Contents

Introduction

Heavy metal pollution due to urbanization has a serious impact on humans and animals. In addition, the exposure to those toxicants can influence the negative effects of virus infections on individual hosts and alter animal movement (Kessler et al. 2018). To understand this, a hypothetical flying fox species is infected with a virus and a mathematical model explores the infection dynamics in toxicant-contaminated landscapes. *LINKJE MAKEN MET INFECTION, MOVEMENT EN DEMOGRAPHY*

Flying foxes are often used as bioindicators for heavy metal pollution, because they have a broad range of different habitats (Pulscher et al. 2020). They feed on fruiting plants in human environments, where they face exposure to heavy metals. Another reason why flying fox species are used in this model is because they are reservoir hosts of a virus named henipavirus. This virus can be transmitted to humans and other animals (Croser and Marsh 2013).

Toxicants can increase the infection susceptibility, but also influence animal movement. Toxicants can reduce movement capacity directly or indirectly. It can directly influence physical activity or indirectly affect memory or navigation ("Emerging Henipaviruses and Flying Foxes - Conservation and Management Perspectives" 2006). In the case of flying foxes, the human environments attract them as a result of their food consumption. This means that flying foxes are unlikely to move back to pristine environments. Infected flying foxes may also be incapable of moving away from contaminated areas.

NOG EVEN WAT ZEGGEN OVER DEMOGRAPHY

The model gives an insight in how the flying fox population size, infection prevalence and zoonotic spillover depend on the contamination rate of the landscape and the effect of toxicant exposure on infection, movement and survival (Sánchez, Altizer, and Hall 2020). *UIT LEGGEN WAT INFECTION PREVELANCE IS, NAMELIJK DE HOEVEELHEID INDIVIDUEN DIE IN EEN POPULATIE GEINFECTEERD ZIJN*

Methods

The model that describes the infection dynamics in toxicant-contaminated landscapes is characterized by four differential equations shown in figure 1. The four equations describe the population size of flying foxes in different habitats. A landscape is divided into a contaminated (T) and a pristine (P) area, and the flying foxes are classified by their infection status; infected (I) or susceptible (S). The model is written in R (version 4.1.3) and the DeSolve package (version 1.32) is imported in order to model the differential equations.

$$\frac{dS_P}{dt} = \left(b_0 - \frac{b_1(S_P+I_P)}{1-f}\right)(S_P+I_P) - mS_P - \beta_P S_P I_P + \gamma I_P - \sigma f S_P + \sigma(1-c_\sigma)(1-f)S_T$$

$$\frac{dI_P}{dt} = \beta_P S_P I_P - \gamma I_P - (m+\mu)I_P - \sigma f I_P + \sigma(1-c_\sigma)(1-f)I_T$$

$$\frac{dS_T}{dt} = \left(b_0 - \frac{b_1(S_T+I_T)}{f}\right)(S_T+I_T) - \frac{m}{1-c_m}S_T - \beta_T S_T I_T + \gamma I_T + \sigma f S_P - \sigma(1-c_\sigma)(1-f)S_T$$

$$\frac{dI_T}{dt} = \beta_T S_T I_T - \gamma I_T - \frac{m+\mu}{1-\alpha c_m} I_T + \sigma f I_P - \sigma(1-c_\sigma)(1-f)I_T$$

Figure 1: *differential equations used by the model. Each differential equation is highlighted by different color; green represents demography paramters, orange represents infection paramters and purple represents movement paramters. Each equation calculates the population size of a different group. The groups are: susceptible animals in a pristine habitat (S_P), infected animals in a pristine habitat (I_P,) susceptible animals in a toxic contaminated habit (S_T) and infected aminals in a toxid contamindated area (I_T). Image obtained from (Sánchez, Altizer, and Hall 2020)*

In figure 1 four differential equations are shown. Firstly, $\frac{dS_P}{dt}$ calculates the population size of the susceptible flying foxes which are located in a pristine area. Secondly, $\frac{dI_P}{dt}$ calculates the amount of infected flying foxes in a pristine area. Next, $\frac{dS_T}{dt}$ calculates the amount of flying foxes which are susceptible and in a toxic area. Finally, $\frac{dI_T}{dt}$ calculates the population size of the flying foxes which are infected and located in a toxic area.
Additionally, parts of the differential equations in figure 1 are colored. Each color represents a different process which may affect the population size with that infection status and habitat. Green is used to indicate demography, orange to indicate infection and purple to indicate movement.

