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Vaccinating behaviour, information, and the dynamics of SIR vaccine preventable diseases

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Abstract

The increasing level of disease control by vaccination jointly with the growing standard of living and health of modern societies could favour the spread of exemption as a "rational" behaviour towards vaccination. Rational exemption implies that families will tend to relate the decision to vaccinate their children to the available information on the state of the disease. Using an SIR model with information dependent vaccination we show that rational exemption might make elimination of the disease an unfeasible task even if coverages as high as 100% are actually reached during epochs of high social alarm. Moreover, we show that rational exemption may also become responsible for the onset of sustained oscillations when the decision to vaccinate also depends on the past history of the disease.

Keywords: SIR models with vaccination; Rational exemption; Social alarm; Global stability; Oscillations

1. Introduction

Vaccines have been a central factor in improving the standards of living, and the standards of health (Bloom and Cannings, 2004; Livi Bacci, 2005). Mass vaccination has allowed increasing levels of disease control worldwide, which has recently culminated in the elimination of indigenous measles in Finland (Peltola et al., 1997) and of poliomyelitis in many areas of the world (CDC, 2004). A further positive effect of some mass vaccinations is the reduction of the incidence of virus-related tumours (Chang et al., 1997). For example, the anti-HBV vaccines may be considered a preventive anti-tumour vaccine (Lollini et al., 2006).

Nonetheless the recent experience of developed countries shows instances of declines in vaccination coverage for several diseases. In some cases this is a consequences of rumours and adverse publicity against vaccines. For example, the decline in coverage of the Measles–Mumps–-Rubella vaccine (MMR) recently observed in the UK (EURO SURVEILLANCE, 1998; CDR, 1998, 2002, 2004) has been explained by the role of adverse publicity about possible links between the vaccine, autism, and Crohn's disease (Wright and Polack, 2005). Similar facts have been found for Scotland (Friederichs et al., 2006). Another example is the decline in HBV coverage due to the "Thimerosal" case (Luman et al., 2004). In the future negative effects on coverage could derive from the argument, often raised by anti-vaccination movements, that vaccines could favour the onset of allergic diseases, a point that is still debated by the scientific literature (Koppen et al., 2004; Berndsen, 2004; Souza da Cunha, 2004; Schattner, 2005).

From a wider perspective, the phenomenon of coverage upswing has been common in the history of modern societies, often as a consequence of the tension between public health targets and individual freedom, for example between compulsory vaccination and conscientious or philosophical exemption (Salmon et al., 2006). Exemption against childhood immunization is a good example of this phenomenon: the tension stemming from the fear of

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damages due to the vaccine is emphasized when compulsory vaccination diminishes parents' autonomy as regards the decisions on their children health. Such tension can in many cases prove beneficial for the society as a whole, in that it can push research toward better outcomes and eventually lead to an improvement in the safety of vaccines, which is a major target of public health. In the short-term however the main consequence of coverage decline, or of delayed vaccination, is always an increase in susceptibility (CDR, 2004), and thus in the risk of resurgence of diseases that were perhaps thought to be well controlled.

An increasing number of studies deal with the motivations underlying parents' choices to vaccinate or not their children (Maayan-Metzger et al., 2005; Wright and Polack, 2005; Wroe et al., 2005; Friederichs et al., 2006). Besides the role played by conscientious exemption, these studies suggest the possibility of an "inverted U" relationship between education and income on one hand and propensity to vaccinate on the other. Two main remarks thus arise: first, the increasing well-being of modern societies could, in prospective terms, lead to increasing difficulties in maintaining high coverages. Second, an ultimate responsible in coverage decline is vaccination itself, i.e. the vaccination success in controlling diseases, which tends to encourage forms of "rational exemption". The argument underlying rational exemption is simple. Consider for example the cases of poliomyelitis and measles control. In several countries the increasing coverage with MMR within the WHO Plan for global measles elimination has driven circulation of the disease to minimal levels or even zero incidence, i.e. a situation where the few observed cases can be traced back to immigration. As the incidence of the diseases continues to decline thanks to vaccination, families become increasingly concerned with the risks associated with vaccines (WHO, 2006). If families start perceiving that the chance of acquiring infection for their children is lower compared to the risk of experiencing damages from the vaccine (this is actually so for poliomyelitis), they could believe it rational not to vaccinate their children, particularly if they perceive that the rest of the population will, instead, vaccinate. This rationality is of course myopic since the decision to not vaccinate should be forward looking and taking into account also expectations of future resurgence of infection due to declining coverage, and not just the currently observed regime of low incidence and high coverage. Moreover, it is an example of "free riding" (Stiglitz, 2000), as by the way all types of exemptions (Salmon et al., 2006).

The widespread adoption of rational exemption would lead to a situation where at least a part of families relate their decision to vaccinate to the available information on the state of the disease, vaccinating more, and promptly, under circumstances of high social alarm due to the disease, and little (and later) otherwise. Such a behaviour always existed, as pointed out by Salmon et al.: "…vaccination rates fell, although uptake tended to increase when outbreaks occurred" (Salmon et al., 2006, p. 438).

Motivated by the above considerations, in this paper we study the dynamic implications of information dependent vaccination for SIR vaccine preventable childhood diseases. The underlying idea is that the vaccine coverage is the outcome of decisions, to vaccinate or not their children, which are partly based on the publicly available information on the state of the disease. There is a growing body of literature on information-dependent vaccination and vaccination choice, and their implications for the dynamics of SIR models for vaccine preventable diseases. Since the seminal paper by Fine and Clarkson (1986), Brito et al. (1991) have explored the conditions under which the free-rider problem can actually be overcome without compulsory vaccination, through the use of taxes and subsidies. Geoffard and Philipson (1997) use SIR-type models to explore the difficulty of eradicating a disease in presence of rational exemption, even if incentives such as subsidies are included. Bauch and Earn (2004) develop a game theoretical interpretation based on an SIR model of the rational exemption phenomenon, and show that under a purely voluntary policy, rational exemption makes eradication impossible. Reluga et al. (2006) expand Bauch and Earn (2004) by setting the game theoretic approach within the "viability" approach, and study the dynamical consequences of rational exemption under both current and delayed information. Bauch (2005) studies SIR-type differential equations with information dependence and analyze a model similar to the one in the present manuscript. Both the latter studies show the existence of oscillations and the impossibility of eradicating the disease due to rational exemption. A further related study is Auld (2003), who models the issue of vaccination choice within the framework of an agent-based model.

The present work aims to contribute to this literature by (a) incorporating information dependence not only on current disease levels but also on the history of disease in the population, (b) including the possibility of catch-up vaccination as a strategy for those who decided to not vaccinate during epochs of low perceived risk, (c) providing more general mathematical result: for instance all our stability results on the model with vaccination dependent on current information are shown to hold globally.

More specifically, we consider some SIR models in which the vaccination coverage of newborn is the sum of two components: a steady one, given by the fraction of parents who, while taking the decision to immunize their children are not affected by the state of information on the disease, and an "information-dependent" one, which is taken to be an increasing function of the perceived risk (or the social alarm) due to the disease, as summarized by some information variable depending on the current and past state of the disease. We feel that our assumptions on coverage capture well the idea of rational exemption.

Our results are as follows. First, if the information function only summarizes the current state of the disease, then unless the steady component is above the elimination threshold, a unique endemic state will exist and is globally asymptotically stable (GAS). This result continues to hold even when we allow in the model delayed catch-up vaccination of older individuals as a "recuperation strategy" for families that did not vaccinate their children during epochs of low perceived risk. Second, if the information function also summarizes the past history of the disease according to an exponentially fading memory then we can also observe the emergence of stable oscillations through Hopf bifurcation of the endemic state, i.e. delayed state-dependent vaccination can be a source of steady oscillations for common childhood diseases. Analysis of selected subcases and numerical simulations gives insight on the conditions under which stable oscillations are more likely, and on the amplitude of the inter-epidemic period that would result as a consequence of the interaction between the factors traditionally included in SIR models, average age at infection, vaccination, and demographics, on the one hand, and those due to social behaviour by individuals on the other hand. Numerical simulations also suggest that the involved limit cycles are globally stable.

The paper is organized as follows. In Section 2 we introduce a general model encompassing the various special models considered. Section 3 reports some results on equilibria and local stability of the general model. Sections 4 and 5 report, respectively, the stability analysis of the undelayed and of the delayed case. Examples, numerical results, and a discussion of the implications of information dependent vaccination for the period of oscillations, are reported in Sections 6 and 7. Concluding remarks follow.

2. A family of models for information-related vaccinating behaviour

We consider the following family of SIR models for a nonfatal disease in a constant homogeneously mixing population, with state-dependent vaccination coverage:

$$\begin{aligned} X' &= \mu N(1-p(M)) - \mu X - \beta(t)\frac{XY}{N}, \\ Y' &= \beta(t)\frac{XY}{N} - (\mu+\nu)Y, \\ Z' &= \nu Y - \mu Z, \\ V' &= \mu N p(M) - \mu V, \end{aligned} \tag{1}$$

where X, Y, Z, V are functions of time, respectively denoting the number of susceptibles, infectious (and infectives), immune and vaccinated individuals at time t. Moreover, $\mu > 0$ denotes the birth and death rate, which are assumed identical, $\nu > 0$ the rate of recovery from infection, $\beta(t) > 0$ the transmission rate, which is assumed to be constant or bounded and periodically varying with minimal period θ usually equal to 1 year (Anderson and May, 1991), and $N = X + Y + Z + V$ is the total population, constant over time. Thus, it is useful to introduce the epidemiological fractions, i.e. the variables

$$S = X/N, \quad I = Y/N, \quad R = Z/N, \quad U = V/N. \tag{2}$$

The main novelty of (1) is the function p which denotes, assuming a 100% effective vaccine, the actual vaccination coverage at birth, which is assumed to be a function of the information variable M. We consider two distinct possibilities: (a) M only summarizes information about the current state of the disease, i.e. M only depends on current values of state variables, and (b) M also summarizes information about past values of state variables.

