Modelling the Effect of Vaccination and Human Behaviour on the Spread of Epidemic Diseases on Temporal Networks

Modelling the Effect of Vaccination and Human Behaviour on the Spread of Epidemic Diseases on Temporal Networks

Kathinka Frieswijk, Lorenzo Zino, and Ming Cao

Abstract— **Motivated by the increasing number of COVID-19 cases that have been observed in many countries after the vaccination campaign and relaxation of non-pharmaceutical interventions (NPIs), we propose a network model for the spread of recurrent epidemic diseases in a partially vaccinated population. The model encapsulates several realistic features, such as different vaccine efficacy against transmission and development of severe symptoms, testing practices, implementation of NPIs, isolation of detected individuals, and human behaviour. Using a mean-field approach, we analytically derive the epidemic threshold of the model and, if the system is below such a threshold, we compute the epidemic prevalence at the endemic equilibrium. These theoretical results show that precautious human behaviour and effective testing practices are key towards avoiding epidemic outbreaks. Interestingly, we found that, in many realistic scenarios, vaccination is successful in mitigating the outbreak by reducing the prevalence of seriously ill patients, but it could be a double-edged sword, favouring resurgent outbreaks, and it thus calls for higher testing rates, more cautiousness and responsibility among the population, or the reintroduction of NPIs to achieve full eradication.**

I. Introduction

The COVID-19 pandemic shook the world to its core, spreading quickly, while leaving death, economical distress and despair in its path [1]. To control the spread of the disease, unrivalled efforts have been directed towards the development of effective vaccines [2]. Although COVID-19 vaccines offer protection against the development of severe symptoms and transmission, they do not provide full immunity [3]. Hence, it is unclear whether a high vaccination coverage alone is sufficient to eradicate the pandemic, as massive outbreaks have been recently registered even in countries with high vaccination rates [1], as soon as non-pharmaceutical interventions (NPIs) were relaxed. To gain insight into the mechanics behind the spread of infections, it is standard practice within the scientific community to employ mathematical models [4]–[7]. In particular, epidemic models on temporal networks have become very popular in the last decade for their ability to capture the complex and time-varying patterns of human encounters, through which epidemic diseases are transmitted [8], [9]. The analysis of such models leads to knowledge that can be used to inform control and intervention strategies [5], [6], [9], [10]. During the past phases of the COVID-19 health crisis, the systems and control community has worked incessantly towards developing models to predict the spread of the pandemic [11]–[13], understand the effectiveness of NPIs [14]–[16], and optimise the planning of vaccination campaigns [17]–[19]. Hence, mathematical modelling can be a key tool for studying the current challenges of the COVID-19 pandemic, specifically those related to the effectiveness of vaccination and the possibility to fully eradicate the disease.

To this aim, we propose a network model for the spread of recurrent epidemic diseases, for instance those caused by fast mutating viruses (e.g. influenza viruses) or those that do not provide permanent immunity (e.g. COVID-19). In our model, we use a mechanism inspired by continuous-time activity-driven networks [20], [21] to generate the time-varying pattern of physical encounters at close promixity, through which the disease is transmitted. The proposed mechanism takes into account the specific human behaviour in the form of a responsibility level, which represents the probability that an individual will choose to protect others (e.g. by maintaining distance), when only mild symptoms of the infection are apparent. To incorporate this human behaviour, we add extra compartments to a standard susceptible–infected–susceptible (SIS) model [9], to account for individuals that are mildly symptomatic and for those that have severe symptoms, and are thus restrained from having social interactions at close proximity. In our model, we include three control measures which impact the spreading of the virus: i) *vaccination*, where we have distinct factors for capturing its efficacy against transmission and developing serious illness; ii) *NPIs*, such as mandatory face masks and physical distancing; and iii) *testing campaigns*, which aim at identifying mildly symptomatic individuals and isolate them, thus reducing the contagions.

The main contribution of this paper is three-fold. First, we propose a parsimonious yet flexible epidemic model that incorporates human behaviour, vaccination and its efficacy, testing, and NPIs. Second, we perform a theoretical analysis of the proposed epidemic model, utilising a mean-field approach in the limit of large-scale populations [22]. Our analysis allows to compute the epidemic threshold and the endemic equilibrium (EE), that is, the epidemic prevalence if the outbreak trespasses the epidemic threshold and the disease becomes endemic. Third, we discuss a case study calibrated on the COVID-19 pandemic. Our findings elucidate the role of vaccination efforts on the spreading of fast transforming viruses, and suggest that although vaccines are typically highly effective in mitigating an epidemic outbreak by reducing the population with severe symptoms, they may make controlling local outbreaks more challenging.

Notation. The set of strictly positive integer, real non-

The authors are with the Faculty of Science and Engineering, University of Groningen, The Netherlands, 9747 AG Groningen, e-mail: {k.frieswijk,lorenzo.zino,m.cao}@rug.nl. The work was partially supported by the European Research Council (ERC–CoG–771687).

negative, and strictly positive real numbers is denoted by $\mathbb{N}$, $\mathbb{R}_{\geq 0}$, and $\mathbb{R}_{>0}$, respectively. Given a set $\mathcal{S}$, $|\mathcal{S}|$ denotes its cardinality. Given a function $x(t)$ with $t \in \mathbb{R}_{\geq 0}$, we define $x(t^+) = \lim_{s \searrow t} x(s)$, and $x(t^-) = \lim_{s \nearrow t} x(s)$.

II. Model

We consider n individuals labelled as $\mathcal{V} = \{1, \dots, n\}$ who interact on an undirected network $(\mathcal{V}, \mathcal{E}(t))$, whose edge set evolves in continuous time $t \in \mathbb{R}_{\geq 0}$. If $(j,k) \in \mathcal{E}(t)$, then a physical encounter in close proximity is occurring between individuals j and k at time t.

