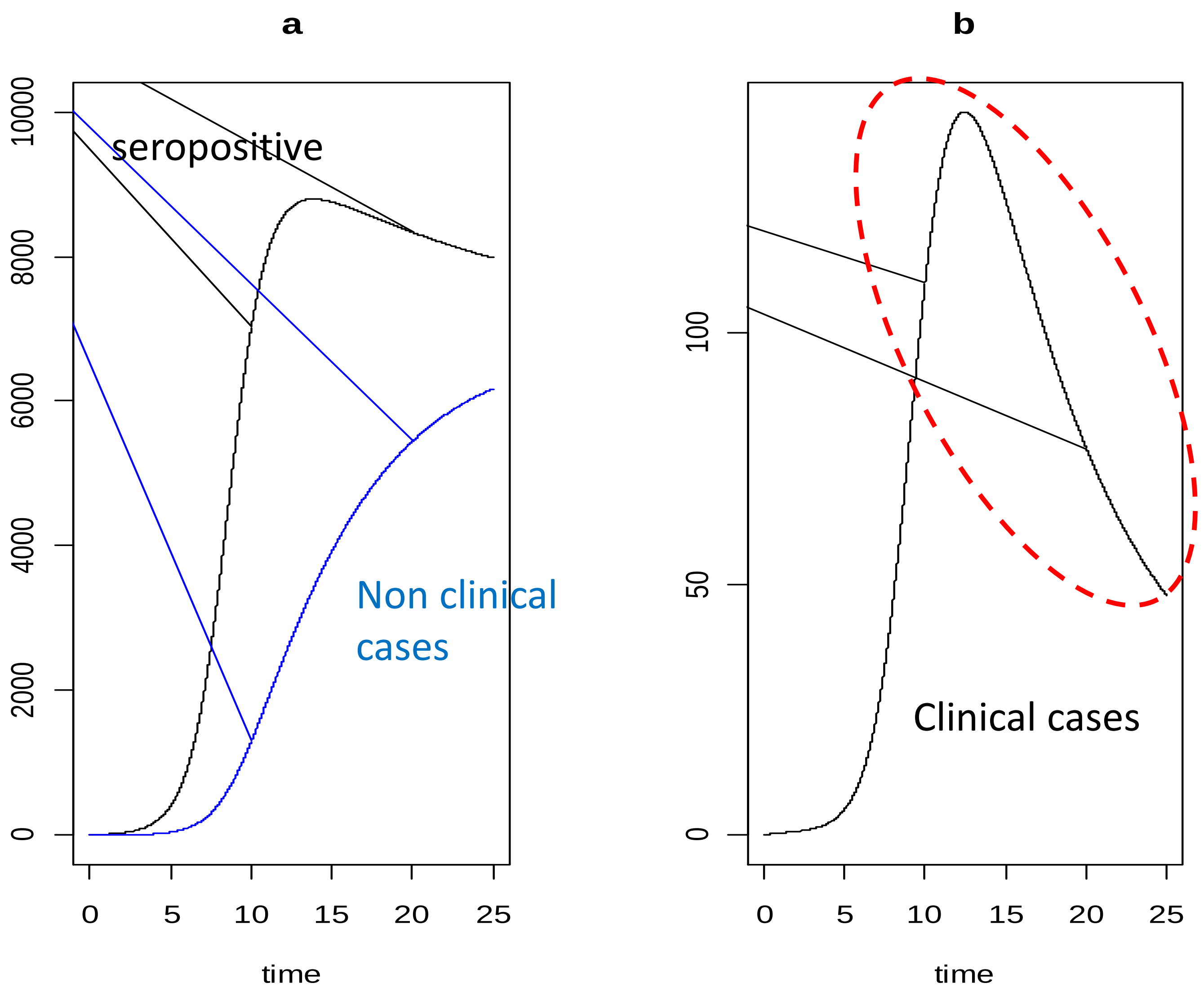
```
times<-seq(0,20,by=0.01)
require(deSolve)
out <- as.data.frame(ode(y=state,times=times,func=AIDS,parms=parameters))
```