Each equation is broken down into its parameters and are listed in figure 2.

process	parameter	definition	units	value
demography	m	natural mortality rate	year^{-1}	0.1
	b_0	maximum *per capita* birth rate	host^{-1} year^{-1}	0.4
	b_1	density-dependent per capita birth rate	year^{-1}	$(b_0-m)/50000 = 6e-6$
	c_m	cost of toxicants to survival		0.2
infection	β_P	transmission rate in pristine habitat	host^{-1} year^{-1}	0.006
	β_T	transmission rate in toxicant-contaminated habitat	host^{-1} year^{-1}	0.0015, 0.006, 0.0105
	γ	recovery rate	year^{-1}	36.5
	μ	disease-induced mortality rate	year^{-1}	0.25
	α	synergistic effect of infection and toxicants on survival		2
movement	f	fraction of the landscape that is toxicant-contaminated		0.01–0.99
	σ	*per capita* dispersal rate	year^{-1}	–log 0.1
	c_σ	cost of toxicants to dispersal		0.2, 0.8

Figure 2: *all of the paramters, definitoins, units and values used in the differential equations. The paramters are divided by demography, infection and movement. Image is obtained from (Sánchez, Altizer, and Hall 2020)*

As shown in figure 2; β_T, f and c_σ have different parameter values. These are used to modulate six different scenarios in which f is being changed, ranging from 0.01 to 0.99. This is the fraction of a landscape that is contaminated by toxicants. For each f, the model is initiated with a population of 50 000 , of which 100 where infected, and has run for a timespan of 50 years, the last values are then stored. This timespan is chosen because all differential equations are then at equilibrium.
The six scenarios can be divided into two parts. These parts are based upon the two different values of c_σ (see figure 2). c_σ is the cost of toxicants to dispersal of the animal. That is, the ability of an animal of switching from a toxic contaminated habitat to a pristine habitat. When c_σ is low the animal can easily move from the toxic to the pristine habitat. On the contrary, if c_σ is high it is hard for the animal to move from the toxic to the pristine habitat.
In both parts the effect of different transmission rates in a toxic contaminated habitat with respect to the transmission rate in a pristine habitat are simulated. This is done by keeping a constant β_P value and the changing the β_T values, resulting in three different scenarios per part:

- $\beta_T < \beta_P$: transmission in toxicant-contaminated habitat is lower than in pristine habitat.
- $\beta_T = \beta_P$: transmission is equal in both habitats.
- $\beta_T > \beta_P$: transmission in toxicant-contaminated habitat is enhanced.

Transmission in this case is the transferring of a pathogen or virus from host to host.

For all six scenarios the population size, infection prevalence and spillover risk are being calculated using the following equations:

$$\text{Population size} = S_P + I_P + S_T + I_T$$

$$\text{Infection prevelance} = \frac{I_T}{\text{population size}}$$

$$\text{Spillover risk} = \frac{I_T}{f}$$

Results

As mentioned earlier, six scenarios are being modulated. These scenarios are divided into two parts, in the first part a c_σ value of 0.2 is used and in the second part a value of 0.8. In both parts the different transmission rates are simulated. For each simulation the the population size, infection prevalence and spillover risk are shown in a plot.
In the first part of the results section compares all the different transmission rates to one and another. The second part compares the c_σ values.

