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Beyond R_0: Exploring New Approaches

Más allá de R_0: Explorando Nuevos Enfoques

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ABSTRACT

The basic reproduction number, denoted as R_0, is a crucial parameter in infectious disease modeling and serves as a key element for designing control strategies.
Calculating R_0 can be challenging in certain situations due to the complexity of the model. This complexity often hinders the explicit computation of R_0 and makes it difficult to understand how different populations and parameters influence its value. Recent research has introduced the concept of the target reproduction number as an alternative to R_0 (Shuai *et al.*, 2013).
The target reproduction number demonstrates how it is possible to exert control over the entire system, by analyzing some subsystems that describe the behavior of an infectious disease, it is possible to exert control over the entire system. The target reproduction number offers a framework for making decisions in public health. In this study, we apply it to two models: a model involving incomplete vaccination and a model for leptospirosis. The presented models showcase two fundamental features of the target reproduction number. Firstly, its expression's simplicity compared to the basic reproduction number. Secondly, its behavior analogous to R_0 at 1.

Keywords:

Target reproduction number, Failed vaccination model, Basic reproduction number, Mathematical Epidemiology.

RESUMEN

El número básico de reproducción, en la modelización de enfermedades infecciosas es un valor fundamental para diseñar estrategias de control. Calcular el valor de R_0 puede ser difícil en algunas situaciones debido a la complejidad del modelo. Esta complejidad a menudo obstaculiza el cálculo explícito de R_0 y dificulta la comprensión de cómo diferentes poblaciones y parámetros influyen en su valor. Trabajos recientes han propuesto el número de reproducción objetivo como alternativa al R_0 (Shuai *et al.*, 2013).
El número de reproducción objetivo muestra cómo, a través del análisis de algunos de los subsistemas que describen el comportamiento de una enfermedad infecciosa, es posible ejercer control sobre todo el sistema. El número de reproducción objetivo puede proporcionar un marco para la toma de decisiones en salud pública. En este trabajo lo aplicamos a dos modelos: un modelo con vacunación incompleta y un modelo para la leptospirosis.
Los modelos presentados exhiben dos características fundamentales del número de reproducción objetivo. En primer lugar, la simplicidad de su expresión en comparación con el número de reproducción básico. En segundo lugar, su comportamiento análogo al R_0 en 1.

Palabras Claves:

Número de reproducción objetivo, Modelo de vacunación imperfecta, Número de reproducción básico, Epidemiología Matemática.

2020 AMS Mathematics Subject Classification: Primary: 92B05; Secondary:

1 INTRODUCTION

On infectious disease modeling, the basic reproduction number (R_0) is crucial. It indicates the average number of secondary infections generated by an infectious individual in a fully susceptible population during its infectious period. Calculating R_0 is essential because it provides vital information for assessing the likelihood of an epidemic outbreak and understanding how diseases will spread. Moreover, it aids in the development of effective strategies to control and prevent infectious diseases (van Den Driessche and Watmough, 2002). In mathematical models involving multiple infectious compartments, computing the basic reproduction number R_0 can be challenging (Saldaña and Barradas, 2018), as it involves intricate parameter relationships resulting in complex expressions. Even if an explicit expression for R_0 is derived, identifying which parameters impact its reduction most significantly is not always straightforward. The expression's complexity often hampers direct analysis. The challenge of calculating and modifying R_0 has direct implications when designing strategies for controlling and preventing infectious diseases. Without a clear understanding of the factors that influence R_0 and how to intervene in them, devising effective measures to contain disease spread becomes more difficult.

The aforementioned challenges highlight the necessity on calculating a value that is easy to determine and enables the design of control strategies in a clear manner. In this way, the work presented by (Heesterbeek, 2007) introduces the concept of target reproduction number. This approach provides a significantly simpler expression in comparison to the originally proposed basic reproduction number.

This perspective concentrates on implementing specific strategies within a subsystem of the disease propagation model, provided that the remaining subsystems are under control. The objective is to exert control over the disease spread.

The target reproduction number estimates the level of effort required to eliminate an infectious disease when control is applied to a specific subpopulation (Driessche, 2017).
An illustrative example could arise in the context of a disease where diverse infection groups coexist, such as in the case of leptospirosis, where infectious groups encompass both animals and bacteria, with humans as the susceptible classes. Assuming that certain transmission routes have been controlled due to prior measures, for instance, transmission between humans and bacteria through interventions like water treatment, the focus might shift to controlling other transmission routes, specifically infections between animals and bacteria. The target reproduction number offers a tool to regulate the subsystem related to the intended control pathways. Consequently, it becomes feasible to achieve control over the entire system, provided the other subsystems associated with the remaining transmission routes have already been managed.

A fundamental property of the target reproduction number resides in its value being 1 when the basic reproduction number is also equal to 1. This characteristic implies that control strategies implemented to attain a value of 1 in the target reproduction number will also place R_0 at 1. Depending on the model's characteristics, for example, if the model does not exhibit a backward bifurcation at $R_0 = 1$, this could lead to disease elimination through control strategies as mentioned.
The target reproduction number is not unique, as it depends on the population to which the control strategy is applied. This implies that the value of the target reproduction number can vary based on the considered population.

