Human prophylaxis driven by risk may cause oscillations in sexually transmitted diseases

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Abstract

Infectious diseases often display oscillations in the number of infected cases through time. Sometimes the ups and downs are caused by seasonal, exogenous events, such as the increase of influenza cases in winter, or the increase of vector-borne diseases during rainy seasons. Other times, the infection displays non-seasonal periodic oscillations, like syphilis, which oscillates with a period of 8-11 years. Several mathematical models aim to capture these oscillations, either by including a period in the transmission rate, by allowing link rewiring in contact networks, or by considering models with temporary immunization. Here we present a stochastic, yet analytically solvable, epidemic spreading model where the individuals of the population decide whether to take preventive measures or not depending on the global extent of the disease, being this an assessment of their infection risk. We show that the combined feedback between the human decision on prophylaxis, and the perceived epidemic risk, are sufficient conditions for the emergence of self-sustained oscillations in diseases well-described by the Susceptible-Infected-Susceptible (SIS) compartmental model, as it is the case for many sexually transmitted diseases (STDs). Finally, we propose plausible mechanisms to damp out the oscillations. Our study prompts to the design of persistent prevention campaigns, substantiated on not only perceived but real risks, to improve human prophylactic behavior and contain the recently reported raise of STDs and the consequent re-emergence of HIV.
It is known that individual human responses to the presence of infectious diseases in a population alter the spreading dynamics and can cause a systematic bias in the disease forecast if not taken into account\cite{1,2}. In the past years, substantial efforts have been made by governments and policy makers to monitorize the spreading of diseases and implement effective containment measures. Most of those measures often rely on changing individual’s behaviors towards other individuals or themselves. From wearing face masks or increasing hand hygiene to prevent influenza-like illnesses to using condoms to stop sexually transmitted diseases, every simple measure helps counteracting the spread of an infectious disease if it is adopted by a significant part of the population. The problem often lies on convincing a sufficient fraction of the pool of individuals to adopt these measures consistently in time. It is known that awareness campaigns and word-of-mouth play a crucial role in reducing epidemics if these campaigns are sustained through time\cite{3,5}. However, most of the times the personal decision on taking preventive measures is based on the individual perceived risk of getting infected, which may depend on present circumstances\cite{6-8}. In general, individuals have a sense of risk, roughly calculated taking into account one’s perceived susceptibility, the number of reported cases of diseased individuals, the distance to the focus of the epidemic, the cost of the measures to be taken, etc. All these factors help the individual to make the decision on whether it is worth it to take prophylactic measures or not. In this paper we assume that individuals are willing to take preventive behaviors if their perceived risk exceeds the cost associated to taking the prophylactic measure. We take the number of infections in the whole population as the proxy of the individual’s perceived risk, and we formulate the decision problem as a two-strategy game theory dilemma. One strategy is to take protective measures against the disease, in which case we say that the agent is protected (P); the other strategy is to disregard any behavioral change and stay not protected (NP). Taking the protective measures will imply, in terms of the epidemics, that this individual will have a lower chance of getting infected if she is susceptible, and that she will be less infectious to others in case she is infected. We couple this decision game with an epidemic process, modeled by a standard SIS model — in which agents can either be susceptible (S) or infected (I)— and we let both processes evolve simultaneously. The decision on whether to adopt protective measures is made according to global information, whereas the epidemics propagates in a contact network. We call this model “risk–driven epidemic spreading” given that the epidemics is palliated by the individual prophilaxis driven by their risk perception.
For sexually transmitted diseases the propagation substrate are sexual contact networks\textsuperscript{9–11}. In these networks, the distribution of the number of sexual partners is heterogeneous, with few individuals having a number of sexual contacts orders of magnitude larger than the average. Previous studies approximated the distribution of the number of sexual contacts, $P(k)$, with a power law $P(k) \sim k^{-\gamma}$, being $k$ the number of sexual contacts. These studies\textsuperscript{11, 12} identified scaling exponents between $1.5 < \gamma < 3.5$. More specifically, they state that sexual contact networks have different scaling exponents depending on whether they depict relationships between men, men and women, or among women. For the sake of simplicity, and without loss of generality, we will focus on men–men sexual contact networks. We will study the coupled disease-decision dynamics on synthetic networks that are built to resemble the structure of real men–men sexual contact networks.

In our risk–driven epidemic spreading model, agents can be in four possible states: Infected and protected, infected and not protected, susceptible and protected, or susceptible and not protected. Formally speaking, let us define the macroscopic quantities $I_p(t)$, $I_{np}(t)$, $S_p(t)$, and $S_{np}(t)$ as the fraction of the population in each of the former possible states at time $t$, respectively.