As regards case (a), one could take any empirically observed quantities published in usual statistics of infectious diseases, for instance:

- $M = \alpha\beta XY/N$, i.e. M is the currently reported absolute incidence where $\alpha > 0$ is the reporting rate. Alternatively, as public data report standardized rather than absolute incidence of diseases, one could take $M = \alpha\beta XY/N^2 = \alpha\beta SI$;
- $M = kI$ ($k > 0$), i.e. M is a linear function of the current prevalence of the disease, representing for instance the current standardized incidence of serious cases of the disease;
- $M = \alpha\beta I/(\mu + \alpha\beta I)$, i.e. M is a nonlinear increasing function of standardized incidence which can be taken as a measure of the perceived risk of infection (Reluga et al., 2006).

Generalizing the examples above, we shall assume that M is given by a function g of the fractions S, I. The function g is assumed to be continuous, increasing in the I variable, whereas we do not state hypotheses on the behaviour in dependence on S. For example, g can be independent of S (as in the case $g(S,I) = kI$), or increasing with S (as in the case $g(S,I) = \alpha\beta SI$). Furthermore, it is natural to assume $g(S,0) = 0$ for all S.

Case (b) in which M also depends on past values of state variables appears more realistic for many endemic disease where information comes after rather long routine procedures (such as laboratory confirmations, reporting delay in the transmission of information to public health and statistics authorities, etc) and when awareness of these phenomena to the general population takes time. In this case the information function M would be given by the delayed values of a function g of S and I with the same properties as in the unlagged case.

As known from the literature there are several routes to model time delays. The formulation adopted in this paper is

$$M(t) = \int_{-\infty}^{t} g(S(\tau), I(\tau))K(t-\tau)\,d\tau, \tag{3}$$

where K is the delaying kernel (MacDonald, 1989). In the stability analysis of Section 5, as a compromise between realism and tractability, we will only consider Erlangian kernels defined by the probability density function

$$Erl_{n,a}(x) = \frac{a^n}{(n-1)!}x^{n-1}e^{-ax} \quad x, a \in \mathbb{R}_+, \ n \in \mathbb{N}_+ \tag{4}$$

for which the mean delay is given by $T = n/a$ and the standard deviation by $\mathfrak{S} = \sqrt{n}/a$. Of special relevance in the Erlangian family is the first element $Erl_{1,a}$ called *exponentially fading memory* because it pays a declining weight to the past. On the other hand the second element $Erl_{2,a}$ defines the simpler "humped" Erlangian memory.

We have preferred infinitely supported distributed delays, as the Erlangian ones, to fixed lags, i.e. to kernels having the Dirac's form $K(t) = \delta(t - \tau_p)$, which lead to delay differential equations, because of their greater realism (Lloyd, 2001). First, fixed delays embed the idea that the past is reminded in terms of "events" rather than its whole history. Second, at the population level they require that individuals are homogeneous in their patterns of delay.

Finally, integro-differential systems with Erlangian delays are reducible to ordinary differential equations, thereby making their analysis simpler compared to other types of distributed delays (MacDonald, 1989). Note that (3) also embeds the unlagged case (a) discussed previously when

$$K(t) = \delta(t). \tag{5}$$

This allows us to consider (3) as a general representation for both cases (a) and (b).

Remark 1. Note that by assumptions on β and g it follows that M is bounded, taking all the values of an interval $\mathscr{I} = [0, M^{\sup})$, where $M^{\sup} = \sup_t M(t)$.

The coverage function p is defined as

$$p(M) = p_0 + p_1(M) \quad 0 < p_0 < 1, \ \ M \in \mathscr{I} \tag{6}$$

i.e. it is the sum of two components, a fixed one or "baseline" p_0, meaning that a fraction of the population is resilient to rumours and continues to vaccinate their children whatever be the state of publicly available information M, and a variable one $p_1(M)$. We assume that $p_1(M)$ essentially mirrors the reaction of families to the social alarm caused by the disease, according to the idea of rational exemption.[1] Thus, we assume that p_1 is an increasing function of M. In real situations we expect that p_1 is often S-shaped, very slowly increasing for low levels of M, and thereafter quickly increasing but saturating to some level $p_1^{\text{sat}} = p_1(M^{\sup})$ less or equal than $1 - p_0$. If inequality $p_1^{\text{sat}} < 1 - p_0$ holds then a positive fraction of individuals is never reached by vaccination, a fact well documented by the public health practice, due to the presence of anti-vaccinating movements and the cost to reach the more elusive population groups. As a consequence, we formally assume that

- $0 \leqslant p_1(M) \leqslant 1 - p_0$ for all $M \in \mathscr{I}$;
- $p_1(0) = 0$;
- p_1 is continuous and differentiable, except, in some cases, at a finite number of points, and increasing.

[1] The idea of rational exemption, or free riding, fits well in the scheme. Indeed the behaviour of the free rider is to vaccinate less when the fraction immune $R + U$ increases, i.e. $\partial p_1/\partial(R + U) < 0$. Since $R + U = 1 - S - I$ this implies that p_1 remains an increasing function of both its arguments (S, I).

Thus, if we take M to be the currently observed incidence of the disease, our formulation amounts to saying that when the disease incidence is high, families tend to react by increasing the vaccination coverage of their children. Conversely, when incidence declines to low levels, families react by vaccinating less.

Combining (1) and (3), our general model is given by the following nonlinear integro-differential system:

$$\begin{aligned} S' &= \mu(1 - p_0 - p_1(M)) - \mu S - \beta(t)SI, \\ I' &= I(\beta(t)S - (\mu + v)), \\ M &= \int_{-\infty}^{t} g(S(\tau), I(\tau))K(t - \tau)\, d\tau, \end{aligned} \tag{7}$$

where we have discarded variables R and U because their dynamics follow trivially from the dynamics of S, I and M.

If (5) holds, then $M = g(S, I)$, and (7) reduces to the unlagged two-dimensional system:

$$\begin{aligned} S' &= \mu(1 - p_0 - p_1(g(S, I))) - \mu S - \beta(t)SI, \\ I' &= I(\beta(t)S - (\mu + v)). \end{aligned} \tag{8}$$

If instead M obeys (4) then, depending on the order of Erlangian kernel, we obtain a family of models. In what follows we will investigate analytically the first Erlangian element $Erl_{1,a}$ which leads to the three-dimensional system:

$$\begin{aligned} S' &= \mu(1 - p_0 - p_1(M)) - \mu S - \beta(t)SI, \\ I' &= I(\beta S - (\mu + v)), \\ M' &= a(g(S, I) - M). \end{aligned} \tag{9}$$

Generalizations for higher order Erlangian kernels easily follow.

3. Properties of the general model

Let us consider initially the unlagged model (8) with constant transmission rate. This model differs from the standard text-book SIR model with vaccination at birth (Capasso, 1993) by the appearance of the state-dependent component of coverage $p_1(M)$. Obviously if the maximal coverage $p_0 + p_1^{\text{sat}}$ is below the critical coverage (or elimination threshold) $p_c = 1 - 1/R_0$, where $R_0 = \beta/(\mu + v)$ is the corresponding basic reproduction number, we cannot expect outcomes different from the standard one, i.e. the disease will persist. Similarly, if the baseline coverage p_0 exceeds the elimination threshold then state dependent vaccination can only accelerate elimination. Thus, the case of interest is when the elimination threshold lies in between the baseline and the maximal coverage. Two basic questions arise. First, can strong information-dependent vaccination allow elimination of the disease even though the baseline policy p_0 would not? Think to situations where social alarm pushes people to vaccinate for a while much in excess of the elimination threshold, for instance to temporary vaccinate 98% of newborn, when the elimination threshold is, say, 75%. Second, can state-dependent vaccination affect the stability of the endemic state?

Passing to more complex formulations as (9), since the inclusion of the delay only affects the stability of the system but not its equilibria, the main questions obviously become: in what manner the stability of the endemic state is affected when people react to past rather than current values of observed epidemiological variables? Can the delay trigger more complex behaviour, e.g. stable oscillations?

We start our analysis by noting that model (7) always admits the disease-free equilibrium:

$$DFE = (1 - p_0, 0, 0). \tag{10}$$

The stability properties of DFE are analyzed in the following proposition (proof in the Appendix A.1).

Proposition 2. *Both in case of θ-periodic or constant β, a sufficient condition for the GAS of the disease-free state DFE (10) is*

$$\frac{1-p_0}{\mu+v}\frac{1}{\theta}\int_0^{\theta}\beta(u)\,du \leqslant 1. \tag{11}$$

Remark 3. Notice that if β is constant condition (11) becomes the usual one

$$(1-p_0)R_0 \leqslant 1. \tag{12}$$

When condition (12) does not hold it is possible to show that there is a unique endemic equilibrium.

Proposition 4. *If β is constant and*

$$(1-p_0)R_0 > 1 \tag{13}$$

there exists a unique endemic equilibrium $EE = (S_e, I_e, M_e)$ for (7).

Proof. Observe preliminarly that if (7) admits an endemic equilibrium (S_e, I_e, M_e), then from (3) it must be

$$M_e = g(S_e, I_e)\int_0^{+\infty} K(\tau)\,d\tau = g(S_e, I_e) \tag{14}$$

and therefore $p_1(M_e) = p_1(g(S_e, I_e))$. Setting $I' = 0$ and disregarding the solution $I = 0$, we obtain

$$S_e = \frac{\mu+v}{\beta} = \frac{1}{R_0}. \tag{15}$$

Defining

$$\widehat{p}_1(I) = p_1(g(R_0^{-1}, I)) \tag{16}$$

it follows that there exists a unique solution I_e of the equation $S' = 0$:

$$1 - \frac{1}{R_0} - \frac{\mu+v}{\mu}I = p_0 + \widehat{p}_1(I). \tag{17}$$

Indeed the function defined by $f_2(I) = p_0 + \widehat{p}_1(I)$ by assumption is strictly increasing, whereas the linear function

$$f_1(I) = 1 - \frac{1}{R_0} - \frac{\mu+v}{\mu}I$$

is strictly decreasing. Hence condition (13) is equivalent to state that

$$f_1(0) = 1 - \frac{1}{R_0} > p_0 = f_2(0)$$

and by

$$f_1(1) = -\frac{1}{R_0} - \frac{v}{\mu} < 0 < p_0 + \widehat{p}_1(1) = f_2(1)$$

the conclusion follows. Notice that I_e will always be epidemiologically meaningful (i.e. $0 < I_e < 1$). $\square$

Remark 5. Eq. (17) implies

$$I_E^{\infty} < I_e < I_E^{o}, \tag{18}$$

where

$$I_E^{\infty} := \frac{\mu R_0(1 - R_0^{-1} - (p_0 + p_1^{\text{sat}}))}{\beta} \tag{19}$$

and

$$I_E^{o} := \frac{\mu R_0(1 - p_0 - R_0^{-1})}{\beta}. \tag{20}$$

Note that I_E^{∞} is equal to the infectious fraction obtainable in the SIR model with constant vaccination rate at birth equal to $p_0 + p_1^{\text{sat}}$, whereas I_E^{o} is equal to the infectious fraction in the SIR model with constant vaccination when only the baseline vaccination rate p_0 is considered.

