

Sensitivity Analysis of Markovian Exact Reproduction Numbers

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Abstract. In this investigation a sensitivity analysis is presented by computing the partial derivatives and elasticities of several summary statistics with respect to parameters of the exact reproduction numbers, R_{e0} and R_p, for the stochastic SVIS model with an external source of infection and imperfect vaccine. These epidemic quantifiers are significant improvements over the basic reproductive number, R_0, to study the potential transmission of an epidemic under a stochastic approach. Our research provides theoretical and algorithmic results for understanding the impact of vaccination strategies on the spread of epidemics. We provide efficient tools to evaluate the importance of each model parameters in the propagation of the pathogen which have significant implications for public health policies aimed at controlling and preventing infectious disease outbreaks. We illustrate our methodology in the context of the transmission of the diphtheria virus.

Keywords: Stochastic epidemic model · Basic reproduction number · Perturbation problem · Imperfect vaccine

1 Introduction

Reproduction numbers are fundamental measures used to quantify the potential transmission of an epidemic in public health practice. There are several quantities that can be classified as reproduction numbers but the basic reproductive number, R_0, is probably the most widely used descriptor of disease spread and plays a privileged role in epidemiology under a deterministic approach. It represents the average number of secondary infections that result from a single infected individual over the course of his/her infectious period in a fully susceptible population. In simpler terms, R_0 measures how contagious a disease is and it is used to assess the potential for an epidemic or pandemic to occur. For example, for an SIS model high values of R_0 are associated with epidemics that persist for long time. In contrast, short epidemics are identified by lower values of the basic reproduction number [1].

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In a compartmental deterministic framework where population size is, as a premise infinite, the probability that two specific individuals have contact equals zero. However, in real-world situations, this behaviour is not true at all.

Moreover, the deterministic approach takes into account only average values and neglects that the agent itself diminishes the availability of susceptible individuals [2,3]. This has a bad consequence in the computation of R_0 because there is an overestimation of the number of contacts and secondary infections produced by the typical individual as authors discuss in [3]. Contacts of infectious individuals to whom have been previously infected should be eliminated [4,5]. Consequently, it seems relevant to explore alternative measures to R_0.

In a Markovian framework, these alternative measures are the exact reproduction number, R_{e0} and the population reproduction number, R_p. Both descriptors were described in 2013, by Artalejo and Lopez-Herrero, in [1], for stochastic SIS and SIR epidemic models. The authors described R_{e0} as a random variable that counts the exact number of secondary cases, produced by a typical infective individual during its entire period of infectiousness. R_p is a random variable that counts the number of infections produced by the whole infectious group no matter who is the spreader, prior the first recovery occurs. The main feature of the exact reproduction numbers is that they do not take into account contacts to previously infected individuals.

In [6], we extended the above mentioned work by including vaccination as strategy for controlling disease transmission in non-isolated populations. More precisely, we studied both exact reproduction numbers for a stochastic SVIS model with an external source of infection and imperfect vaccine.

In the present investigation our interest is in complementing the work in [6] by providing a local sensitivity analysis for both exact reproduction numbers.

In general a sensitivity analysis is a technique used to study perturbation effects of parameters that define a mathematical model on outputs of this model [7]. Recently, this methodology has been applied to various subjects of study as demography, ecology [8] and epidemiology [9]. In the context of stochastic epidemic models, this methodology can help us to identify which parameters have the greatest impact on the probabilistic behaviour of measures related to the spread of a pathogen. There is a vast literature that addresses this problem, for example in [10], author uses matrix calculus to obtain sensibilities and elasticities for moments of the random variable time until absorption, time spent in transitory states and number of visits to transitory states before the absorption in a continuous-time Markov chain. In [11], authors determine the most influential parameters in the spread of malaria by computing sensitivity indices of the basic reproduction number. In [12], authors analyze the perturbation problem through matrix calculus in a LD-QBD process and provide algorithms to compute elasticities related to the random variable maximum visits to a state before absorption. To supplement information, we refer the interested reader to the following works for further investigation on the topic [13–15].

The remainder of the present paper is organized as follows. In Sect. 2, we give a description of the stochastic SVIS model with an external source of infection

and imperfect vaccine, and introduce the exact reproduction numbers R_{e0} and R_p. In Sects. 3 and 4, a local sensitivity analysis is conducted via derivatives and elasticities for the exact reproduction numbers. Finally, in Sect. 5 and for diphtheria outbreaks, we illustrate theoretical and algorithmic derivations provided in previous sections by presenting numerical results related to disease spread, followed by some conclusions.

2 Quantifying the Potential Transmission in a Stochastic SVIS Model with an External Source of Infection and Imperfect Vaccine

The stochastic SVIS model with an external source of infection and imperfect vaccine was introduced in [6]. There we consider a constant and moderate size population, N, that is afflicted by a disease that does not confers immunity. Individuals in the population are well mixed and the topological structure of the contact network established by the individuals of the host population is not important to describe the expansion of the epidemic. Population is not closed and in the sense that, the pathogen can be transmitted by direct contact with an infected individual within or outside of the population. The internal and external transmission rates are β and ξ, respectively. Each infected individual recovers from the disease at rate γ. Prior the start of the epidemic and to assure herd immunity, a percentage of the population is vaccinated to be protected from the disease. However, this vaccine is not perfect and it fails with probability h.

We define the random variables, $V(t)$, $I(t)$ and $S(t)$ that count the number of vaccinated, infected and susceptible individuals at any time $t \geq 0$, respectively. As we are considering a constant size population, the number of susceptible individuals can be calculated as $S(t) = N - V(t) - I(t)$. According to above hypotheses, the evolution of the epidemic process is modeled as the following bi-dimensional Markov chain,

$$X = \{(V(t), I(t)), t \geq 0\}.$$

The state space of the Markov chain, X, is $\mathsf{S} = \{(v, i) : 0 \leq v \leq v_0,\ 0 \leq i \leq N - v\}$ and includes $(v_0 + 1)\,(N + 1 - v_0/2)$ states.