state variables

The model

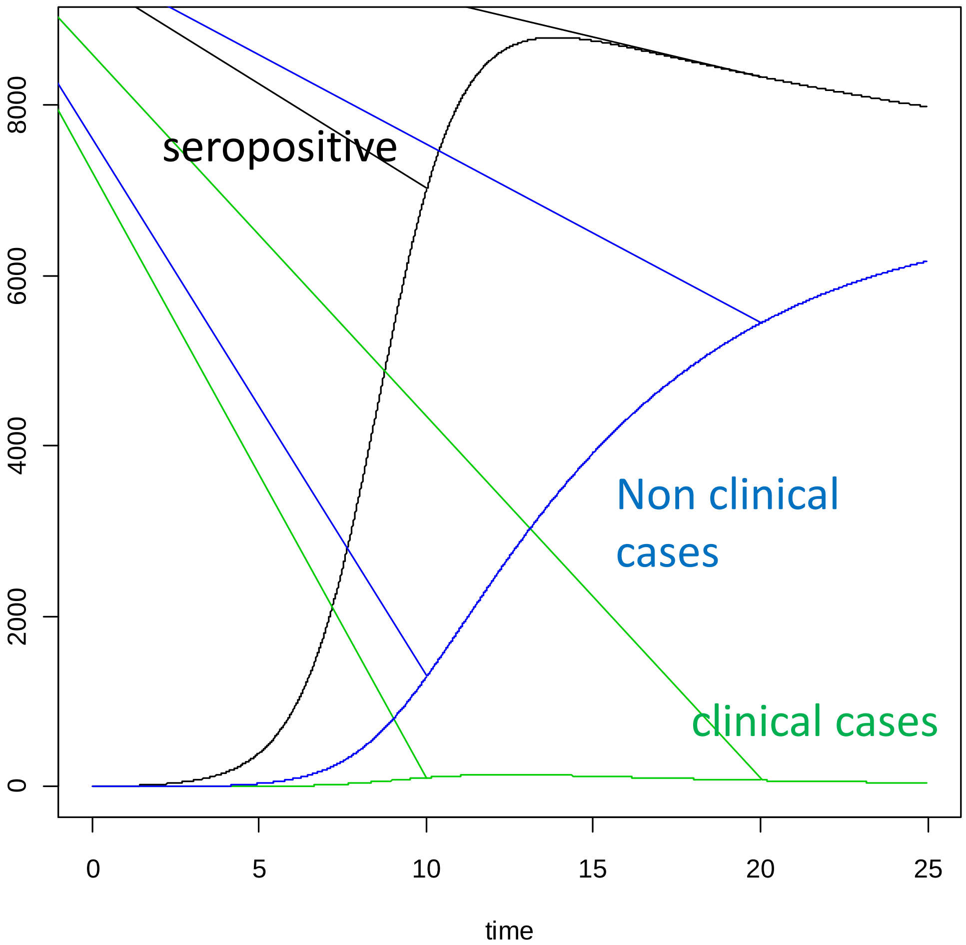
model parameters

Solution



a
b
seropositive
Non clinical
cases
Clinical cases
10000
8000
6000
4000
2000
0
100
50
0
0
5
10
15
20
25
time
time

Solution



Why we do not see so many clinical cases ?