Remark 6. In the piece-wise linear case $p_1(M) = \min\{cM, 1 - p_0\}$ if

$$g(S, I) = I \cdot \varphi(S)$$

Eq. (17) is analytically solvable and:

$$\begin{aligned} I_e &= \frac{\mu+v}{\mu+v+c\mu\varphi R_0^{-1}} \cdot \frac{\mu}{\mu+v} \cdot \frac{(1-p_0)R_0 - 1}{R_0} \\ &= \frac{\mu+v}{\mu+v+c\mu\varphi R_0^{-1}} \cdot I_E^{o}. \end{aligned} \tag{21}$$

Remark 7. It is well known that, in case of instability of the disease-free equilibrium, if the contact rate $\beta(t)$ is periodic, then the behaviour of a nonlinear epidemic model may be very complex. For example, at the best of our knowledge, there is no analytical demonstration of the strong persistence of the classical no-vaccination SIR model with periodic $\beta(t)$. As far as the persistence, we performed intensive numerical simulations, and in all cases we obtained that the system is strongly persistent. Epidemiologically, this means that the disease remains endemic since, roughly speaking, there are no long-term "oscillation-induced" eradications.

4. Stability analysis of the endemic equilibrium in the unlagged case

We now focus on the stability of the endemic state $EE = (S_e, I_e)$ in the no delay case (8) under the assumption of a constant transmission rate β. We assume that p_1 is differentiable. The following general result holds (proof postponed to the Appendix A.2):

Proposition 8. *Let β be constant, and $(1-p_0)R_0>1$. Then the unique endemic state EE of system* (8):

1. *if*
$$-p_1'(M_e)\frac{\partial g}{\partial S}(S_e,I_e)<1+\frac{\beta I_e}{\mu} \tag{22}$$
is LAS;
2. *if, in particular,*
$$\frac{\partial g}{\partial S}\geqslant 0 \tag{23}$$
is GAS in the positively invariant set:

$$\Omega^{**}=\{(S,I)\mid S\geqslant 0,\ I>0,\ S+I\leqslant 1,\ S\leqslant 1-p_0\}. \tag{24}$$

In the undelayed system limit cycles may be possible when the function g is decreasing with respect to the proportion of susceptible subjects, as the following proposition illustrates (proof in the Appendix A.3).

Proposition 9. *If β is constant, $(1-p_0)R_0>1$, and*
$$-p_1'(M_e)\frac{\partial g}{\partial S}(S_e,I_e)>1+\frac{\beta I_e}{\mu} \tag{25}$$
then system (8) *has at least one LAS limit cycle in Ω^{**}.*

4.1. A noteworthy extension: adding vaccination of susceptibles at ages different from birth

Previous results are quite general. Indeed they hold for the following more general model which also allows, compared to the basic model (8), "catch-up" vaccination of older individuals:

$$\begin{aligned} S' &= \mu(1-p_0-p_1(M))-(q_0+q_1(M))S-\mu S-\beta SI,\\ I' &= I(\beta S-(\mu+\nu)). \end{aligned} \tag{26}$$

The quantities q_0 and $q_1(M)$, respectively, denote the steady and information dependent components of the rate of vaccination of susceptibles at ages different from birth, in particular $q_1(M)$ fulfills the same assumptions as $p_1(M)$. This is a more robust formulation of our state-dependent vaccination problem because it allows to families that decided to not vaccinate their children during epochs of low social alarm the further possibility to "run to vaccinate" them at a later age during a subsequent period of high social alarm. It is possible to check that if the basic program (p_0,q_0) is insufficient to eliminate the disease, then also the "expanded" programme (p_0+p_1,q_0+q_1) will be incapable to achieve elimination. Proceeding as in the previous sections, we may, when the function g is increasing in the susceptible fraction, demonstrate these two propositions (we omit the easy proofs) extending Propositions 2 and 8:

Proposition 10. *A sufficient condition for the GAS of the disease-free state DFE of system* (26) *is*
$$\frac{\mu(1-p_0)}{\mu+q_0}\frac{1}{\mu+\nu}\frac{1}{\theta}\int_0^\theta \beta(u)\,du\leqslant 1. \tag{27}$$

Proposition 11. *If β is constant and*
$$\frac{\mu(1-p_0)}{\mu+q_0}R_0>1 \tag{28}$$
then model (26) *admits a unique endemic equilibrium and it is GAS in the set*:

$$\Gamma=\{(S,I)|S\geqslant 0, I>0, 0\leqslant S+I\leqslant 1\}.$$

We are now ready to get back to the two main questions we have raised on the potential role of state-dependent vaccination. Our main result of this section shows that: (a) if the baseline vaccination coverage is below the critical elimination threshold, then elimination is definitely an unfeasible task, even if during epochs of social alarm due to the disease coverage in the newborn could temporary achieve levels close to 100%! (b) things do not change when also state-dependent catch-up of older individuals is allowed; (c) the existence of state-dependent vaccination coverage can change the stability character of the *EE*, when g is decreasing in the susceptible fraction, from point stability to locally stable oscillations.

5. Onset of stable oscillations under exponentially fading memories

In this section we prove that when the actual coverage also depends on past information then stable oscillations may appear even under the simplest pattern of delay, i.e. the exponentially fading memory $Erl_{1,a}$. To make computations simpler we assume $g(S,I)=kI$ in (3), obtaining from (9), under the assumption of constant β, the following three-dimensional system:

$$\begin{aligned} S' &= \mu(1-p_0-p_1(M))-\mu S-\beta SI,\\ I' &= I(\beta S-(\mu+v)),\\ M' &= a(kI-M). \end{aligned} \tag{29}$$

As we have seen in Proposition 4, under condition $(1-p_0)R_0>1$, system (29) has the unique endemic equilibrium $EE=(S_e,I_e,M_e)$.

The local stability of *EE* depends on the delay parameter a defined in (4) as it is shown in the following proposition.

Proposition 12. *If and only if*
$$(\beta I_e+\mu)^2-\beta I_e\mu kp_1'(M_e)+2(\beta I_e+\mu)\sqrt{\beta I_e(v+\mu)}<0 \tag{30}$$
there exist two values a_1, a_2 with $0<a_1<a_2$ for the parameter a such that EE is unstable for $a\in(a_1,a_2)$, whereas it is LAS for $a\notin[a_1,a_2]$. At the points a_1 and a_2 Hopf bifurcations occur.

Proof. The stability analysis at EE leads to the following characteristic equation:

$$\lambda^3 + b_2\lambda^2 + b_1\lambda + b_0 = 0, \tag{31}$$

with coefficients

$$\begin{aligned} b_2 &= \beta I_e + \mu + a > 0, \\ b_1 &= \beta I_e(\mu + v + a) + a\mu > 0, \\ b_0 &= a\beta I_e(k\mu p_1'(M_e) + (\mu + v)) > 0. \end{aligned} \tag{32}$$

The positivity of b_j, by Descartes theorem, rules out the possibility of real positive eigenvalues, so that stability losses can only occur via Hopf bifurcations. Since a affects only the stability of EE and not its location and delay parameters are most often destabilizing (MacDonald, 1989), we use a as bifurcation parameter.

From Routh–Hurwitz theorem EE will be LAS if and only if $b_2b_1 - b_0 > 0$ equivalently written as

$$f(a) = B_2a^2 + B_1a + B_0 > 0, \quad a \in \mathbb{R}_+, \tag{33}$$

where

$$B_2 = \beta I_e + \mu, \tag{34}$$

$$B_1 = (\beta I_e + \mu)^2 - \beta I_e \mu k p_1'(M_e), \tag{35}$$

$$B_0 = \beta I_e(\beta I_e + \mu)(v + \mu). \tag{36}$$

The coefficients B_2, B_0 are positive, whereas B_1 has variable sign. Thus, if $B_1 \geqslant 0$ EE is always LAS independently on the delay. On the other hand, if $B_1 < 0$ instability is possible. Note that since $f(0) > 0$, $f(\infty) > 0$ the endemic equilibrium is however always LAS for both large or small values of the delay parameter a, i.e. for large mean delays $(T = 1/a \to +\infty)$ and for small mean delays $(T = 1/a \to 0)$.

Thus, stability continues to prevail if the discriminant

$$\Delta = B_1^2 - 4\beta I_e(v + \mu)(\beta I_e + \mu)^2 \tag{37}$$

is negative or null, whereas if $\Delta > 0$ there are two positive distinct solutions a_1 and a_2 for the equation $f(a) = 0$, i.e. two meaningful bifurcating values of the delay parameter a.

By simple algebra we can write Δ as

$$\Delta = \left(B_1 - 2(\beta I_e + \mu)\sqrt{\beta I_e(v + \mu)}\right) \times \left(B_1 + 2(\beta I_e + \mu)\sqrt{\beta I_e(v + \mu)}\right). \tag{38}$$

Since we are supposing $B_1 < 0$, then $\Delta > 0$ if and only if (30) holds.

It is finally trivial to demonstrate that a_1 and a_2 fulfill the test for nonzero speed (Guckenheimer and Holmes, 1983). Indeed as far as a_1 and a_2 are distinct roots of $f(a) = 0$ then

$$\left[\frac{d(b_2b_1 - b_0)}{da}\right]_{a=a_i} = \left[\frac{df(a)}{da}\right]_{a=a_i} \neq 0, \quad i = 1, 2. \qquad \square$$

Intuition would suggest that the onset of oscillations critically depends on the interaction between the information delay $a = T^{-1}$, and the shape of the extra-vaccination coverage p_1, particularly its slope p_1' evaluated at the endemic equilibrium. This intuition is not easy to be proved analytically from condition (30). We therefore move now to simulation in order to complete and illustrate our findings.