The exact reproduction number, R_{e0}, quantifies the potential transmission of an epidemic and it is described as the number of infections produced by a marked individual during its entire infectious period. To quantify the global potential transmission of an epidemic, we introduce the exact population number, R_p, that counts infections produced by the entire infectious population previously to the first recovery occurs. Both random measures are directly related to the recovery time of infectious individuals. Throughout this interval of time population contains at least one infected individual. Consequently, the CTMC, X, evolves in the following subset of S, which is decomposed in levels according to the number of vaccine-protected individuals

$$\widehat{S} = \bigcup_{v=0}^{v_0} \widehat{L}(v) = \bigcup_{v=0}^{v_0} \{(v, i) : 1 \leq i \leq N - v\}.$$

The perturbation analysis will be conducted for performance measures of the exact reproduction numbers, R_{e0} and R_p. In that sense, we introduce factorial moments of both variables. Factorial moments of the exact reproduction number, R_{e0}, conditioned to a generic state $(v,i) \in \widehat{S}$ are defined as follows

$$m^k_{v,i} = \begin{cases} 1, & \text{if } k = 0, \\ E\left[R_{e0}\left(R_{e0}-1\right)\cdots\left(R_{e0}-k+1\right)|(V(0)=v, I(0)=i)\right], & \text{if } k > 0. \end{cases}$$

Factorial moments of the population reproduction number conditioned to a generic state $(v,i) \in \widehat{S}$ is defined as follows

$$M^k_{v,i} = \begin{cases} 1, & \text{if } k = 0, \\ E\left[R_{p}\left(R_{p}-1\right)\cdots\left(R_{p}-k+1\right)|(V(0)=v, I(0)=i)\right], & \text{if } k > 0. \end{cases}$$

3 Sensitivity Analysis of the Factorial Moments of R_{e0}

The sensitivity analysis is relevant in the modeling of epidemics, particularly when the model parameters are estimated from a given data set. This methodology allows researchers to assess the robustness of their model, ensuring that it provides accurate and reliable insights into the spread and control of infectious diseases. In that sense, our interest is to quantify how small variations in each model parameter can affect in mathematical epidemic model output and to evaluate the importance and the influence of each model parameter in the expansion of an epidemic.

The perturbation problem will be approached through derivatives and elasticities of expected values and standard deviations of the exact reproduction numbers, that provide information about model parameters.

The elasticity of a general random variable, Y, respect to a model parameter, θ, is defined as

$$\varepsilon_Y = \frac{(\partial Y/\partial\theta)}{(Y/\theta)}. \tag{1}$$

To address this study we rely on matrix calculus and we start by computing first derivative of conditional factorial moments of order k of R_{e0}, $m^k_{v,i}$, for any $(v,i) \in \widehat{\mathcal{S}}$ and $k \geq 1$, with respect to the whole set of model parameters $\theta = (\theta_1, \theta_2, \theta_3, \theta_4)^T = (\beta, \xi, \gamma, h)^T$, where T denotes matrix transposition.

The first partial derivative of the factorial moments of order $k \geq 0$, regarding parameter θ_r, with $r \in \{1,2,3,4\}$ is denoted by $\frac{\partial m^k_{v,i}}{\partial \theta_r}$, and gives the exchange rate of $m^k_{v,i}$, for changing values of θ_r, when the rest of the parameters are constant. We compute them as follows.

We recall that Equation (7) in [6], involves factorial moments of order k, $m^k_{v,i}$, has the following expression for any $(v,i) \in \widehat{\mathcal{S}}$ and are computed, starting from boundary conditions $m^0_{v,i} = 1$, by applying Algorithm 1 in [6].

$$m_{v,i}^k = (1-\delta_{v,0})\left(\frac{\beta_{v,i}}{q_{v,i}} m_{v-1,i+1}^k + k\frac{\beta_v^*}{q_{v,i}} m_{v-1,i+1}^{k-1}\right) + \frac{\gamma_{i-1}}{q_{v,i}} m_{v,i-1}^k$$
$$+(1-\delta_{i,N-v})\left(\frac{\alpha_{v,i}}{q_{v,i}} m_{v,i+1}^k + k\frac{\alpha_{v,i}^*}{q_{v,i}} m_{v,i+1}^{k-1}\right), \tag{2}$$

where $\delta_{a,b}$ denotes the Dirac's delta function (defined as 1 when $i=j$, and 0 otherwise) and coefficients, for any $(v,i) \in \widehat{\mathcal{S}}$, are $\alpha_{v,i} = \left(\frac{\beta i}{N} + \xi\right)(N-v-i)$, $\alpha_{v,i}^* = \frac{\beta}{N}(N-v-i)$, $\beta_{v,i} = h\left(\frac{\beta i}{N} + \xi\right)v$, $\beta_v^* = h\frac{\beta}{N}v$ and $\gamma_i = \gamma i$.

In what follows we omit the corresponding Dirac's delta terms to ease notation.

Taking derivatives on (2) respect to each single parameter of the model and keeping the others constant, we obtain the following expression that involves both factorial moments and its derivatives, conditioned to a generic state $(v,i) \in \widehat{\mathcal{S}}$, for any $k > 0$.

$$-\gamma_{i-1}\frac{\partial m_{v,i-1}^k}{\partial\theta_r} + q_{v,i}\frac{\partial m_{v,i}^k}{\partial\theta_r} - \alpha_{v,i}\frac{\partial m_{v,i+1}^k}{\partial\theta_r} = \beta_{v,i}\frac{\partial m_{v-1,i+1}^k}{\partial\theta_r} \tag{3}$$
$$+ k\beta_v^*\frac{\partial m_{v-1,i+1}^{k-1}}{\partial\theta_r} + k\alpha_{v,i}^*\frac{\partial m_{v,i+1}^{k-1}}{\partial\theta_r} + \frac{\partial\beta_{v,i}}{\partial\theta_r} m_{v-1,i+1}^k + k\frac{\partial\beta_v^*}{\partial\theta_r} m_{v-1,i+1}^{k-1}$$
$$+ k\frac{\partial\alpha_{v,i}^*}{\partial\theta_r} m_{v,i+1}^{k-1} + \frac{\partial\gamma_{i-1}}{\partial\theta_r} m_{v,i-1}^k - \frac{\partial q_{v,i}}{\partial\theta_r} m_{v,i}^k + \frac{\partial\alpha_{v,i}}{\partial\theta_r} m_{v,i+1}^k.$$

We continue introducing the following notation for the derivatives of conditional moments of order $k \geq 0$ respect to each parameter θ_j, with $r \in \{1,2,3,4\}$

$$\frac{\partial m_{v,i}^k}{\partial\theta_r} = A_{v,i}^k(\theta_r)$$

and we define $\rho_{v,i}^k(\theta_r)$ as

$$\rho_{v,i}^k(\theta_r) = \frac{\partial\beta_{v,i}}{\partial\theta_r} m_{v-1,i+1}^k + k\frac{\partial\beta_v^*}{\partial\theta_r} m_{v-1,i+1}^{k-1} + k\frac{\partial\alpha_{v,i}^*}{\partial\theta_r} m_{v,i+1}^{k-1}$$
$$+\frac{\partial\gamma_{i-1}}{\partial\theta_r} m_{v,i-1}^k - \frac{\partial q_{v,i}}{\partial\theta_r} m_{v,i}^k + \frac{\partial\alpha_{v,i}}{\partial\theta_r} m_{v,i+1}^k.$$