The agents will choose between the two possible strategies according to the difference of payoffs of each strategy. The payoff of being protected ($P_p$) and the payoff of disregarding protection ($P_{np}$) are:

\begin{equation}
P_p(t) = -c - T \frac{I_p(t)}{I_p(t) + S_p(t)}
\end{equation}

\begin{equation}
P_{np}(t) = -T \frac{I_{np}(t)}{I_{np}(t) + S_{np}(t)}
\end{equation}

The parameter $c$ refers to the cost associated to taking the protective measures. This cost may refer to the monetary cost that the individual has to assume for adopting the protection, but also to other related costs, like the side effects provoked by the protection, or other personal concerns regarding the measures to be taken. The parameter $T$ accounts for the cost of contracting an infection, that is, how severe are the consequences of an infection. The quantities $\frac{I_p(t)}{I_p(t) + S_p(t)}$ and $\frac{I_{np}(t)}{I_{np}(t) + S_{np}(t)}$ refer to the probability to be infected given that the agent is protected, and the probability to be infected given that the agent is not protected, respectively. These quantities are informative of the risk of infection depending on the chosen strategy. Therefore, the cost $T$ multiplied by the risk of infection refers to the expected cost associated to an infection.
The transition probabilities between strategies are defined as a function of the difference in payoffs $\Delta P_{np-p}(t) = P_{np}(t) - P_{p}(t)$ and $\Delta P_{p-np}(t) = P_{p}(t) - P_{np}(t)$, respectively. In this sense, agents will transition to the strategy which is providing a greater payoff at the current time with a given probability. These transition probabilities are those leading to the replicator dynamics at the population level \(^{[13]}\), i.e.:

$$T_{p \rightarrow np}(t) = \frac{\Delta P_{np-p}(t)}{T + c} \Theta(\Delta P_{np-p}(t))$$

$$T_{np \rightarrow p}(t) = \frac{\Delta P_{p-np}(t)}{T + c} \Theta(\Delta P_{p-np}(t)),$$

with $\Theta$ representing the Heaviside function, where $\Theta(x) = 1$ if $x \geq 0$ and $\Theta(x) = 0$ if $x < 0$, and $(T + c)$ the normalizing factor that is equal to the maximum possible payoff difference between P and NP strategists.

In general, behavioral changes towards protection do not imply an absolute protection from the disease (e.g. the efficacy of condoms for the transmission of HIV is approximately 80\%\(^{[14]}\)). For this reason, we define also a parameter $\gamma$ as the probability of the preventive measures failing, where $\gamma = 1$ means that the prevention strategy is useless and both protected and unprotected users will get infected with the same probability. On the other hand, if $\gamma = 0$, a susceptible protected agent will be totally immune against getting infected, and an infected protected agent will absolutely not transmit the disease to anyone else. The protection mechanism is bilateral, meaning that as long as one of the two parties participating in an infection contact is protected, the other party is protected as well. This is reflected by the linear reduction of the infection rate as two agents with strategies P and NP meet. The transition probabilities for changing the epidemic compartment can be summarized as the following reactions between agents $i$ and $j$:

$$S_{np}^{i} + I_{np}^{j} \xrightarrow{\lambda} I_{np}^{i} + I_{np}^{j}$$

$$S_{np}^{i} + I_{p}^{j} \xrightarrow{\gamma \lambda} I_{np}^{i} + I_{p}^{j}$$

$$S_{p}^{i} + I_{np}^{j} \xrightarrow{\gamma \lambda} I_{p}^{i} + I_{np}^{j}$$

$$S_{p}^{i} + I_{p}^{j} \xrightarrow{\gamma \lambda} I_{p}^{i} + I_{p}^{j},$$

where $\lambda$ is the infectivity rate of the epidemic and $\gamma$ is the aforementioned probability that preventive measures fail. The variables $S_{p}^{i}, I_{p}^{i}, S_{np}^{i}, I_{np}^{i}$ with $i = 1, 2, \ldots, N$ describe the state of the $N$ agents in the population.
Now, by using all of the above definitions, we can write the dynamical equations of the coupled the risk-driven epidemic model through the following set of recurrence relations:

\[
S^i_p(t + 1) = (1 - T_{p\rightarrow np}(t)) \left[ S^i_p(t)(1 - q^i_p(t)) + I^i_p(t)\mu \right] + T_{np\rightarrow p}(t) \left[ S^i_{np}(t)(1 - q^i_{np}(t)) + I^i_{np}(t)\mu \right]
\]
\[
S^i_{np}(t + 1) = T_{p\rightarrow np}(t) \left[ S^i_p(t)(1 - q^i_{np}(t)) + I^i_p(t)\mu \right] + (1 - T_{np\rightarrow p}(t)) \left[ S^i_{np}(t)(1 - q^i_{np}(t)) + I^i_{np}(t)\mu \right]
\]
\[
I^i_p(t + 1) = (1 - T_{p\rightarrow np}(t)) \left[ S^i_p(t)q^i_p(t) + I^i_p(t)(1 - \mu) \right] + T_{np\rightarrow p}(t) \left[ S^i_{np}(t)q^i_{np}(t) + I^i_{np}(t)\mu \right] + (1 - T_{np\rightarrow p}(t)) \left[ S^i_{np}(t)q^i_{np}(t) + I^i_{np}(t)(1 - \mu) \right]
\]
\[
I^i_{np}(t + 1) = T_{p\rightarrow np}(t) \left[ S^i_p(t)q^i_{np}(t) + I^i_p(t)(1 - \mu) \right] + (1 - T_{np\rightarrow p}(t)) \left[ S^i_{np}(t)q^i_{np}(t) + I^i_{np}(t)(1 - \mu) \right]
\]