Transmission rates

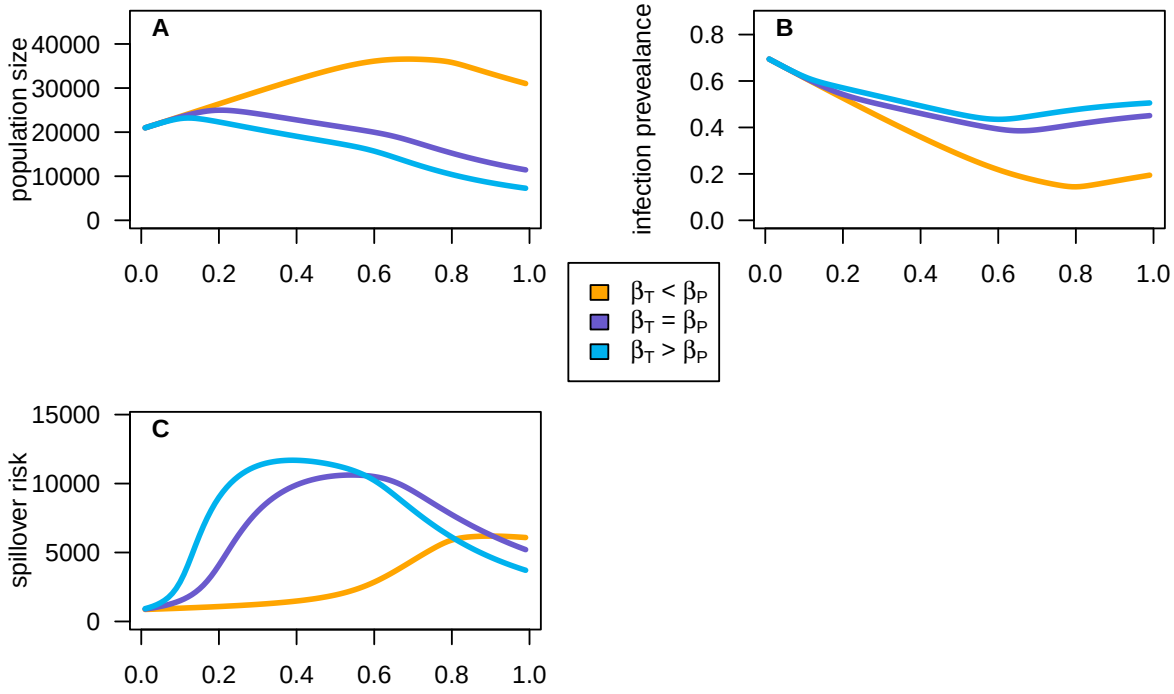

Figure 3: *modulated population size (A), infection prevalence (B) and spillover risk (C) with respect to the fraction of toxic-contaminated habitat. In all plots the line colors orange, purple and blue indicate* $beta_T < beta_P$, $beta_T = beta_P$ *and* $beta_T < beta_P$, *respectively. A* c_sigma *value of 0.2 was used.*

In figure 3 the population size, infection prevalence and spillover risk are shown with varying β_t values.

In figure 3A $\beta_T = \beta_P$ and $\beta_T > \beta_P$ show a similar trend. When the fraction of contaminant habitat (f) increases, the population size first increases a little and then declines slowly. However, the population size of $\beta_T = \beta_P$ has a higher increase until it declines resulting in a higher population size at different f's. Interestingly, when looking at $\beta_T < \beta_P$ an increase can be seen until an f of 0.7 is reached, which is way higher when compared to the other scenarios where it increased until approximately 0.15. After an f of 0.7 it declines.

In figure 3B $\beta_T = \beta_P$and $\beta_T > \beta_P$ are again very similar. A slow decline of infection prevalence can be seen until an f of approximately 0.65 is reached, after which it increases. Furthermore, $\beta_T < \beta_P$ shows a steeper and longer decrease as f increases. It then increases in the same way as $\beta_T = \beta_P$ and $\beta_T > \beta_P$.

