Mathematical modeling of Nipah virus transmission

Outline of Doctoral Thesis

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Szeged
2023

Introduction

This doctoral thesis is concerned with the transmission dynamics of the Nipah virus by using compartmental models, both autonomous and non-autonomous. The main aim of the thesis was to investigate all possible transmissions of the Nipah virus and determine which parameters are the most influential in this regard.

The basic reproduction number ($\mathscr{R}_0$) describes the dynamics of the system, as also demonstrated in the case of our autonomous model to be a threshold parameter concerning disease extinction or persistence. For periodic compartmental models, $\mathscr{R}_0$ is defined as the spectral radius of an integral operator acting on the space of continuous periodic functions. In our non-autonomous model, our goal is to demonstrate that for $\mathscr{R}_0 < 1$, the disease-free periodic solution of our model is globally asymptotically stable, whereas, for $\mathscr{R}_0 > 1$, the disease remains endemic and there exists at least one positive periodic solution. Additionally, a modeling analysis to assess the effect of disease transmission from deceased individuals and an *SIRS* epidemic model for a zoonotic disease with a general nonlinear incidence rate assuming that the animal population has already reached an endemic equilibrium are analyzed in this dissertation.

The author's publications listed below serve as the foundation for the thesis, the last three of which are submitted to journals, and the first one is accepted:

(1) Saumen Barua, Attila Dénes. Global dynamics of a compartmental model for the spread of Nipah virus. Accepted in *Heliyon*.

(2) Saumen Barua, Attila Dénes. Global stability in an SIRS model with zoonotic transmission, nonlinear incidence rate and temporary immunity, submitted.

(3) Saumen Barua, Attila Dénes. A compartmental model for the spread of Nipah virus with periodic outbreaks, submitted.

(4) Saumen Barua, Attila Dénes. Global dynamics of a compartmental model to assess the effect of transmission from deceased. Accepted in *Math. Biosci.*

Global dynamics of a compartmental model for the spread of Nipah virus

Nipah virus (NiV) is a zoonotic virus meaning that it is transmitted between species from animals to humans and causes outbreaks of fatal disease in humans [1]. After the first identification of the virus in pig-farming villages in Peninsular Malaysia, outbreaks were seen in Singapore, Bangladesh, and India [2, 3, 4]. This emerging infectious disease has become one of the most alarming threats to public health due to its periodic outbreaks and extremely high mortality rate. WHO has included Nipah virus in its blueprint list including ten diseases and pathogens to be prioritized for R&D [5]. The disease has influenza-like symptoms including fever, headache, muscle pain, vomiting and pain in the throat. In critical cases inflammation of the brain and uncontrolled electrical activity take place in the brain, progressing to coma within 24 to 48 hours [6]. The animal host reservoir for NiV is the fruit bat also known as the flying fox, belonging to the *Pteropus* genus in the *Pteropodidae* family [7]. We establish and study a novel SIRS model to describe the dynamics of Nipah virus transmission, considering human-to-human as well as zoonotic transmission from bats and pigs. We determine the basic reproduction number which can be obtained as the maximum of three threshold parameters corresponding to various ways of disease transmission and determine in which of the three species the disease becomes endemic. By constructing appropriate Lyapunov functions, we completely describe the global dynamics of our model depending on these threshold parameters. Numerical simulations are shown to support our theoretical results and assess the effect of various intervention measures.

Model formulation

We develop a compartmental model considering transmission from bats to humans, bats to pigs, bats to bats, pigs to humans, pigs to pigs, and from humans to humans. That is, we do not consider transmission from humans to any of the two animal species and pig-to-bat transmission either as these ways of transmission have a negligible probability.

The total human population $N(t)$ at time t is divided into susceptibles ($S(t)$), infected ($I(t)$) and recovered ($R(t)$). Hence, $N(t) = S(t) + I(t) + R(t)$. The total pig (intermediate host) population $N_p(t)$ at time t is divided into susceptible ($S_p(t)$), infected ($I_p(t)$) and recovered ($R_p(t)$) individuals, so that $N_p(t) = S_p(t) + I_p(t) + R_p(t)$, similarly the total

bat population (host reservoir) $N_b(t)$ at time t is divided into susceptible ($S_b(t)$), infected ($I_b(t)$) and recovered ($R_b(t)$) individuals, such that $N_b(t) = S_b(t) + I_b(t) + R_b(t)$.