In practice, it is recognized that different control strategies can lead to disease eradication. Therefore, it is necessary to evaluate which strategy requires lower implementation costs.
To illustrate the calculation of the target reproduction number, in this work two examples are presented. The first model, proposed in (Gandon *et al.*, 2003), addresses a scenario of failed vaccination where the infectious disease can persist despite vaccination. This model is known as the incomplete vaccination model.
On the other hand, the second model is about leptospirosis, presented in (Baca *et al.*, 2015). In this work an analysis is conducted on a model representing leptospirosis, a disease in which humans become infected through direct or indirect contact with the urine of infected animals, wounds, or other bodily fluids. In this work, numerical simulations will be presented to illustrate the obtained results. These simulations will illustrate how, by implementing control strategies constructed based on the target reproduction number, the infected curves tend towards zero as time increases. This implies the eradication of the disease.

In this article, the emphasis lies on the significance of the target reproduction number as an alternative to the basic reproduction number, facilitating more detailed analyses and employing simpler expressions. We refer to prior investigations conducted by (Roberts and Heesterbeek, 2003) and (Driessche, 2017). This paper is structured as follows. In Section 2 it is elaborated on the concept of the target reproduction number, detailing the steps and calculations required for its construction. In Section 3 it is shown two specific examples in which target reproduction number is employed to underscore its utility in concrete situations. Additionally, this section includes simulations to verify the effectiveness of the target reproduction number as a control strategy. In the last section, the discussion is presented, highlighting the main results obtained in the analyses, along with the effectiveness of implementing the strategy based on target reproduction number.

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2 CONSTRUCTION OF THE TARGET REPRODUCTION NUMBER

In this section, the construction of the target reproduction number will be performed using the methodology proposed by (Roberts and Heesterbeek, 2003) and (Lewis *et al.*, 2019).

In this analysis, the study addresses an infectious disease that spreads among susceptible individuals using a system of differential equations. Specifically, the existence of n infectious compartments is considered. To understand and analyze the disease spreading dynamics, we will start by using the next-generation matrix, referred to as $K = [k_{ij}]$. This matrix, as described in the study by (van Den Driessche and Watmough, 2002), characterizes the interactions and connections among the distinct infectious compartments, playing a fundamental role in determining the target reproduction number.

Each element k_{ij} in the matrix K represents the expected number of secondary infections in the compartment i that can be caused by an infected individual in the compartment j, considering a fully susceptible population during their infectious period. These matrix components reflect the potential for disease the propagation among the different compartments.

To explain the methodology, we will begin with the first infectious compartment. That is in a fully susceptible population, the introduction of an infected individual belonging to compartment 1 will be considered. Subsequently, the matrix K will be used to calculate the expected number of individuals in all infectious compartments in the next generation of infection, due to an infectious individual from the first compartment.

Considering the canonical vector $e_1 = (1,0,\ldots,0)$ of the standard basis in $\mathbb{R}^n$, we will compute Ke_1. The i-th component of this vector represents the expected number of new infections in compartment i produced by an in individual from compartment 1. Specifically, the first component of this vector represents the expected number of new cases in the infectious compartment 1 in the next generation of infection, caused by an infectious individual from compartment 1.

To identify all new infections in compartment 1, it is necessary to consider infections generated by individuals from other compartments. To achieve this, the first position of the vector (Ke_1) is removed. This is accomplished through the expression $(I-P)(Ke_1)$, where $P = [p_{ij}]$ is the projection matrix defined by:

$$\begin{cases} p_{ij} = 1 & \text{if} \quad i = j = 1, \\ p_{ij} = 0 & \text{otherwise.} \end{cases}$$

Subsequently, the matrix K is applied again to the resulting vector $(I-P)(Ke_1)$, allowing us to obtain the expected number of infected individuals from classes 2 to n that are generated by an infectious individual from class 1 during the second generation of infection.

In the third generation of infection, the vector $K(I-P)(Ke_1)$ is calculated. The expected number of infected individuals of type 1 is obtained using the expression $PK(I-P)(Ke_1)$.
On the other hand, the term $(I-P)(K(I-P)(Ke_1))$ represents the expected number of infected individuals of types 2 to n. This term takes into account infections that occur in intermediate generations of the infection without the involvement of infectious individuals of type 1.
After $j+1$ generations of infection, the value $e_1^T K((I-P)K)^{j-1} e_1$ represents the expected number of infected individuals of type 1 that arise during the infection cycle without the intervention of an infectious individual from the same group in an intermediate generation. Therefore, the value representing the number of secondarily infected individuals of type 1 originating from an infected individual of type 1 is:

$$\Gamma_1 = e_1^T K \sum_{j=0}^{\infty} ((I-P)K)^j . \tag{1}$$

The spectral radius of the matrix $(I-P)K$ is denoted as $\rho(I-P)K$. If $\rho((I-P)K) < 1$, then the sum, given in (1), converges to:

$$\Gamma_1 = e_1^T K (I-(I-P)K)^{-1} e_1. \tag{2}$$

In the realm of numerous infectious diseases, different groups of infected individuals are often encountered. Previously, the focus was solely on counting the expected number of infected individuals from the first group. However, it is now possible to generalize this concept by considering the existence of l classes of infected individuals, where l can be less than or equal to n. The following definition is provided:

Definition 1 *The target reproduction number Γ_l is defined as the spectral radius of the $l \times l$ matrix M_l, given by:*

$$M_l = E_l^T K (I-(I-P_l)K)^{-1} E_l. \tag{3}$$

With E_l and P_l are matrices of size $n \times l$ and $n \times n$ respectively, defined as:

$$\begin{cases} (P_l)_{ii} = (E_l)_{ii} = 1 & \text{if} \quad i = 1,\ldots l, \\ (P_l)_{ij} = (E_l)_{ij} = 0 & \text{otherwise.} \end{cases}$$

From this point onward, we will employ the matrices: $D = P_l K$ and $B = (I-P_l)K$, which were used in the equation given in (3). Note that $D+B = K$.

A related method regarding the matrices D and B, as proposed by (Driessche, 2017), is presented in the next. Suppose that a control strategy is to be applied and the parameters describing the infection behavior in the next-generation matrix

K are modified. Let S be the set of entries in K that will be modified by the control strategy τ. Additionally, let l be the classes of infectives from which Γ_l was constructed. In this context, the matrix $P_l = [p_{ij}]$ is:

$$\begin{cases} p_{ii} = 1 & \text{if} \quad i = 1, ...l, \\ p_{ij} = 0 & \text{otherwise.} \end{cases}$$

The matrix $D = [d_{ij}]$ will be referred to as the target matrix. It contains the entries that will be modified in the matrix K through the control strategy τ. On the other hand, $B = [b_{ij}] = (I - P_l)K$ contains the entries of K that will not be modified. To ensure an effective control strategy over the terms of the matrix K that will not be modified, it is required that the spectral radius of the matrix $B = (I - P_l)K$, denoted as $\rho(B) = \rho((I - P_l)K)$, be less than 1, as established in (1). This ensures that the non-modified terms do not significantly contribute to the disease's spread. The target reproductive number can be defined based on the aforementioned matrices B and D as follows (Driessche, 2017):

$$\Gamma_l = \rho\left(D(I - B)^{-1}\right). \tag{4}$$

With $\rho\left(D(I - B)^{-1}\right)$ being the spectral radius of the matrix $D(I - B)^{-1}$, and I being the identity matrix of size $n \times n$. Associated with the target reproduction number, the control matrix is constructed as defined below.

Definition 2 (Control Matrix) *The control matrix associated with the target matrix D is defined as $K_{C(\tau)} = B + \frac{D}{\tau}$. τ represents a control applied to the matrix D, which in turn represents the implementation of a control policy within the population.*

According to the above definition, the components d_{ij} of the matrix D are transformed to $\frac{d_{ij}}{\tau}$. The following theorem describes some characteristics of the target reproduction number as a threshold parameter, as well as its effectiveness as a control policy. The complete proofs of these theorems can be found in (Driessche, 2017).

In this section, we make use of the definition of a non-negative matrix, where all its entries are greater than or equal to zero. Additionally, we consider an irreducible matrix, characterized by the property that all its elements can be related to one another, either directly or indirectly, through a finite number of steps. This implies that there are no isolated submatrices where there is no connection between rows and columns. The main characteristic of the target reproduction number is manifested through the following theorem, which explicitly establishes the relationship between the control strategy τ applied to the population and the reproduction objective number. Γ_l, defined in equation (4).

Theorem 1 *Let K, B, D be non-negative $n \times n$ matrices with $K = B + D$ is irreducible, $D \neq 0$, and $\rho(B) < 1$. Then, $\rho(K_{C(\tau)}) = 1$ if and only if $\tau = \Gamma_l$.*

The following theorem demonstrates that the target reproduction numbers associated with different control strategies share similar characteristics, as they are threshold parameters at 1. Additionally, they offer the advantage of having much simpler expressions compared to the basic reproduction number, R_0.

Theorem 2 *Let K, B, and D be non-negative irreducible matrices with $K = B + D$, $D \neq 0$, and $\rho(B) < 1$. Then, the following propositions hold:*

i) $\rho(K) < 1$ *if and only if* $\Gamma_D < 1$.

ii) $\rho(K) = 1$ *if and only if* $\Gamma_D = 1$.

iii) $\rho(K) > 1$ *if and only if* $\Gamma_D > 1$.

This theorem establishes a relationship between the target reproductive numbers and their behavior around the threshold value of 1.

Theorem 3 *Let K, B, B', D, and D' be non-negative matrices, with $K = B + D = B' + D'$, and all of them are irreducible. $D \neq 0$, $D' \neq 0$, $\rho(B) < 1$, and $\rho(B') < 1$. If $D' < D$, then one and only one of the following propositions holds:*

i) $1 < \Gamma_D < \Gamma_{D'}$.

ii) $1 = \Gamma_D = \Gamma_{D'}$.

iii) $\Gamma_{D'} < \Gamma_D < 1$.