where \( \mu \) is the epidemic recovery rate. The terms in brackets in the equations refer to the epidemic spreading dynamics, which describe the transit between the compartments \( S \Rightarrow I \). The other terms refer to the game dynamics, allowing the transition between the compartments \( P \Rightarrow NP \). The quantities \( q^i_p(t) \) and \( q^i_{np}(t) \) express the probability that agent \( i \) will get infected at time \( t \) if she is protected or not protected, respectively, and read:

\[
q^i_p(t) = 1 - \prod_{j=1}^{N} \left[ 1 - A_{ij}\lambda\gamma(I^j_p(t) + I^j_{np}(t)) \right] \tag{13}
\]
\[
q^i_{np}(t) = 1 - \prod_{j=1}^{N} \left[ 1 - A_{ij}\lambda(\gamma I^j_p(t) + I^j_{np}(t)) \right] \tag{14}
\]

where \( A_{ij} \) refers to the adjacency matrix of the epidemic process and defines the sexual contacts among agents.

Solving numerically the equations of the risk-driven epidemic model (Eqs. (9)-(12)) we observe that the incidence of the epidemics, \( I \), as well as the number of protected individuals, \( P \), oscillates in time in a sustained way, see Fig. 1(a). In Fig. 1(b) we unveil the mechanism behind the oscillations (see gray area): when \( P_{np} \) is higher than \( P_p \), individuals cease to protect themselves, and this implies that the number of infected individuals start to increase. When this happens, the payoff of the strategy protected \( (P_p) \) becomes larger than \( P_{np} \), provoking individuals to start protecting themselves, and thus the number of infected individuals is again reduced, sustaining the limit cycle observed in the evolution of \( I \) and \( P \).

An interesting question is whether oscillations disappear or are reduced for certain values of the parameters. We explored how the cost of contracting the disease \( T \) affects the aforementioned oscillations. We observe that higher values of \( T \) (higher cost) generate smaller oscillations (see Fig. 1(c) left plot), given that when the cost of contracting an infection is really high, almost all individuals adopt the protected strategy. However, when plotting the
relative amplitude of the oscillations in (see Fig. 1(c)(right)) we observe that for all values of $T$ the relative amplitude has the same order of magnitude. We conclude that the cost of contracting the disease $T$ does not induce the oscillations to vanish.

One would think that the probability that preventive measures fail ($\gamma$) and the infectivity rate ($\lambda$) are able to shape the oscillations as well. We explore this in Fig. 1(d), and find that oscillations are only present for low values of $\gamma$ and low values of $\lambda$, pointing out that only when the preventive measure is very effective and the disease is not very contagious that individuals face the dilemma on whether to protect themselves that ultimately leads to the aforementioned oscillatory behavior. Outside this area of the parameters, either the disease is very contagious, or the measures are useless, or a combination of both. In any case, the number of infected individuals grows larger and we do not observe oscillations. We also see that as the infection cost $T$ grows larger, the region of parameters that presents oscillations becomes smaller, but the relative oscillations are higher.

Note that for oscillations to emerge, the system must be constantly reacting, i.e., the disease transmission has to be slower than the strategic updates. Otherwise, the epidemics reaches faster its stationary state than game dynamics, since agents have complete and precise information about the system thus taking more accurate decisions. This allows the system to reach its equilibrium steady state. On the other hand, when agents evaluate their payoffs before the disease has reached its equilibrium, the success of each strategy (used in Eqs. (1) and (2)) to update the prophylactic behavior) does not capture the actual risk of getting infected. In other words, agents take their decisions based on information, which is delayed in time. This is precisely the most common scenario for many epidemic outbreaks.

Interestingly, in [15] time delay is seen to enhance the oscillatory behavior observed in an adaptive network model [16] in which susceptible nodes rewire those links with infected ones. In [15] the authors extend the model in [16] by adding a time delay before agents rewire a link, which was previously cut with an infected agent. The introduced time delay in [15] substantially increased the parameter space, in which oscillations emerge. Similarly, it was shown that cyclical SIRS models can exhibit oscillations if a time delay is introduced before agents become susceptible again [17]. The only coevolutionary mode exhibiting an oscillatory behavior is [18]. The study analyzes the vaccination uptake against childhood diseases. As observed in our risk-driven epidemic spreading model, if the time scale of the game is too slow, the oscillations disappear.
FIG. 1. Risk-driven epidemic spreading model. Numerical results of the risk–driven epidemic spreading model on a power-law network of size $N = 2000$ and exponent 2.5. Default parameters are $c = 1$, $\mu = 0.1$, $T = 10$, $\lambda = 0.05$, and $\gamma = 0.1$. (a) Fraction of Protected ($P = S_p + I_p$) and Infected ($I = I_p + I_{np}$) individuals as a function of time. We observe an oscillatory behavior that is sustained in time. (b) Amplitudes of the oscillations in the fraction of infected individuals as a function of time. Left plot depicts the absolute value of the amplitude, while the right one depicts the relative one, all of them for three values of $T$, the cost of infection. Higher values of $T$ (higher cost) generate smaller oscillations (see left plot). On the right, we can see that all amplitude of oscillations are of the same order of magnitude, when calculated relatively to the fraction of infected individuals. (c) Detail of the oscillations. The red and blue lines indicate the fraction of Infected and Protected individuals, respectively. The black dashed line plots the payoff of the strategy not protected ($P_{np}$) while the solid black line is the payoff of the protected strategy ($P_p$). (d) Average relative amplitudes of the fraction of infected individuals in the steady state, for all range of $\gamma$ (the probability of protection failure) and $\lambda$ (the infectivity rate), for different values of $T$. We observe that as the infection cost increases, the area where the oscillations are present is reduced, but the oscillations themselves are larger.

