

Attack rates of seasonal epidemics

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ARTICLE INFO

Article history:

Received 20 February 2011

Received in revised form 22 October 2011

Accepted 24 October 2011

Available online 9 November 2011

Keywords:

Seasonal epidemics

SIR model

Seasonal forcing

Attack rate

Vaccination

ABSTRACT

We study the attack rate, that is the total fraction of the population infected each year, for a disease with seasonally varying transmission rate. The attack rate is shown to be governed by both the reproductive number, reflecting the transmissibility of the disease, and the birth rate, which provides a source of new susceptibles. For the case of epidemics which have an annual period (like the seasonality), we prove inequalities which show that the attack rate is close to that of the non-seasonal model, so that it is nearly independent of the strength of the forcing, despite the fact that the shape of the epidemic curve depends strongly on the degree of seasonality of the forcing. Numerical simulations show that this holds to an even stronger extent than is implied by our rigorous results. When the system has subharmonic or chaotic solutions, we show that similar results hold when the attack rate is replaced by the average attack rate over several years. Consequences of these findings for analyzing the effect of vaccination in seasonally-forced models are noted.

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1. Introduction

1.1. Seasonal epidemics

When a new infectious agent invades a population without prior immunity, the size of the resulting epidemic is determined by the reproductive number \mathcal{R}_0 , which is itself dependent on the duration of infection and on its transmissibility. Once the infectious agent has been circulating for a while, the size of recurrent epidemics depends crucially also on the degree of immunity which has developed in the population due to previous exposures, or in other words on the fraction of susceptibles in the population. This fraction is itself governed by the size of previous epidemics, as well as by the rate of replenishment of susceptibles, either through demographic processes (births or immigration) or through the loss of previously acquired immunity. In this work we consider the former, in which case the simplest model for describing the process is the well-known SIR model. Moreover, since a constant coefficient SIR model leads to damped oscillations converging to an endemic equilibrium, explanation of recurrent epidemics which occur during specific months of the year requires the positing of a seasonally-dependent transmission coefficient. The seasonality in the transmission can be due to climatic factors influencing pathogen survival outside the host, or to seasonal changes in host immune function or host behavior, see [1,9,19].

We thus consider the seasonally forced SIR model

$$S' = \mu(1 - S) - \beta(t)SI, \quad (1)$$

$$I' = \beta(t)SI - (\gamma + \mu)I, \quad (2)$$

$$R' = \gamma I - \mu R. \quad (3)$$

Here S, I, R are the fractions of susceptible, infective and recovered individuals in the population, $\frac{1}{\gamma}$ is the mean duration of infectiousness of an infected individual, and μ is the birth and death rate. $\beta(t)$ is the seasonally-dependent transmission rate:

$$\beta(t+T) = \beta(t), \quad \beta(t) \geq 0,$$

where T is the annual period, which we break up as

$$\beta(t) = \bar{\beta} + \beta_0(t), \quad \bar{\beta} = \frac{1}{T} \int_0^T \beta(t) dt, \quad \int_0^T \beta_0(t) dt = 0.$$

For example, the seasonality is often modeled by the term $\beta_0(t) = \delta \bar{\beta} \cos(\omega t)$, $0 < \delta < 1$. This model and variants of it have been studied by many investigators, both due to its relevance to the understanding of the epidemiology of seasonal infectious diseases and to the rich dynamical phenomena that it generates [2,7,8,10,13,15,18,19]. Our aim here is to study factors which govern the expected size of annual epidemics generated by this model.

As the forced SIR model is one of the paradigmatic models of mathematical epidemiology, gaining understanding of its behavior is of fundamental interest, and is essential in order to be able to evaluate its capacity to reproduce observed patterns of epidemics. In particular, since the attack rate is the most basic measurable quantity related to an epidemic, studying its dependence on the parameters of the SIR model is of obvious importance. In recent work, Bacaer and Gomes [3] have examined the attack rate (final size) of

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a single epidemic in the seasonally-forced SIR model, in which case the demographic (birth–death) terms are unimportant, and revealed some counter-intuitive behaviors. In particular, they showed that a higher reproductive number \mathcal{R}_0 may sometimes result in a lower attack rate. This work differs from [3] in that we concentrate on the long-term behavior of the model with demographical turnover, in which case the replenishment of susceptibles by new births is essential in determining the annual attack rate. In [3] the fraction of the population susceptible at the beginning of the epidemic is an exogenous parameter, which is appropriate for the case of an infection which has newly-emerged in a certain population. In the long-term scenario considered here, the fraction of susceptibles at the beginning of each epidemic season is endogenously determined by previous epidemics and demographic turnover, a description appropriate for endemic childhood diseases.