We denote the birth and death rates of humans by Λ and μ, respectively. There is also a disease-induced death rate, denoted by δ. Rates of human-to-human, pig-to-human and bat-to-human transmission are denoted by β_I, β_{ph} and β_{bh}, respectively. The rate of transmission among bats is denoted by β_b, while that of transmission among pigs by β_p. Transmission from bats to pigs is given by β_{bp}.

Infected humans are transferred to the recovered compartment at the rate γ (i.e. the average duration of the infectious period is $1/\gamma$ days) and θ is the rate of loss of temporary immunity acquired by recovered individuals, meaning that recovered individuals remain immune for $1/\theta$ days on average. We define all other parameters for pigs and bats in an analogous way, for these parameters, we introduce the subscripts p and b, respectively.

The system of differential equations established considering the above assumptions takes the form

$$\begin{aligned} S'(t) &= \Lambda - \beta_I S(t)I(t) - \beta_{ph} S(t)I_p(t) - \beta_{bh} S(t)I_b(t) - \mu S(t) + \theta R(t), \\ I'(t) &= \beta_I S(t)I(t) + \beta_{ph} S(t)I_p(t) + \beta_{bh} S(t)I_b(t) - (\mu + \delta + \gamma)I(t), \\ R'(t) &= \gamma I(t) - (\mu + \theta)R(t), \end{aligned} \tag{1a}$$

$$\begin{aligned} S_p'(t) &= \Lambda_p - \beta_p S_p(t)I_p(t) - \beta_{bp} S_p(t)I_b(t) - \mu_p S_p(t) + \theta_p R_p(t), \\ I_p'(t) &= \beta_p S_p(t)I_p(t) + \beta_{bp} S_p(t)I_b(t) - (\mu_p + \delta_p + \gamma_p)I_p(t), \\ R_p'(t) &= \gamma_p I_p(t) - (\mu_p + \theta_p)R_p(t), \end{aligned} \tag{1b}$$

$$\begin{aligned} S_b'(t) &= \Lambda_b - \beta_b S_b(t)I_b(t) - \mu_b S_b(t) + \theta_b R_b(t), \\ I_b'(t) &= \beta_b S_b(t)I_b(t) - (\mu_b + \delta_b + \gamma_b)I_b(t), \\ R_b'(t) &= \gamma_b I_b(t) - (\mu_b + \theta_b)R_b(t), \end{aligned} \tag{1c}$$

with nonnegative initial conditions.

It is important to note that due to the asymmetric transmission possibilities among the three species, subsystem (1c) can be decoupled from the rest of the equations of (4), furthermore, the subsystem consisting of equations (1b) and (1c) can also be decoupled from the human equations.

Basic properties

Lemma 1. *All solutions of model* (4) *started from nonnegative initial conditions will remain nonnegative for all forward time and will eventu-*

ally approach the forward invariant set $\Gamma = \{S, I, R, S_p, I_p, R_p, S_b, I_b, R_b \in \mathbb{R}^3_+ \times \mathbb{R}^3_+ \times \mathbb{R}^3_+ : 0 < N \leq \Lambda/\mu, 0 < N_p \leq \Lambda_p/\mu_p, 0 < N_b \leq \Lambda_b/\mu_b\}$.

Basic reproduction number

The basic reproduction number is given by $\mathscr{R}_0 = \max\{\mathscr{R}_0^1, \mathscr{R}_0^2, \mathscr{R}_0^3\}$, where $\mathscr{R}_0^1 = \frac{\beta_I \Lambda}{\mu(\gamma+\delta+\mu)}$, $\mathscr{R}_0^2 = \frac{\beta_p \Lambda_p}{\mu_p(\gamma_p+\delta_p+\mu_p)}$, $\mathscr{R}_0^3 = \frac{\beta_b \Lambda_b}{\mu_b(\gamma_b+\delta_b+\mu_b)}$.

Existence of endemic equilibria

Lemma 2. *The human-only endemic equilibrium* $\hat{E} := \big(\hat{S}, \hat{I}, \hat{R}, \hat{S}_p, 0, \hat{R}_p, \hat{S}_b, 0, \hat{R}_b,\big)$ *exists if and only if* $\mathscr{R}_0^1 > 1$.