Once explored the nature of the oscillatory dynamic we now characterize to what extent the quality of the protective measures affects the spreading of the disease. In Fig. 2(a) we plot the steady state fraction of both $I$ and $P$ individuals as a function of the epidemic infectivity $\lambda$, for different protection effectivity values $\gamma$. When $\gamma = 1$, the prevention measures are useless and thus we recover the second order phase transition typical of an SIS model. For very effective measures ($\gamma \approx 0$), a majority of the population adopts the protective behavior and thus the number of infected individuals is almost zero. For intermediate values of
the protection effectivity \( \gamma = 0.5 \) the effect is interesting: for values of the infectivity sufficiently low (but above the critical threshold), a fraction of individuals adopt protection, but as the infectivity increases, for this particular value of the effectivity \( \gamma \), prophylaxis is not enough as to prevent infection and thus agents cease to protect themselves. We see that the adoption of protection in this region of \( \lambda \) leads to a decrease in the number of infections, but this range is small and we see that intermediate values of \( \gamma \) are not able to contain the disease.

Actually, the epidemic is only fully eradicated when the disease is intrinsically highly noninfectious, i.e. \( \lambda \) is below its critical value, \( \lambda_c \). To investigate this, we need to find out the equilibrium condition of this coupled system. Regarding the game, the equilibrium is reached when agents keep the same strategy over time. Regarding the epidemics, stability is achieved when the fraction of susceptible and infected individuals is constant over time. When both dynamics are stable, we can say that the coupled system is in equilibrium. Consequently, we can find out the exact conditions for which the equilibrium condition for the game is reached. For an agent to keep the same strategy over a period of time, it must happen that no other strategy provides a better payoff than the one provided by the current strategy. In our case, this happens when \( T_{np\rightarrow p} = T_{p\rightarrow np} = 0 \), which in turn requires that both payoffs are equal, i.e. \( P_p = P_{np} \). This equality implies:

\[
\frac{c}{T} = \frac{I_{np}}{I_{np} + S_{np}} - \frac{I_p}{I_p + S_p}.
\]

(15)

Which means that the probability of infection if the agent is not protected minus the probability of infection if the agent is protected must be equal to the ratio between the cost of the prophylaxis and the cost of infection, in order to reach equilibrium.

At the epidemic threshold, \( \lambda_c \), the fraction of infected agents is almost 0, i.e. \( I_p, I_{np} \approx 0 \). Therefore, inserting \( I_p, I_{np} \approx 0 \) in Eq. (15), we obtain \( c/T = 0 \), which does not hold for \( c > 0 \). Consequently, all the agents choose the NP strategy, and the epidemic threshold is the usual in the SIS model:

\[
\lambda_c = \mu/\Lambda_{\text{max}}(A),
\]

(16)

where \( \Lambda_{\text{max}}(A) \) refers to the maximum eigenvalue of the adjacency matrix \( A \). The fact that the epidemic threshold does not depend on the protection mechanism illustrates the general dilemma underlying voluntary protection mechanisms: Individuals adopt the protection solely if the infection risk is imminent. Therefore, the disease is only contained but
not eradicated, meaning that the epidemic threshold is not increased, see the red line in Fig. 2(b)(left).

Regarding the incidence of the protection, we observe in Fig. 2(b)(right) that agents only take a protective behavior when the infectivity rate is low and the preventive measures are reasonably efficient. In analogy to the epidemic threshold, we define the threshold $\tilde{\lambda}$, such that agents start protecting themselves. The protection threshold $\tilde{\lambda}$, can be calculated in a well-mixed population supposing that the fraction of protected agents is negligible in comparison to the fraction of non-protected ones (see Methods), and we obtain:

$$\tilde{\lambda}^\pm = \frac{2\mu}{1 - \frac{\gamma}{T} \mp \sqrt{(1 - \frac{\gamma}{T})^2 - 4\frac{\mu}{1 - \frac{\gamma}{T}}}}.$$  \hspace{1cm} (17)

The equation for the threshold has two solutions: $\tilde{\lambda}^-$ and $\tilde{\lambda}^+$. The threshold $\tilde{\lambda}^-$ describes the critical infectivity rate above which agents start protecting themselves. In other words, below $\tilde{\lambda}^-$ there is still no risk of infection sufficiently high as to consider taking preventive measures. On the other hand, the threshold $\tilde{\lambda}^+$ is the point where agents stop adopting the protective behavior, since the protection is not sufficient to combat to the high infection risk. From Eq. 17 we obtain $\lim_{\gamma \to 0} \tilde{\lambda}^+ = \infty$. This means that, under the condition where protection leads to complete immunization ($\gamma = 0$), an increasing infectivity rate does not stop agents from taking preventive measures against the disease and the disease is controlled independently of the infection probability. The real parts of both solutions $\tilde{\lambda}^-$ and $\tilde{\lambda}^+$ are displayed in Fig. 2(b)(right) as a single blue curve over the phase space of the incidence of the protected. Note that even though this threshold is calculated using a mean-field approximation, it nicely matches to the results of our model using heterogeneous networks.