3 THE TARGET REPRODUCTIVE NUMBERS

In this section, we will apply the methodology proposed in (Shuai *et al.*, 2013) to calculate the target reproductive numbers for different epidemiological models in order to demonstrate the advantages of this technique.

Example 1**.** In this example, we examine the model proposed in (Gandon *et al.*, 2003). The model describes the dynamics of an infectious disease when a vaccination strategy is being implemented in the susceptible population. In this model, it is assumed that the vaccine is imperfect. The model is presented below:

$$\begin{aligned} S' &= \Lambda(1-p) - \mu S - (\beta_{uu} I + \beta_{vv} I_v) S, \\ S'_v &= -p\Lambda - \mu S_v - (\beta_{uv} I + \beta_{vu} I_v) S_v, \\ I' &= (\beta_{uu} I + \beta_{vv} I_v) S - (\mu + \nu) I, \\ I'_v &= (\beta_{uv} I + \beta_{vu} I_v) S_v - (\mu + \nu_v) I_v. \end{aligned} \tag{5}$$

In the design of control strategies, it is useful to have a tool that allows me to determine whether an epidemic outbreak will occur. In the introduction of this paper, it is mentioned that the basic reproductive number is the commonly used epidemiological threshold parameter to determine infectious dynamics at the onset of the disease.

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The next-generation matrix for model (5) is shown below.

$$K = \begin{bmatrix} \dfrac{\beta_{uu}S_0^*}{\mu+\nu} & \dfrac{\beta_{uv}S_0^*}{\mu+\nu_v} \\ \dfrac{\beta_{vu}S_{0v}^*}{\mu+\nu} & \dfrac{\beta_{vv}S_{0v}^*}{\mu+\nu_v} \end{bmatrix}, \tag{6}$$

When calculating the spectral radius of matrix K with $E_0 = (S_0, S_{0v}, 0, 0) = \left(\frac{\Lambda(1-p)}{\mu}, \frac{p\Lambda}{\mu}, 0, 0\right)$, the basic reproductive number associated with the model given in (5) is:

$$R_0 = \frac{1}{2}\left(\frac{\beta_{uu}S_o^*}{(\nu+\mu)} + \frac{\beta_{vv}S_{ov}^*}{(\nu_v+\mu)} + \sqrt{\left(\frac{\beta_{uu}S_o^*}{(\nu+\mu)} + \frac{\beta_{vv}S_{ov}^*}{(\nu_v+\mu)}\right)^2 - 4\left(\frac{\beta_{uu}S_0^*\beta_{vv}S_{ov}^* - \beta_{uv}\beta_{vu}S_{ov}^*S_{ou}^*}{(\nu+\mu)(\nu_v+\mu)}\right)}\right). \tag{7}$$

Consequently, the disease-free equilibrium E_0 is locally asymptotically stable if and only if $R_0 < 1$. Therefore, a control strategy involves adjusting one or more parameters of the model in such a way that the value of R_0 decreases below 1.

Note that the effects on R_0 when applying a control strategy to reduce the transmission rate among the non-vaccinated population β_{uu} are not clear. The same ambiguity applies to the other effective contact rates β_{vv}, β_{vu}, and β_{uv}. Let us consider a control strategy aimed at decreasing the spread of infections among the non-vaccinated individuals, assuming that transmissions among vaccinated individuals are under control.

This strategy can be implemented by reducing mobility among the non-vaccinated individuals. Next, we proceed to calculate the value of target reproductive number associated with this strategy, as per the definition established in equation (4). However, before performing this calculation, it is necessary to obtain the matrix $D(I-B)^{-1}$.

The expression that defines $D(I-B)^{-1}$ is as follows:

$$\begin{bmatrix} \dfrac{\frac{\beta_{uu}S_o^*}{(\nu+\mu)}\left(1-\frac{\beta_{vv}S_{ov}^*}{(\nu_v+\mu)}\right)}{1-\frac{\beta_{vv}S_{ov}^*}{(\nu_v+\mu)} - \frac{\beta_{uv}S_o^*}{(\nu_v+\mu)}\frac{\beta_{vu}S_{ov}^*}{(\nu+\mu)}} & \dfrac{\frac{\beta_{uu}S_o^*}{(\nu+\mu)}\frac{\beta_{vv}S_{ov}^*}{(\nu_v+\mu)}}{1-\frac{\beta_{vv}S_{ov}^*}{(\nu_v+\mu)} - \frac{\beta_{uv}S_o^*}{(\nu_v+\mu)}\frac{\beta_{vu}S_{ov}^*}{(\nu+\mu)}} \\ 0 & 0 \end{bmatrix}. \tag{8}$$