Lemma 3. *The human- and pig-endemic equilibrium* $\tilde{E} := \big(\tilde{S}, \tilde{I}, \tilde{R}, \tilde{S}_p, \tilde{I}_p, \tilde{R}_p, \tilde{S}_b, 0, \tilde{R}_b\big)$ *exists if* $\mathscr{R}_0^2 > 1$.

Lemma 4. *The endemic equilibrium* $E^* := \big(S^*, I^*, R^*, S_p^*, I_p^*, R_p^*, S_b^*, I_b^*, R_b^*\big)$ *with the disease being endemic in all three species exists if and only if* $\mathscr{R}_0^3 > 1$ *and* $\mathscr{R}_0^2 > 1$

Stability analysis

Local stability of the equilibria

Theorem 5. *The disease free equilibrium* $E_0\big(\frac{\Lambda}{\mu}, 0, 0, \frac{\Lambda_p}{\mu_p}, 0, 0, \frac{\Lambda_b}{\mu_b}, 0, 0\big)$ *is locally asymptotically stable if* $\mathscr{R}_0^1 < 1, \mathscr{R}_0^2 < 1, \mathscr{R}_0^3 < 1$, *while* E_0 *is unstable if any one of the inequalities altered.*

Global stability of the equilibria

Theorem 6. *The disease-free equilibrium* $E_0\big(\frac{\Lambda}{\mu}, 0, 0, \frac{\Lambda_p}{\mu_p}, 0, 0, \frac{\Lambda_b}{\mu_b}, 0, 0\big)$ *is globally asymptotically stable* $\Gamma := \{(S(t), I(t), R(t), S_p(t), I_p(t), R_p(t), S_b(t), I_b(t), R_b(t)) \in \mathbb{R}^9_+\}$ *if* $\mathscr{R}_0 < 1$.

Theorem 7. *The human-only endemic equilibrium* $\hat{E} := \big(\hat{S}, \hat{I}, \hat{R}, \hat{S}_p, 0, \hat{R}_p, \hat{S}_b, 0, \hat{R}_b\big)$ *is globally asymptotically stable in*

$$\Gamma := \{(S(t), I(t), R(t), S_p(t), I_p(t), R_p(t), S_b(t), I_b(t), R_b(t)) \in \mathbb{R}^9_+\}$$

if $\mathscr{R}_0^1 > 1$, $\mathscr{R}_0^2 < 1$ *and* $\mathscr{R}_0^3 < 1$.

Theorem 8. *The equilibrium* $\tilde{E} := \big(\tilde{S}, \tilde{I}, \tilde{R}, \tilde{S}_p, \tilde{I}_p, \tilde{R}_p, \tilde{S}_b, 0, \tilde{R}_b\big)$, *where the disease is endemic among humans and pigs, is globally asymptotically stable in* $\Gamma := \{(S(t), I(t), R(t), S_p(t), I_p(t), R_p(t), S_b(t), I_b(t), R_b(t)) \in \mathbb{R}^9_+\}$ *if* $\mathscr{R}_0^2 > 1$ *and* $\mathscr{R}_0^3 < 1$.

Theorem 9. *The endemic equilibrium* $E^* := \big(S^*, I^*, R^*, S_p^*, I_p^*, R_p^*, S_b^*, I_b^*, R_b^*\big)$ *is globally asymptotically stable if* $\mathscr{R}_0^3 > 1$.

Numerical simulations

We performed numerical simulations to validate our model and to assess the efficiency of various possible intervention strategies. We fitted our model to real-world data. We chose the outbreak in 1999 in the Malaysian state Negeri Sembilan [8]. We also conducted an analysis using the Latin Hypercube Sampling along with the Partial Rank Correlation Coefficient (PRCC) method with $10,000$ Monte Carlo simulations per run. The input parameters considered for our PRCC analysis included all transmission rates and recovery rates, while the output parameter was chosen as the cumulative number of infected until the end of the time period under consideration in the fitting. Our results confirmed the important role of pigs in disease transmission and that decreasing the number of pigs by culling might be an efficient tool to eradicate the epidemic.