Model parameters in R

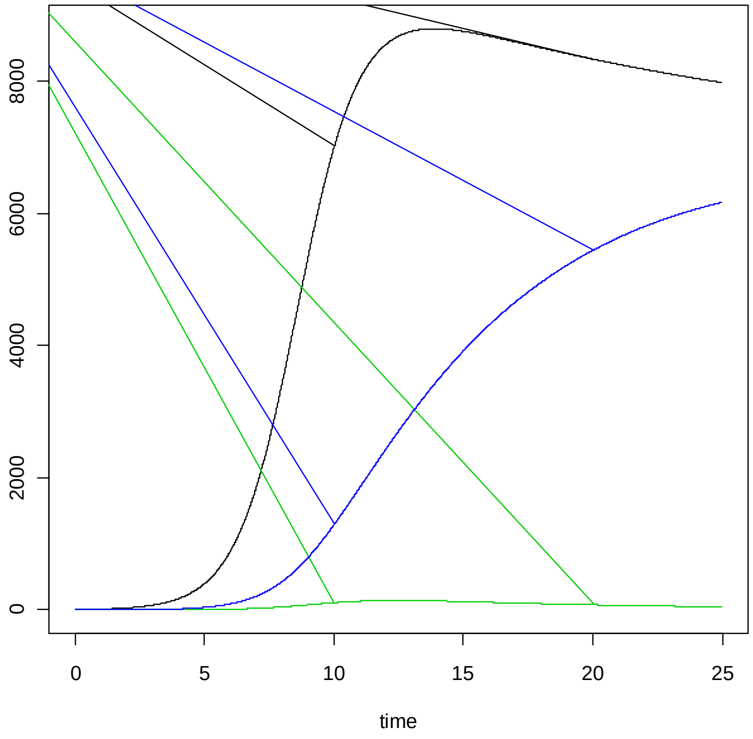
Model parameters:

1. Life expectancy: 75 years.
2. Incubation period: 8 years.
3. Proportion of individuals develop clinical AIDS 20%.
4. life expectancy with clinical AIDS: 1 year ➡ 10 years.

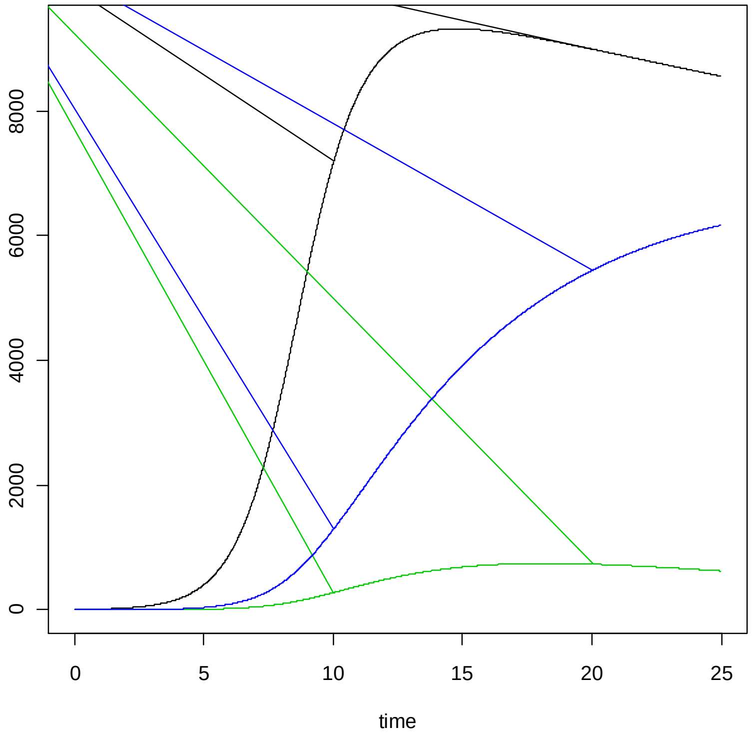
```
> parameters <- c(B=10000,mu=1/75,v1=1/8,v2=1/8,f=0.2,alpha=0.1)
> parameters
            B            mu            v1            v2             f 
alpha
1.000000e+04 1.333333e-02 1.250000e-01 1.250000e-01 2.000000e-01 
1.000000e-01
```