Hence, for any $(v,i) \in \widehat{\mathcal{S}}$, Eq. (3) and boundary conditions can be expressed as follows

$$-\gamma_{i-1}A_{v,i-1}^k(\theta_r) + q_{v,i}A_{v,i}^k(\theta_r) - \alpha_{v,i}A_{v,i+1}^k(\theta_r) = \tag{4}$$
$$\beta_{v,i}A_{v-1,i+1}^k(\theta_r) + k\beta_v^*A_{v-1,i+1}^{k-1}(\theta_r) + k\alpha_{v,i}^*A_{v,i+1}^{k-1}(\theta_r) + \rho_{v,i}^k(\theta_r),$$

$$A^0_{v,i}(\theta_r) = 0. \tag{5}$$

Taking derivatives of rates $\alpha^*_{v,i}$, $\alpha_{v,i}$, β^*_v, $\beta_{v,i}$, γ_{i-1} and $q_{v,i}$ regarding each model parameter, $\theta_r \in \{\beta, \xi, \gamma, h\}$, we obtain that

$$\rho^k_{v,i}(\theta_r) = \begin{cases} \frac{N-v-i}{N}(km^{k-1}_{v,i+1} + im^k_{v,i+1} - im^k_{v,i}) & \\ +\frac{hv}{N}(km^{k-1}_{v-1,i+1} + im^k_{v-1,i+1} - im^k_{v,i}), & \text{if } \theta_j = \beta, \\ hv(m^k_{v-1,i+1} - m^k_{v,i}) + (N-v-i)(m^k_{v,i+1} - m^k_{v,i}), & \text{if } \theta_j = \xi, \\ (i-1)(m^k_{v,i-1} - m^k_{v,i}), & \text{if } \theta_j = \gamma, \\ v(\frac{\beta i}{N} + \xi)(m^k_{v-1,i+1} - m^k_{v,i}) + k\frac{\beta v}{N} m^{k-1}_{v-1,i+1}, & \text{if } \theta_j = h. \end{cases}$$

We obtain the related derivatives by solving the system of Eqs. (3). These equations can be expressed in matrix form and they can be solved by applying an inverse matrix method in a recursively way for each parameter, θ_r and taking into account the boundary conditions (5). This result is summarized in Theorem 1.

Theorem 1. *Given a fixed initial number of vaccinated individuals, v_0 and for each model parameter, $\theta_r \in \{\beta, \xi, \gamma, h\}$ derivatives in the set $\{A^k_{v,i}(\theta_r) : (v,i) \in \widehat{\mathcal{S}}\}$ are recursively computed from the following equations for any $k \geq 0$ and any level $0 \leq v \leq v_0$ as follows*

$$\mathbf{A^0_v}(\theta_\mathbf{r}) = \mathbf{0}_{N-v}, \text{ for } 0 \leq v \leq v_0, \tag{6}$$

$$\begin{aligned} \mathbf{R_v A^k_v}(\theta_\mathbf{r}) &= (1-\delta_{v,0})(\mathbf{D}_{\beta,v}\widehat{\mathbf{A}}^k_{\mathbf{v-1}}(\theta_r) + k\mathbf{D}^*_{\beta,v}\widehat{\mathbf{A}}^{k-1}_{\mathbf{v-1}}(\theta_r)) + k\mathbf{D}^*_{\alpha,v}\widetilde{\mathbf{A}}^{k-1}_{\mathbf{v}}(\theta_r) \\ &+ (1-\delta_{v,0})(\mathbf{D}'_{\beta,v}\widehat{\mathbf{m}}^k_{\mathbf{v-1}} + k(\mathbf{D}^*_{\beta,v})'\widehat{\mathbf{m}}^{k-1}_{\mathbf{v-1}}) \\ &+ k(\mathbf{D}^*_{\alpha,v})'\widetilde{\mathbf{m}}^{k-1}_{\mathbf{v}} - \mathbf{R_v}'\mathbf{m_v}^k, \end{aligned} \tag{7}$$

where matrices appearing in Eqs. (6) and (7) are described as the following $\mathbf{R_v}$ and its gradient matrix $\mathbf{R_v}'$ are tridiagonal square matrices of dimension $N-v$ with non-null entries given by

$$\mathbf{R_v}(i,j) = \begin{cases} -\gamma_{i-1}, \text{ if } j = i-1 \text{ and } 2 \leq i \leq N-v, \\ q_{v,i}, \quad \text{if } j = i \text{ and } 1 \leq i \leq N-v, \\ -\alpha_{v,i}, \text{ if } j = i+1 \text{ and } 1 \leq i \leq N-v-1, \end{cases}$$

$$\mathbf{R_v}'(i,j) = \begin{cases} -\frac{\partial \gamma_{i-1}}{\partial \theta_r}, \text{ if } j = i-1 \text{ y } 2 \leq i \leq N-v, \\ \frac{\partial q_{v,i}}{\partial \theta_r}, \quad \text{if } j = i \text{ and } 1 \leq i \leq N-v, \\ -\frac{\partial \alpha_{v,i}}{\partial \theta_r}, \text{ if } j = i+1 \text{ and } 1 \leq i \leq N-v-1. \end{cases}$$

$\mathbf{D}_{\beta,\mathbf{v}}$, $\mathbf{D}^*_{\beta,\mathbf{v}}$ $\mathbf{D}^*_{\alpha,\mathbf{v}}$ and their respective gradient matrices $\mathbf{D}'_{\beta,\mathbf{v}}$, $(\mathbf{D}^*_{\beta,\mathbf{v}})'$ and $(\mathbf{D}^*_{\alpha,\mathbf{v}})'$ are diagonal matrices of dimension $(N-v)$, with non-null diagonal elements given by $\mathbf{D}_{\beta,v}(i,i) = \beta_{v,i}$, $\mathbf{D}^*_{\beta,v}(i,i) = \beta^*_{v,i}$, $\mathbf{D}^*_{\alpha,v}(i,i) = \alpha^*_{v,i}$, $\mathbf{D}'_{\beta,\mathbf{v}}(i,i) = \frac{\partial \beta_{v,i}}{\partial \theta_r}$, $\mathbf{D}^*_{\beta,\mathbf{v}}{}'(i,i) = \frac{\partial \beta^*_{v,i}}{\partial \theta_r}$, $\mathbf{D}^*_{\alpha,\mathbf{v}}{}'(i,i) = \frac{\partial \alpha^*_{v,i}}{\partial \theta_r}$, for $1 \leq i \leq N-v$.