Global stability in an SIRS model with zoonotic transmission, nonlinear incidence rate and temporary immunity

Zoonotic spillover is the transmission of pathogens from vertebrate animals to humans and it is related to the direct or indirect interaction of humans with different animal species and pathogens they host, including handling, poaching, and consumption of meat from wild animals. Recently, there has been an increase in the occurrence rate of novel zoonotic illnesses, including Ebola virus disease, many strains of bird flu and swine flu, COVID-19, West Nile fever, Lassa fever, Nipah fever. In most of the mathematical models for zoonotic diseases, animals are included by considering analogous compartments as for humans. Our aim was to establish a simple, but general model for zoonotic diseases, incorporating many characteristics of them and assuming that the animal population has already reached an endemic equilibrium, making it possible to only consider human compartments establishing a novel type of model.

Model formulation

A simple *SIRS* model for a zoonotic disease can be established as

$$\begin{aligned} S'(t) &= \Lambda - f(I)S(t) - f_z(I_a(t))S(t) - \mu S(t) + \theta R(t), \\ I'(t) &= f(I)S(t) + f_z(I_a(t))S(t) - (\mu + \delta + \gamma)I(t), \\ R'(t) &= \gamma I(t) - (\mu + \theta)R(t), \end{aligned} \tag{2a}$$

$$\begin{aligned} S_a'(t) &= \Lambda_a - f_a(I_a(t))S_a(t) - \mu_a S_a(t) + \theta_a R_a(t), \\ I_a'(t) &= f_a(I_a(t))S_a(t) - (\mu_a + \delta_a + \gamma_a)I_a(t), \\ R_a'(t) &= \gamma_a I_a(t) - (\mu_a + \theta_a)R_a(t), \end{aligned} \tag{2b}$$

where S stands for susceptible, I for infected, R for recovered humans. Human-to-human transmission is described by a nonlinear incidence function f and zoonotic transmission by f_z. Human birth and death rates are denoted by Λ and μ, respectively. Disease-induced death rate is denoted by δ. Infected humans are transferred to the recovered compartment at the rate γ and θ is the rate of loss of temporary immunity acquired by recovered individuals. Compartments and parameters of the animal subsystem are introduced in an analogous way, with a lower index a.We assume that the disease is only transmitted from animals to humans but not the opposite way, enabling us to decouple the animal subsystem (2b) from the human subsystem (2a). It follows from [9, Theorem 3] that depending on the basic reproduction number, either the disease-free or the unique endemic equilibrium (S_a^*, I_a^*, R_a^*) of the animal subsystem is globally asymptotically stable. Here we assume that the disease is endemic among animals, hence, all solutions with positive initial conditions tend to the endemic equilibrium. We assume that the animal population has already reached this equilibrium, so, by substituting the limit value I_a^* of infected animals into the human subsystem (2a) and introducing the parameter $\xi := f_z(I_a^*)$, we may rewrite the human subsystem (2a) as

$$\begin{aligned} S'(t) &= \Lambda - f(I)S(t) - \xi S(t) - \mu S(t) + \theta R(t), \\ I'(t) &= f(I)S(t) + \xi S(t) - (\mu + \delta + \gamma)I(t), \\ R'(t) &= \gamma I(t) - (\mu + \theta)R(t), \end{aligned} \tag{3}$$

with nonnegative initial conditions.

Lemma 10. *All solutions of model 3 with nonnegative initial conditions have a positive invariant solution in the region* $\Omega = \{S, I, R \in \mathbb{R}_+^3 : 0 < N \leq \Lambda/\mu\}$.

Lemma 11. *Model* (3) *has a unique endemic equilibrium.*

Theorem 12. *The endemic equilibrium E^* is a globally asymptotically stable equilibrium of* (3)*.*

A compartmental model for the spread of Nipah virus in a periodic environment

Since the outbreak, very few mathematical models are available for the studies of the Nipah virus disease. Although some models [10, 11, 12] demonstrate that little research has been done regarding its transmission most of the models did not consider periodicity in the spread of the disease. Additionally, several studies focused on optimal control problems rather than the dynamics of the proposed models. So we tried to follow [13, 14, 15, 16] to observe NiV transmission in a periodic environment. Moreover, we have considered all possible transmissions from humans to animals and animals to humans.

Model formulation

We develop a compartmental model considering all possible transmissions from animals to humans, animals to animals, and from humans to animals with periodicity.

Total human population $N(t)$ at time t is divided into susceptibles $(S(t))$, exposed $(E(t))$, infected $(I(t))$ and recovered $(R(t))$. Hence, $N(t) = S(t) + E(t) + I(t) + R(t)$.