solution

life expectancy with clinical AIDS: 1 year



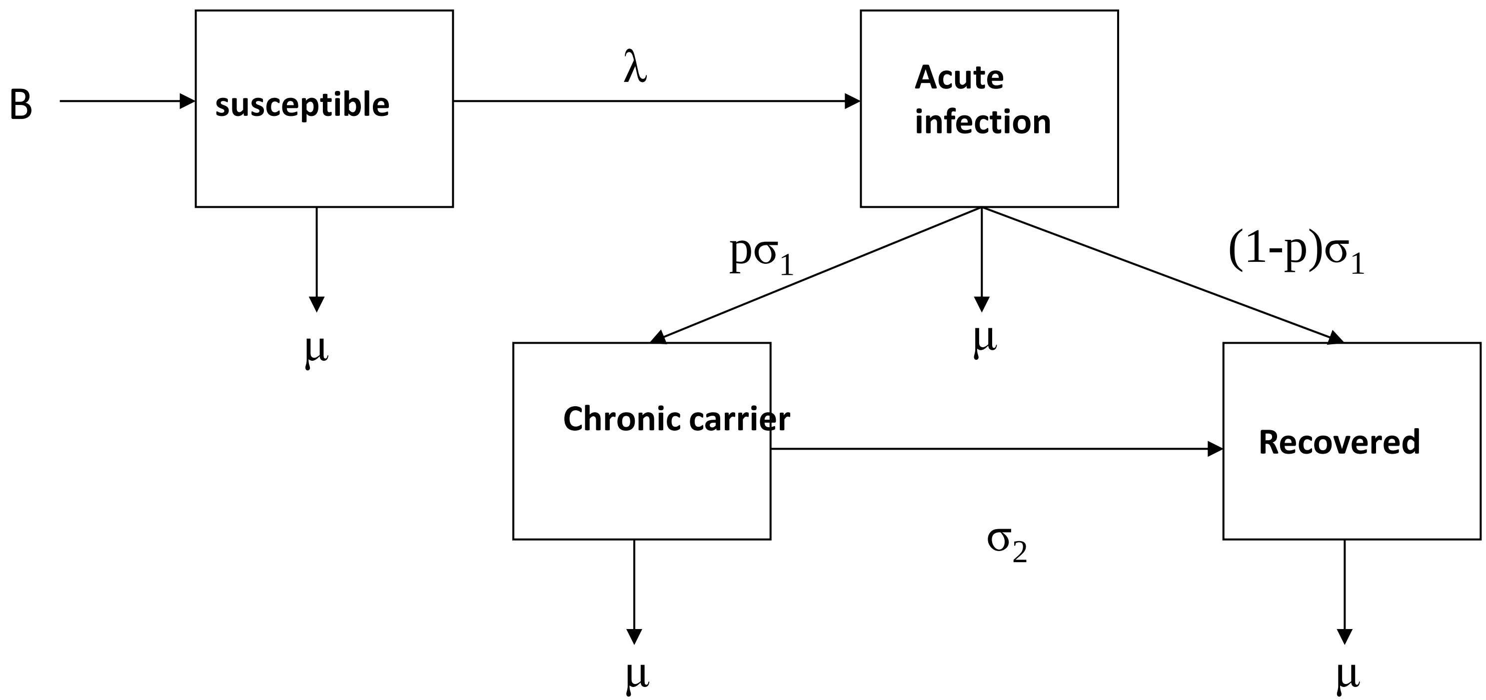
life expectancy with clinical AIDS: 10 years



Part 2:

Transmission model for hepatitis C among IDUs

A simple transmission model for hepatitis C model

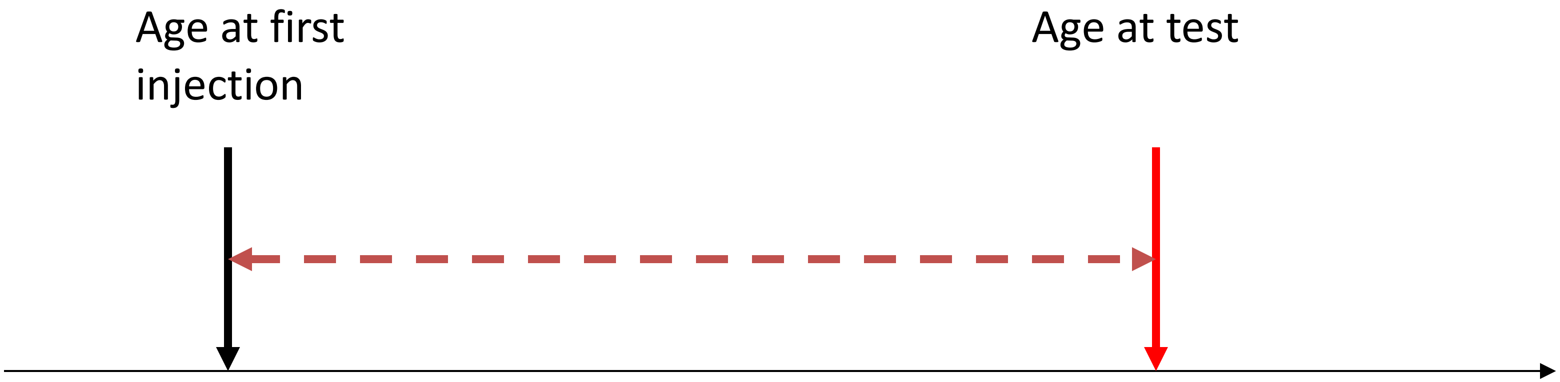


(ref: Monograph of EMCDDA 2004, chapter 5)

A simple transmission model for hepatitis C model

- Transmission model for hepatitis C among injecting drug users (IDUs).
- Transmission is related to the injecting process.
- Very high prevalence in the IDU population but low prevalence in the general population.

Exposure time



The time scale is the exposure time: the difference between the age at first injection and the age at test.

The ODE system

The model

$$\frac{dS(t)}{dt} = B\mu - \lambda(t)S(t) - \mu S(t)$$

$$\frac{dA(t)}{dt} = \lambda(t)S(t) - (P\sigma_1 + \mu)A(t)$$

$$\frac{dC(t)}{dt} = P\sigma_1 A(t) - \sigma_2 C(t) - \mu C(t)$$

$$\frac{dR(t)}{dt} = (1-P)\sigma_1 A(t) + \sigma_2 C(t) - \mu R(t)$$

Model parameters

B	Rate of entry to the IDU population.
$\lambda(t)$	Force of infection.
σ_1	Recovery rate.
P	Proportion of IDUs with carrier state.
σ_2	Recovery rate (carriers).
μ	Death rate.

The force of infection

Transmission
probability per contact

$$\lambda(t) = k\frac{(c_1 A(t) + c_2 C(t))}{N}$$

Rate of sharing injecting materials
(represent risk behavior factor)

Population
size

Specification of model parameters in R

Model parameters:

1. "Life expectancy" in the IDU population: 25 years.
2. Rate of sharing materials 15.
3. Transmission probabilities 0.3 (acute to susceptible)
4. Transmission probabilities 0.03 (carrier to susceptible)
5. Recovery rate (acute): ~2.5 months.
6. Duration as carrier: ~ 20 years.
7. Proportion of infected IDU that will be carrier: ~70%

```
>paraameters <- c(B=0.05,mu=0.05,k=15,ba=0.3,bc=0.05,sigma1=5,sigma2=0.05,rho=0.7)
> parameters
      B      mu       k      ba      bc  sigma1  sigma2     rho
   0.05    0.05   15.00    0.30    0.05    5.00    0.05    0.70
```

State variables

```
> state <- c(y1=0.99,y2=0.01,y3=0,y4=0)
> state
  y1   y2   y3   y4
0.99 0.01 0.00 0.00
```

At time zero: 99% are susceptible and 1% are infected.

Specification the transmission model in R

$$\frac{dS(t)}{dt} = B\mu - \lambda(t)S(t) - \mu S(t)$$

$$\frac{dA(t)}{dt} = \lambda(t)S(t) - (P\sigma_1 + \mu)A(t)$$

$$\frac{dC(t)}{dt} = P\sigma_1 A(t) - \sigma_2 C(t) - \mu C(t)$$

$$\frac{dR(t)}{dt} = (1-P)\sigma_1 A(t) + \sigma_2 C(t) - \mu R(t)$$

```
SIR<-function(t,state,parameters)
{
with(as.list(c(state, parameters)),
{
dy1 = B-k*ba*y1*y2-k*bc*y3*y1-mu*y1
dy2 = k*ba*y1*y2+k*bc*y3*y1-sigma1*y2-mu*y2
dy3 = rho*sigma1*y2-sigma2*y3-mu*y3
dy4= (1-rho)*sigma1*y2+sigma2*y3-mu*y4;
list(c(dy1,dy2,dy3,dy4))
})
}
```