1.2. Attack rates

Given a solution $S(t), I(t), R(t)$ of (1)–(3), the attack rate, or size of the epidemic in year n is defined as the fraction of the population which is infected during this year. Since the incidence of new cases is $\beta(t)S(t)I(t)$, the attack rate in year n is given by

$$A_n = \int_{nT}^{(n+1)T} \beta(t)S(t)I(t)dt. \tag{4}$$

Dynamics of the forced SIR model can be complicated, including the possibilities of subharmonic (multi-year) oscillations, chaos, and several coexisting attractors. However, we first concentrate on parameter regimes for which there exists a globally stable periodic solution $S_p(t), I_p(t), R_p(t)$ with a 1-year period:

$$S_p(t + T) = S_p(t), \quad I_p(t + T) = I_p(t), \quad R_p(t + T) = R_p(t), \quad \forall t.$$

We shall later consider also the subharmonic and chaotic regimes.

Since, by the above assumption, all solutions converge to the periodic solution, we then have, for any solution of (1)–(3),

$$\lim_{n \rightarrow \infty} A_n = A = \int_0^T \beta(t)S_p(t)I_p(t)dt. \tag{5}$$

In other words, after the transients die down, the annual attack rate will be that associated with the periodic solution. Therefore, assuming that the process has been ongoing for a number of years, the annual attack rate is given by A . Investigating the quantity A is the focus of this paper.

In the special case where $\beta(t) = \bar{\beta}$ (constant transmission rate), when $\mathcal{R}_0 > 1$, where

$$\mathcal{R}_0 = \frac{\bar{\beta}}{\gamma + \mu}, \tag{6}$$

(1)–(3) has a globally stable equilibrium given by

$$S^* = \frac{1}{\mathcal{R}_0}, \quad I^* = \frac{\mu}{\gamma + \mu} \left(1 - \frac{1}{\mathcal{R}_0}\right), \quad R^* = \frac{\gamma}{\gamma + \mu} \left(1 - \frac{1}{\mathcal{R}_0}\right), \tag{7}$$

hence, using (5), the attack rate in the steady-state is given by

$$A^* = T\mu \left(1 - \frac{1}{\mathcal{R}_0}\right). \tag{8}$$

This expression shows that A^* vanishes when $\mathcal{R}_0 = 1$ and increases as $\mathcal{R}_0 > 1$ increases, but it saturates at the finite value $T\mu$ so that beyond a certain point, an increase in \mathcal{R}_0 leads to a negligible increase of the attack rate. The intuitive explanation for this is simple: at the steady state, the attack rate is restricted by the replenishment of susceptibles provided by births. The inequality $A^* \leq T\mu$ says that, at steady state, the attack rate is less than the annual number of births, no matter how high the transmission rate.

We now turn to the case of a seasonal periodic forcing, wishing to investigate the attack rate and its dependence on the parameters. In the case of a non-trivial forcing a closed form expression for the attack rate A in terms of the parameters $\gamma, \mu, \beta(t)$ cannot be obtained. We therefore first perform some numerical experimentation, whose results are displayed in Fig. 1. In this example we take $T = 1, \mu = 0.04$ (a 4% annual birth rate), $\gamma = \frac{14}{365}$ (a two-week average infectious period) and seasonal forcing of the form

$$\beta(t) = \bar{\beta}(1 + \delta \cos(2\pi t)),$$

and $\mathcal{R}_0 = 40$, so that $\bar{\beta} = \mathcal{R}_0(\gamma + \mu) = 1044.45$. We note that according to recent model-fitting studies of measles, this value of \mathcal{R}_0 is within the realistic range [11,12]. He et al. [11] give point estimates of \mathcal{R}_0 for different cities in the UK ranging from 21 to 57. For the above choice of parameters, the long time behavior of the system is periodic with a 1-year period, for any value of the seasonality $\delta \in (0, 1)$. We observe that the shape of the epidemic curve changes considerably as the strength of seasonality varies (see left part of Fig. 1). However, when we compute the attack rate for different values of δ (see right part of Fig. 1), we observe that the change in the attack rate is very small – and the attack rate remains close to its value for the unforced case ($A = 0.039$) even when the seasonality parameter δ is close to 1. For the three epidemic curves in the left part of the figure the attack rates are $A = 3.9002\%$ for $\delta = 0.1$, $A = 3.9034\%$ for $\delta = 0.3$, $A = 3.9121\%$ for $\delta = 0.8$.