The rest of vectors are defined as follows: $\mathbf{A_v^k} = (A_{v,1}^k, ..., A_{v,N-v}^k)^T$, $\widetilde{\mathbf{A}}_\mathbf{v}^\mathbf{k} = (A_{v,2}^k, ..., A_{v,N-v}^k, 0)^T$, $\widehat{\mathbf{A}}_\mathbf{v}^\mathbf{k} = (A_{v,2}^k, ..., A_{v,N-v}^k)^T$, $\mathbf{m_v^k} = (m_{v,1}^k, ..., m_{v,N-v}^k)^T$, $\widetilde{\mathbf{m}}_\mathbf{v}^\mathbf{k} = (m_{v,2}^k, ..., m_{v,N-v}^k, 0)^T$, $\widehat{\mathbf{m}}_\mathbf{v}^\mathbf{k} = (m_{v,2}^k, ..., m_{v,N-v}^k)^T$, *and* $\mathbf{0}_{N-v}$ *is a all-zeros vector of dimension* $N - v$.

Algorithm 1 shows how to proceed to compute the related derivatives in an ordered and efficient way, starting from $k = 0$ in natural order and for $0 \leq v \leq v_0$.

Algorithm 1. The derivatives of the moments of order $k \geq 0$, $m_{v,i}^k$ can be determined numerically according to the following scheme

Input: α, β, γ, h, k_{max}, θ_r, $m_{v,i}^k$ *for any* $(v,i) \in \widehat{S}$ *and* $0 \leq k \leq k_{max}$

Step 1: Set $A_{N-v}^0 = 0_{N-v}$ for $0 \leq v \leq N - v$.

Step 2: Set $k = 1$ and $v = 0$

Step 2a: Compute

$$\mathbf{A^1_{N-v}}(\theta_r) = \mathbf{R_v^{-1}}((\mathbf{D}^*_{\alpha,v})'(\theta_r)\widetilde{\mathbf{m}}_\mathbf{v}^{k-1} - \mathbf{R}'_\mathbf{v})$$

Step 2b: Set $v = v + 1$ and compute

$$\mathbf{A^1_{N-v}}(\theta_r) = \mathbf{R_v^{-1}}(\mathbf{D}_{\beta,v}\widehat{\mathbf{A}}^k_{\mathbf{v-1}}(\theta_r) + (\mathbf{D}'_{\beta,v}(\theta_r)\widehat{\mathbf{m}}^1_{\mathbf{v-1}}(\mathbf{D}^*_{\beta,v})'(\theta_r)\widehat{\mathbf{m}}^0_{\mathbf{v-1}}) + (\mathbf{D}^*_{\alpha,v})'(\theta_r)\widetilde{\mathbf{m}}^0_\mathbf{v} - \mathbf{R}'_\mathbf{v}(\theta_r)).$$

Step 2c: If $v < v_0$ go to Step 2b.

Step 3: Set $k = k + 1$ and $v = 0$

Step 3a: Compute

$$\mathbf{A^k_{N-v}}(\theta_r) = \mathbf{R_v^{-1}}(k\mathbf{D}^*_{\alpha,v}\widetilde{\mathbf{A}}^{k-1}_\mathbf{v}(\theta_r) + k(\mathbf{D}^*_{\alpha,v})'(\theta_r)\widetilde{\mathbf{m}}_\mathbf{v}^{k-1} - \mathbf{R}'_\mathbf{v}(\theta_r)\mathbf{m_v}^k).$$

Step 3b: Set $v = v + 1$ and compute

$$\begin{aligned}\mathbf{A^1_{N-v}}(\theta_r) = \quad & \mathbf{R_v^{-1}}(\mathbf{D}_{\beta,v}\widehat{\mathbf{A}}^k_{\mathbf{v-1}}(\theta_r) + k\mathbf{D}^*_{\beta,v}\widehat{\mathbf{A}}^{k-1}_{\mathbf{v-1}}(\theta_r) + k\mathbf{D}^*_{\alpha,v}\widetilde{\mathbf{A}}^{k-1}_\mathbf{v}(\theta_r) + \mathbf{D}'_{\beta,v}(\theta_r)\widehat{\mathbf{m}}^k_{\mathbf{v-1}} \\ & + k(\mathbf{D}^*_{\beta,v})'(\theta_r)\widehat{\mathbf{m}}^{k-1}_{\mathbf{v-1}}) + k(\mathbf{D}^*_{\alpha,v})'(\theta_r)\widetilde{\mathbf{m}}_\mathbf{v}^{k-1} - \mathbf{R}'_\mathbf{v}(\theta_r)\mathbf{m_v}^k).\end{aligned}$$

Step 3c: If $v < v_0$ go to Step 3b.

Step 3d: If $k < k_{max}$ go to Step 3.

Output: $A_{v,i}^k(\theta_r)$ *for any* $(v,i) \in \widehat{S}$ *and* $0 \leq k \leq k_{max}$

When conducting sensitivity analysis in conditional moments, it is not sufficient to rely on a single derivative. Instead, we must solve Eq. (7) once for each parameter. This is particularly relevant for models with a large number of parameters, where an approach to differentiating matrix-valued functions of vector arguments is needed. Matrix calculus allows us to collect partial derivatives with respect to a vector into vectors and matrices of derivatives, which simplifies the process of solving systems of differential equations. A helpful resource for reviewing the notation and properties of matrix calculus can be found in [18]. Furthermore, from Eq. (7) in Theorem 1 and applying the mentioned methodology we derive the following expression