To complete the study about the adoption of prophylactic behavior in Fig. 2(c) we show the partition of the population across the four compartments ($S_{np}$, $S_p$, $I_{np}$ and $I_{up}$) as a function of $\lambda$ and $\gamma$. As expected, for values of $\lambda$ lower than $\lambda_c$ there is no infection and all agents are in the $S_{np}$ compartment. In the range of values of $\lambda$ above $\lambda_c$ and low values of $\gamma$ the disease is present (the number of infected individuals is very small but different from zero) but it is very contained. In the plot depicting the behavior of compartment $S_p$ we observe that the effect of preventive measures on the epidemic is largely noticeable. Outside the region of low $\gamma$ and low $\lambda$, the disease cannot be contained for two different reasons, as we can see in Fig. 2(c). In one case individuals choose to take protection measures but they
are too inefficient to actually protect them (i.e. most individuals are in the $I_p$ compartment). In the other, they disregard protection altogether, transferring to the $I_{np}$ compartment.

FIG. 2. **Effectiveness of the prevention method.** Numerical results of the proposed model on a power-law network of size $N = 2000$ and exponent 2.5. Default parameters are $c = 1$, $\mu = 0.1$, and $T = 10$. (a) Fraction of infected individuals ($I = I_{np} + I_p$) and fraction of protected individuals ($P = S_p + I_p$) in the steady state as a function of the epidemic infectivity probability $\lambda$, for different values of the probability of preventive measures failing ($\gamma$). (b) Phase-space diagrams of the incidence on the number of Infected (left) and number of Protected individuals (right). Red line in left plot denotes the epidemic threshold of our model, as calculated by (16). The blue line on the right plot is the protection threshold as obtained in (17). (c) Phase-space diagrams of the incidence for each one of the four compartments of our model, at the steady state, for all range of $\lambda$ and $\gamma$. Darker colour denotes higher incidence. The black line indicates the epidemic threshold in the case of a fully protected population.

Once understood human prophylaxis can cause oscillations in the disease incidence, we now focus on possible intervention strategies to contain the disease. An intervention strategy will basically act on the parameters in the model. The transmission probability $\lambda$ is intrinsic to the specific disease, i.e. a biological constant, and is thus not subject to any intervention.
In contrast, the recovery rate $\mu$ may be increased through advances in the treatment of the disease. However, such advances require costly research and guaranteeing the access to new therapies will be financially demanding. Similarly, any improvement in the quality of the protection $\gamma$ requires time and financially intensive technological advances. The protection cost $c$ is not solely a financial cost but also related to the availability of the protection. However, in particular for western countries, neither the availability nor the financial cost of contraceptives seem to leave room for substantial improvements. Accordingly, the only parameter we are left with is $T$, the infection cost. The infection cost depends on the perceived risk of the disease. Information campaigns can raise the awareness of the severity of STDs and the existing infection risk. We will focus on two types of campaigns: targeted information campaigns as the disease is on the rise, and, a sustained increase of the awareness in time. In the latter, this simply leads to an increased infection risk $T + \Delta T$. Whereas in the former, the payoffs are modified in the following form:

$$P_p(t) = -c - (T + \Delta T \Theta[I(t) - I(t-1)]) \frac{I_p(t)}{I_p(t) + S_p(t)}$$

$$P_{np}(t) = -(T + \Delta T \Theta[I(t) - I(t-1)]) \frac{I_{np}(t)}{I_{np}(t) + S_{np}(t)}.$$  

Accordingly, information campaigns, which raise the awareness for the severity of STDs and the imminent infection risk, are launched as prevalence is on the rise. Intuitively, a sustained increase of awareness should be more effective in containing the disease. However, considering the results in Fig. 3 the opposite is the case. In particular, targeted interventions prove much more effective in combating the maxima in the prevalence, in i.e. modulating the amplitude. In this sense, targeted information campaigns act like pulse vaccination programs through the intermediate of a behavioral adaption. In contrast, persisting awareness appears to mainly act like a baseline shift of the oscillations in the disease incidence. Pulse vaccination programs were initially designed to counteract measles outbreaks[19], whereas India implemented pulse vaccination programs against Polio[20]. Our results indicate that targeted, i.e. pulsed, information campaigns may prove equally fruitful in combating outbreaks of STDs.