Let the set of indices $S = \{(i,j) \mid 0 \le i,j \le n\}$ correspond to the entries of the matrix K given in (6). According to the definition established in (4), the target reproduction number Γ_l for (5), associated with the index set $S = \{(1,1)\}$, is given by the following expression:

$$\Gamma_l = \frac{\frac{\beta_{uu}S_o^*}{(\nu+\mu)}\left(1-\frac{\beta_{vv}S_{ov}^*}{(\nu_v+\mu)}\right)}{1-\frac{\beta_{vv}S_{ov}^*}{(\nu_v+\mu)} - \frac{\beta_{uv}S_o^*}{(\nu_v+\mu)}\frac{\beta_{vu}S_{ov}^*}{(\nu+\mu)}}. \tag{9}$$

It is essential to highlight the simplicity of the target reproduction number as defined in equation (9), compared to the basic reproduction number established in equation (7). Although the expression for the target reproduction number is much simpler, its value equals is 1 when the basic reproduction number R_0 is also equal to 1. However, another important aspect is to consider its effectiveness in guiding the control of disease spread. This happens once a specific control strategy that modifies transmission rates has been implemented.

To demonstrate the effectiveness of the target reproduction number, numerical simulations will be conducted. The expression given in (1) asserts that by applying a control strategy to the parameters related to disease transmission in the entries of the next-generation matrix K and adjusting these parameters through the control strategy to make τ equal to the target reproduction number, the new basic reproduction number associated with the control matrix $K_{C(\tau)}$ will be equal to 1.This condition, in turn, ensures that the solution curves of system (5) approach to zero as time approaches to infinity, provided initial conditions are near the equilibrium point. Additionally, it is essential that system (5) has no endemic points in order to develop the strategy associated with the target reproduction number, the following set of parameters is considered: $\theta = (\beta_{uu}, \beta_{vv}, \beta_{uv}, \beta_{vu})$ that are related to the target reproduction number Γ_l defined in equation (9). The implementation of the control strategy involves dividing certain parameters associated with the next-generation matrix of the model by the value of the target reproduction number. In practice, this represents the minimum value to which infections must be reduced to ensure the epidemic's extinction (Saldaña and Barradas, 2018).

Contemplating controlling transmission within the unvaccinated population, entailing an adjustment to the parameter β_{uu}. Contemplating controlling transmission within the unvaccinated population, entailing an adjustment to the parameter β_{uu} will be made. This modification is defined by the new value βuu, which is calculated as $\beta uu^* = \frac{\beta_{uu}}{\Gamma_l}$. The following graphs show the temporal evolution of the curves of infected individuals before and after the implementation of the control strategy through parameter modification. These graphs illustrate the curves of infected individuals both before and after the parameter modification.

Figure (1) shows the impact on the spread of the epidemic in the unvaccinated population. It can be observed that as control is implemented, the curve showing the evolution of the infected population tends to zero as time approaches to infinity. This result is explained by the expression given in (1), which states that the control measure is effective if the transmission rate is reduced in accordance with the values specified by the target reproduction number (Saldaña and Barradas, 2018). According to the theorem presented in (3),

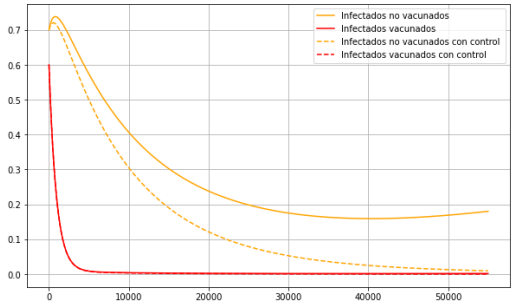

Figure 1: The graph depicts the prevalence of the infection in the non-vaccinated population over time, represented by a continuous curve in the absence of control and a dashed curve in the presence of control.
The parameter values used are: $\beta_{uu} = 0.0002$, $\beta_{vv} = 0.00009$, $\beta_{uv} = 0.000009$, $\beta_{vu} = 0.000003$, $v = 0.0001$, $v_v = 0.00011$, $p = \frac{1}{5}$, $\mu = \frac{1}{365\times 20}$, $\Lambda = 3\times\mu$

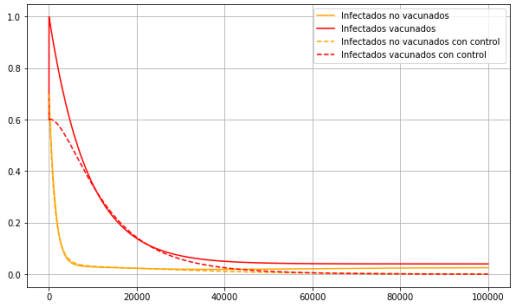

Figure 2: The graph depicts the prevalence of the disease infection in the vaccinated and unvaccinated populations over time, represented by continuous curves in the absence of control and dashed curves in the presence of control. The parameter values used are: $\beta_{uu} = 0.00000002$, $\beta_{vv} = 0.9$, $\beta_{uv} = 0.000009$, $\beta_{vu} = 0.000003$, $v = 0.001$, $v_v = 0.0001$, $p = \frac{1}{5}$, $\mu = \frac{1}{36520}$, $\Lambda = 3\mu$