$$\begin{aligned}\frac{d\mathbf{m_v^k}}{d\boldsymbol{\theta}'} &= -(\mathbf{R_v^{-1}}(\mathbf{D}_{\beta,v}\widehat{\mathbf{m}}_{\mathbf{v-1}}^{\mathbf{k}} + \mathbf{D}_{\beta,v}^{*}\widehat{\mathbf{m}}_{\mathbf{v-1}}^{\mathbf{k-1}} + k\mathbf{D}_{\alpha v}^{*}\widetilde{\mathbf{m}}_{\mathbf{v-1}}^{\mathbf{k-1}})' \otimes \mathbf{R_v^{-1}})\frac{dvec\mathbf{R_v}}{d\boldsymbol{\theta}'} \\ &+ \mathbf{R_v^{-1}}(\mathbf{D}_{\beta,v}\widehat{\mathbf{A}}_{\mathbf{v-1}}^{\mathbf{k}}(\theta) + \mathbf{D}_{\beta,v}^{*}\widehat{\mathbf{A}}_{\mathbf{v-1}}^{\mathbf{k-1}}(\theta) + k\mathbf{D}_{\alpha,v}^{*}\widetilde{\mathbf{A}}_{\mathbf{v}}^{\mathbf{k-1}}(\theta)) \\ &+ ((\widehat{\mathbf{m}}_{\mathbf{v-1}}^{\mathbf{k}} \otimes \mathbf{R_v^{-1}})\frac{dvec\mathbf{D}_{\beta,\mathbf{v}}}{d\boldsymbol{\theta}'} + (\widehat{\mathbf{m}}_{\mathbf{v-1}}^{\mathbf{k-1}} \otimes \mathbf{R_v^{-1}})\frac{dvec\mathbf{D}_{\beta,\mathbf{v}}^{*}}{d\boldsymbol{\theta}'} \\ &+ k(\widehat{\mathbf{m}}_{\mathbf{v}}^{\mathbf{k-1}} \otimes \mathbf{R_v^{-1}})\frac{dvec\mathbf{D}_{\beta,\mathbf{v}}^{*}}{d\boldsymbol{\theta}'},\end{aligned} \tag{8}$$

and initial conditions $\frac{\partial \mathbf{m_v^0}}{\partial \boldsymbol{\theta}'} = \mathbf{0}_{(N-v)\times 4}$, for any $0 \leq v \leq v_0$ and $k \geq 1$, where $\frac{d\mathbf{m_v^k}}{d\boldsymbol{\theta}'}$ is the Jacobian matrix with entries given by $\frac{dm_{v,i}^{k}}{d\theta_r}$, $\otimes$ represents Kronecker product and $vec(A)$ is the column-wise vectorization of the matrix A.

Following we derive explicit expressions for the expected and standard deviation elasticises of R_{e0} that are needed to obtain the numerical results in Sect. 5.

For a given state $(v,i) \in \widehat{\mathsf{S}}$, derivatives of conditioned expected values and standard deviations respect to any model parameter, θ_r, denoted by $\frac{\partial E[R_{e0}]}{\partial \theta_r}$ and $\frac{\partial Sd[R_{e0}]}{\partial \theta_r}$ respectively, can be computed as follows

$$\frac{\partial E[R_{e0}]}{\partial \theta_r} = \frac{\partial m_{v,i}^{1}}{\partial \theta_r} = A_{v,i}^{1}(\theta_r), \tag{9}$$

$$\begin{aligned}\frac{\partial Sd[R_{e0}]}{\partial \theta_r} &= \frac{\partial (m_{v,i}^{2} + m_{v,i}^{1} - (m_{v,i}^{1})^2)^{\frac{1}{2}}}{\partial \theta_r} \\ &= \frac{A_{v,i}^{2}(\theta_r) + A_{v,i}^{1}(\theta_j) - 2m_{v,i}^{1}A_{v,i}^{1}(\theta_r)}{2Sd[R_{e0}]}.\end{aligned} \tag{10}$$

Applying elasticity definition (1) and Expressions (9) and (10), the elasticities for the mean and standard deviation of R_{e0}, conditioned to any state $(v,i) \in \widehat{\mathcal{S}}$, respect to each model parameter θ_r are given by

$$\varepsilon_{E[R_{e0}]} = \frac{\partial E[R_{e0}]/\partial \theta_r}{E[R_{e0}]/\theta_r} = \frac{A_{v,i}^{1}(\theta_r)}{m_{v,i}^{1}/\theta_r},$$

$$\varepsilon_{Sd[R_{e0}]} = \frac{\partial Sd[R_{e0}]/\partial \theta_r}{Sd[R_{e0}]/\theta_r} = \frac{\theta_r(A_{v,i}^{2}(\theta_r) + A_{v,i}^{1}(\theta_r) - 2m_{v,i}^{1}A_{v,i}^{1}(\theta_r))}{2Sd^2[R_{e0}]}.$$

4 Sensitivity Analysis of the Factorial Moments of R_p

In this section we derive a sensitivity analysis for the random variable, R_p.

We apply an analogous methodology as in the previous section so we omit the procedure and only we give the results obtained.

We recall that in [6], we obtained the following equations involving R_p-Factorial moments of order $k \geq 1$, for any $(v,i) \in \widehat{\mathcal{S}}$

$$q_{v,i}M_{v,i}^{k} = \alpha_{v,i}\left(kM_{v,i+1}^{k-1} + M_{v,i+1}^{k}\right) + \beta_{v,i}\left(kM_{v-1,i+1}^{k-1} + M_{v-1,i+1}^{k}\right), \tag{11}$$

with boundary conditions

$$M^0_{v,i} = 1.$$

These factorial moments are necessary to obtained the related derivatives and it can be done with the help of Theorem 2 in [6].

We introduce the following notation for the first derivatives of the R_p-Factorial moments order k, respect to each parameter θ_r, $\frac{\partial M^k_{v,i}}{\partial \theta_r}$, and $\widetilde{\rho}^k_{v,i}(\theta_r)$

$$\begin{aligned}\frac{\partial M^k_{v,i}}{\partial \theta_r} &= \mathbb{A}^k_{v,i}(\theta_r),\\ \widetilde{\rho}^k_{v,i}(\theta_r) &= -\frac{\partial q_{v,i}}{\theta_r} M^k_{v,i} + \frac{\partial \alpha_{v,i}}{\theta_r}[kM^{k-1}_{v,i+1} + M^k_{v,i+1}]\\ &\quad + \frac{\partial \beta_{v,i}}{\partial \theta_r}[kM^{k-1}_{v-1,i+1} + M^k_{v-1,i+1}].\end{aligned}$$