6. Examples and numerical simulations

In this section we report some numerical simulation of system (29) under three noteworthy functional forms of the function p_1. We focus on the relation between patterns of information delay and the reactivity of information-dependent vaccination in determining the onset of oscillations. Subsequently we shall discuss in greater detail the implications for the period of inter-epidemic oscillations.

Most our computations will be based on the following benchmark parameter constellation roughly mimicking measles: $\mu = (1/L)\,\text{days}^{-1}$ where $L = 75 \times 365$ days is the life expectancy at birth, $v = (1/\mathscr{D})\,\text{days}^{-1}$ where $\mathscr{D} = 7$ days is the average duration of infection, $R_0 = 10$ ($\beta \approx 1.43\,\text{days}^{-1}$). In a standard SIR model without information dependent coverage these values would imply a susceptible fraction at equilibrium $S_e = 0.1$, and critical coverage $p_c = 0.90$. In addition we take a baseline coverage $p_0 = 0.75$, which for $p_1 = 0$ implies an infective fraction at equilibrium equal to 3.83×10^{-5}. Finally, just to fix the ideas we set $k = 1$. This amounts to say that all cases of the disease are considered to be "serious cases".

Example (*Piece-wise linear varying vaccination coverage*). Let it be

$$p_1(M) = \min\{cM, 1 - p_0\}, \quad M \in \mathscr{I},$$

where c is a positive constant, representing the proportional change in the extra-vaccination coverage p_1 for an infinitesimal change or proportional change in delayed disease incidence M. This case has some pedagogic interest and moreover is a local approximation to more general coverage functions. The condition for instability (30) may be written as $\Psi(c) < 0$ where

$$\Psi(c) = \left(\frac{H_1}{H_2 + \mu ck} + \mu\right)^2 - \frac{\mu ck H_1}{H_2 + \mu ck} + 2\left(\frac{H_1}{H_2 + \mu ck} + \mu\right)\sqrt{\frac{H_1H_2}{H_2 + \mu ck}} \tag{39}$$

and

$$H_1 = \mu(\mu + v)(R_0(1 - p_0) - 1) > 0,$$
$$H_2 = \mu + v > 0.$$

Note that

$$\Psi(0) = \left(\frac{H_1}{H_2} + \mu\right)^2 + 2\left(\frac{H_1}{H_2} + \mu\right)\sqrt{H_1} > 0, \tag{40}$$

$$\Psi(\infty) = \mu^2 - H_1. \tag{41}$$

Thus, since the function Ψ is strictly decreasing in c, if $\Psi(\infty) < 0$, there exists a unique threshold c^* such that if

$c > c^*$ the instability condition is fulfilled. We note that the condition $\Psi(\infty) < 0$ holds for $R_0(1 - p_0)$ large enough. This means that oscillations are more likely to occur for infectious diseases with a large reproduction number, or under moderate control circumstances. Moreover, a longer period of infectiousness is, other things being equal, a further factor favouring oscillations.

Fig. 1 reports the shape of the function f for distinct values of c. For low values of c (say $c = 200$), f is always positive, but as c increases its graph shifts downward and intersections with the axis occur, thereby leading to bifurcations. Oscillations thus require quite large c values, since we need a high reactivity of p_1 at the scale of $M_e = kI_e$.

Example (*Michaelis–Menten type coverage*). Let us consider a more realistic case, namely the Michaelis–Menten function (Murray, 1989)

$$p_1(M) = \frac{CM}{DM + 1}, \quad C, D \in \mathbb{R}_+, \ \ M \in \mathscr{I}. \tag{42}$$

This function is concave and saturating with $C = p_1'(0)$ (thus $p_1(M) \leqslant CM$). It is convenient to reparametrize it as

$$p_1(M) = (1 - p_0 - \varepsilon)\frac{DM}{DM + 1}, \tag{43}$$

where we have set $C/D = 1 - p_0 - \varepsilon$, $\varepsilon \in \mathbb{R}_+$. This parametrization would imply a "roof" in the overall coverage given by $p_0 + (1 - p_0 - \varepsilon) = 1 - \varepsilon$ if we could let M go to $+\infty$. Though M is bounded, by choosing D sufficiently large, p_1 will reach values sufficiently close to its asymptote even for rather small values of M, which is satisfactory for practical purposes. Here we take $\varepsilon = 0.01$ potentially implying a roof coverage of 99% under circumstances of high perceived risk. Keeping constant the roof coverage the reactivity of p_1 is tuned by D.

Numerical computations show how the onset of oscillations is governed by the interaction between a and D. This is illustrated in Fig. 2 reporting the $f(a)$ function governing the stability of the endemic state for different values of D (under the benchmark parametric set). For small values of D, $f(a)$ is always positive and the endemic state is always locally stable. As D further increases, $f(a)$ intersects the horizontal axis, thus leading to instability. For instance for $D = 1500$ the system, which is stable for large values of a, is destabilized for $a \cong 0.005\,\text{days}^{-1}$ corresponding to an average delay $T \cong 200$ days. Further decreasing a, i.e. further increasing the mean delay T, leads to limit cycles whose amplitude is increasing up to a maximum and then decreasing until $a \cong 0.0015\,\text{days}^{-1}$, corresponding to $T \cong 660$ days, where oscillations disappear and the stability of the endemic state is restored. The shape of the bifurcation locus (a, D), given by the union of the solutions a_1, a_2 of the equation $f(a) = 0$, as functions of D, is illustrated in Fig. 3 for the benchmark parameter set, against two different cases, respectively, with $R_0 = 8$ and 6 (other parameters as the benchmark set). The corresponding mean bifurcating delays, i.e. the quantities $T_i(D) = 1/a_i(D)$, $i = 1, 2$ are reported in Fig. 4. Fig. 5 depicts the bifurcation locus as function of D for different values of the recovery rate $v = 1/\mathscr{D}$ ($\mathscr{D} = \text{benchmark} = 7$ days against $\mathscr{D} = 21$ and 35 days) which confirms the result found in the linear case: other things being equal an increase in the duration of the infectious period $\mathscr{D}$ favours the onset of oscillations.

As regards the dynamics of the model, we now consider numerical simulations of the model in the cyclic zone for $D = 5000$ ($I_e = 2.61 \times 10^{-5}$), implying (Fig. 3) that the first stability loss occurs for a around $0.017\,\text{days}^{-1}$, i.e. an average delay of about two months, and that the cyclical regime persist up to average delays in excess of 6 years,

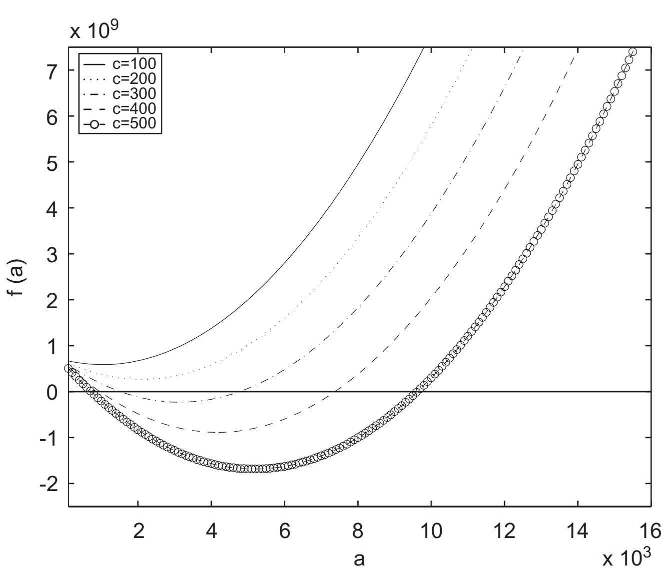

Fig. 1. The piece-wise linear case: shape of $f(a)$, for different values of c, from $c = 100$ (higher curve) to $c = 500$ (lower curve).

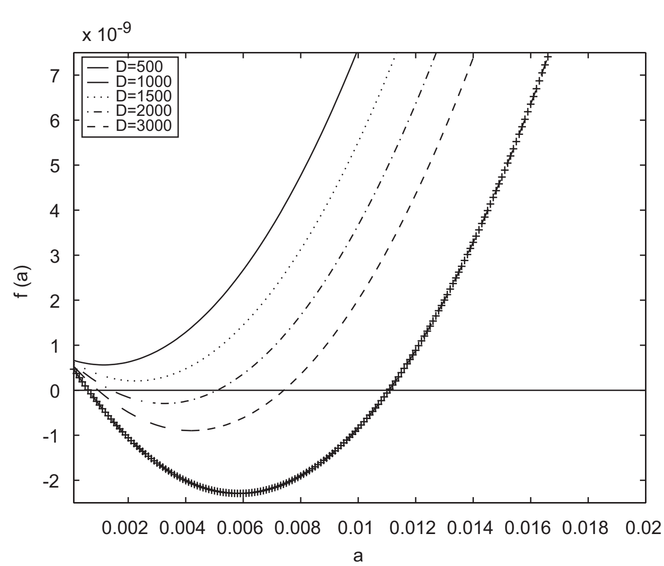

Fig. 2. The Michaelis–Menten case: shape of f as a function of the delay parameter a, for different values of D, from $D = 500$ (higher curve) to $D = 3000$ (lower curve).