The total population of pigs (intermediate host) $N_p(t)$ at time t is divided into susceptible (S_p), exposed $(E_p(t))$, infected $(I_p(t))$ and recovered $(R_p(t))$ individuals, so that $N_p(t) = S_p(t) + E_p(t) + I_p(t) + R_p(t)$.

Similarly the total bat population (animal host reservoir) $N_b(t)$ at time t is divided into susceptible (S_b), exposed $(E_b(t))$, infected $(I_b(t))$ and recovered $(R_b(t))$ individuals, such that $N_b(t) = S_b(t)+E_b(t)+I_b(t)+R_b(t)$.

We denote the birth and death rates of humans by Π and μ, respectively. There is also a disease-induced death rate, denoted by δ. The force of infection for humans to humans, pigs, and bats for NiV transmission is given by $\beta I, \beta_{hp} I, \beta_p I$ and $\beta_{hb} I$ respectively. Again force of infection for Niv transmission from pigs to humans, pigs, and bats is expressed here as $\beta_{ph} I_p, \beta_p I_p$ and $\beta_{pb} I_p$. Furthermore, the force of infection for Niv transmission from bats to humans, pigs, and bats is expressed here as $\beta_{bh}(t) I_b, \beta_b I_b$

and $\beta_{bp}(t)I_b$. Here the parameters are the effective contact rate of susceptible individuals, who become infected from either humans or animals who became NiV infected.

Here the average duration of the infectious period is $1/\gamma$ days, so infected individuals are transferred to the recovered compartment at the rate γ and θ is the rate of loss of temporary immunity acquired by recovered individuals, meaning that recovered individuals remain immune for $1/\theta$ days on average. We define all other parameters for pigs and bats and apply the subscript p and b respectively for them. Note that time-dependent parameters in this model are $\beta_{bh}(t), \beta_{bp}(t)$ and $\Pi_b(t)$. So our model takes the form

$$\begin{aligned}
\frac{dS}{dt} &= \Pi - \beta SI - \beta_{ph} SI_p - \beta_{bh}(t) SI_b - \mu S + \theta R, \\
\frac{dE}{dt} &= \beta SI + \beta_{ph} SI_p + \beta_{bh}(t) SI_b - \nu E - \mu E, \\
\frac{dI}{dt} &= \nu E - (\mu + \delta + \gamma) I, \\
\frac{dR}{dt} &= \gamma I - (\mu + \theta) R,
\end{aligned} \tag{4a}$$

$$\begin{aligned}
\frac{dS_p}{dt} &= \Pi_p - \beta_p S_p I_p - \beta_{hp} S_p I - \beta_{bp}(t) S_p I_b - \mu_p S_p + \theta_p R_p, \\
\frac{dE_p}{dt} &= \beta_p S_p I_p + \beta_{hp} S_p I + \beta_{bp}(t) S_p I_b - \nu_p E_p - \mu_p E_p, \\
\frac{dI_p}{dt} &= \nu_p E_p - (\mu_p + \delta_p + \gamma_p) I_p, \\
\frac{dR_p}{dt} &= \gamma_p I_p - (\mu_p + \theta_p) R_p,
\end{aligned} \tag{4b}$$

$$\begin{aligned}
\frac{dS_b}{dt} &= \Pi_b(t) - \beta_b S_b I_b - \beta_{hb} S_b I - \beta_{pb} S_b I_p - \mu_b S_b + \theta_b R_b, \\
\frac{dE_b}{dt} &= \beta_b S_b I_b + \beta_{hb} S_b I + \beta_{pb} S_b I_p - \nu_b E_b - \mu_b E_b, \\
\frac{dI_b}{dt} &= \nu_b E_b - (\mu_b + \delta_b + \gamma_b) I_b, \\
\frac{dR_b}{dt} &= \gamma_b I_b - (\mu_b + \theta_b) R_b.
\end{aligned} \tag{4c}$$

The following initial conditions are associated with system (4), define $\phi = (S(0), E(0), I(0), R(0),$
$S_p(0), E_p(0), I_p(0), R_p(0), S_b(0), E_b(0), I_b, R_b(0))$ where $S(0) > 0$, $E(0) \geq$

0, $I(0) \geq 0$, $R(0) \geq 0$, $S_p(0) > 0$, $E_p(0) \geq 0$, $I_p(0) \geq 0$, $R_p(0) \geq 0$, $S_b(0) > 0$, $E_b(0) \geq 0$, $I_b(0) \geq 0$, and $R_b(0) \geq 0$.