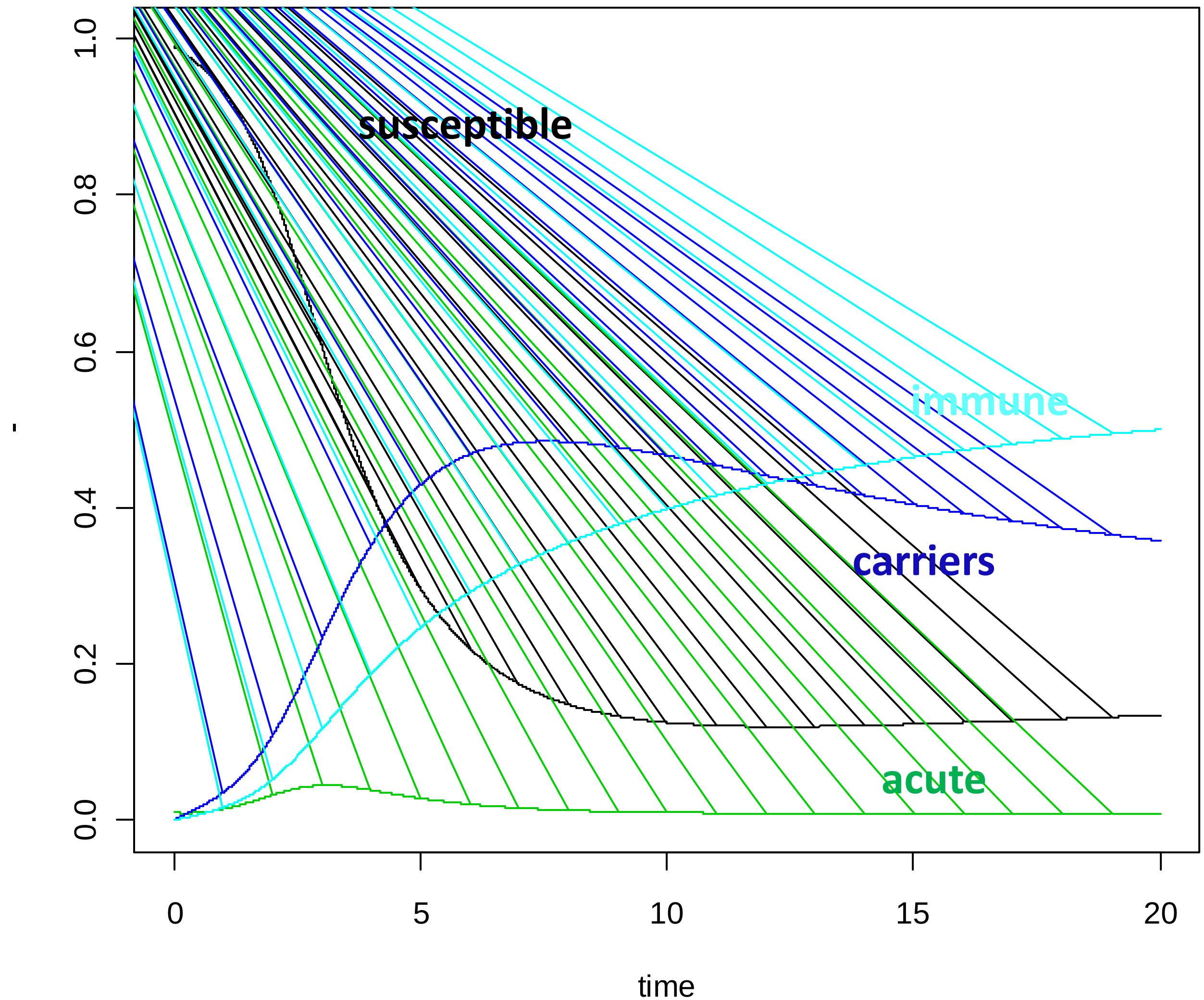
Specification the transmission model in R