Taking derivatives on Eq. (11), respect to each parameter θ_r and applying the above notation, we obtain the following equations for any $k \geq 0$ and any $(v,i) \in \widehat{\mathcal{S}}$

$$\begin{aligned}q_{v,i}\mathbb{A}^k_{v,i}(\theta_r) - \alpha_{v,i}\mathbb{A}^k_{v,i+1}(\theta_r) &= \alpha_{v,i}k\mathbb{A}^{k-1}_{v,i+1}(\theta_r) + \beta_{v,i}[k\mathbb{A}^{k-1}_{v-1,i+1}(\theta_r)\\ &\quad + \mathbb{A}^k_{v-1,i+1}(\theta_r)] + \widetilde{\rho}^k_{v,i}(\theta_r),\end{aligned} \tag{12}$$

with boundary conditions

$$\mathbb{A}^0_{v,i}(\theta_r) = 0, \tag{13}$$

and

$$\widetilde{\rho}^k_{v,i}(\theta_r) = \begin{cases} \frac{(N-v-i)i}{N}[kM^{k-1}_{v,i+1} + M^k_{v,i+1} - M^k_{v,i}] & \\ +\frac{hvi}{N}[kM^{k-1}_{v-1,i+1} + M^k_{v-1,i+1} - M^k_{v,i}], & \text{if } \theta_r = \beta,\\ (N-v-i)[kM^{k-1}_{v,i+1} + M^k_{v,i+1} - M^k_{v,i}] & \\ +hv[kM^{k-1}_{v-1,i+1} + M^k_{v-1,i+1} - M^k_{v,i}], & \text{if } \theta_r = \xi,\\ -iM^k_{v,i}, & \text{if } \theta_r = \gamma,\\ (\frac{\beta i}{N} + \xi)v[kM^{k-1}_{v-1,i+1} + M^k_{v-1,i+1} - M^k_{v,i}], & \text{if } \theta_r = h. \end{cases}$$

At any level $0 \leq v \leq v_0$, Eqs. (12) can be solved by applying matrix techniques for $k > 0$ and $1 \leq i \leq N - v$, and derivatives of factorial moments of order $k \geq 0$ of the conditioned variables of R_p are obtained with the help of Theorem 2.

Theorem 2. *Given a fixed initial number of vaccinated individuals, v_0 and for each model parameter, $\theta_r \in \{\beta, \xi, \gamma, h\}$ derivatives in the set $\{\mathbb{A}^k_{v,i}(\theta_r) : (v,i) \in \widehat{\mathcal{S}}\}$ are recursively computed from the following equations for any $k \geq 0$ and any level $0 \leq v \leq v_0$ as follows*

$$\begin{aligned}\mathbf{A^0_v}(\theta_\mathbf{r}) &= \mathbf{0}_{N-v}, \\ \mathbf{H_v A^k_v}(\theta_\mathbf{r}) &= k\mathbf{L_v}\widehat{\mathbf{A}}^{\mathbf{k-1}}_{\mathbf{v}}(\theta_\mathbf{r}) + \mathbf{D_v}[k\widetilde{\mathbf{A}}^{k-1}_{v-1}(\theta_r) + \widetilde{\mathbf{A}}^k_{v-1}(\theta)] - \mathbf{H}'_v(\theta_r)\mathbf{M}^k_v\end{aligned} \tag{14}$$

$$+ \mathbf{D}'_{\mathbf{v}}(\theta_r)[\widetilde{\mathbf{M}}^{k-1}_{v-1} + \widetilde{\mathbf{M}}^{k}_{v-1}] + k\mathbf{L}'_{\mathbf{v}}(\theta_r)\widehat{\mathbf{M}}^{k-1}_{v}, \tag{15}$$

where $\mathbf{A}^k_v = (\mathbb{A}^k_{v,1}, ..., \mathbb{A}^k_{v,N-v})^T$, $\widetilde{\mathbf{A}}^k_{v-1} = (\mathbb{A}^k_{v-1,2}, ..., \mathbb{A}^k_{v-1,N-v+1})^T$, $\widehat{\mathbf{A}}^{k-1}_v = (\mathbb{A}^{k-1}_{v,2}, ..., \mathbb{A}^{k-1}_{v,N-v}, 0)^T$, $\widetilde{\mathbf{M}}^k_{v-1} = (M^k_{v-1,2}, ..., M^k_{v-1,N-v+1})^T$, $\widehat{\mathbf{M}}^{k-1}_v = (M^{k-1}_{v,2}, ..., M^{k-1}_{v,N-v}, 0)^T$. $\mathbf{H_v}$ *and its gradient matrix* $\mathbf{H}'_{\mathbf{v}}$ *are squared bi-diagonal matrices of dimension* $(N-v)$*, with non-null entries given by*

$$\mathbf{H_v}(i,j) = \begin{cases} q_{v,i}, & \text{if } j = i \text{ and } 1 \le i \le N-v, \\ -\alpha_{v,i}, & \text{if } j = i+1 \text{ and } 1 \le i \le N-v-1, \end{cases}$$

$$\mathbf{H}'_{\mathbf{v}}(i,j) = \begin{cases} \frac{\partial q_{v,i}}{\partial \theta_r}, & \text{if } j = i \text{ and } 1 \le i \le N-v, \\ \frac{-\partial \alpha_{v,i}}{\partial \theta_r}, & \text{if } j = i+1 \text{ and } 1 \le i \le N-v-1. \end{cases}$$

$\mathbf{D_v}$, $\mathbf{L_v}$ *and their respective gradient matrices,* $\mathbf{D}'_{\mathbf{v}}$ *and* $\mathbf{L}'_{\mathbf{v}}$ *are diagonal matrices of dimension* $(N-v)$*, with non-null diagonal elements given by* $\mathbf{D_v}(i,i) = \beta_{v,i}$, $\mathbf{D}'_{\mathbf{v}}(i,i) = \frac{\partial \beta_{v,i}}{\partial \theta_r}$, $\mathbf{L_v}(i,i) = \alpha_{v,i}$, $\mathbf{L}'_{\mathbf{v}}(i,i) = \frac{\partial \alpha_{v,i}}{\partial \theta_r}$.

We compute factorial moments of the related random variable with the help of Algorithm 2.

Algorithm 2. The derivatives of the moments of order $k \ge 0$, $M^k_{v,i}$, can be determined numerically according to the following scheme

Input: α, β, γ, h, k_{max}, θ_r, $M^k_{v,i}$ *for any* $(v,i) \in \widehat{S}$ *and* $0 \le k \le k_{max}$

Step 1: Set $A^0_{N-v} = 0_{N-v}$ for $0 \le v \le N-v$.