This surprising phenomenon of near independence of the attack rate on the strength of seasonal forcing is quite general and appears, in our numerical experiments, for all values of the parameters for which the steady state is periodic. However, we are not aware of this phenomenon having been mentioned in any of the previous studies of the forced SIR model. Attempting to explain this phenomenon mathematically is the main motivation and aim of this paper.

As noted above, the mechanisms driving seasonality in transmission rates of various infectious diseases remain unknown, with different hypotheses proposed [1,9]. Under most of these hypotheses, it is likely that the strength of seasonality would vary in different regions of the world, according to local conditions, whether related to climatic factors or to host behavioral patterns. Our

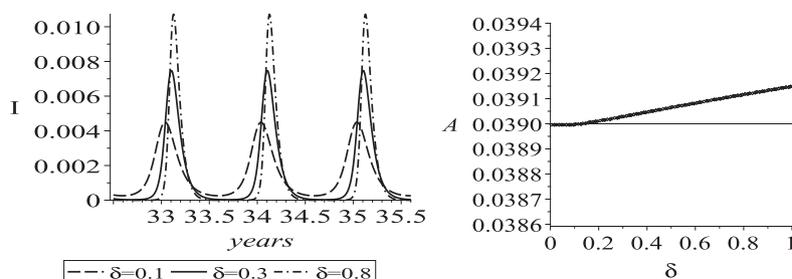


Fig. 1. Left: Solution curves $I(t)$ for the forced SIRS model, with sinusoidal forcing, $T = 1, \mu = 0.04, \gamma = \frac{365}{14}, \mathcal{R}_0 = 40$, for three values of the seasonality δ . Right: Attack rates as a function of the seasonality parameter δ . The horizontal line is the attack rate for the non-forced case.

results show that, insofar as the forced SIR provides an appropriate account of the dynamics of seasonal infections, different strength of seasonality will *not* lead to significantly different attack rates in different locations, as long as the reproductive number \mathcal{R}_0 is similar in these locations. Conversely, if significantly different attack rates are observed in different regions, this cannot be explained as due to different strength of seasonality alone, but indicates that \mathcal{R}_0 must differ among these regions. Moreover, as the attack rate is given to a very good approximation by the value (8) provided by the non-seasonal model, which saturates at high values of \mathcal{R}_0 , large differences in \mathcal{R}_0 may be needed in order to explain rather small differences in attack rates. This may explain the wide range of estimates of values of \mathcal{R}_0 obtained when fitting models to measles data from different cities in the UK in [11]. Some further epidemiological implications are noted in Section 5.

1.3. Bounding attack rates

Since analytic formulas for the attack rate are not available for the forced case, our mathematical investigation proceeds by proving rigorous upper and lower bounds on the attack rate in terms of the parameters, which show that the attack rate in the seasonal case is in fact close to the attack rate A^* in the non-seasonal model, when $\beta(t)$ is replaced by the average $\bar{\beta}$, as given by (8). While our inequalities are strong enough to show that, for all practical purposes, attack rates of the seasonal model can be approximated by the attack rates of the corresponding non-seasonal model, they do not fully explain the numerical observations, in the sense that the actual attack rates, computed numerically, are considerably closer to the non-seasonal attack rates than our inequalities require. Thus there is still room for further investigation of the phenomenon.

As an appetizer, let us derive a very simple upper bound for the attack rate. Assuming (S, I, R) is a T -periodic solution (1)–(3) (from now on we drop the subscript p), we integrate both sides of (1) over $[0, T]$, and using the fact that

$$\int_0^T S'(t)dt = S(T) - S(0) = 0,$$

and that $0 \leq S(t) < 1$, we get that

$$A = \int_0^T \beta(t)S(t)I(t)dt = \mu \int_0^T (1 - S(t))dt < T\mu. \tag{9}$$

Thus, as for the non-seasonal model, the attack rate, in the case that the asymptotic behavior is periodic with an annual period, is bounded by the number of births per year. We shall later see that this result is *not* valid when the periodicity is of higher order. We record this basic result as