The disease-free periodic solution

Existence and uniqueness of the disease-free ω-periodic solution

The system (4) has a unique disease-free periodic solution

$$E^* = (S_h^*, 0, 0, 0, S_p^*, 0, 0, 0, S_b^*(t), 0, 0, 0),$$

where $S_h^* = \Pi/\mu$ and $S_p^* = \Pi_p/\mu_p$.

To introduce the following result, we set $h^L = \sup_{t\in[0,\omega)} h(t)$ for a positive, continuous ω-periodic function $h(t)$.

Lemma 13. *There is $N_b^* = \frac{\Pi_b^L}{\mu_b} > 0$ such that each solution in $\mathbb{R}_+^{12}$ of (4) eventually enters*

$$G_{N^*} = \{(S, E, I, R, S_p, E_p, I_p, R_p, S_b, E_b, I_b, R_b) \in \mathbb{R}_+^{12} : N_h \leq N_h^*, N_p \leq N_p^*, N_b \leq N_b^*\},$$

and for each $N_b(t) \geq N_b^*$, G_{N^*} is positively invariant for system (4).

Theorem 16. *The disease-free periodic solution E^* of (4) is locally asymptotically stable if $\mathscr{R}_0 < 1$, whereas it is unstable if $\mathscr{R}_0 > 1$.*

Global stability of the disease-free solution

Theorem 18. *The disease-free periodic solution E^* of (4) is globally asymptotically stable if $\mathscr{R}_0 < 1$ and unstable if $\mathscr{R}_0 > 1$.*

Proposition 19. *The set X_0 and ∂X_0 are both positively invariant w.r.t. the flow defined in (4).*

Lemma 20. *If $\mathscr{R}_0 > 1$, then there exists a $\sigma > 0$ such that for any $x^0 \in X_0$, with $\|x^0 - E^*\| < \sigma$ we have $\limsup_{m\to\infty} d(\mathscr{P}^m(x^0), E^*) \geq \sigma$.*

Theorem 21. *Let $\mathscr{R}_0 > 1$. Then system (4) has at least one positive periodic solution and there exists an $\epsilon_1 > 0$ such that*

$$\liminf_{t\to\infty} (E(t), I(t), R(t), E_p(t), I_p(t), R_p(t), E_b(t), I_b(t), R_b(t))^T \geq (\epsilon_1, \epsilon_1, \epsilon_1, \epsilon_1, \epsilon_1, \epsilon_1, \epsilon_1, \epsilon_1, \epsilon_1)^T,$$

for all $\phi \in X_0$.

Global dynamics of a compartmental model to assess the effect of transmission from deceased

Several infectious diseases caused by pathogenic microorganisms (e.g. bacteria, viruses, parasites, or fungi) can be spread directly or indirectly, from person to person, however, apart from infection from infectious individuals, also corpses of those deceased due to a given epidemic may pose a risk of transmission, especially under special circumstances like natural disasters, an overwhelmed health care system, or due to traditional funerary practices. Examples for this phenomenon include plague, cholera, typhoid fever, tuberculosis, anthrax, smallpox, and influenza. Our aim was to establish and study a model highlighting on the effect transmission of pathogens from the deceased in general and also including partially protective vaccination.

Model formulation

We divide the total active human population, denoted by $N(t)$ at time t, into the following compartments: susceptibles ($S(t)$), vaccinated ($V(t)$), exposed ($E(t)$), infected ($I(t)$) and recovered ($R(t)$). Hence, $N(t) = S(t) + V(t) + E(t) + I(t) + R(t)$. An additional compartment D is introduced for deceased humans who passed away due to virus infection and have not been buried yet.