when considering a different index set for the matrix K, the associated target reproductive number for that index set exhibits the same behavior around 1 as any other reproductive number associated with a different strategy.
In this context, let us consider the index set $S = \{(2,2)\}$. This index set is related to a new control strategy linked to the vaccinated population. Imagine a scenario where the epidemic spread in the non-vaccinated population is already under control, possibly due to the isolation of this population. However, the vaccinated population is allowed to circulate freely. Despite this situation, there still exists a possibility of transmission within this vaccinated group. Now, let us proceed to calculate the target reproductive number $\Gamma_{D'}$ for infections generated by a vaccinated individual in the vaccinated susceptible population. We follow a similar process as shown the previous steps for the model given in (5) with the values provided in (7), and with the matrix $D = [d_{ij}]$ with:

$$\begin{cases} d_{ij} = k_{ij} & \text{if} \quad i = j = 2, \\ d_{ij} = 0 & \text{otherwise.} \end{cases}$$

If $\rho(B) < 1$, the objective reproductive number $\Gamma_{D'}$ exists and is given by:

$$\Gamma_{D'} = \frac{\frac{\beta_{vv}S^*_{ov}}{(v_v+\mu)}\left(1 - \frac{\beta_{uu}S^*_o}{(v+\mu)}\right)}{1 - \frac{\beta_{uu}S^*_o}{(v+\mu)} - \frac{\beta_{uv}S^*_o}{(v_v+\mu)}\frac{\beta_{vu}S^*_{ov}}{(v+\mu)}}. \tag{10}$$

The target reproductive number $\Gamma_{D'}$ represents the average number of vaccinated individuals infected by another vaccinated individual in a population that is completely susceptible to the disease. The infection can spread from one vaccinated individual to another or through unvaccinated individuals.

In this context, the goal is to put in place a control strategy to reduce the spread of the epidemic among the vaccinated population, assuming that the epidemic is already under control among the unvaccinated population. To achieve this, a set of parameters $\theta = (\beta_{uu}, \beta_{vv}, \beta_{uv}, \beta_{vu})$ related to the target reproductive number $\Gamma_{D'}$ defined in (4) is taken into consideration.

Firstly, a study was conducted on the effect of vaccination on the disease spread. For this purpose, the dynamics of the epidemic in the absence of control measures on the population were analyzed, and the parameters $\theta = (\beta_{uu}, \beta_{vv}, \beta_{uv}, \beta_{vu})$ corresponding to the initial situation were obtained. Subsequently, a numerical simulation of the epidemiological model was performed using the parameters θ, in order to obtain the prevalence curves of the disease both in the vaccinated and unvaccinated populations.

Once these curves were obtained, the control strategy was implemented by adjusting the parameters $\theta_0 = (\beta_{uu}, \beta^*_{vv}, \beta_{uv}, \beta_{vu})$, where $\beta^*_{vv} = \frac{\beta_{vv}}{\Gamma_{D'}}$, with the aim of reducing the reproductive number of the disease. In practice, this could be achieved by implementing specific control measures, such as reducing the mobility of the vaccinated population, among other strategies.

Figures 1 and 2 show how, by applying control strategies based on target reproductive numbers, the curves representing the behavior of the infected individuals experience a significant decrease. This implies that, in the context of the model, the disease tends to disappear.

Example 2. The following example, presented in (Baca *et al.*, 2015), deals with human infection caused by bacteria from the environment or contact with infected animals. The mathematical model describes how an epidemic spreads, with contact with infected animals and environmental bacteria being the main sources of new infections in both animals

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and humans. Below is the detailed model:

$$\begin{aligned} S_A' &= -(C_1 I_A + C_2 B) S_A + \beta N_A - \alpha_2 S_A, \\ I_A' &= (C_1 I_A + C_2 B) S_A - \alpha_2 I_A, \\ S_H' &= -(C_3 I_A + C_4 B) S_H + \alpha_1 I_H, \\ I_H' &= (C_3 I_A + C_4 B) S_H - \alpha_1 I_H, \\ B' &= C_5 I_A + C_6 I_H - kB. \end{aligned} \tag{11}$$

By setting the direction field given in (11) equal to zero, an infection-free equilibrium is obtained with the following components:

$$X_0 = (S_{A0}, S_{H0}, I_{A0}, I_{H0}, B) = \left(\frac{N\beta}{\alpha_2}, N_H, 0, 0, 0\right). \tag{12}$$

The next-generation matrix K associated with the model described in (11) is displayed.

$$K = \begin{bmatrix} \frac{C_1 N_A}{\beta} & 0 & \frac{C_2 N_A}{K} \\ \frac{C_3 N_H}{\beta} & 0 & \frac{C_4 N_H}{K} \\ \frac{C_5}{\beta} & \frac{C_6}{\alpha_1} & 0 \end{bmatrix}. \tag{13}$$

The characteristic polynomial of (13) is defined as follows:

$$P(\lambda) = -\lambda^3 + R_1 \lambda^2 + \left(R_4^2 + R_6^2\right) \lambda + \overline{R}^3 - R_1 R_4^2. \tag{14}$$