Summarizing, in previous works analyzing the adaptive behavior in the presence of a disease, models explicitly fixed the behavior of the agents. Agents did not evaluate the utility of adapting the behavior. The protection was implicitly considered beneficial. Here we presented a framework in which agents adopt protection mechanisms by evaluating their
FIG. 3. **Intervention strategies.** Time evolution of the disease incidence in the presence of a pulsed information campaign (a) and persisting campaign (b) for different values of the perceived risk increment $\Delta T$. (c) Average prevalence in time for a pulsed information campaign (cross) and a persisting campaign (dot). The contact networks is a power-law network of size $N = 2000$ and exponent 2.5. Default parameters are $c = 1$, $\mu = 0.1$, and $T = 10$. The pulsed information campaign allows the suppression of the oscillatory incidence, while the persisting campaign not.

utility. Our framework applies to a variety of behavioral changes. It may describe the usage of condoms as well as individuals reducing their interaction rate due to the infection risk, allowing to quantify the adoption of protective behaviors in the presence of the disease outbreaks. The adaption of behavior emerges by comparing the infection risk with the associated protection costs. The adoption of protection mechanisms does not affect the epidemic threshold, $\lambda_c$. This is a general dilemma if individuals protect themselves on a voluntary basis. Nevertheless, we observed that the voluntary adoption of protection mechanisms can cause an oscillatory behavior of the disease dynamics. More precisely, delayed information regarding the infection risk lead to oscillations in the epidemic incidence. This mechanism has shed light on possible policies aimed at suppressing the oscillatory trends in the incidence, such as those observed in mycoplasma pneumoniae or syphilis. Our results point out that adopting targeted information campaigns as the disease incidence is on the rise is much more effective than sustained campaigns to combat the recent rise of STDs such as Gonorrhoea and Syphilis[21].
**METHODS**

**Equilibrium**

For characterizing the equilibrium of Eqs. (9)-(12), we first focus on the condition such that the system can reach the equilibrium state. Can the system reach the equilibrium state if the transition probabilities are non zero, $\Gamma_{a \rightarrow b} \neq 0$? Intuitively, since the game and disease dynamics are decoupled, it should not be possible. For proofing so, let us consider the following new set of variables:

$$P^i \equiv I^i_p + S^i_p$$  \hspace{1cm} (20)
$$NP^i \equiv I^i_{np} + S^i_{np}$$  \hspace{1cm} (21)
$$I^i_p \equiv I^i_p$$  \hspace{1cm} (22)
$$I^i_{np} \equiv I^i_{np}$$  \hspace{1cm} (23)

where the variables $P$ and $NP$ represent the probability of an agent adopting the protection mechanism, respectively not adopting the protection mechanism. With these variables the recurrence relations become:

$$\Delta P^i = P^i(t+1) - P^i(t) = NP^iT_{np \rightarrow p} - P^iT_{p \rightarrow np}$$  \hspace{1cm} (24)
$$\Delta NP^i = NP^i(t+1) - NP^i(t) = -NP^iT_{np \rightarrow p} + P^iT_{p \rightarrow np}$$  \hspace{1cm} (25)
$$\Delta I^i_p = I^i_p(t+1) - I^i_p(t) = -\mu I^i_p + (P^i - I^i_p)\lambda\gamma(I^i_p + I^i_{np}) - T_{np \rightarrow p}I^i_{np} + T_{p \rightarrow np}I^i_p$$  \hspace{1cm} (26)
$$\Delta I^i_{np} = I^i_{np}(t+1) - I^i_{np}(t) = -\mu I^i_{np} + (NV^i - I^i_{np})\lambda(\gamma I^i_p + I^i_{np}) + T_{p \rightarrow np}I^i_p - T_{np \rightarrow p}I^i_{np}.$$  \hspace{1cm} (27)

Since the transition probabilities $T_{np \rightarrow p}$ and $T_{p \rightarrow np}$ contain a Heavyside function $\Theta(P_p - P_{np})$ and $\Theta(P_{np} - P_p)$, respectively (see Eqs. (3) and (4)), they cannot be non zero simultaneously. Consequently, the two terms in the first two equations in Eqs. (24) and (25) cannot compensate each other such that $\Delta P^i = \Delta NP^i = 0$. Therefore, equilibrium can only be reached if $T_{np \rightarrow p} = T_{p \rightarrow np} = 0$, i.e. $P_p = P_{np}$ (see Eq. (15)).

**Well mixed population**

Analyzing analytically the coupled dynamics in a networked population proofs difficult due to the $4N$ nonlinear and coupled recurrence relations (see Eqs. (9)-(12)). However, in
order to get an understanding about the dynamics of the system we may consider a well mixed instead of a networked population. In the well mixed population, agents interact randomly. Accordingly, the interactions are not structured and thus the probability for an agent to be in a given compartment is the same in the whole population. Therefore, the system can be described by only four variables: \( S_p, S_{np}, I_p, I_{np} \). Accordingly, the recurrence relations take the same form as in Eqs. (9)-(12) but without the label \( i \):

\[
S_p(t+1) = (1 - T_{p \rightarrow np}) [S_p(1 - q_p) + I_p \mu] + T_{np \rightarrow p} [S_{np}(1 - q_{np}) + I_{np} \mu] \\
S_{np}(t+1) = T_{p \rightarrow np} [S_p(1 - q_{np}) + I_p \mu] + (1 - T_{np \rightarrow p}) [S_{np}(1 - q_{np}) + I_{np} \mu] \\
I_p(t+1) = (1 - T_{p \rightarrow np}) [S_p q_p + I_p (1 - \mu)] + T_{np \rightarrow p} [S_{np} q_{np} + I_{np} (1 - \mu)] \\
I_{np}(t+1) = T_{p \rightarrow np} [S_p q_{np} + I_p (1 - \mu)] + (1 - T_{np \rightarrow p}) [S_{np} q_{np} + I_{np} (1 - \mu)].
\]