We denote the birth and natural death rates by Λ and μ, respectively. A fraction ρ (with $0 < \rho < 1$) of newborns not vaccinated after birth enter the susceptible compartment, while the remaining fraction enters the vaccinated compartment. The force of infection is given by $\lambda(t) = (\beta_1 I(t) + \beta_2 D(t))$, where β_1 represents the effective contact rate of susceptibles to get an infection from visibly infected individuals and β_2 is the effective unprotected contact rate of susceptibles, who become infected from dead bodies. Since vaccines are not fully efficient enough for a disease, we consider vaccine efficiency by introducing the parameter $\eta \in [0, 1]$. Infected individuals progress from the exposed to the infectious compartment at rate σ, and further, they leave the visibly infected compartment at rate γ (i.e. the average duration of the latent period is $1/\sigma$ days and that of the infectious period is $1/\gamma$ days). Disease-induced death affects individuals in the infected compartment. A fraction $0 < \delta < 1$ of those leaving the infectious compartment will die due to the infection and arrive in the D class, while the remaining fraction recovers and moves to the recovered compartment R. Infected corpses are buried at the rate α, i.e. the average time until the burial equals $1/\alpha$ days. Besides vaccination

right after birth, we also consider v as the vaccination rate of adults and with that, susceptible individuals are transferred to the vaccinated compartment. With the above notations and assumptions, our model takes the form

$$\begin{aligned} S'(t) &= \rho\Lambda - (\beta_1 I(t) + \beta_2 D(t))S(t) - vS(t) - \mu S(t), \\ V'(t) &= (1-\rho)\Lambda - \eta(\beta_1 I(t) + \beta_2 D(t))V(t) + vS(t) - \mu V(t), \\ E'(t) &= (\beta_1 I(t) + \beta_2 D(t))(S(t) + \eta V(t)) - (\sigma + \mu)E(t), \\ I'(t) &= \sigma E(t) - (\gamma + \mu)I(t), \\ R'(t) &= (1-\delta)\gamma I(t) - \mu R(t), \\ D'(t) &= \delta\gamma I(t) - \alpha D(t). \end{aligned} \tag{5}$$

The following initial conditions are associated with the system (5): $S(0) > 0, V(0) \geq 0, E(0) \geq 0, I(0) \geq 0, R(0) \geq 0, D(0) \geq 0$. We note that system (5) is similar to the model studied in [17], where the compartment of low-risk susceptibles corresponds to our vaccinated compartment. Apart from the main difference, the presence of vaccination of susceptible individuals (i.e. movement from the S class to the V class, which term clearly cannot be present in [17] due to the different meaning of the corresponding compartments), another important difference is that we use mass action incidence, which allows us to prove global asymptotic stability of the endemic equilibrium without additional conditions.

To obtain our analytical results described in Sections and , for technical reasons we will omit vaccination of adults, hence, we study the reduced system

$$\begin{aligned} S'(t) &= \rho\Lambda - (\beta_1 I(t) + \beta_2 D(t))S(t) - \mu S(t), \\ V'(t) &= (1-\rho)\Lambda - \eta(\beta_1 I(t) + \beta_2 D(t))V(t) - \mu V(t), \\ E'(t) &= (\beta_1 I(t) + \beta_2 D(t))(S(t) + \eta V(t)) - (\sigma + \mu)E(t), \\ I'(t) &= \sigma E(t) - (\gamma + \mu)I(t), \\ R'(t) &= (1-\delta)\gamma I(t) - \mu R(t), \\ D'(t) &= \delta\gamma I(t) - \alpha D(t) \end{aligned} \tag{6}$$

with the initial conditions $S(0) \geq 0, V(0) \geq 0, E(0) \geq 0, I(0) \geq 0, R(0) \geq 0, D(0) \geq 0$. We note that the assumption of omitting vaccination of older individuals is not merely technical: in the case of several childhood diseases, vaccination almost entirely takes place within a short time after birth and vaccination of older individuals is negligible.

Basic properties

Lemma 22. *All solutions of system* (6) *with non-negative initial conditions will enter the invariant region* $\phi = \{S, V, E, I, R, D \in \mathbb{R}^6_+ : 0 < N \leq \Lambda/\mu\}$.

The basic reproduction number

The basic reproduction number $\mathscr{R}_0$ is obtained as

$$\mathscr{R}_0 = \frac{(\alpha\beta_1+\beta_2\gamma\delta)\Lambda(\eta(1-\rho)+\rho)\sigma}{\alpha\mu(\gamma+\mu)(\mu+\sigma)}.$$