Step 2: Set $k = 1$ and $v = 0$

Step 2a: Compute

$$\mathbf{A^1_{N-v}}(\theta_r) = \mathbf{H_v}^{-1}(\mathbf{L}'_{\mathbf{v}}(\theta_r)\widehat{\mathbf{M}}^{\mathbf{0}}_{\mathbf{v}} - \mathbf{H_v}'(\theta_r)\mathbf{M^1_v})$$

Step 2b: Set $v = v+1$ and compute

$$\mathbf{A^1_{N-v}}(\theta_r) = \mathbf{H_v}^{-1}(\mathbf{D_v}\widetilde{\mathbf{A}}^{\mathbf{1}}_{\mathbf{v-1}}(\theta_r) + \mathbf{D_v}'(\theta_r)(\widetilde{\mathbf{M}}^{0}_{\mathbf{v-1}} + \widetilde{\mathbf{M}}^{1}_{\mathbf{v-1}}) + \mathbf{L}'_v(\theta_r)\widehat{\mathbf{M}}^{0}_{\mathbf{v}} - \mathbf{H}'_{\mathbf{v}}(\theta_r)\mathbf{M^1_v}).$$

Step 2c: If $v < v_0$ go to Step 2b.

Step 3: Set $k = k+1$ and $v = 0$

Step 3a: Compute

$$\mathbf{A^k_{N-v}}(\theta_r) = \mathbf{H_v}^{-1}(k\mathbf{L_v}\widehat{\mathbf{A}}^{k-1}_{\mathbf{v}}(\theta_r) + k\mathbf{L_v}'(\theta_r)\widehat{\mathbf{M}}^{k-1}_{\mathbf{0}} - \mathbf{H_v}'(\theta_r)\mathbf{M_0}^k).$$

Step 3b: Set $v = v+1$ and compute

$$\mathbf{A_{N-v}}^1(\theta_r) = \mathbf{H_v}^{-1}(k\mathbf{L}_v(\widehat{\mathbf{A}}^{k-1}_{\mathbf{v}}(\theta_r) + \mathbf{D}_v(k\widetilde{\mathbf{A}}^{k-1}_{\mathbf{v-1}}(\theta_r) + \widetilde{\mathbf{A}}^{k}_{\mathbf{v-1}}(\theta_r)) + \mathbf{D}'_v(\theta_r)(\widetilde{\mathbf{M}}^{k-1}_{\mathbf{v-1}} + \widetilde{\mathbf{M}}^{k}_{\mathbf{v-1}}) + k\mathbf{L}'_v(\theta_r)\widehat{\mathbf{M}}^{k-1}_{\mathbf{v}} - \mathbf{H_v}'(\theta_r)\mathbf{M_v}^k).$$

Step 3c: If $v < v_0$ go to Step 3b.

Step 3d: If $k < k_{max}$ go to Step 3.

Output: $A^k_{v,i}(\theta_r)$ *for any* $(v,i) \in \widehat{S}$ *and* $0 \le k \le k_{max}$

Applying some basic rules and properties of calculating differentials, we obtain the following expression that involves more than one partial derivative

$$\begin{aligned}\frac{d\mathbf{M_v^k}}{d\boldsymbol{\theta}'} &= -(\mathbf{H_v^{-1}}(\mathbf{D_v}(k\widehat{\mathbf{M}}_{\mathbf{v-1}}^{\mathbf{k-1}} + \widehat{\mathbf{M}}_{\mathbf{v-1}}^{\mathbf{k}}) + k\widetilde{\mathbf{D}}_{\mathbf{v}}\widetilde{\mathbf{M}}_{\mathbf{v}}^{\mathbf{k-1}})' \otimes \mathbf{H_v^{-1}})\frac{\partial vec\mathbf{H_v}}{\partial \boldsymbol{\theta}'} \\ &+ \mathbf{H_v^{-1}}(\mathbf{D_v}(k\widetilde{\mathbf{A}}_{\mathbf{v-1}}^{\mathbf{k-1}}(\theta) + \widetilde{\mathbf{A}}_{\mathbf{v-1}}^{\mathbf{k}}(\theta)) + k\widetilde{\mathbf{D}}_{\mathbf{v}}\widetilde{\mathbf{A}}_{\mathbf{v}}^{\mathbf{k-1}}(\theta)) \\ &+ ((\mathbf{k}\widehat{\mathbf{M}}_{\mathbf{v-1}}^{\mathbf{k-1}} + \widehat{\mathbf{M}}_{\mathbf{v-1}}^{\mathbf{k}})' \otimes (\mathbf{H_v})^{-1})\frac{\partial vec\mathbf{D_v}}{\partial \boldsymbol{\theta}'} + ((\mathbf{k}\widetilde{\mathbf{M}}_{\mathbf{v}}^{\mathbf{k-1}})' \otimes \mathbf{H_v^{-1}})\frac{\partial vec\mathbf{D_v}}{\partial \boldsymbol{\theta}'},\end{aligned} \tag{16}$$

and initial conditions $\frac{\partial \mathbf{M_v^0}}{\partial \theta'} = \mathbf{0}_{(N-v)\times 4}$, for any $0 \le v \le v_0$ and $k \ge 1$.

For a given state $(v, i) \in \widehat{\mathcal{S}}$, first derivatives of conditioned expected values and standard deviations of R_p, respect to any parameter, θ_r, can be calculated as follows

$$\frac{\partial E[R_p]}{\partial \theta_r} = \frac{\partial M_{v,i}^1}{\partial \theta_r} = \mathbb{A}_{v,i}^1(\theta_r),$$

$$\frac{\partial Sd[R_p]}{\partial \theta_r} = \frac{\partial (M_{v,i}^2 + M_{v,i}^1 - (M_{v,i}^1)^2)^{\frac{1}{2}}}{\partial \theta_r} = \frac{\mathbb{A}_{v,i}^2(\theta_r) + \mathbb{A}_{v,i}^1(\theta_r) - 2M_{v,i}^1\mathbb{A}_{v,i}^1(\theta_r)}{2Sd[R_p]}.$$

For any $0 \le v \le v_0$ and $1 \le i \le N - v$, elasticities for the conditioned mean and standard deviation, for each parameter θ_r, are given by

$$\varepsilon_{E[R_p]} = \frac{\partial E[R_p]/\partial \theta_r}{E[R_p]/\theta_r} = \frac{\mathbb{A}_{v,i}^1(\theta_r)}{M_{v,i}^1/\theta_r},$$

$$\varepsilon_{Sd[R_p]} = \frac{\partial Sd[R_p]/\partial \theta_r}{Sd[R_p]/\theta_r} = \frac{\theta_r(\mathbb{A}_{v,i}^2(\theta_r) + \mathbb{A}_{v,i}^1(\theta_r) - 2M_{v,i}^1\mathbb{A}_{v,i}^1(\theta_r))}{2Sd^2[R_p]}.$$

5 Numerical Analysis

The aim of this section is to study the relative importance of the model parameters for transmission of diphtheria virus. Diphtheria is a highly infectious bacterial disease caused by the bacterium Corynebacterium diphtheriae. It primarily affects the respiratory system but can also affect other organs. The disease is characterized by the formation of a thick gray or white membrane in the throat, which can lead to severe breathing difficulties and even death. The transmission of diphtheria occurs through direct contact with an infected person's respiratory secretions or by touching contaminated objects. Diphtheria remains a significant public health concern, particularly in areas with low vaccination coverage and poor living conditions.