In figure 3C $\beta_T = \beta_P$ and $\beta_T > \beta_P$ repeatedly show similar trends. They both have a sharp S-shaped increase with respect to an increasing value of f. Hereafter it declines. The same S-shaped increase can be seen when looking at

$\beta_T < \beta_P$. However, this increases is less steep and the optimum is reached at a higher f. Furthermore, when the optimum is reached it does not decline at all.

Altogether it seems like a similar trend in all graphs of figure 3 can be seen. $\beta_T = \beta_P$ and $\beta_T > \beta_P$ show very similar curves, where $\beta_T = \beta_P$ is delayed or more spread out. When looking at $\beta_T < \beta_P$ the same phenomenon can be seen, but more extreme. The increases and decreases are less steep and take longer with respect to an increasing f.

Comparing c_σ values

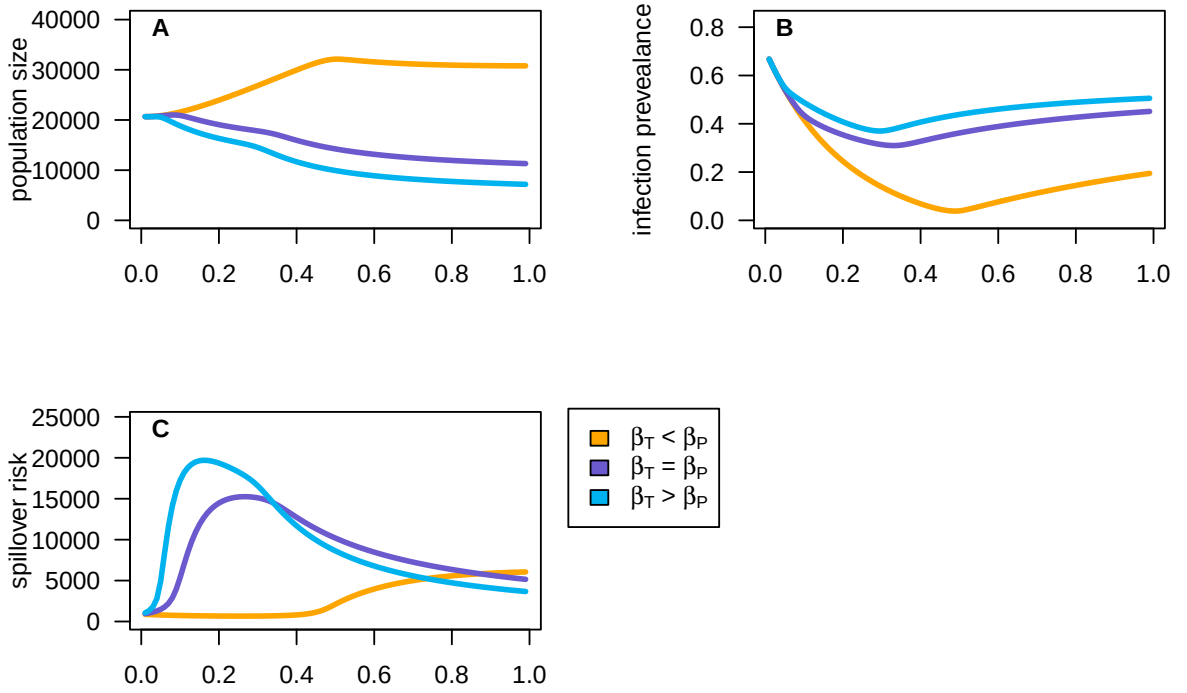

Figure 4: *modulated population size (A), infection prevalence (B) and spillover risk (C) with respect to the fraction of toxic-contaminated habitat. In all plots the line colors orange, purple and blue indicate* $beta_T < beta_P$, $beta_T = beta_P$ *and* $beta_T < beta_P$, *respectively. A* c_sigma *value of 0.8 was used.*

In figure 4 the population size, infection prevalence and spillover risk are shown with varying β_T values. These graphs will be mostly compared to the graphs in figure 3. In figure 4 a c_σ value of 0.8 was used, wheras figure 3 uses a c_σ of 0.2.