The force of infection depends on the duration of injection.

```
SIR<-function(t,state,parameters)
{
with(as.list(c(state, parameters)),
{
dy1 = B-k*ba*y1*y2-k*bc*y3*y1-mu*y1
dy2 = k*ba*y1*y2+k*bc*y3*y1-sigma1*y2-mu*y2
dy3 = rho*sigma1*y2-sigma2*y3-mu*y3
dy4= (1-rho)*sigma1*y2+sigma2*y3-mu*y4;
list(c(dy1,dy2,dy3,dy4))
})
}
```

$$\boxed{\lambda(t) = k\frac{(c_1 A + c_2 C)}{N}}$$

Solution

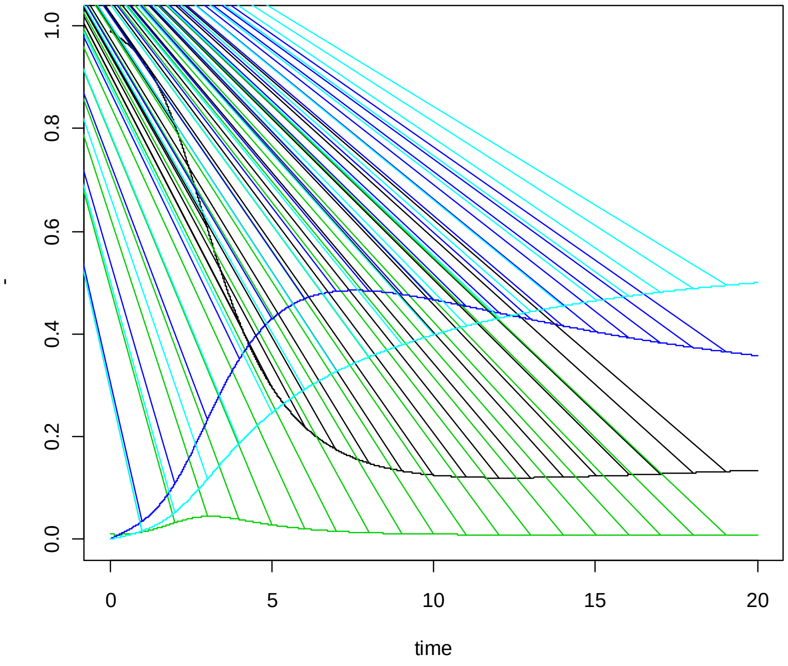


susceptible
immune
carriers
acute
1.0
0.8
0.6
0.4
0.2
0.0
0
5
10
15
20
time
-

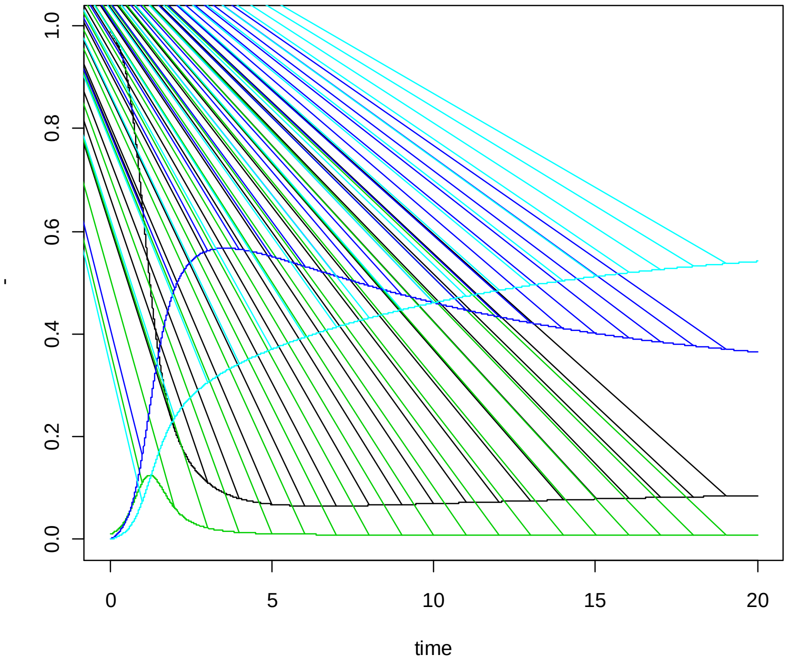
Change in sharing rate

The sharing rate increase from 15 to 25 (represent a population with higher risk behavior).