A. Disease transmission model

We extend the classical network SIS model [9] by dividing infected individuals in two separate compartments: *infectious* (i.e. infected individuals who are untested and mildly symptomatic) and *quarantined* (due to the presence of severe symptoms or of a positive test). We assume that individuals with severe symptoms are always quarantined. Hence, the health state of individual $j \in \mathcal{V}$ at time $t \in \mathbb{R}_{\geq 0}$ is defined by the variable $X_j(t) \in \{\mathrm{S}, \mathrm{I}, \mathrm{Q}\}$, denoting susceptible (S), infectious (I), and quarantined infected individuals (Q).

Here, we make the assumption that quarantined individuals (Q) do not actively participate in the society because they are too unwell or due to prohibitions enforced by public health authorities. Infectious individuals with mild symptoms (I) can participate, however. Specifically, we introduce a parameter $\sigma \in [0,1]$ that captures the individuals' level of *responsibility*. If an individual j is mildly symptomatic, they choose to protect others and maintain physical distance with probability σ; whereas with probability $1-\sigma$, j disregards the symptoms and physically interacts with others in close proximity. We assume that each individual makes their decision independently of the others and of the past. For the sake of simplicity, we will assume that all the individuals have the same level of responsibility, but heterogeneous responsibilities could easily be introduced in the model.

The time-varying network of physical encounters in close proximity is generated in a stochastic fashion. Inspired by continuous-time adaptive activity-driven networks [21], we attach to each individual a Poisson clock with unit rate[1], ticking independently of the others. If the clock associated with individual $j \in \mathcal{V}$ ticks at time $t \in \mathbb{R}_{\geq 0}$, then j activates and has an interaction with another individual k, selected uniformly at random from $\mathcal{V} \setminus \{j\}$. Whether a susceptible individual has an encounter in close proximity depends on the state and responsibility level of the individuals involved in the interaction. Specifically, if j is susceptible at the moment of activation ($X_j(t^-) = \mathrm{S}$) and selects an infected and mildly symptomatic individual ($X_k(t^-) = \mathrm{I}$), then the encounter takes place in close proximity with probability equal to $1-\sigma$; while if k is susceptible ($X_k(t^-) = \mathrm{S}$), then a physical encounter in close proximity always takes place. If an individual j who is infected and mildly symptomatic ($X_j(t^-) = \mathrm{I}$) activates and selects a susceptible individual k ($X_k(t^-) = \mathrm{S}$), then the encounter occurs in close proximity with probability $1-\sigma$; if j selects another mildly symptomatic individual k ($X_k(t^-) = \mathrm{I}$), then they interact in close proximity with probability $(1-\sigma)^2$ (i.e. if both individuals disregard the symptoms). Quarantined individuals ($X_k(t^-) = \mathrm{Q}$) do not participate in any (risky) encounters. If a physical encounter in close proximity occurs, then the ephemeral edge (j,k) is added to the edge set $\mathcal{E}(t)$, and immediately removed afterwards.

The health state of an individual $j \in \mathcal{V}$ evolves over time according to the following two mechanisms.

Contagion. Infection transmission occurs through pairwise physical encounters at close proximity, hereafter denoted by *contacts*. Specifically, if a susceptible individual j ($X_j(t^-) = \mathrm{S}$) has contact with an infected individual k with $X_k(t^-) = \mathrm{I}$, i.e. $(j,k) \in \mathcal{E}(t)$, the infection is transmitted to j with *per-contact infection probability* $\lambda \in [0,1]$. We assume that contact with an infected individual k ($X_k(t^-) = \mathrm{Q}$) does not lead to transmission of the infection, since they will use protections, as they are aware of the risk. After being infected, individual j will develop severe symptoms ($X_j(t^+) = \mathrm{Q}$) with probability $p_{\mathrm{q}} \in [0,1]$, while j will be mildly symptomatic ($X_j(t^+) = \mathrm{I}$) with probability $1 - p_{\mathrm{q}}$.

Recovery. An infected individual ($X_j(t^-) \in \{\mathrm{I}, \mathrm{Q}\}$) spontaneously recovers according to a Poisson clock with rate $\beta \in \mathbb{R}_{>0}$, becoming again susceptible ($X_j(t^+) = \mathrm{S}$).

B. Control measures

We introduce three control measures that public health authorities can take to control the spread of a disease.

Vaccination. We reduce the probability of infection transmission and the probability of the development of severe symptoms. To model these effects, we introduce the parameters $\gamma_{\mathrm{t}} \in [0,1]$ and $\gamma_{\mathrm{q}} \in [0,1]$, respectively. Let $v \in [0,1]$ denote the vaccination coverage of the population, i.e. the probability that a generic individual is vaccinated. The effect of vaccination is implemented in the model in a mean-field fashion, by multiplying the per-contact infection probability λ and the probability of developing severe symptoms p_{q} by the re-scaling factors $(1-\gamma_{\mathrm{t}} v)$ and $(1-\gamma_{\mathrm{q}} v)$, respectively.

NPIs. We introduce a parameter $\eta \in [0,1]$ that models the effectiveness of the NPIs implemented in preventing transmission. Hence, their effect is modelled by multiplying the per-contact infection probability λ by the quantity $(1-\eta)$.

Testing. By offering free testing campaigns, individuals with mild symptoms ($X_j(t) = \mathrm{I}$) are triggered to get tested. To quantify the effect of this measure, we introduce a Poisson clock with rate $c_{\mathrm{t}} \in \mathbb{R}_{\geq 0}$, representing the rate at which testing takes place. Thus, mildly symptomatic infectious individuals ($X_j(t^-) = \mathrm{I}$) are diagnosed according to a Poisson clock with rate c_{t}. After diagnosis, the infectious individuals quarantine themselves ($X_j(t^+) = \mathrm{Q}$), whereby they avoid having (risky) encounters, until they recover.

III. Dynamics

All the mechanisms described in Sec. II are prompted by independent Poisson clocks, so the n-dimensional state of the

[1] A Poisson clock with rate ζ is a continuous-time stochastic process that ticks in a time-interval of length Δt with probability $\zeta \Delta t + o(\Delta t)$.