In a similar way, the infection probabilities \( q_p \) and \( q_{np} \) are given by:

\[
q_p(t) = \lambda (\gamma I_p(t) + I_{np}(t)) \\
q_{np}(t) = \lambda \gamma (I_p(t) + I_{np}(t)).
\]

**Equilibrium point**

The payoffs of the two strategies must be equivalent in equilibrium. Setting the transitions probabilities to 0 in Eqs. (28)-(31), the equilibrium conditions \( S_p(t+1) = S_p(t) \) and \( I_p(t+1) = I_p(t) \) become equivalent. Equally, the conditions \( S_{np}(t+1) = S_{np}(t) \) and \( I_{np}(t+1) = I_{np}(t) \) become equivalent. Consequently, together with Eq. (15) we have three independent equations. This stems from the three independent variables in the system. Due to the conservation condition \( S_p + S_{np} + I_p + I_{np} = 1 \), one of the variables is redundant. For convenience, we will solve the system of equations with the three variables \( NP = I_{np} + S_{np}, I_p \) and \( I_{np} \). With this three variables the system of equations is given by:

\[
\frac{c}{T} = \frac{I_{np}}{NP} - \frac{I_p}{1 - NP} \\
I_p = \frac{\gamma \lambda}{\mu} (1 - NP - I_p)(I_{np} + I_p) \\
I_{np} = \frac{\lambda}{\mu} (NP - I_{np})(I_{np} + \gamma I_p).
\]

Using Eq. (34) allow us to express \( I_p \) as a function of \( I_{np} \) and \( NP \):

\[
I_p = (1 - NP) \left[ \frac{I_{np}}{NP} - \frac{c}{T} \right].
\]
The above expression contains two intuitive results. If \( NP = 1 \), we have \( I_p = 0 \), since none of the agents adopt the protection mechanism. Equally, if the adoption cost, \( c \), is higher than the recovery cost, \( T \), \( I_p < 0 \) since \( NV < I_{np} \) and \( c > T \). Consequently, as expected, none of the agents will adopt the protection mechanisms if \( c > T \). We can now insert the expression of \( I_p \) in Eq. (37) into Eq. (36) in order to find an expression of \( I_{np} \) as a function of \( NP \). As a matter of fact, we find a quadratic equation given by:

\[
I_{np}^2 \left[ 1 + \frac{\gamma(1-NP)}{NP} \right] + I_{np} \left[ \frac{\mu}{\lambda} - NP - (1 + \frac{c}{T})\gamma(1-NP) \right] + \frac{c}{T}NP(1-NP)\gamma = 0. \tag{38}
\]

Similarly, the above Eq. (38) reproduces trivial solution. If none of the agents adopt the protection mechanism, \( NP = 1 \), Eq. (38) becomes \( I_{np} = 1 - \mu/\lambda \), which is the standard solution of the SIS model. In the case of a perfect protection mechanism, \( \gamma = 0 \), we find \( I_{np} = NP(1-\mu/\lambda NP) \). This corresponds to the reduced transmission rate \( \lambda' = \lambda(1-P) \). A numerical exploration let us decide which is the physical solution in the quadratic equation in Eq. (38), leading to:

\[
I_{np} = \frac{-b + \sqrt{b^2 - 4ad}}{2a}. \tag{39}
\]

The expression of \( I_{np} \) as a function of \( NP \) allows us equally to express \( I_p \) as a function of \( NP \) by inserting it into Eq. (37). Consequently, replacing \( I_p \) and \( I_{np} \) in Eq. (35) by its expression as a function of \( NP \) allows to find a transcendental equation for \( NP \), which can be solved numerically. As oscillations are not present, the system reaches this equilibrium point.

The case \( \gamma = 0 \) In the case that the change of behavior allows for complete protection, \( \gamma = 0 \), the expression of the equilibrium point can be found analytically. Actually, for \( \gamma = 0 \), the dimensionality of the system is reduced. An agent adopting strategy \( P \) cannot get infected if \( \gamma = 0 \). Consequently, we have \( I_p = 0 \). In this case, the equilibrium conditions in Eqs. (34)-(36) become:

\[
\frac{c}{T} = \frac{I_{np}}{I_{np} + S_{np}} \tag{40}
\]

\[
I_{np} = \frac{\lambda}{\mu} S_{np} I_{np}. \tag{41}
\]
Solving the above equations, we find the equilibrium point as:

\[
S_{np} = \frac{\mu}{\lambda} \tag{42}
\]

\[
S_p = \frac{1}{(1-cT)} \left[ 1 - \frac{\mu}{\lambda} - \frac{c}{T} \right] \tag{43}
\]

\[
I_{np} = \frac{1}{(\frac{c}{T}-1)} \mu \cdot \tag{44}
\]