Existence of equilibria and stability analysis

Existence of endemic equilibrium

To determine the existence of endemic equilibria, we let the right-hand sides of all equations in (6) to be equal to zero. Solving the last three equations we get $E = \frac{I(\gamma+\mu)}{\sigma}, R = \frac{I\gamma(1-\delta)}{\mu}$ and $D = \frac{I\gamma\delta}{\alpha}$. Substituting these values in the first three equations, the system becomes

$$\begin{aligned} S\left(I\left(\beta_1 + \tfrac{\beta_2\gamma\delta}{\alpha}\right) + \mu\right) &= \Lambda\rho, \\ IV\left(\beta_1 + \tfrac{\beta_2\gamma\delta}{\alpha}\right)\eta + V\mu &= \Lambda(1-\rho), \\ t\frac{(\gamma+\mu)(\mu+\sigma)}{\sigma} &= \left(\beta_1 + \tfrac{\beta_2\gamma\delta}{\alpha}\right)(S + \eta V). \end{aligned} \tag{7}$$

Solving the first two equations of (7) for S and V in terms of I, we get $S = \frac{\alpha\Lambda\rho}{I(\alpha\beta_1+\beta_2\gamma\delta)+\alpha\mu}$ and $V = \frac{\alpha\Lambda(1-\rho)}{I(\alpha\beta_1+\beta_2\gamma\delta)\eta+\alpha\mu}$. Substituting these values in the third equation of (7) we get the quadratic equation $aI^2+bI+c=0$, where

$$\begin{aligned} a &= (\gamma+\mu)(\mu+\sigma)(\alpha\beta_1+\beta_2\gamma\delta)^2\eta, \\ b &= (\alpha\beta_1+\beta_2\gamma\delta)(\alpha\mu\eta(\gamma+\mu)(\mu+\sigma) + \alpha\mu(\gamma+\mu)(\mu+\sigma)(1-\mathscr{R}_0) \\ &\quad + \Lambda\sigma\rho(1-\eta)(\alpha\beta_1+\beta_2\gamma\delta)), \\ c &= \alpha^2\mu^2(\gamma+\mu)(\mu+\sigma)(1-\mathscr{R}_0). \end{aligned}$$

Clearly, $c < 0$ holds if and only if $\mathscr{R}_0 > 1$. As $a > 0$ independently of the parameters, using Vieta's formulas, we obtain that for $\mathscr{R}_0 \geq 1$, there is exactly one positive solution of the quadratic equation, while if $\mathscr{R}_0 < 1$, there is no positive solution. Therefore, there is no endemic equilibrium if $\mathscr{R}_0 < 1$ and there exists a unique endemic equilibrium if $\mathscr{R}_0 \geq 1$.

Local stability of the equilibria

Theorem 23. *The disease-free equilibrium* $E_0\left(\frac{\rho\Lambda}{\mu}, \frac{(1-\rho)\Lambda}{\mu}, 0, 0, 0, 0\right)$ *is locally asymptotically stable if* $\mathscr{R}_0 < 1$*, while* E_0 *is unstable otherwise.*

Global stability of the equilibria

Lemma 24. *For the limit superior of* $S(t)$ *and* $V(t)$*, the inequalities* $S^\infty \leq \frac{\rho\Lambda}{\mu}$ *and* $V^\infty \leq \frac{(1-\rho)\Lambda}{\mu}$ *hold.*

Theorem 25. *The disease-free equilibrium* $E_0\left(\frac{\rho\Lambda}{\mu}, \frac{(1-\rho)\Lambda}{\mu}, 0, 0, 0, 0\right)$ *is globally asymptotically stable in* $\Gamma := \{(S, V, E, I, R, D) \in \mathbb{R}^6_+\}$ *if* $\mathscr{R}_0 < 1$.

Theorem 26. *The endemic equilibrium* $E^* := \left(S^*, V^*, E^*, I^*, R^*, D^*\right)$ *is globally asymptotically stable in* $\Gamma := \{(S(t), V(t), E(t), I(t), R(t), D(t)) \in \mathbb{R}^6_+\}$ *if* $\mathscr{R}_0 > 1$.

Assessing the effects of transmission by deceased on disease spread

We performed numerical simulations to estimate the disease burden due to infection via contact with deceased individuals selecting three recent epidemics with different characteristics: Ebola, COVID-19, and Nipah fever. The simulations suggest that for such epidemics, a very efficient way to reduce the epidemic spread is to diminish this way of transmission as much as possible. On the contrary, generalizing the results of our simulations regarding the COVID-19 epidemic, we may conclude that if corpses are handled in a safe and adequate way and contact of susceptibles with them is reduced, then even in the case of a large-scale epidemic, one may more or less eliminate the contribution of deceased to disease spread.

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