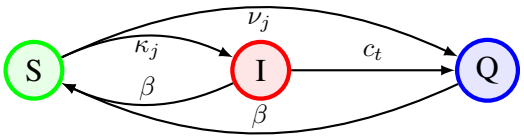


Fig. 1: State transitions of the epidemic model for $j \in \mathcal{V}$.

population $X(t) := (X_1(t)\ X_2(t) \cdots X_n(t)) \in \{\mathrm{S}, \mathrm{I}, \mathrm{Q}\}^n$ evolves according to a continuous-time Markov process [23]. As shown in Fig. 1, an individual can undergo five different state transitions, governed by the mechanisms of contagion, recovery, and testing, as described above. The three transitions triggered by recovery and testing are spontaneous processes, which occur with rate β and c_t, as detailed in Secs. II-A and II-B, respectively. The two triggered by contagion, instead, involve interactions between individuals and the corresponding rates are derived as follows.

If $X_j(t^-) = \mathrm{S}$, then j can become infected if they have contact with an infectious mildly symptomatic individual (I). Such a contact occurs with rate equal to $2\frac{1-\sigma}{n-1} \cdot |\{k \in \mathcal{V} : X_k(t) = \mathrm{I}\}|$, where the term 2 comes from the fact that both j and k can initiate the encounter. If such a contact occurs, j becomes infected with probability λ, reduced by the presence of NPIs and the efficacy of vaccination against transmission. Then, j becomes severely symptomatic with probability equal to $p_\mathrm{q}(1-\gamma_\mathrm{q} v)$, otherwise they become infectious. We conclude that $X_j(t^-) = \mathrm{S}$ becomes infectious ($X_j(t^+) = \mathrm{I}$) according to a Poisson clock with rate

$$\kappa_j := 2(1-\eta)\lambda\,(1-\gamma_\mathrm{t} v) \cdot [1 - p_\mathrm{q}\,(1-\gamma_\mathrm{q} v)]\,\frac{1-\sigma}{n-1} \sum_{k \in \mathcal{V}: X_k = \mathrm{I}} 1,$$

while they become quarantined ($X_j(t^+) = \mathrm{Q}$) according to a Poisson clock with rate

$$\nu_j := 2(1-\eta)\lambda\,(1-\gamma_\mathrm{t} v) \cdot p_\mathrm{q}\,(1-\gamma_\mathrm{q} v)\,\frac{1-\sigma}{n-1} \sum_{k \in \mathcal{V}: X_k = \mathrm{I}} 1.$$

For a generic j^{th} entry of the Markov process $X(t)$, the transition rate matrix is $Q_j = \begin{bmatrix} -\kappa_j - \nu_j & \kappa_j & \nu_j \\ \beta & -\beta - c_\mathrm{t} & c_\mathrm{t} \\ \beta & 0 & -\beta \end{bmatrix}$, where the rows (columns) correspond to state S, I, and Q, respectively. For any $p, q \in \{\mathrm{S}, \mathrm{I}, \mathrm{Q}\}$ with $p \neq q$, $\lim_{\Delta t \searrow 0} \mathbb{P}[X_j(t+\Delta t) = q \,|\, X_j(t) = p]/\Delta t = (Q_j)_{pq}$. We begin our analysis by noting that the first row of the transition rate matrix Q_j depends on the states of the other individuals. Hence, the individual dynamics cannot be decoupled, complicating the analysis for large-scale populations, where the state space dimension grows exponentially with n. Thus, as is common practice in the study of these complex systems [10], [22], we employ a continuous-state deterministic mean-field relaxation of the system. In particular, instead of studying the actual evolution of the health state for each individual $j \in \mathcal{V}$, we study the evolution of the probabilities that the individual is susceptible, infectious, or quarantined, denoted as $s_j(t) := \mathbb{P}[X_j(t) = \mathrm{S}]$, $i_j(t) := \mathbb{P}[X_j(t) = \mathrm{I}]$, and $q_j(t) := \mathbb{P}[X_j(t) = \mathrm{Q}]$, respectively. In the mean-field approximation, the evolution of these probabilities is

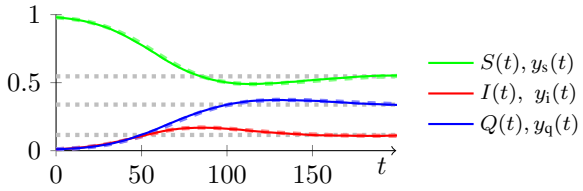


Fig. 2: Simulated trajectories of the Markov process (solid curves) and its deterministic approximation (dashed curves). The grey dotted lines are the EE, from Theorem 2. Here, $n = 10\,000$, $\sigma = 0.4$, $\lambda = 0.2$, $p_\mathrm{q} = 0.2$, $\beta = 0.02$, $v = 0.5$, $\gamma_\mathrm{t} = 0.5$, $\gamma_\mathrm{q} = 0.9$, $\eta = 0.2$, and $c_\mathrm{t} = 0.05$.