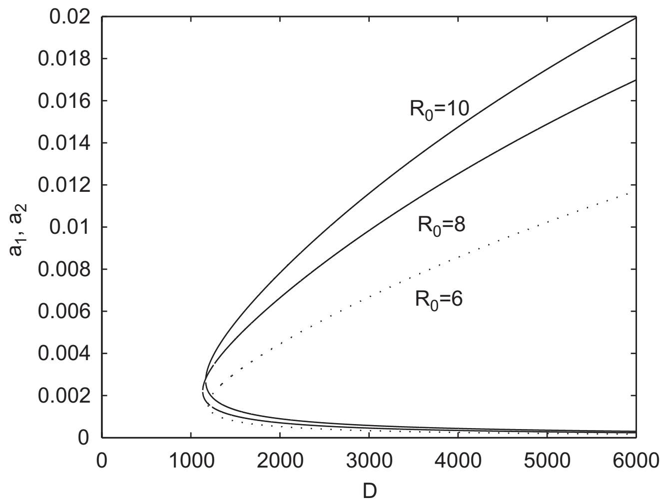

Fig. 3. The Michaelis–Menten case: shape of the bifurcation locus in the (a, D) plane for three different values of R_0 ($R_0 = 10, 8, 6$). The "low" ("high") branch of each curve is the graph of the smaller (larger) bifurcation value a_1 (a_2) as a function of the D parameter tuning curve (42).

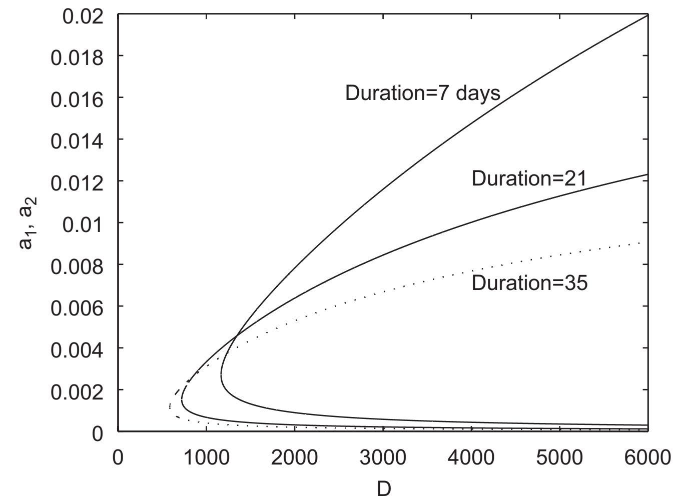

Fig. 5. The Michaelis–Menten case: shape of the bifurcation locus (a, D) for three different values of the duration of infection $\mathscr{D}$ ($\mathscr{D} = 7, 21, 35$ days). The "low" ("high") branch of the curve is the graph of the smaller (larger) bifurcation value a_1 (a_2) as a function of the D parameter tuning curve (42).

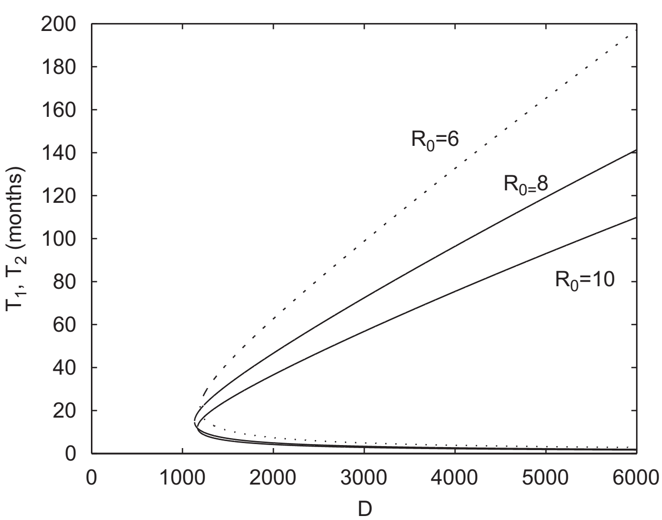

Fig. 4. The Michaelis–Menten case: shape of the bifurcation locus of Fig. 3 on the (T, D) plane for three different values of R_0 ($R_0 = 10, 8, 6$). The "low" ("high") branch of each curve is the graph of the smaller (larger) bifurcating delay $T_2 = 1/a_2$ ($T_1 = 1/a_1$) as a function of the D parameter tuning curve (42).

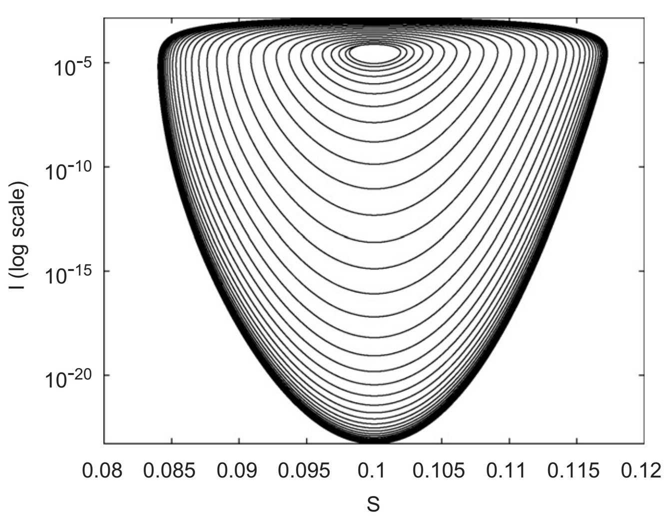

Fig. 6. The Michaelis–Menten case in the cyclic regime: transient and long-term dynamics in the (S, I) plane.

where the local stability of the endemic equilibrium is restored. Simulations for an average delay $T = 1$ year, which in many cases appears a reasonable figure for the information delay, are reported in Figs. 6 and 7. The initial conditions S_0, I_0 and M_0 were chosen by slightly perturbing the endemic state of the basic SIR model with constant vaccination coverage $p_0 = 0.75$: $S_0 = 1/R_0 = 0.1$, $I_0 = 0.00038$, and taking $M_0 = kI_0$. The convergence to the limit cycle predicted by Proposition 12 is illustrated in Fig. 6 which reports the phase plane dynamics in the (S, I) plane (I in log scale) until the emergence of the long-term pattern. The values of I during cycle troughs can appear very small but are comparable with those emerging in the periodically forced SIR model with vaccination.

Fig. 7 reports with time span 350 years, the corresponding transient (left-hand side) and long-term (right-hand side) time paths of susceptibles (top), infectives normalized to their equilibrium value (medium), and of the coverage function p_1 (bottom), jointly with its time average. The period of the oscillation sharply switches over time from a value which is initially close to the quasi-period of about 6 years predicted by the SIR model with constant baseline vaccination at birth only ($p_0 = 0.75$), to a long-term value close to 19 years. Moreover p_1 peaks up to 17% during epochs of high perceived risk, implying that overall coverage can peak to levels as high as 92% i.e. significantly

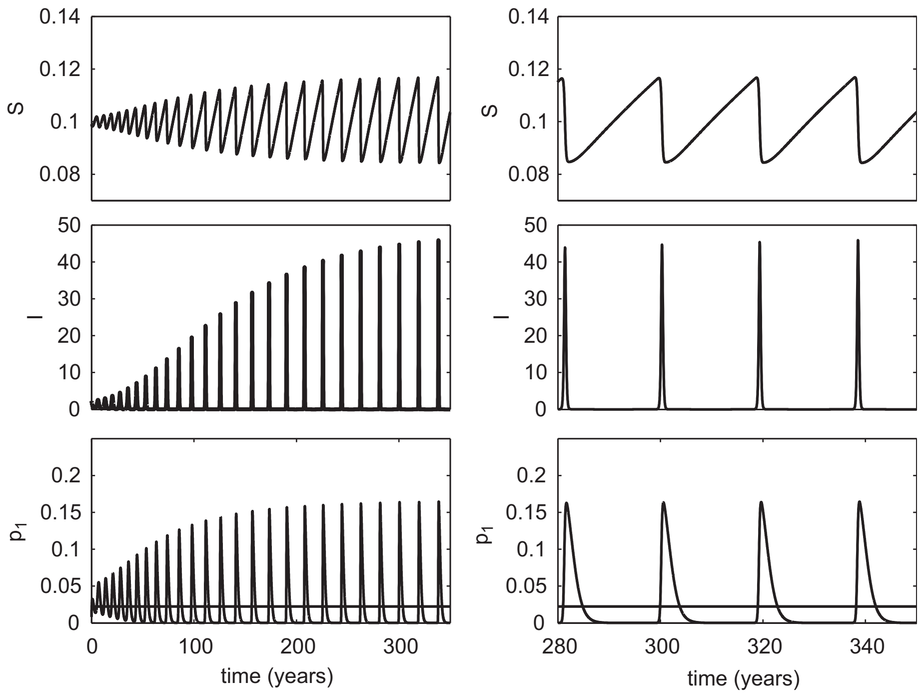

Fig. 7. The Michaelis–Menten case in the cyclic "zone": transient (left-hand side) and long-term (right-hand side) time paths of S, I, and p_1, showing convergence to a stable limit cycle. The dynamics of p_1 is compared with its time average (the flat line in the bottom graph).

in excess of the critical coverage. Elimination does not occur however, and this is understood by the low average level achieved by the extra coverage over time, which is less than 3%, implying that the overall average coverage does not exceed 78%.

Example (*Holling-type 2 S-shaped coverage*). Let us finally consider the following S-shaped function:

$$p_1(M) = \frac{C_2 M^2}{1 + D_2 M^2}, \quad C_2, D_2 \in \mathbb{R}_+, \quad M \in \mathscr{I} \tag{44}$$

which is a two-parameter Holling-type 2 curve (other choices are possible, for instance we also explored logistic-like functions, but the results are largely similar). We parametrize it in a manner analogous to what done for the Michaelis–Menten curve:

$$p_1(M) = (1 - p_0 - \varepsilon)\frac{D_2 M^2}{1 + D_2 M^2}. \tag{45}$$

In this case the parameter tuning the reactivity of p_1 is D_2. We still keep $\varepsilon = 0.01$. Though analytical computations become nasty in this case the S-shaped form is probably the one which better approximates real behaviour. Thus, we use this case to illustrate more in depth the relation between information-dependent vaccination and information delays. Under the benchmark parameter constellation values of D_2 in excess of 10^6 are necessary to generate oscillations. Setting, respectively, D_2 and T to the benchmark values $D_2 = 50 \times 10^6$ and $T = T_1 = 1$ year, Fig. 8 reports the time paths (until the long-term regime is achieved) of S, I and p_1. The period of oscillations steadily increases until a long-term figure of about 19 years; in addition the p_1 function approaches, during epochs of high social alarm, levels as high as 22% so that the overall coverages reaches levels as high as 97%. As already occurred in the Michaelis–Menten example, elimination of the disease cannot occur: the average coverage (not reported on the graph) during any inter-epidemic period, never exceeds 3%.