For all experiments we consider a population of $N = 100$ individuals where prior the start of epidemic a percentage of the population, $v_0 \in \{20, 60, 90\}$ has received a vaccine to prevent infection. The epidemic is detected as soon as the

first case of infection is produced and in consequence, the initial state of the Markov chain describing the evolution of the infectious process is $(V(0), I(0)) = (v_0, 1)$. We fix the time unit to be the expected infectious time of an infected individual, therefore we take $\gamma = 1.0$. The internal rate of transmission is $\beta = 10.0$, that is taken by considering a basic reproduction number $R_0 = \frac{\beta}{\gamma} = 10.0$ and a vaccine failure probability, $h = 0.03$, according to the information presented in [16,17]. Infections produced from an external source of infection occur at rate $\xi = 0.01$, indicating that most of infections occur within the population and to guarantee the reintroduction of the disease when there are not infected individuals in the community.

In Table 1, we present values for mean and standard deviation of R_{e0} and R_p, under different coverage values to enhance understanding of the numerical results appearing in Table 2. We can see that increasing vaccine coverage conducts to a decrease in the number of infections produced by the index case and the entire infected population. We recall that these values are obtained applying theoretical and algorithm results in [6]. Our goal is to study if elasticities for a given parameter present a similar behaviour when increasing vaccine coverage and to find the most significant model parameters in the potential transmission of the pathogen.

Table 2 presents elasticities of the expected and standard deviation of the random variables, R_{e0} and R_p. Elasticities were computed numerically by appealing theoretical and algorithmic results in Sect. 3 and 4. To interpreter the elasticity values respect to each model parameter we keep all other parameter fixed. Regardless vaccine coverage sign patterns for elasticities of $E[R_{e0}]$ and $E[R_p]$ in Table 2 indicate that the most influential parameters are the external rate transmission β and the recovery rate γ but have opposite effect. In particular increasing β or decreasing γ by a 1% increases the expected number of secondary infections produced by the index case by a 0.3%, a 0.5% and a 0.9% when considering vaccine coverage of 20, 60 and 90, respectively. For the random variable R_p, these quantities are always between 0.85% and 0.92%. For the exact reproduction number, R_{e0}, when considering low vaccine coverage the external transmission rate is more sensitive than the vaccine failure probability h and have opposite effects. Increasing h by a 1% increases the expected number of secondary infections produced by the index case by a 0.007% and decreasing ξ by a 1% increases these infections by a 0.01%. In contrast, when prior the start of epidemic the percentage of the vaccinated individuals is larger the parameter h is more sensitive than the external contact rate ξ. In particular when increasing h by a 1% increases the expected number of secondary infections produced by the index case by a 0.24% and decreasing ξ only by a 0.004%. Regarding the elasticities of the number of infections produced by all the entire population for the parameter ξ and γ we notice the same behaviour as R_{e0} but they do not have an opposite effect. In addition, changes in parameters have larger effect on both random variables when vaccine coverage is larger. The stochastic uncertainty of the exact reproduction numbers, is more affected by perturbations in β or γ.

Table 1. Expected and standard deviation values for $N = 100$

Coverage	$E[R_{e0}]$	$\sigma(R_{e0})$	$E[R_p]$	$\sigma(R_p)$
$v_0 = 20$	4.20352	2.94801	7.42982	1.18173
$v_0 = 60$	2.98428	2.60305	3.86460	1.43269
$v_0 = 90$	1.11003	1.38102	1.15562	0.97599

Table 2. R_{e0}-Elasticities versus vaccine coverage for $N = 100$

Coverage	Parameter	$E[R_{e0}]$	$\sigma(R_{e0})$	$E[R_p]$	$\sigma(R_p)$
$v_0 = 20$	β	+0.33949	-0.00082	+0.86997	+30.3866
	ξ	−0.01657	−0.01378	+0.02402	+0.36422
	h	+ 0.00782	+ 0.00790	+0.00812	+0.16152
	γ	−0.32291	+0.02105	−0.89437	−13.2925
$v_0 = 60$	β	+0.55173	+0.21260	+0.85942	+5.68674
	ξ	−0.01322	−0.01335	+0.03485	+0.10997
	h	+0.04304	+0.03995	+0.04727	+0.19232
	γ	−0.53850	−0.17349	−0.89428	−2.75651
$v_0 = 90$	β	+ 0.92055	+0.75071	+ 0.85362	+1.27075
	ξ	−0.00432	-0.00409	+0.05748	+0.05036
	h	+0.24911	+0.24025	+0.24301	+ 0.29031
	γ	−0.91622	−0.66947	−0.91110	−0.88260

6 Conclussions and Future Work

In this investigation we analyzed the influence of parameter variation on the exact reproduction numbers R_{e0} and R_p by performing a local sensitivity analysis for a stochastic SVIS model with an external source of infection and imperfect vaccine. To measure the potential transmission of an epidemic, under a stochastic framework and for moderate size populations, the exact reproduction numbers are preferable to the deterministic quantifier R_0. In that context, the basic reproduction number overestimates the average number of secondary infections produced by the index case while R_{e0} and R_p provide exact measures of the disease spread.

We performed the sensitivity analysis via derivatives and elasticises. These quantities are obtained with the help of the Algorithm 1 and 2 which were implemented in R software environment.

Regarding the CPU times for Algorithms 1 and 2, we obtain that these quantities are similar but a bit larger for the computation of the derivatives of factorial moments of order k of R_{e0}. These times depend on the population size and when considering larger populations we obtain larger execution times. In particular, the average times to execute Algorithm 1 for a population of

$N = 100$, 500 and 1000 individuals are 0.22, 12.2 and 78.07, respectively and for Algorithm 2 these times are 0.21, 10.03 and 60.23.

Results can be used to help institution authorities to identify the most effective prevention control health strategies such as revaccination campaigns, social distancing measures or contact tracing efforts. The methodology can be applied to other epidemic models and descriptors of disease propagation and we are considering to extend the analysis to epidemic models with latency period or recovery, involving vaccines that wane the effect along time.

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