governed by the system of ordinary differential equations $\left(\dot{s}_j\ \dot{i}_j\ \dot{q}_j\right) = \left(s_j\ i_j\ q_j\right) Q_j$, or equivalently

$$\begin{aligned}
\dot{s}_j &= -2s_j(1-\eta)\lambda\,(1-\gamma_\mathrm{t} v) \cdot \frac{1-\sigma}{n-1} \sum_{k \in \mathcal{V}\setminus\{j\}} i_k + \beta i_j + \beta q_j, \qquad (1)\\
\dot{i}_j &= 2s_j(1-\eta)\lambda\,(1-\gamma_\mathrm{t} v)\,[1 - p_\mathrm{q}\,(1-\gamma_\mathrm{q} v)] \cdot \frac{1-\sigma}{n-1} \sum_{k \in \mathcal{V}\setminus\{j\}} i_k - (\beta + c_\mathrm{t}) i_j,\\
\dot{q}_j &= 2s_j(1-\eta)\lambda\,(1-\gamma_\mathrm{t} v)\,p_\mathrm{q}\,(1-\gamma_\mathrm{q} v) \cdot \frac{1-\sigma}{n-1} \sum_{k \in \mathcal{V}\setminus\{j\}} i_k + c_\mathrm{t} i_j - \beta q_j,
\end{aligned}$$

for all $j \in \mathcal{V}$. Before moving to the mean-field analysis of the system, we define $y_\mathrm{s} := \frac{1}{n}\sum_{j \in \mathcal{V}} s_j$, $y_\mathrm{i} := \frac{1}{n}\sum_{j \in \mathcal{V}} i_j$, and $y_\mathrm{q} := \frac{1}{n}\sum_{j \in \mathcal{V}} q_j$, which is the average probability for a randomly selected individual to be in state S, I, and Q, respectively. For a sufficiently large enough n and for any finite time-horizon, the fraction of individuals in a certain state can be arbitrarily closely approximated by the average probabilities, i.e. $S(t) := \frac{1}{n}|\{j \in \mathcal{V} : X_j(t) = \mathrm{S}\}| \approx y_\mathrm{s}$, $I(t) := \frac{1}{n}|\{j \in \mathcal{V} : X_j(t) = \mathrm{I}\}| \approx y_\mathrm{i}$, and $Q(t) := \frac{1}{n}|\{j \in \mathcal{V} : X_j(t) = \mathrm{Q}\}| \approx y_\mathrm{q}$ [21], [24], as illustrated in Fig. 2. This supports the use of the mean-field approximation to study the emergent behaviour of the system for large populations employing (y_s, y_i, y_q) and (1).

IV. Main Results

Here, we rigorously analyse the system in (1), to elucidate the role of vaccination and the level of responsibility in the epidemic spreading. Before presenting the main results, we show that the system in (1) is well-defined, i.e. that $(s_j\ i_j\ q_j)$ is a probability vector for all $j \in \mathcal{V}$ and $t \in \mathbb{R}_{\geq 0}$.

Lemma 1. *For all $j \in \mathcal{V}$, the set $\{(s_j\ i_j\ q_j) : s_j, i_j, q_j \geq 0, s_j + i_j + q_j = 1\}$ is positive invariant under* (1).

Proof. Observe that if one of the probabilities governed by (1) is equal to zero, then its respective time-derivative is always non-negative. Furthermore, $\dot{s}_j + \dot{i}_j + \dot{q}_j = 0$, for all $j \in \mathcal{V}$, so $s_j + i_j + q_j = 1$ for all $t \in \mathbb{R}_{\geq 0}$. □

Lemma 1 also implies that only $2n$ of the $3n$ equations are linearly independent, as $s_j(t) + i_j(t) + q_j(t) = 1$, for all $t \in \mathbb{R}_{\geq 0}$ and $j \in \mathcal{V}$, simplifying the analysis of the system.

The first thing we want to investigate is whether a local outbreak of the infection will escalate into a pandemic. Theorem 1 presents the required conditions for (local) asymptotic stability of the disease-free equilibrium (DFE) of system (1),

which is coined as the *epidemic threshold*. The threshold is presented as a critical value for the rate of testing c_t. If the testing rate is larger than $\bar{c}_\mathrm{t}$, as defined below, then the local outbreak is quickly extinguished; if not, it becomes endemic.

Theorem 1. *Consider the dynamical system in* (1)*. In the thermodynamic limit of large-scale systems $n \to \infty$, the epidemic threshold is equal to*

$$\bar{c}_\mathrm{t} := 2(1-\eta)(1-\sigma)\lambda\,(1-\gamma_\mathrm{t} v)\,[1-p_\mathrm{q}\,(1-\gamma_\mathrm{q} v)]-\beta. \quad (2)$$

In particular, if $c_\mathrm{t} > \bar{c}_\mathrm{t}$, the DFE (with $y_\mathrm{i} = y_\mathrm{q} = 0$) is locally asymptotically stable.

Proof. First, we immediately verify that the disease-free state of (1), that is, $(s_j, i_j, q_j) = (1, 0, 0)$ for all $j \in \mathcal{V}$, is always an equilibrium of the dynamics, as it nullifies the right-hand side of (1). To study its local stability, we consider a system made of the three macroscopic variables y_s, y_i, y_q, where its dynamics can be derived from (1) as

$$\begin{aligned}
\dot{y}_\mathrm{s} =& -2(1-\eta)\lambda\,(1-\gamma_\mathrm{t} v)\,(1-\sigma) y_\mathrm{i} y_\mathrm{s} + \beta y_\mathrm{i} + \beta y_\mathrm{q}, \quad (3)\\
\dot{y}_\mathrm{i} =& 2(1-\eta)\lambda\,(1-\gamma_\mathrm{t} v)\,[1-p_\mathrm{q}\,(1-\gamma_\mathrm{q} v)]\,(1-\sigma) y_\mathrm{i} y_\mathrm{s} - (\beta + c_\mathrm{t}) y_\mathrm{i},\\
\dot{y}_\mathrm{q} =& 2(1-\eta)\lambda\,(1-\gamma_\mathrm{t} v)\,p_\mathrm{q}\,(1-\gamma_\mathrm{q} v)\,(1-\sigma) y_\mathrm{i} y_\mathrm{s} + c_\mathrm{t} y_\mathrm{i} - \beta y_\mathrm{q}.
\end{aligned}$$

Since $y_\mathrm{s} + y_\mathrm{i} + y_\mathrm{q} = 1$ (as a consequence of Lemma 1), the system in (3) can be reduced to a planar system. For our analysis, we take the second and third equation of (3). Due to the definition of the macroscopic variables, the DFE of (1) is asymptotically stable if and only if the origin is asymptotically stable for the planar system $(y_\mathrm{i}, y_\mathrm{q})$. We subsequently linearize (3) around the origin in the limit of large-scale systems, $n \to \infty$, and obtain