In order to better illustrate the impact of the information delays we have also investigated the sensitivity of output to changes in the fundamental parameters, by considering three distinct values of the average delay T, i.e. besides the benchmark delay $T_1 = 1$ year, the values $T_2 = 6$ months, $T_3 = 18$ months. This has been repeated for: (a) the benchmark parameter set (B), (b) a first "alternative" parameter set A1, considering a larger value of R_0, i.e. $R_0 = 15$ (a more standard value for measles in developed countries); (c) a second "alternative" parameter set A2 considering a faster response of vaccination to changing epidemiological conditions, with $D_2 = 100 \times 10^6$.

Fig. 9 provides a summary plot of the time paths of the susceptible fraction (left-hand side) and the information-dependent component of coverage p_1 (right-hand side) for this set of cases. The main facts can be summarized as follows:

(1) increasing information delays lead, coeteris paribus, to increasing periods of the long-term oscillation. For instance in the A1 scenario ($R_0 = 15$) the period increase from less than 12 years for an average delay

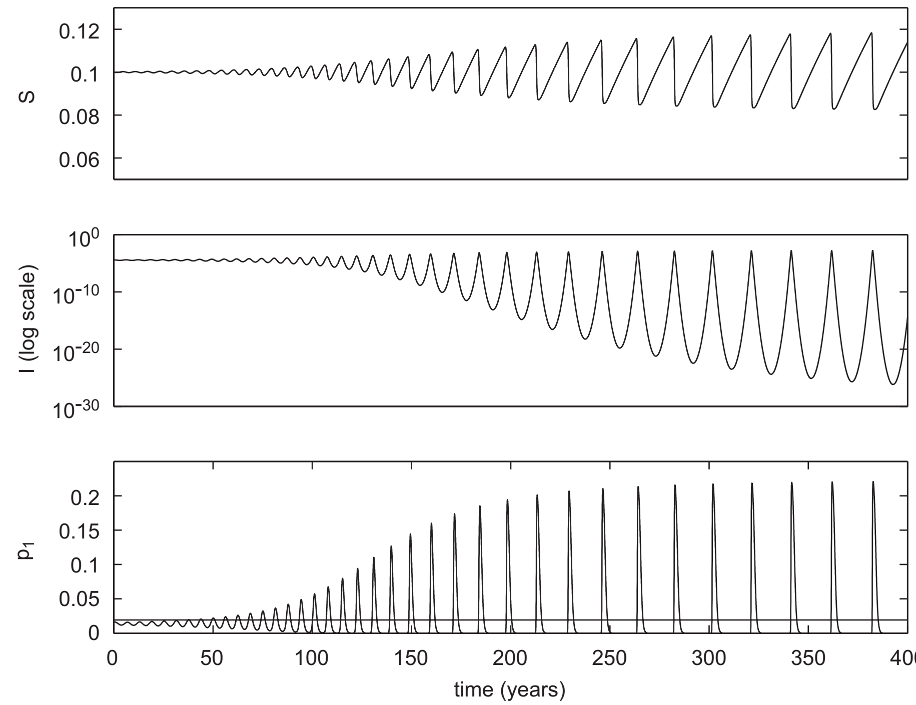

Fig. 8. The S-shaped case in the cyclic "zone": time paths of S, I (log scale), and p_1.

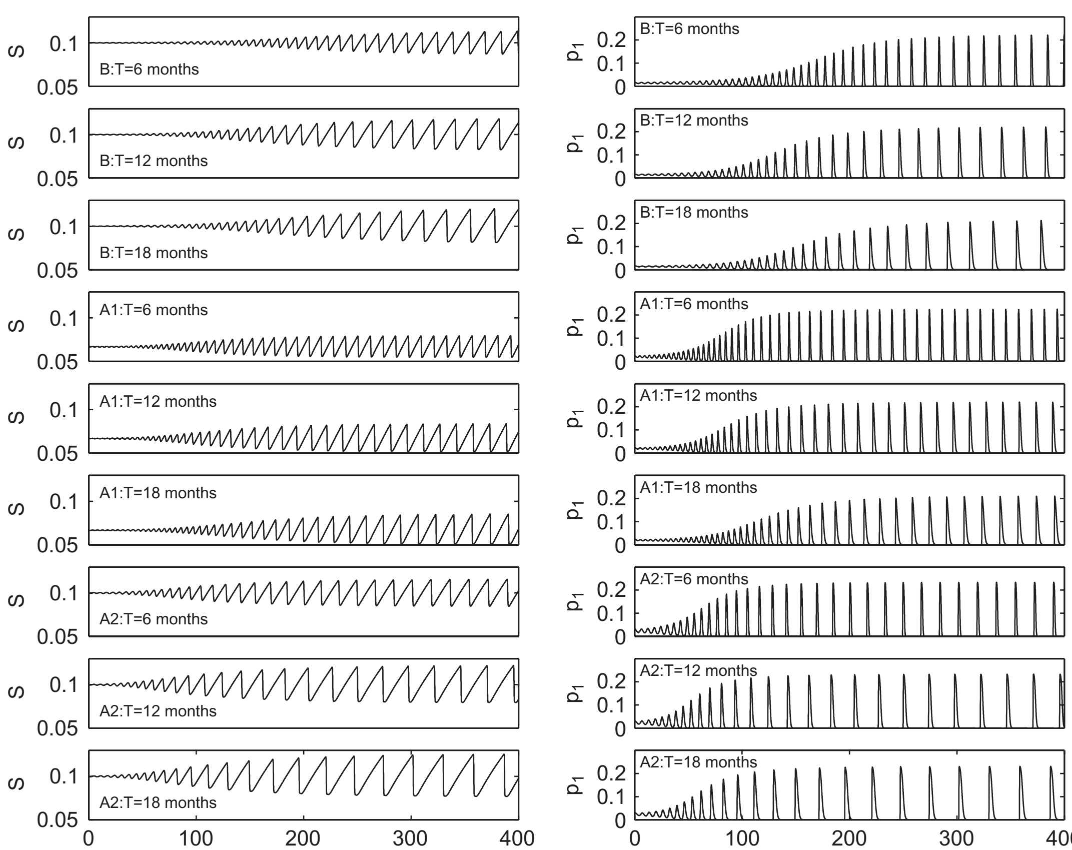

Fig. 9. The S-shaped case in the cyclic "zone". Summary plot of the time paths of S (left-hand side) and p_1 (right-hand side) for the three scenarios: B, A1,A2. Each scenario considers three distinct values of the average delay: $T = 6$ months, $T = 12$ months, $T = 18$ months.

$T=6$ months to about 14 years for $T=12$ months, and to about 16 years for $T=18$ months (similar things occur for scenarios B, A2);

(2) the increase in the inter-epidemic period observed in (1) in presence of longer memories leads to larger oscillations of the susceptible fraction, consistently with the larger susceptible replenishment due to the larger spacing between major epidemics;

(3) increasing the reactivity of vaccination through increasing D_2 also leads to increasing periods. For instance comparing scenarios B and A2 under $T=18$ months (similar for the other values) the inter-epidemic period grows from little in excess of 20 years to more than 30;

(4) increasing the reactivity of vaccination through increasing D_2 (compare B with A2) allows the overall coverage p_0+p_1 to more closely approach its "roof". However, as already pointed out eradication never occurs.

Remark 13. In addition to the results reported here, numerical simulations suggest that the closed orbit emerging via Hopf bifurcation of the endemic state in Proposition 12 is unique; moreover, the results of this Proposition seem to hold globally: when the endemic state is stable it appears to be GAS, and similarly when it switches its stability with the limit cycle. Finally, the results of this section extend straightforwardly to other choices of the information function M, for instance when it is given by the past reported incidence of the disease, and other types of delaying kernels in the Erlangian family.

7. The period of oscillations

The previous simulation results suggest the possibility that information delays in vaccination behaviour might yield a wide range of outcomes in terms of the period of the ensuing long-term sustained oscillation, compared to the basic (i.e. nonperiodically forced) SIR model. In the SIR model without vaccination only damped oscillations occur and are generated by the interplay of the epidemic mechanism, i.e. exhaustion of susceptibles, and the demographic one, i.e. regeneration of susceptibles via new births. For short diseases occurring early in life the quasi-period of the corresponding oscillations about the endemic state is well approximated by the simple formula (Anderson and May, 1991) $\tau \cong 2\pi\sqrt{\mathscr{A}\mathscr{D}}$ where $\mathscr{A}$ is the average age at which infection was acquired, also called the pre-vaccination average age at infection. When vaccination at birth is introduced it is well known that if the disease is not eliminated (i.e. the coverage is below the critical threshold $1-1/R_0$) the average age at infection increases and this consequently raises the inter-epidemic period. For example under the benchmark parametric set we find $\tau \cong 2.5$ years, and $\tau_{Vacc} \cong 6.1$ years.

7.1. The inter-epidemic quasi-period of the unlagged model

To clarify how information-dependent vaccination can affect the period of oscillations, we start from our two-dimensional undelayed model, which only has damped oscillations, and thus is straightforwardly comparable with the basic SIR model with vaccination. The question here is to what extent can (current) information-dependent vaccination interact with the mechanisms operating in the basic SIR model (transmission, demographics, "baseline" vaccination) and affect the inter-epidemic quasi-period? In our unlagged model the quasi-period of linearized oscillations is available in closed form. Choosing $g(S,I)=kI$ we have

$$\tau_{unlagged} = \frac{4\pi}{\sqrt{-(\mu+\beta I_e)^2 + 4\beta I_e(\mu k p_1'(kI_e)+\mu+v)}}, \tag{46}$$

with dumping time

$$\mathrm{dump} = \frac{2}{\mu+\beta I_e}. \tag{47}$$

It is possible to investigate the dependency of the length of the quasi-period (46) on the parameters tuning the shape of the information-dependent coverage p_1. We focus our analysis to the case of short diseases ($\mu \ll v$) occurring early in life.