Figure 4A and figure 3A the lines of $\beta_T = \beta_P$ and $\beta_T > \beta_P$ are in both graphs very close together and show a similar trend. These lines show in figure 3A a small initial increase, which can not be seen in figure 4A. $\beta_T < \beta_P$ does have an initial increase in figure 4A and shows more of a kink at the inflection point, compared to a curve in figure 3A. This inflection point is also at a lower f, that is, it is shifted to the right. $\beta_T < \beta_P$ also has a lower maximum at this point of inflection.

The graph illustrated in figure 4B and figure 3B show a similar pattern in a way that $\beta_T = \beta_P$, $\beta_T > \beta_P$ and $\beta_T < \beta_P$ and first decline and then increase. In addition, the values of where the lines start and end are the same in figure 4B and 3B. However, the point of inflection happens at a lower f and the minimum of the line is lower. This results in a more stiff decrease and increase.

When looking at figure 4C compared to figure 3C, the following can be noticed. The lines in figure 4C are similar but more compressed and shifted to the left. In addition, the spillover risk values of the peaks are higher. This results in a more steep increase. Interestingly, when looking at $\beta_T < \beta_P$ in figure 4C a flat-line can be seen until an f of 0.4 is reached.

Collectively, all graphs in figure 4 are unlike in way that the lines are shifted to the right when compared to figure 3. On the contrary, similar values of the start and stop values can be seen in all graphs (A, B and C) and lines.

Discussion

With the model two different figures where created. The first one had a lower cost of toxicants to dispersal, in which different transmission rates were shown. In the second figure the different transmission rates with a higher cost of toxicants to dispersal was shown. First a possible explanation of the trends shown in figure 3 are given.

When the virus is less transmissible in toxicant-contaminated habitat then in pristine habitat (\textcolor{orange}{$\beta_T < \beta_P$), lower fractions of the toxicants might not have a large effect on transferring the the virus from host to host, this might mean that less flying foxes are infected with the virus (a lower infection prevalence) and less flying foxes die from infection (higher population size). The infection prevalance decreases because there are less infected flying foxes in toxic-contaminated habitat and a larger population size.

But when a virus is equally ($\beta_T = \beta_P$) or more ($\beta_T > \beta_P$) transmissible in toxicant-contaminated habitat, there is also a small increase in population size and a decrease in infection prevalence. However, in both situations the population size decreases sooner. This is because toxicants might amplify the negative effects of the virus, causing the virus to go from host to host sooner and therefor infect more flying foxes with the virus, When looking at the infection prevalence plot this might seem contradictory, since the infection prevalence is the ratio between infected animals in toxic-contaminated habitat and the population size, more infected animals might mean a lower population size, causing less infected animals in toxic-contaminated habitat and a lower population size, therefor a decline in infection prevalence.

It appears that in all three scenarios when there is a very high fraction of contaminated habitat, the population size (further) decrease. When looking at the equations there is a direct relation between f and demography and movement. In the equations about the toxicant-contaminated habitat, a higher f leads to less movement from the contaminated habitat to pristine habitat (- σ * (1 - c_σ) * (1 - f)I_T). This means that toxicant-contaminated habitats contain more flying foxes than pristine habitats. Assumed that a higher toxicant-contaminated habitat is also more urbanized, leading to more food sources for flying foxes, the exposure of toxicants to the flying foxes are higher and can cause more fatal cases. This leads to a decline in population size. Then the ratio of population size and amount of infected flying foxes in the toxicant habitat increase.