The equation (18) define the values of R_1, R_4, R_6, and $\overline{R}$ in terms of the parameters C_1, C_2, C_4, and C_5. N_A and N_H represent the total populations of animals and humans, respectively.

$$R_1 = c_1 N_A \beta. \tag{15}$$

$$R_4 = \sqrt{\frac{C_4 C_6 N_H}{\alpha_1 k}}. \tag{16}$$

$$R_6 = \sqrt{\frac{C_2 C_5 N_A}{\beta k}}. \tag{17}$$

$$\bar{R} = \sqrt[3]{\frac{C_2 C_3 C_6 N_A N_H}{\alpha_1 \beta k}}. \tag{18}$$

The basic reproduction number R_0 associated with model (11) is defined as follows:

$$R_0 = \frac{1}{3} R_1 + z^{\frac{1}{3}} + \frac{|z|^{\frac{2}{3}}}{z^{\frac{1}{3}}}. \tag{19}$$

With

$$\begin{aligned} z = &\frac{\bar{R}^3}{2} + \frac{R_1^3}{3} + \frac{R_1 R_6^2}{6} - \frac{R_1 R_4^2}{3} + \\ &\sqrt{\frac{\bar{R}^6}{4} + \frac{R_1 R_6^2 \bar{R}_3}{6} + \frac{R_1^3 \bar{R}^3}{27} + \frac{2 R_1^2 R_4^2}{27} - \frac{R_1^4 R_4^2}{27}} \\ &- \frac{5 R_1^2 R_4^2 R_6^2}{27} - \frac{R_1^2 R_6^4}{108} - \frac{R_1^2 R_4^2 \bar{R}^3}{3} - \left(\frac{R_4^2 + R_6^2}{27}\right)^3. \end{aligned} \tag{20}$$

In the current scenario, we consider a situation where the control of transmission between humans and animals, as well as between humans and bacteria, is already controlled, possibly through control campaigns. Now, the focus is on maintaining control both between animals and between animals and bacteria, possibly through hygienic measures involving animal food consumption. With this consideration, we will proceed to calculate the value of the reproduction number associated with this control strategy. It is important to highlight that identifying which parameters are most sensitive becomes significantly more challenging when examining the entire system, due to the complexity of the expressions involved, as shown in the equation given in (20). However, by focusing the analysis on the subsystem related to a specific strategy, this task simplifies, especially if the other subsystems are already under control. Using the previous definition given in (4), the matrix B is defined as:

$$B = \begin{bmatrix} 0 & 0 & 0 \\ \frac{C_3 N_H}{\beta} & 0 & \frac{C_4 N_H}{k} \\ \frac{C_5}{\beta} & \frac{C_6}{\alpha_1} & 0 \end{bmatrix}.$$

According to the definition given in equation (4), the target reproduction number Γ_l, for (11), associated with the index set $S = \{(1,1), (1,2)\}$, is given by the following expression:

$$\rho(D(I-B)^{-1}) = \frac{(C_1 k + C_2 C_5) N_A \alpha_1 + (C_2 C_3 - C_1 C_4) C_6) N_A N_H}{(k\alpha_1 - C_4 C_6 N_H)\beta}. \tag{21}$$

It is important to highlight the simplicity of the target reproduction number in comparison to R_0 given by (20). This expression remains valid whenever the condition $\rho(B) < 1$ is satisfied, which is equivalent to:

$$\sqrt{\frac{C_4 C_6 N_H}{k\alpha_1}} < 1.$$

Next, numerical simulations will be permormed. These simulations will be carried out before applying the control strategy and after applying the control strategy using the target reproduction number. Given the target reproduction number Γ_l, as defined in equation (21), the set of parameters $\theta = (C_1, C_2, C_3, C_4, C_5, C_6)$ is taken into consideration. The strategy involves controlling the transmission rates between animals and bacteria, which leads to the modification of the parameters C_1 and C_2. New parameters are derived from the value of target reproduction number using the following expressions for C_1 and C_2, denoted as $C_1^* = \frac{C_1}{\Gamma_l}$ and $C_2^* = \frac{C_2}{\Gamma_l}$. In Figure presented show the temporal evolution of the infected individuals, including the curves of infected individuals before and after of the parameter modification.

Figure 3 illustrates how the application of combined control strategies, based on target reproduction number, manages to reduce infections in both animals and humans. The curves representing the behavior of infected individuals tend to zero, indicating that the disease tends to disappear.

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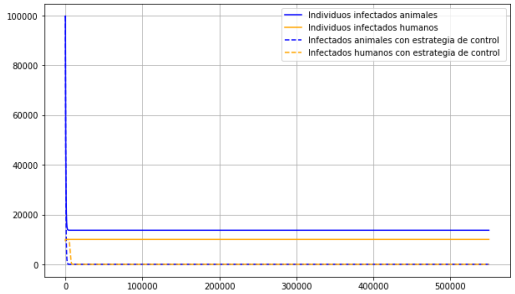

Figure 3: The graph displays the prevalence of infection by the disease in the population over time, represented by continuous curves in the absence of control and dashed curves in the presence of control. The simulation uses the following parameter values: $\beta = \frac{1}{3560}$, $C_1 = 5 \times 10^{-3}$, $C_2 = 5 \times 10^{-3}$, $C_3 = 65 \times 10^{-2}$, $C_4 = 6 \times 10^{-2}$, $C_5 = 2 \times 10^{-2}$, $C_6 = 2.15 \times 10^{-6}$, $\alpha_1 = \frac{1}{20}$, $\alpha_2 = \frac{1}{500}$, and $k = \frac{1}{18}$.