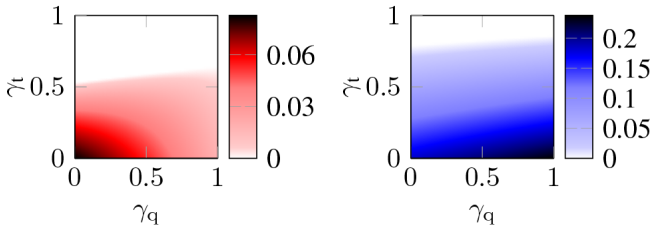
$$\begin{aligned}
\dot{y}_\mathrm{i} =& 2(1-\eta)\lambda\,(1-\gamma_\mathrm{t} v)\,[1-p_\mathrm{q}\,(1-\gamma_\mathrm{q} v)]\,(1-\sigma) y_\mathrm{i} - (\beta + c_\mathrm{t}) y_\mathrm{i},\\
\dot{y}_\mathrm{q} =& [2(1-\eta)\lambda\,(1-\gamma_\mathrm{t} v)\,p_\mathrm{q}\,(1-\gamma_\mathrm{q} v)\,(1-\sigma) + c_\mathrm{t}]\,y_\mathrm{i} - \beta y_\mathrm{q}. \quad (4)
\end{aligned}$$

The eigenvalues of the Jacobian matrix are given by $-\beta < 0$, and $2(1-\eta)(1-\sigma)\lambda\,(1-\gamma_\mathrm{t} v)\,[1-p_\mathrm{q}\,(1-\gamma_\mathrm{q} v)]-\beta-c_\mathrm{t}$, where the latter is negative if and only if $c_\mathrm{t} > \bar{c}_\mathrm{t}$. □

This theoretical result provides a rigorous tool to shed light on how the effectiveness of the vaccine and human behaviour impact the epidemic threshold of an infection, and thereby determine whether an epidemic outbreak could be easily controlled, or if higher testing efforts or more severe NPIs should be implemented. This will be discussed in the following remarks, and illustrated in the next section.

Remark 1. *From* (2)*, we observe that $\frac{\partial \bar{c}_\mathrm{t}}{\partial \gamma_\mathrm{t}} < 0$ and $\frac{\partial \bar{c}_\mathrm{t}}{\partial \gamma_\mathrm{q}} > 0$. Hence, while high vaccine efficacy against transmission favours the control of an epidemic outbreak, high efficacy against severe illness hinders complete eradication. We compute $\frac{\partial \bar{c}_\mathrm{t}}{\partial v} = 2(1-\eta)(1-\sigma)\lambda[p_\mathrm{q}\gamma_\mathrm{q} - \gamma_\mathrm{t}(1-p_\mathrm{q}) - 2p_\mathrm{q}\gamma_\mathrm{t}\gamma_\mathrm{q} v]$, finding that whether an increase in the vaccination coverage facilitates complete eradication is non-trivial and depends on p_q, γ_t, γ_q, and v. Interestingly, at the beginning of the vaccination campaign, only vaccines with $\gamma_\mathrm{t}/\gamma_\mathrm{q} > p_\mathrm{q}/(1-p_\mathrm{q})$ favour complete eradication.*

The following theorem characterises the global behaviour of the system in (1) and provides an analytical expression



(a) Seriously ill ξ (b) Threshold $\bar{c}_\mathrm{t}$

Fig. 3: (a) Fraction of seriously ill population ξ and (b) epidemic threshold $\bar{c}_\mathrm{t}$ for different levels of efficacy against severe illness γ_q and against transmission γ_t. Common parameters are $\sigma = 0.4$, $v = 0.821$, $\eta = 0.19$, $c_\mathrm{t} = 0.06$ $\lambda = 0.36$, $p_\mathrm{q} = 0.19$, and $\beta = 0.1$.

of the EE of the system, when the DFE is unstable. The simulation in Fig. 2 confirms our theoretical findings.

Theorem 2. *Consider the dynamical system in* (1)*, in the thermodynamic limit of large-scale systems $n \to \infty$. If $c_\mathrm{t} \geq \bar{c}_\mathrm{t}$, the system converges to the DFE $(y_\mathrm{s}, y_\mathrm{i}, y_\mathrm{q}) = (1, 0, 0)$. If $c_\mathrm{t} < \bar{c}_\mathrm{t}$ and $y_\mathrm{i}(0) > 0$, then the system converges to the EE $(y_\mathrm{s}^*, y_\mathrm{i}^*, y_\mathrm{q}^*)$, where $y_\mathrm{q}^* = 1 - y_\mathrm{s}^* - y_\mathrm{i}^*$,*

$$\begin{aligned}
y_\mathrm{s}^* =& \tfrac{\beta + c_\mathrm{t}}{2(1-\eta)(1-\sigma)\lambda(1-\gamma_\mathrm{t} v)[1-p_\mathrm{q}(1-\gamma_\mathrm{q} v)]},\\
y_\mathrm{i}^* =& \tfrac{\beta[1-p_\mathrm{q}(1-\gamma_\mathrm{q} v)]}{\beta + c_\mathrm{t}} - \tfrac{\beta}{2(1-\eta)(1-\sigma)\lambda(1-\gamma_\mathrm{t} v)}.
\end{aligned} \quad (5)$$