The piece-wise linear case: Under a piece-wise linear p_1 function: $p_1(M)=\min\{cM, 1-p_0\}$, it is possible to show (Appendix A.4), studying $\tau_{unlagged}$ as a function of c only (other parameters being equal, but $\mu \ll v$), that $\tau_{unlagged}(c)$ is monotonically decreasing over the whole range of c and

$$\tau_{unlagged}(0) \approx \tau_{unlagged}(+\infty). \tag{48}$$

This means that $\tau_{unlagged}(c)$ is indeed almost flat in this case. To sum up, in the piece-wise linear case we have the surprising result that the quasi-period does not differ from the corresponding quasi-period of the basic SIR model with vaccination at the baseline level p_0, whatever be the magnitude of c!

The Michaelis–Menten case: Different phenomena occur for Michaelis–Menten-type p_1 functions. Some analytical considerations are still possible. The adopted parametrization (42) makes p_1 dependent on two parameters, D and ε, implying that the quasi-period of the model is a function $\tau_{unlagged}(D,\varepsilon)$ of both such parameters. Fig. 10 shows the relation between the quasi-period and D, for $\varepsilon=0.01$ as in our simulation run, other parameters as in the benchmark set, for a very wide range of D values. Fig. 10 confirms that $\tau_{unlagged}(D, 0.01)$ is an eventually increasing function of D (it can indeed have a through, though not pronounced, for very small D values) ranging from the value of about 6.1 years observed in the underlying SIR model with only the baseline vaccination schedule $p_0=0.75$ (this corresponds to $D=0$) up to a maximum around 10 years for very large levels of D

($D = 10^6$). The flat lines denote the quasi-period in the underlying SIR models (a) without vaccination, and (b) with baseline coverage $p_0 = 0.75$, reported for reference. Fig. 11 shows the overall shape of $\tau_{unlagged}(D, \varepsilon)$. The dependency on ε is nonmonotonic but this depends mainly on the fact that the manner in which D, ε affect p_1 is not independent, i.e. for a given D, increasing values of ε promote steeper shapes of p_1, which lead to smaller endemic infected fractions, and so on.

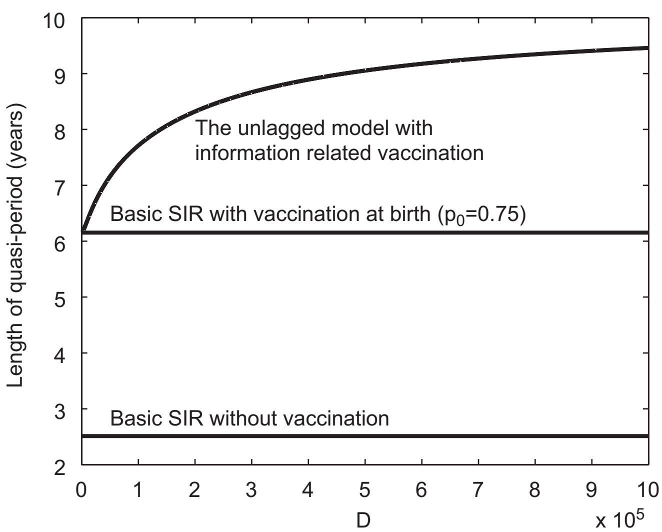

Fig. 10. The unlagged model, Michaelis–Menten case. The quasi-period $\tau_{unlagged}$ of the endemic oscillation as a function of D, for $\varepsilon = 0.01$, other parameters as in the benchmark set.

7.2. The inter-epidemic period of the delayed model

The delayed model exhibits both damped oscillations when the endemic state is LAS and genuine stable oscillations in the regime induced by the Hopf bifurcations. The inclusion of the delay has the potential to affect the period of oscillations in both such cases, but little can be said analytically on the dependence of the period or quasi-period on the shape of the vaccination function p_1. For instance as regards the damped oscillations about the endemic state, the eigenvalues can still be found in closed form but the problem of interpretation becomes formidable.

7.2.1. The period at the onset of the Hopf bifurcation

The true period of the (degenerate) cycle that occurs at the appearance of the Hopf bifurcation can be found explicitly. At a bifurcation point the system has a real negative eigenvalue, call it A, and a purely imaginary pair $\pm\omega i$, where ω denotes the frequency of the oscillations, related to the period τ by $\tau = 2\pi/\omega$. Thus, the characteristic polynomial at the bifurcation point can be factored as follows: $P(\lambda) = (\lambda^2 + \omega^2)(\lambda - A)$. Comparing this expression with the characteristic polynomial (31)–(32) of our delayed model (29), we obtain $\omega^2 = \beta I_e(\mu + v + a) + a\mu$ and remembering that we need to consider parameter constellations belonging to the bifurcation locus, i.e. for $b_2 b_1 - b_0 = f(a) = 0$, the frequency of the degenerate cycle is

$$\omega_H = \left(\sqrt{\beta I_e(\mu + v + a) + a\mu}\right)_{f(a)=0} \tag{49}$$

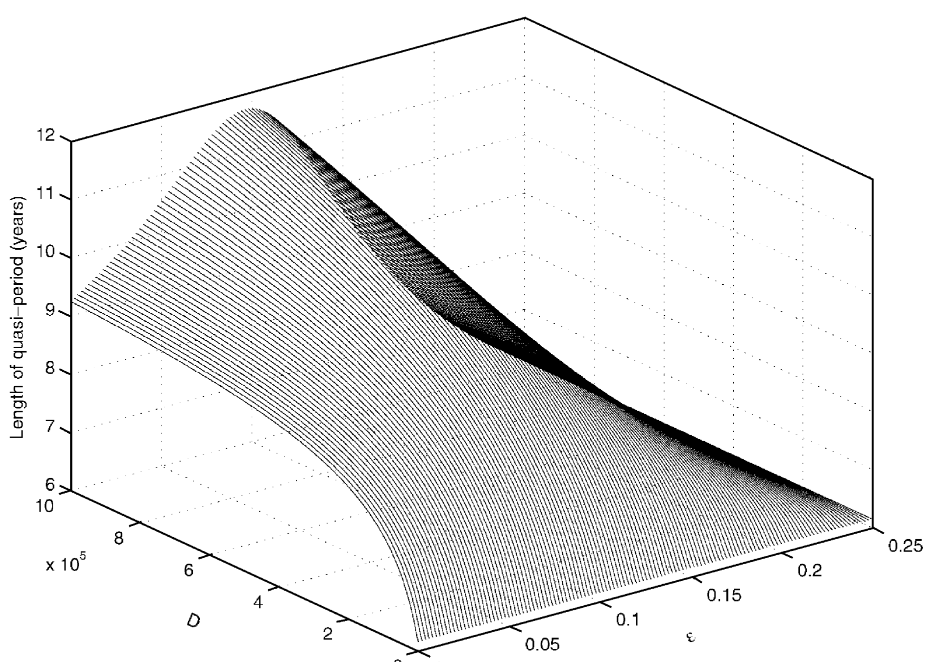

Fig. 11. The unlagged model, Michaelis–Menten case. The quasi-period $\tau_{unlagged}$ of the endemic oscillation as a joint function of D, ε, other parameters as in the benchmark set.

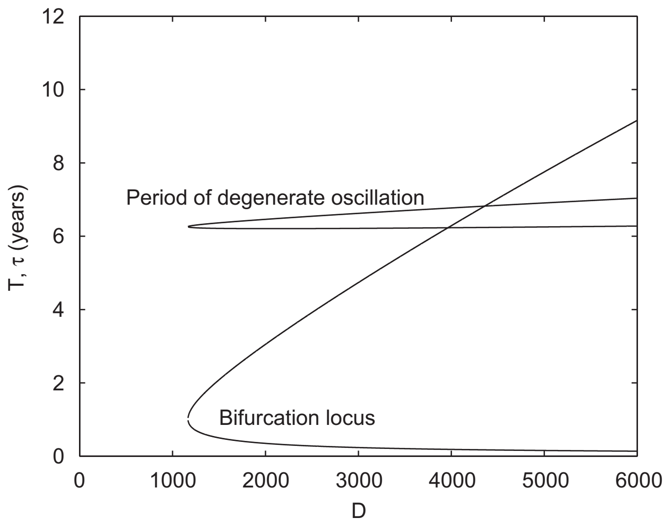

Fig. 12. The Michaelis–Menten case. Bifurcating delay versus the corresponding bifurcating period (benchmark parametric set).

and the corresponding period is

$$\tau_{delay\_Bif} = \left(\frac{2\pi}{\sqrt{\beta I_e(\mu + v + a) + a\mu}} \right)_{f(a)=0}. \tag{50}$$

This allows us to look at how the period of the degenerate oscillations is influenced by the parameters tuning the vaccination function p_1.

For example, for the Michaelis–Menten case, Fig. 12 adds to the graph of the bifurcation locus of Fig. 4, the graph of the amplitude of the period of the degenerate cycle occurring on each point of the bifurcation locus. The interpretation of Fig. 12 is the following: for example for $D = 3000$ the "small delay" bifurcation occurs for a value of T around 3 months. At this point a degenerate cycle occurs having period little in excess of 6 years. Briefly Fig. 12 shows that the period at the onset of the bifurcation is rather insensitive to "where the bifurcation actually occurs", particularly the bifurcation occurring for small delays (the lower branch of the bifurcation locus) causes degenerate cycles whose period never differ significantly from the period of the basic SIR model with baseline vaccination.