It seems that,when a virus is equally or more transmissible in toxicant-contaminated habitat that the spill-over risk occur at lower proportions of toxicant-contaminated habitat. Meaning that less flying foxes are needed to spill over diseases to humans. However when the transmission rate is less, the virus is only being spilled over at a high f. This could be because a higher fraction of contaminated habitat could mean more urbanization and more human-wildlife contact, and therefor an increase in spill-over risk.

When the cost of toxicants to dispersal (c_σ) is increased, it is harder for an animal to move from a toxic-contaminated habitat to a pristine habitat. This means that the chance of animal staying in the toxic-contaminated habitat is greater. This results in that the survival chance of an animal exposed to toxicants decreases, because it is difficult for the animal to move out of this harmful habitat. This effect can be seen in the results (figure 4AB), where the maximum population size is lower and this maximum is reached at a lower fraction of toxic-contaminated habitat. The rest of the explanations for the plots as described for c_σ = 2 are similar to the the movement of the lines in figure 4. A higher cost of toxicant dispersal simply means that the overall population size an prevalence is reduced, and that infections could be transferred to humans at even lower fractions of toxicant-contaminated habitat..

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Apendix

ODE Function

```
## ODE FUNCTION

# Load deSolve package
library(deSolve)

# Function with the models differential equations
wildlife_urbanization_model <- function(t, state, parameters) {
  with(as.list(c(state, parameters)),{

    dSp <- (b0 - (b1 * (Sp + Ip)) /(1-f) ) * (Sp + Ip) - m * Sp -  # demography
      beta_p * Sp * Ip + gamma * Ip -  # infection
      sigma * f * Sp + sigma * (1 - c_sigma) * (1 - f) * St  # movement


    dIp <-  beta_p * Sp * Ip - gamma * Ip -  # infection
      (m + mu) * Ip -  # demography
      sigma * f * Ip + sigma * (1 - c_sigma) * (1 - f) * It  # movement


    dSt <- (b0 - (b1 * (St + It) / f)) * (St + It) - (m / (1 - c_m)) * St -  # demography
      beta_t * St * It + gamma * It +  # infection
      sigma * f * Sp - sigma * (1 - c_sigma) * (1 - f) * St  # movement


    dIt <- beta_t * St * It - gamma * It -  # infection
      ((m + mu) / (1 - alpha * c_m)) * It +  # demography
      sigma * f * Ip - sigma * (1 - c_sigma) * (1 - f) * It  # movement


    list(c(dSp, dIp, dSt, dIt))
  })
}
```

Running the ODE function

```
## MODEL FUNCTION

run_model <- function(population = 50000, infected = 100, m = 0.1, b0 = 0.4,
                      c_m = 0.2, beta_p = 0.006, beta_t = 0.006, gamma = 36.5,
                      mu = 0.25, alpha = 2, sigma = -log(0.1), c_sigma = 0.2){

  # Create a data frame to store needed data
  df <- data.frame(matrix(nrow = 0, ncol = 8))
  colnames(df) <- c('f', 'Sp', 'Ip', 'St', 'It',
                    'pop_size', 'inf_prevalence', 'spillover')

  for (f in seq(0.01, 0.99, 0.01)){
    # Calculate b1 based on the function parameters
    b1 <- (b0 - m) / population

    # Calculate infection status per habitat
    Sp <- (population - infected) * (1 - f)
    Ip <- infected * (1 - f)
    St <- (population - infected) * f
    It <- infected * f

    # Creating a vector with the parameter values
    parameters <- c(m = m, b0 = b0, b1 = b1, c_m = c_m, beta_p = beta_p,
                    beta_t = beta_t, gamma = gamma, mu = mu, alpha = alpha,
                    f = f, sigma = sigma, c_sigma = c_sigma)

    # Creating a vector with the initial values
    state<- c(Sp = Sp, Ip = Ip, St = St, It = It)

    # Time frame of 50 years
    times <- seq(0, 50, 0.05)

    out <- tail(ode(y = state, times = times, func = wildlife_urbanization_model,
                    parms = parameters), 1)

    df[nrow(df) + 1,] <- c(f, out[2:5], sum(out[2:5]),
                           (out[3] + out[5])/sum(out[2:5]), out[5]/f)
    }

  return(df)
}
```