Proof. For this analysis, we use again the fact that $y_\mathrm{s} + y_\mathrm{i} + y_\mathrm{q} = 1$ (Lemma 1) and we take the first and second equation of (3). Note that the domain is bounded (Lemma 1), so we can employ the Bendixson-Dulac theorem [25]. For $\phi(y_\mathrm{s}, y_\mathrm{i}) = (y_\mathrm{s} y_\mathrm{i})^{-1}$ we find $\frac{\partial(\phi \dot{y}_\mathrm{s})}{\partial y_\mathrm{s}} + \frac{\partial(\phi \dot{y}_\mathrm{i})}{\partial y_\mathrm{i}} = -\frac{\beta}{y_\mathrm{s}^2}\left(1 + \frac{1-y_\mathrm{i}}{y_\mathrm{i}}\right) < 0$, so there do not exist periodic solutions of (3). If $c_\mathrm{t} > \bar{c}_\mathrm{t}$, then the DFE $(y_\mathrm{s}, y_\mathrm{i}, y_\mathrm{q}) = (1, 0, 0)$ is the unique equilibrium of (3) and therefore globally asymptotically stable. If $c_\mathrm{t} < \bar{c}_\mathrm{t}$, then one can easily verify that there exists one other equilibrium given by (5). Since there do not exist periodic solutions and the DFE is unstable for $c_\mathrm{t} < \bar{c}_\mathrm{t}$, the EE is asymptotically stable. For $c_\mathrm{t} = \bar{c}_\mathrm{t}$, (5) is equal to the DFE, hence, we conclude that for $c_\mathrm{t} = \bar{c}_\mathrm{t}$, the DFE is asymptotically stable. □

Remark 2. *In the EE* (5)*, with $c_\mathrm{t} < \bar{c}_\mathrm{t}$ for existence, the fraction of seriously ill individuals in the population can be computed as $\xi := (1 - y_\mathrm{s}^*) p_\mathrm{q}\,(1 - \gamma_\mathrm{q} v)$. Using the explicit expression of y_s^*, we can compute $\frac{\partial \xi}{\partial v} = \frac{\beta + c_\mathrm{t}}{(\beta + \bar{c}_\mathrm{t})^2} \frac{\partial \bar{c}_\mathrm{t}}{\partial v} p_\mathrm{q}(1 - \gamma_\mathrm{q} v) - \left(1 - \frac{\beta + c_\mathrm{t}}{\beta + \bar{c}_\mathrm{t}}\right) p_\mathrm{q} \gamma_\mathrm{q}$, where $\bar{c}_\mathrm{t}$ is defined in* (2) *and $\frac{\partial \bar{c}_\mathrm{t}}{\partial v}$ is computed in Remark 1. Hence, vaccination seems beneficial in reducing the fraction of people with severe illness for the set of parameters that satisfy $\frac{\partial \xi}{\partial v} < 0$, which includes all the cases in which the vaccine facilitates the control of the epidemic (Remark 1).*

Our theoretical findings highlight that, for a wide range of parameters (Remark 2), vaccination is a powerful control measure for the mitigation of an epidemic outbreak, as it is able to successfully reduce the number of seriously ill

individuals in the population. However, Remark 1 shows that, in some of these scenarios, vaccination could act as a double-edged sword, whereby, despite reducing severe infections, it could hinder complete eradication of the disease. In these scenarios, the epidemic disease tends to become endemic, unless stronger control measures are enacted (NPIs or efficient testing practices) or people increase their responsibility level, restraining themselves from having interactions with others if they have symptoms, as indicated by Theorem 1. In the next section, we will illustrate this non-trivial effect of vaccination by means of a case study, inspired by the ongoing COVID-19 pandemic and vaccination campaign.

V. Case Study and Discussion

We present a case study to provide insights into the theoretical results presented in Sec. IV. Motivated by the ongoing COVID-19 pandemic and global vaccination campaign, we calibrate our model to reflect some characteristics of COVID-19 and of the situation in the Netherlands as of early November 2021. In [26], it was estimated that the infection probability of a contact is 36%, which was reduced to 29% after governmental NPIs. Thus, we take $\lambda = 0.36$, and derive from $\lambda(1-\eta) = 0.29$ that $\eta = 0.19$. According to clinical data, 81% of COVID-19 cases are classified as mild [27], so we set $p_{\mathrm{q}} = 0.19$. For this choice of parameters, the vaccine seems to be almost always beneficial in mitigating the disease (by checking the condition in Remark 2), but, depending on the characteristics γ_{t} and γ_{q} of the vaccine in question, it may hinder the possibility of fully eradicating the disease without increasing NPIs or testing, or relying on a more responsible population. Vaccine efficacy is dependent on the type of vaccine, the time passed from its administration, and the virus strain, and there is not yet a consensus in the scientific community on reliable estimations for γ_{t} and γ_{q}.

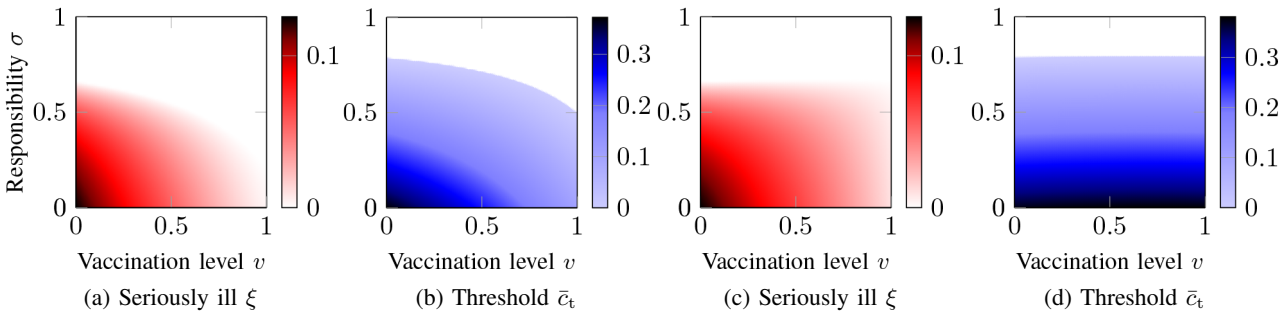
In view of these high levels of uncertainty, we use our theoretical findings to examine the effect of γ_{t} and γ_{q} on the prevalence of severe illness (Fig. 3a) and on the epidemic threshold (Fig. 3b). From Fig. 3, we observe that although a vaccination coverage of 82.1% (that is, the coverage in the Netherlands as of November 5, 2021 [28], [29]) has a strongly beneficial effect on the reduction of the prevalence of seriously ill individuals (Fig. 3a), the epidemic threshold is monotonically increasing in the efficacy against severe illness γ_{q} (Fig. 3b). This implies that, unless testing is performed at a very high rate, the current vaccination coverage in the Netherlands as of early November 2021 is not enough to stop local outbreaks from becoming endemic and completely eradicate the disease. In other words, despite vaccines being highly effective in the prevention of severe illness, thereby reducing the pressure on hospitals, they may complicate the control of local outbreaks. This is a consequence of the increased social activity of infected individuals, who are less likely to develop severe symptoms, and thus are less likely to be detected and isolated.