7.2.2. The true period of the sustained oscillation

The most interesting issue is clearly what happens when we move far away from the bifurcation locus, i.e. what is the dependency of the period of the true sustained oscillation on the amplitude of the average information delay on which families base their vaccination decisions. Our discussion on the shape of the bifurcations locus has shown that for parameters constellations for which cycles exist, they "live" in a very wide range of values of the average delay. By repeated simulations of the model it is possible to draw the dependency of the period of oscillations on the length of the memory. Fig. 13 shows

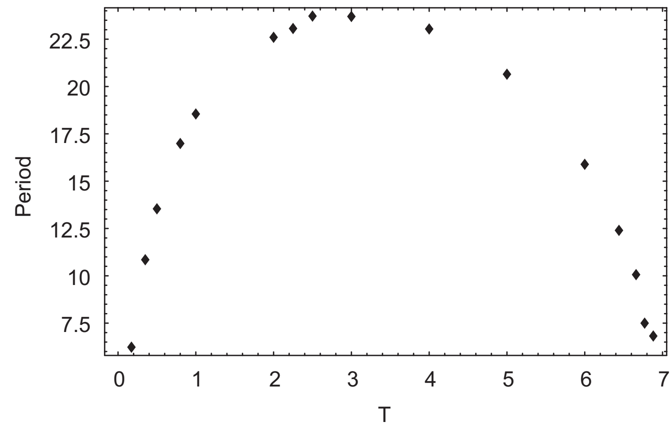

Fig. 13. The Michaelis–Menten case. Period of the sustained oscillations as a function of the average delay (Period and average delay expressed in years, $D = 4400$, $\varepsilon = 0.01$, other parameters as in the benchmark parametric set).

for the Michaelis–Menten case, under a value of D ($D = 4400$) allowing oscillation ($\varepsilon = 0.01$, other parameters as in the benchmark parametric set) the dependency of the period of the stable long-term oscillation on the length of the average delay. Fig. 13 is drawn with reference only to the window of T values for which stable oscillations exist, which is between about two months and 7 years (outside this window no stable oscillations but only damped oscillations toward the steady state exist). The dependency is humped, as it is reasonable, given the shape of the bifurcation locus. In particular the amplitude of the period as a function of the average delay takes values close to the figure predicted by the SIR model with vaccination at the baseline level p_0, i.e. close to about 6.2 years, for small delays, i.e. delays very close to the "small delay" bifurcation value; then it increases with the information delay up to a peak of about 22 years (this occurs when the average information delay is close to 3 years); finally it starts decreasing to re-approach a value close to the period of the SIR model for very large information delays (where cycles disappear).

8. Discussion

This work has investigated the implications of information-dependent vaccination for the dynamics and control of SIR childhood vaccine preventable infectious diseases. Here information-dependent vaccination is used to model the phenomena of rational exemption to vaccination and social alarm as a consequence of the spread of public information on the disease, by assuming that a component of the overall vaccination coverage is positively correlated with the available information on the disease. In simple words this means that a fraction of the families will not vaccinate their children during epochs of low social alarm due to the disease, thereby decreasing the total coverage.

Overall, our results have shown that if the steady component of vaccination is below the critical elimination threshold there is no hope to eliminate the disease even if during epochs of high social alarm coverage at birth could temporary achieve levels as high as 100%, and strong supplementary coverage of adults can be achieved by catch-up policies. A further main consequence of information-dependent vaccination is the onset of sustained oscillations. Such cycles are triggered by a somewhat violent but not instantaneous reaction by people to the social alarm caused by the disease. In other words stable oscillations appear when parents, in deciding on whether to vaccinate or not their children make use of past, and not only current, information about the disease and furthermore tend to react quite violently to epochs of social alarm by promptly and significantly increasing the vaccination coverage.

It is to be noticed that, as regards the cyclic regime, this occurs in a very wide range of information delays, from few months to several years, so that we can correctly say that oscillations are the rule. These oscillations can generate, depending on the form of the information-dependent vaccination curve, a wide range of possible inter-epidemic periods, some of which are completely realistic also from the viewpoint of vaccination programmes. In particular these periods range from a minimum length which is exactly the one found in the SIR model with vaccination and remain within order of magnitude "relevant" for public health purposes provided the delay is not too long.

Additionally, the results found in the paper appear to be robust in that they seem to extend to other choices of the information function, and to other types of delay patterns. Thus, we feel that the mechanisms devised in this paper represent an important source of oscillations of vaccine preventable diseases, up to now little stressed. Concerning the oscillations, another point we are currently investigating is the nonlinear inter-play between these information-related oscillations and seasonal variations in the contact rate (d'Onofrio et al., manuscript in preparation).

We acknowledge that this is just a first step toward more realistic formulations of the problem of the interaction of information and vaccinating behaviour. Future work should (a) include behaviourally founded vaccination functions along the directions indicated for instance in Bauch (2005), Reluga et al. (2006); (b) include more realistic factors particularly age structure. This appears to be the only way to properly deal with the risks of serious side-effects from the diseases, which are age-related, and potential long-term undesired effects of vaccination. Moreover, it is the proper manner to deal with vaccination choices, since fully rational agents (parents) should take into consideration the risk of side effects while forming the decision to vaccinate or not their children. Moreover, the inclusion of age structure would allow a more realistic treatment of "catch-up" vaccination, treated here very coarsely, as a rational strategy for those who decided to not vaccinate their children at the proper age because the perceived risk from the diseases was low; (c) include real data on vaccinating behaviour.

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Appendix A

A.1. Proof of Proposition 2

Defining $\sigma(t) = S(t) + I(t)$ we obtain:

$$\sigma' = \mu(1 - p_0) - \mu\sigma - vI - \mu p_1(M) \leqslant \mu(1 - p_0) - \mu\sigma. \quad (51)$$

By a comparison theorem for ODEs (Hale, 1969), it follows that asymptotically it must be

$$S + I \leqslant 1 - p_0 \quad (52)$$

hence

$$I' \leqslant I(\beta(t)(1 - p_0 - I) - (\mu + v)). \quad (53)$$

From (53) it descends

$$I' \leqslant I(\beta(t)(1 - p_0) - (\mu + v))$$

and if (11) strictly holds, it follows that

$$I(t) \to 0 \quad \Rightarrow \quad S(t) \to 1 - p_0 \quad (54)$$

i.e. the DFE is GAS.

If in (11) the equality holds, we may write

$$(1 - p_0)\beta(t) = (\mu + v) + w(t), \quad (55)$$

where $w(t)$ is a θ-periodic function having null mean value, if $\beta(t)$ is θ-periodic. The case of constant transmission rate may be formally studied as well by considering $w(t) = 0$. Thus, we may rewrite (53) as follows:

$$I' \leqslant w(t)I - \beta(t)I^2 \quad (56)$$

i.e. $I(t) \leqslant z(t)$, where $z(t)$ is the solution of the Riccati's differential equation:

$$z' = w(t)z - \beta(t)z^2, \quad (57)$$

with $z(0) = I(0) \neq 0$. Defining

$$W(t) = \int_0^t w(s)\,ds \quad (58)$$

which is periodic by construction, it turns out that

$$z(t) = \frac{\exp\{W(t)\}}{1/I(0) + \int_0^t \exp\{W(u)\}\beta(u)\,du} \leqslant \frac{\exp(W_{\max})}{1/I(0) + (\beta_{\min}\exp(W_{\min}))t} \to 0^+. \quad (59)$$

Thus, in turn

$$z(t) \to 0^+ \quad \Rightarrow \quad I(t) \to 0^+ \quad \Rightarrow \quad S(t) \to 1 - p_0. \quad (60)$$

A.2. Proof of Proposition 8

1. By Proposition 4 there exists a unique endemic equilibrium $EE = (S_e, I_e)$ for system (8). A linearization of (8) near EE yields the following Jacobian matrix:

$$J(S_e, I_e) = \begin{pmatrix} -\mu p_1'(M_e)\frac{\partial g}{\partial S}(S_e, I_e) - \mu - \beta I_e & -(\beta S_e + \mu p_1'(M_e)\frac{\partial g}{\partial I}(S_e, I_e)) \\ \beta I_e & 0 \end{pmatrix},$$

with eigenvalues having negative real parts, since, by (22) and the assumption $p_1' \geqslant 0$,

$$\mathrm{tr}\, J(S_e, I_e) = -\mu p_1'(M_e)\frac{\partial g}{\partial S} - \mu - \beta I_e < 0, \qquad (61)$$

$$\det J(S_e, I_e) = \beta I_e \left(\beta S_e + \mu p_1'(M_e)\frac{\partial g}{\partial I}(S_e, I_e)\right) > 0. \qquad (62)$$

2. In Ω^{**} there are no closed orbits since, by (23) and $p_1' \geqslant 0$:

$$\mathrm{div}\left(\frac{1}{I}(S', I')\right) = -\frac{\mu}{I} p_1'(M)\frac{\partial M}{\partial S} - \frac{\mu}{I} - \beta < 0.$$

Thus, by the Poincaré–Bendixon thricotomy (Thieme, 2003) it follows that the endemic equilibrium is GAS in Ω^{**}.

A.3. Proof of Proposition 9

With reference to the Proof of Proposition 8, we have from (61) that condition (25) guarantees the instability of EE, and since Ω^{**} is bounded and positively invariant, from the Poincaré–Bendixon's thricotomy it follows the existence of at least one LAS limit cycle.

A.4. Proof on inter-epidemic periods

The undelayed model: piece-wise linear case: In the piece-wise linear case ($p_1(M) = \min\{cM, 1 - p_0\}$) formula (46) implies

$$\tau_{unlagged}(c) = \frac{4\pi}{\sqrt{4(\mu + v)\mu((1 - p_0)R_0 - 1) - \mu^2\left(1 + \frac{(\mu + v)((1 - p_0)R_0 - 1)}{(\mu + v + ck\mu)}\right)^2}}. \qquad (63)$$

Thus, since μ is "small" and $\mu \ll v$, it easily follows

$$\tau_{unlagged}(0) = \frac{4\pi}{\sqrt{4(\mu + v)\mu((1 - p_0)R_0 - 1) - \left(\frac{(1 - p_0)\beta}{1 + v/\mu}\right)^2}} \approx \frac{4\pi}{\sqrt{4(\mu + v)\mu((1 - p_0)R_0 - 1) - \mu^2}} = \tau_{unlagged}(+\infty).$$

Finally, to show the monotonicity of $\tau_{unlagged}(c)$, define

$$\tau_{unlagged}(c) = \frac{4\pi}{\sqrt{ff(c)}}.$$

We have that

$$ff'(c) = k\frac{2\beta\mu^3(1 - (1 - p_0)R_0)(\beta(1 - (1 - p_0)R_0) - R_0(ck\mu + \mu + v))}{R_0^2(ck\mu + \mu + v)^3} > 0$$

for its numerator is the product of two negative quantities if $R_0(1 - p_0) > 1$.

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