Obtaining data function

```
## OBTAIN DATA FUNCTION
obtain_data <- function(c_sigma){
  for (beta_t in c(0.0015, 0.006, 0.0105)){
    df <- run_model(beta_t = beta_t, c_sigma = c_sigma)
    if (beta_t == 0.0015){
      population_all <- data.frame('0.0015' = df$pop_size)
      infection_all <- data.frame('0.0015' = df$inf_prevalence)
      spillover_all <- data.frame('0.0015' = df$spillover)
    }
    if (beta_t == 0.006){
      population_all <- data.frame(population_all, '0.006' = df$pop_size)
      infection_all <- data.frame(infection_all, '0.006' = df$inf_prevalence)
      spillover_all <- data.frame(spillover_all, '0.006' = df$spillover)
    }
    if (beta_t == 0.0105){
      population_all <- data.frame(population_all, '0.0105' = df$pop_size)
      infection_all <- data.frame(infection_all, '0.0105' = df$inf_prevalence)
      spillover_all <- data.frame(spillover_all, '0.0105' = df$spillover)
    }
  }
  return(list(population_all, infection_all, spillover_all))
}
```

Plotting scenarios function

```
## PLOT FUNCTION
plot_scenario <- function(datasets, y_labels, line_cols, legends){
  plot_labels = c("A", "B", "C")
  f_seq = seq(0.01, 0.99, 0.01)
  for (item in 1:length(datasets)){
    data <- datasets[[item]]
    for (scenario in 1:3){
      if (scenario == 1){
        plot(data[,scenario] ~ f_seq, col = line_cols[scenario],
             type = 'l', lwd = 3, ylim = c(0, max(data) * 1.25),
             xlab = 'f', las = 1, ylab = "")
        title(ylab = y_labels[item], line = 3.3)
        text(x=0.05, y=max(data) * 1.2, labels = plot_labels[item], font = 2)
      }
      else{
        lines(data[,scenario] ~ f_seq, col = line_cols[scenario], lwd = 3)
      }
    }
  }
}
```

Running β_t scenarios

```
beta_t_data <- obtain_data(c_sigma = 0.2)
beta_t_labels <- c('population size', 'infection prevealance', 'spillover risk')
beta_t_cols <- c('orange', 'slateblue', 'deepskyblue2')
beta_t_legends <- c(expression(paste(beta[T], " < ", beta[P])),
                    expression(paste(beta[T], " = ", beta[P])),
                    expression(paste(beta[T], " > ", beta[P])))

par(mfrow=c(2,2), mar=c(3.1,5.1,3.1,2.1))
plot_scenario(datasets = beta_t_data, y_labels = beta_t_labels,
              line_cols = beta_t_cols, legends = beta_t_legends)
legend(1.1, 26000, legend = beta_t_legends, fill = beta_t_cols, xpd=NA)
```

Running c_σ scenarios

```
beta_t_data <- obtain_data(c_sigma = 0.8)
beta_t_labels <- c('population size', 'infection prevealance', 'spillover risk')
beta_t_cols <- c('orange', 'slateblue', 'deepskyblue2')
beta_t_legends <- c(expression(paste(beta[T], " < ", beta[P])),
                    expression(paste(beta[T], " = ", beta[P])),
                    expression(paste(beta[T], " > ", beta[P])))


par(mfrow=c(2,2), mar=c(3.1,5.1,3.1,2.1))
plot_scenario(datasets = beta_t_data, y_labels = beta_t_labels,
              line_cols = beta_t_cols, legends = beta_t_legends)
legend(1.1, 26000, legend = beta_t_legends, fill = beta_t_cols, xpd=NA)
```