K=15

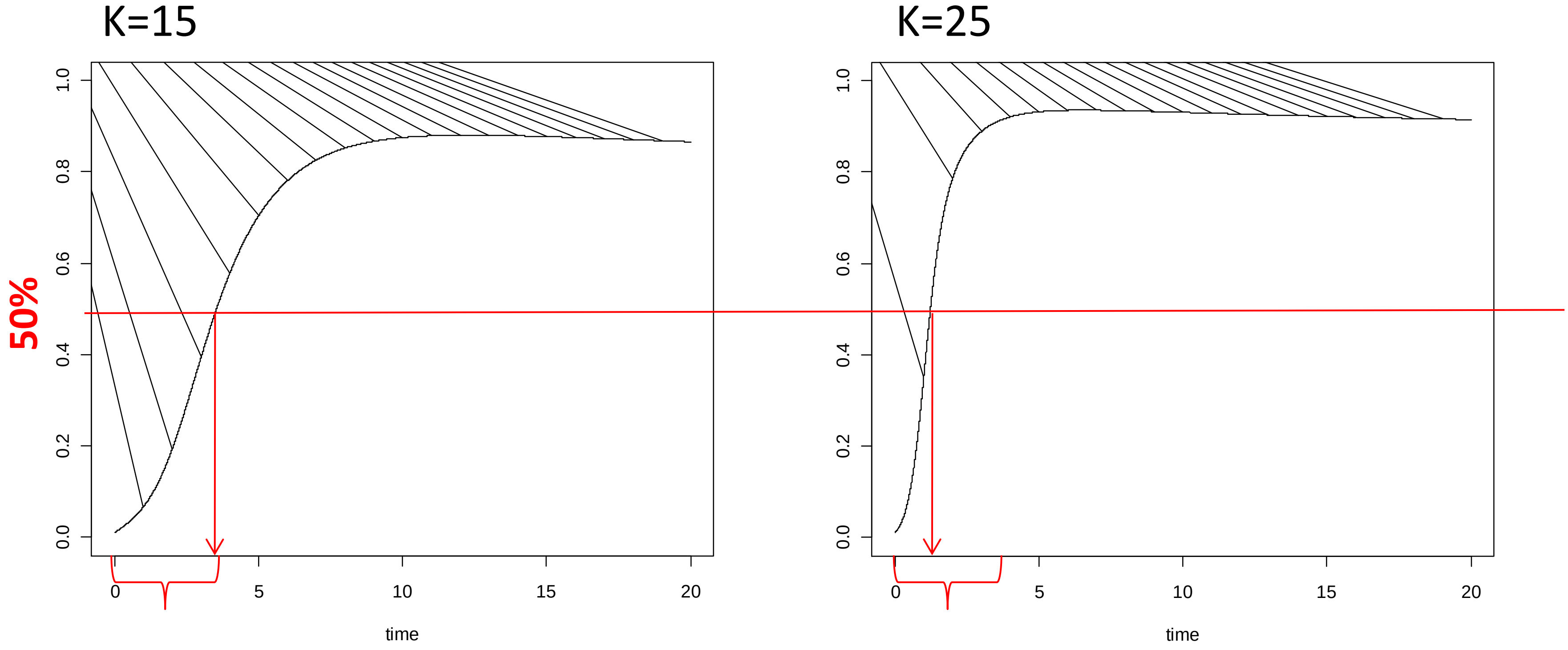


K=25



The prevalence

The duration of injected for a prevalence of 50% in the population.



Data and models

K=25.

Predicted prevalence after 5 years of injection: ~ 70%.