If the ratio between \( c \) and \( T \) is sufficiently high, the epidemics can almost not spread for \( \gamma = 0 \). Additionally, the fraction of infected agents decreases with an increasing transmission rate \( \lambda \) due to the increased adoption of protection mechanisms. However, accordingly to Eq. (40), the fraction of infected agents inside the non protected agents is independent of the transmission probability, \( \lambda \). Therefore, as \( \lambda \) increases the fraction of protected agents increases such that \( I_{np}/(I_{np} + S_{np}) \) stays constant. Consequently, the overall fraction of infected agents decreases with \( \lambda \). Additionally, the above expressions are only valid if the transmission probability, \( \lambda \) is above the classical epidemic threshold, \( \lambda > \mu \). This is due to the fact that the epidemic threshold is not affected by the voluntary adoption of protection mechanisms.

**Protection threshold**

For calculating the threshold, \( \tilde{\lambda} \), for the adaption of behavior, we can make use of the findings regarding the epidemic threshold. We argued that at the epidemic threshold, none of the agents adopt strategy \( p \). Consequently, the strategy \( p \) emerges in the presence of the disease. This allows us to make the following assumptions: \( S_p, I_p \ll S_{np}, I_{np} \) and \( S_p, I_p \ll 1 \). Therefore, we can expand the equilibrium condition for the game in Eq.(15) as:

\[
\frac{c}{T}(I_p + S_p) = \frac{I_{np}}{(I_p + S_p)} (1 - I_p - S_p - I_p) = I_{np}(I_p + S_p) - I_p + O((P)^2). \tag{45}
\]

Since we want to calculate the threshold for the strategy \( p \), we will neglect all the second order and higher order terms in \( P \) subsequently. Consequently, Eq. (45) can be rewritten as:

\[
I_p = (I_p + S_p) \left( I_{np} - \frac{c}{T} \right). \tag{46}
\]

In the equilibrium conditions coming from Eqs. (28)-(31), neglecting the second order terms is equivalent to neglecting the risk that a susceptible agent with strategy \( p \), \( S_p \), gets infected by another agent with strategy \( p \), \( I_p \). Therefore, whether the transmission probability is
reduced linearly or quadratically as two agents with strategy $p$ meet does not influence the threshold. Consequently, the here presented calculation of the threshold would also be valid if we assumed that agents with strategy $p$ reduce their interaction rate. Neglecting the second order terms, the equilibrium conditions become:

$$S_p = \frac{I_p}{I_{np}} \frac{\mu}{\gamma \lambda}$$  \hspace{1cm} (47)

$$I_p = I_{np} \frac{1 - I_{np} - \frac{\mu}{\lambda}}{I_{np}(1 + \gamma) - \gamma + \frac{\mu}{\gamma \lambda}}.$$  \hspace{1cm} (48)

Inserting Eq. (47) into Eq. (46) leads to a quadratic equation for $I_{np}$:

$$I_{np}^2 - I_{np} \left( 1 + \frac{c}{T} - \frac{\mu}{\gamma \lambda} \right) - \frac{c}{T} \frac{\mu}{\gamma \lambda} = 0.$$  \hspace{1cm} (49)

In the quadratic equation, there is only one non negative solution. Consequently, the explicit expression for $I_{np}$ is given by:

$$I_{np} = \frac{1}{2} \left[ 1 - \frac{\mu}{\gamma \lambda} + \frac{c}{T} + \sqrt{\left( \frac{\mu}{\gamma \lambda} + \frac{c}{T} \right)^2 + 4 \frac{\mu}{\gamma \lambda}} \right].$$  \hspace{1cm} (50)

The threshold can now be found if we consider the condition such that $P \neq 0$. Considering Eq.(47), we have $S_p > 0 \iff I_p > 0$. Therefore, the threshold, $\tilde{\lambda}$, is reached as $I_p$ becomes non zero. The denominator in the expression of $I_p$ in Eq. (47) is always positive. This can

$$I_{np}(1 + \gamma) - \gamma + \frac{\mu}{\gamma \lambda} = \frac{1}{2} \left[ 1 - \gamma + \frac{\mu}{\lambda} \left( \frac{1}{\gamma} - 1 \right) + (1 + \gamma) \left( \frac{c}{T \gamma} + \sqrt{\Delta} \right) \right] > 0.$$  \hspace{1cm} (51)

The positivity is guaranteed due to $\gamma \in [0, 1]$. Since the denominator is always positive, the threshold is reached as the numerator becomes non negative. The threshold condition therefore reads: $1 - I_{np} - \mu/\tilde{\lambda} = 0$. Inserting the expression of $I_{np}$ in Eq. (48) into the threshold condition, we find after tedious algebra the threshold, $\tilde{\lambda}$, as presented in Eq. (17).

In order to get a more accurate description of the networked dynamics, we can consider a well mixed population in which agents interact $k$ times at each time step. The number of interactions $k$ is then fixed by the mean degree of the network we want to approximate. The protection threshold is then rescaled as $\tilde{\lambda} \to \tilde{\lambda}k$.

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