Finally, we consider a specific scenario calibrated on the BNT162b2 mRNA vaccine (Comirnaty by Pfizer-BioNTech), which is the most used vaccine in the Netherlands [28]. We consider a scenario in which we set $\gamma_{\mathrm{t}} = 0.65$, as [30] indicated a reduction of the risk of transmission of 65% for Comirnaty. According to clinical studies [31], a full vaccination status reduces the probability of severe symptom development with 92%, so we set $\gamma_{\mathrm{q}} = 0.92$. In Fig. 4, we show that the epidemic threshold and the fraction of seriously ill population are both monotonically decreasing in the vaccination coverage v and the responsibility level σ. However, compared to the responsibility level, vaccination has a lower impact, and does not lead to a complete eradication of the disease at low responsibility levels (Fig. 4a), suggesting that responsibility is key to achieve eradication of the disease. Some recent clinical studies suggest that the efficacy of Comirnaty —in particular against transmission— may quickly wane over the course of a few months after the second shot, calling for the need of a booster shot campaign [32]. While there is still not a consensus in the scientific community about waning immunity and its timing, we perform some further analysis by assuming that, after some months, the efficacy against transmission reduces to a fourth of the nominal value, i.e. $\gamma_{\mathrm{t}} = 0.165$. Our findings suggest that although a high vaccination coverage is still effective in keeping the fraction of seriously ill population under control (Fig. 4c), it is not beneficial in facilitating full eradication of the disease, since the degree of vaccination coverage has no effect on the epidemic threshold (Fig. 4d). Before concluding this paper, we would like to remark that our results are derived with a simple epidemic model that does not capture important features of COVID-19 like latency period and (temporary) immunisation after recovery. Hence, the case study discussed here should be meant as a preliminary qualitative analysis of our theoretical results inspired by a real-world scenario and a motivation to perform future research with more complex epidemic models [11]–[15], towards deriving rigorous quantitative conclusions.

VI. Conclusion

We proposed a mathematical model for the spreading of recurrent epidemic infections in a partially vaccinated population, and studied the impact of vaccination campaigns on the epidemic prevalence and the control of local outbreaks. Employing a mean-field approximation of the system, in the limit of large-scale populations, we derived the epidemic threshold and an expression for the endemic equilibrium. Our theoretical results indicate that although vaccines have a beneficial effect on the prevalence of individuals with severe symptoms, it may impede the control of local outbreaks. To manage such outbreaks, the combination of responsible behaviour of individuals and effective testing practices is key.

Our promising preliminary results pave the way for several avenues of future research. First, we plan to incorporate further compartments, e.g. to capture (temporary) immunity after recovery and latency periods, similar to [11]–[15]. Second, similar to [33]–[35], we aim at encapsulating in the model a game-theoretic decision-making process, whereby individuals make the decision to protect others or vaccinate based on a combination of external factors. Finally, one



(a) Seriously ill ξ (b) Threshold $\bar{c}_{\rm t}$ (c) Seriously ill ξ (d) Threshold $\bar{c}_{\rm t}$

Fig. 4: (a,c) Fraction of seriously ill population ξ and (b,d) epidemic threshold $\bar{c}_{\rm t}$ for different vaccination levels v and responsibility σ. In (a-b), $\gamma_{\rm t} = 0.65$; in (c-d), $\gamma_{\rm t} = 0.165$. Common parameters are $\gamma_{\rm q} = 0.92$, $\eta = 0.19$, $\lambda = 0.36$, $p_{\rm q} = 0.19$, $c_{\rm t} = 0.06$, and $\beta = 0.1$.

may consider interactions between multi-populations with a different vaccination coverage, and study the effect of a community with a very low vaccination rate (e.g. the Bible Belt in the Netherlands [29]) on epidemic spreading.

REFERENCES

[1] World Health Organization. (2022) Coronavirus (COVID-19) dashboard. Available: https://covid19.who.int

[2] World Health Organization. (2022) Draft landscape and tracker of COVID-19 candidate vaccines. Available: https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines

[3] H. N. Altarawneh *et al.*, "Protection against the omicron variant from previous SARS-CoV-2 infection," *N. Engl. J. Med.*, 2022.

[4] R. Pastor-Satorras, C. Castellano, P. Van Mieghem, and A. Vespignani, "Epidemic processes in complex networks," *Rev. Mod. Phys*, vol. 87, no. 3, pp. 925–979, 2015.

[5] C. Nowzari, V. M. Preciado, and G. J. Pappas, "Analysis and control of epidemics: A survey of spreading processes on complex networks," *IEEE Control Syst. Mag.*, vol. 36, no. 1, pp. 26–46, 2016.

[6] W. Mei, S. Mohagheghi, S. Zampieri, and F. Bullo, "On the dynamics of deterministic epidemic propagation over networks," *Annu. Rev. Control*, vol. 44, pp. 116–128, 2017.

[7] P. E. Paré, C. L. Beck, and T. Başar, "Modeling, estimation, and analysis of epidemics over networks: An overview," *Annu. Rev. Control*, vol. 50, pp. 345–360, 2020.