It is noteworthy how it is possible to exert control over the entire system by regulating the subsystem related to transmission between animals and bacteria. This objective is valid as long as the subsystems associated with transmission pathways involving humans are under control. Clearly, this subsystem has a considerably simpler mathematical formulation for analysis compared to the complexity of the entire system. The simplicity in its formulation represents greater efficiency when designing control strategies.

4 Discussion

Calculating the basic reproduction number in situations involving complex interactions among multiple infectious compartments poses significant challenges. The diverse interactions among these compartments, represented by different rates, complicate the derivation of simple formulas for computing R_0. This, in turn, hinders the identification of strategies for controlling the spread of an infectious disease.

In response to this complexity, the concept of the target reproduction number is suggested as a simpler alternative to the original R_0. This strategy focuses on analyzing subsystems related to transmission pathways within an infectious disease system. It shows that by controlling these subsystems, overall system control can be achieved. The target reproduction number facilitates the formulation of more specific control strategies.
By directing efforts towards a subgroup of the population, the target reproduction number provides a tool to control the outbreak of an infectious disease. The target reproduction number offers a clearer understanding of how changes in one part of the system can influence disease spread, thereby enabling more informed decision-making in the implementation of preventive measures.

It is important to highlight that the target reproduction number is supported by results that ensure a similar behavior to R_0 when its value is equal to 1. These results underscore a fundamental aspect: regardless of the strategy used to calculate the target reproduction number, when one of them reaches a value of 1, the others also become 1. Therefore, this property enables the evaluation of various control strategies and their effectiveness. The choice of which strategy to apply should be based on minimizing costs when implementing a control strategy.

To illustrate the applicability of the target reproduction number, two specific models have been used. In the first model, the scenario of incomplete vaccination is addressed, where the infectious disease can persist despite vaccination. In this model, two types of strategies are modeled: the first strategy is linked to controlling the non-vaccinated population. The effectiveness of this control strategy depends on controlling the other subsystem represented by the vaccinated population. Conversely, a control strategy is developed associated with the vaccinated population, assuming control over the non-vaccinated population. The effectiveness of both strategies occurs because changes in the rate values, which are adjusted by the target reproduction number, allow it to reach the threshold of 1. This implies that the respective basic reproduction number for the adjusted system is equal to 1.

Through a detailed calculation of the target reproduction number and the performance of simulations, the effectiveness of this approach as a control strategy in the proposed scenario has been shown. The choice of the most suitable strategy is based on the costs required to control the regulated subsystem. In the second model, an analysis of leptospirosis, a disease with infectious agents including animals and bacteria in the environment, is carried out. A control strategy is proposed that addresses infections between animals and bacteria, assuming transmission to humans is under control. The target reproduction number related to this control strategy is significantly simpler than R_0. The target reproduction number presents itself as an alternative for developing control strategies to contain an epidemic outbreak. It is important to emphasize that by solely controlling the subsystem related to infections between animals and bacteria, it is possible to exert control over the entire system that includes all transmission pathways.

The simulations carried out in the examples have supported the effectiveness of the target reproduction number as a control strategy. In each of the examples, it is illustrated how the curves of infected individuals undergo changes before and after applying the strategy based on the target reproduction number. It is clear that after implementing this strategy, the curve decreases significantly. This contrast highlights the utility of this approach as a control strategy.

A consequence that can be inferred from applying the target reproduction number to the model of incomplete

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vaccination is that when implementing different control strategies based on the target reproduction number, first in the unvaccinated population and then in the vaccinated population, these strategies efficiently achieve disease eradication as time approaches infinity.
An observation that can be made from the analysis of second model is that, despite the simplicity of the target reproduction number, using it as a control strategy on a subpopulation also leads to disease elimination as time tends to infinity.

In conclusion, the target reproduction number provides a valuable alternative to the traditional calculation of R_0 in situations involving complex interactions among multiple infectious classes. Its simplicity make this approach a promising tool for addressing the spread of infectious diseases and designing more effective interventions. By focusing on a specific population group, the target reproduction number allows for a more precise assessment of intervention effectiveness and facilitates informed decision-making regarding prevention and control strategies.

A pathway for future research could involve determining the target reproduction number in models of multiple cities, thus enabling a comparison between the target reproduction number approach for the entire multi-city model and the proposed numbers for each individual city.

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DECLARATION OF USE OF ARTIFICIAL INTELLIGENCE

The autors declare they have not used Artificial Intelligence (AI) tools in the creation of this article.

CONTRIBUTION OF THE AUTHORS (CREDIT)

The authors contributed equally to this work.

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