[8] P. E. Paré, C. L. Beck, and A. Nedić, "Epidemic Processes Over Time-Varying Networks," *IEEE Trans. Control Netw. Syst.*, vol. 5, no. 3, pp. 1322–1334, 2018.

[9] L. Zino and M. Cao, "Analysis, prediction, and control of epidemics: A survey from scalar to dynamic network models," *IEEE Circ. Syst. Mag.*, vol. 21, no. 4, pp. 4–23, 2021.

[10] L. Zino, A. Rizzo, and M. Porfiri, "On assessing control actions for epidemic models on temporal networks," *IEEE Control Syst. Lett.*, vol. 4, no. 4, pp. 797–802, 2020.

[11] G. Giordano, F. Blanchini, R. Bruno, *et al.*, "Modelling the COVID-19 epidemic and implementation of population-wide interventions in Italy," *Nat. Med.*, vol. 26, pp. 855–860, 2020.

[12] F. Della Rossa *et al.*, "A network model of Italy shows that intermittent regional strategies can alleviate the COVID-19 epidemic," *Nat. Comm.*, vol. 11, no. 1, p. 5106, 2020.

[13] G. C. Calafiore, C. Novara, and C. Possieri, "A time-varying SIRD model for the COVID-19 contagion in Italy," *Annu. Rev. Control*, vol. 50, pp. 361–372, 2020.

[14] F. Parino, L. Zino, M. Porfiri, and A. Rizzo, "Modelling and predicting the effect of social distancing and travel restrictions on COVID-19 spreading," *J. R. Soc. Interface*, vol. 18, no. 175, p. 20200875, 2021.

[15] R. Carli, G. Cavone, N. Epicoco, P. Scarabaggio, and M. Dotoli, "Model predictive control to mitigate the COVID-19 outbreak in a multi-region scenario," *Annu. Rev. Control*, vol. 50, pp. 373–393, 2020.

[16] K. Soltesz *et al.*, "The effect of interventions on COVID-19," *Nature*, vol. 588, no. 7839, pp. E26–E28, 2020.

[17] G. Giordano *et al.*, "Modeling vaccination rollouts, SARS-CoV-2 variants and the requirement for non-pharmaceutical interventions in Italy," *Nat Med*, vol. 27, no. 6, pp. 993–998, 2021.

[18] F. Parino, L. Zino, G. C. Calafiore, and A. Rizzo, "A model predictive control approach to optimally devise a two-dose vaccination rollout: A case study on COVID-19 in Italy," *Int J Robust Nonlinear Control*, 2021.

[19] S. M. Grundel, S. Heyder, T. Hotz, T. K. S. Ritschel, P. Sauerteig, and K. Worthmann, "How to coordinate vaccination and social distancing to mitigate SARS-CoV-2 outbreaks," *SIAM J. Appl. Dyn. Syst.*, vol. 20, no. 2, pp. 1135–1157, 2021.

[20] L. Zino, A. Rizzo, and M. Porfiri, "Continuous-time discrete-distribution theory for activity-driven networks," *Phys. Rev. Lett.*, vol. 117, no. 228302, 2016.

[21] ——, "An analytical framework for the study of epidemic models on activity driven networks," *J. Complex Netw.*, vol. 5, no. 6, pp. 924–952, 2017.

[22] P. Van Mieghem, J. Omic, and R. Kooij, "Virus spread in networks," *IEEE/ACM Trans. Netw.*, vol. 17, no. 1, pp. 1–14, 2009.

[23] D. A. Levin, Y. Peres, and E. L. Wilmer, *Markov chains and mixing times*. Providence RI, US: American Mathematical Society, 2006.

[24] T. G. Kurtz, "Limit theorems for sequences of jump Markov processes approximating ordinary differential processes," *J Appl. Prob.*, vol. 8, no. 2, pp. 344–356, 1971.

[25] H. J. Ricardo, *A modern introduction to differential equations*. Academic Press, 2020.

[26] C. Phucharoen, N. Sangkaew, and K. Stosic, "The characteristics of COVID-19 transmission from case to high-risk contact, a statistical analysis from contact tracing data," *EClinicalMedicine*, vol. 27, p. 100543, 2020.

[27] Z. Wu and J. M. McGoogan, "Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72.314 cases from the Chinese Center for Disease Control and Prevention," *JAMA*, vol. 323, no. 13, pp. 1239–1242, 2020.

[28] E. Mathieu *et al.*, "A global database of COVID-19 vaccinations," *Nat. Hum. Behav.*, vol. 5, no. 7, pp. 947–953, 2021.

[29] Government of the Netherlands. (2022) COVID-19 vaccinations. Available: https://coronadashboard.government.nl/landelijk/vaccinaties

[30] B. de Gier *et al.*, "Vaccine effectiveness against SARS-CoV-2 transmission and infections among household and other close contacts of confirmed cases, the Netherlands, February to May 2021," *Eurosurveillance*, vol. 26, no. 31, p. 2100640, 2021.

[31] N. Dagan *et al.*, "BNT162b2 mRNA Covid-19 vaccine in a nationwide mass vaccination setting," *N. Engl. J. Med.*, vol. 384, no. 15, pp. 1412–1423, 2021.

[32] D. W. Eyre *et al.*, "Effect of Covid-19 Vaccination on Transmission of Alpha and Delta Variants," *N. Engl. J. Med.*, vol. 386, no. 8, pp. 744–756, 2022.

[33] K. Frieswijk, L. Zino, and M. Cao, "A time-varying network model for sexually transmitted infections accounting for behavior and control actions," *Int. J. Robust Nonlinear Control*, 2021.

[34] M. Ye, L. Zino, A. Rizzo, and M. Cao, "Game-theoretic modeling of collective decision making during epidemics," *Phys. Rev. E*, vol. 104, p. 024314, 2021.

[35] K. Frieswijk, L. Zino, M. Ye, A. Rizzo, and M. Cao, "A mean-field analysis of a network behavioural-epidemic model," *arXiv preprint arXiv:2203.04016*, 2022.