Theorem 1. *For any T -periodic solution (S, I, R) of (1)–(3) we have*
 $A < \mu T. \tag{10}$

Let us note here that the calculation in (9) yields some insight: since

$$A = \mu T - \int_0^T \mu S(t)dt, \tag{11}$$

and since the first term is the number of births per year and the second (integral) term is the number of deaths of susceptibles per year, we see that A is equal to the difference between the number of susceptible births and susceptible deaths. Indeed, since in the case of a periodic solution the inflow into the susceptible class must be equal to the outflow over a year, and the outflow from the susceptible class consists of deaths and of infections, this result is obvious. Thus calculating the attack rate hinges on the possibility of calculating the number of susceptible deaths per year. In the unforced case

we have, at steady-state, $S(t) = S^* = \frac{1}{\mathcal{R}_0}$, so that the number of annual deaths of susceptibles is $T\mu\frac{1}{\mathcal{R}_0}$, and (11) gives us the formula (8). In the periodically forced case, the integral in (11) can no longer be computed analytically. However, we may still bound it from above and from below, and this leads to inequalities for the attack rate. In Sections 2 and 3 we use this idea to improve upon the simple result of Theorem 1 in several ways:

- We derive stronger upper bounds on the attack rate, which also take into account the effect of the reproductive number \mathcal{R}_0 . These bounds also involve the strength of the seasonality.
- We derive complementary *lower* bounds on the attack rates.

We believe that the ideas used to prove these inequalities (see Section 3) though elementary, are of interest in themselves, as they show how one can obtain some rigorous quantitative results about a nonlinear system which is not solvable in closed form, without imposing ‘small parameter’ assumptions.

In Section 4, we consider the case in which the system exhibits subharmonic (multi-year) oscillations, that is, we assume that there exists a stable solution $S_s(t), I_s(t), R_s(t)$ of (1)–(3) with period nT , for some $n \geq 2$. The attack rates corresponding to periodic solution will then differ from year to year, with an n -year periodicity. Hence, setting

$$A^{(k)} = \int_{kT}^{(k+1)T} \beta(t)S_s(t)I_s(t)dt, \tag{12}$$

we have, by the n -year periodicity of $S_s(t), I_s(t), R_s(t)$,

$$A^{(k+n)} = A^{(k)}, \quad \forall k.$$

Thus, for any initial conditions in the basin of attraction of our nT -periodic solution, the attack rates corresponding to the solution with these initial conditions, defined by (4), will satisfy, for any $1 \leq k \leq n$,

$$\lim_{j \rightarrow \infty} A_{k+jn} = A^{(k+\tau)}$$

for some $1 \leq \tau \leq n$. Thus, if all solutions converge to our nT -periodic solution, then, after transients have died down, the attack rates are given by the numbers $A^{(k)}$ ($1 \leq k \leq n$), repeating periodically. It is then interesting to study these numbers for an arbitrary subharmonic solution. It turns out that these annual attack rates can vary extensively from year to year. In particular, it is *not* the case that these quantities are dominated by the numbers of annual births, that is the inequality $A^{(k)} \leq T\mu$ is *not* valid. However, if we define the average the attack rate over n consecutive years

$$\tilde{A} = \frac{1}{n} \sum_{k=1}^n A^{(k)} = \frac{1}{n} \int_0^{nT} \beta(t)S_s(t)I_s(t)dt, \tag{13}$$

we discover a much tamer behavior. For example the inequality $\tilde{A} \leq T\mu$ is true. Thus although in individual years the attack rate can be much higher than the number of new births, this will be compensated for in other years in which the attack rate will be very small, so that the average attack rate (over n years) will be dominated by the number of new births. The more refined upper and lower bounds for the T -periodic case, presented in Sections 2 and 3, also have their analogs for the subharmonic case. Moreover, numerical investigations show that the average attack rates are remarkably close to the attack rate A^* in the unforced case.

We also show that these results can be partially extended to chaotic solutions, provided that the attack rates are averaged over infinitely many years.

1.4. Exact attack rate for the Bartlett model

Bartlett [4–6] studied the following simplified version of the forced SIR model,

$$S' = \mu - \beta(t)SI, \tag{14}$$

$$I' = \beta(t)SI - \gamma I, \tag{15}$$

$$R' = \gamma I - dR, \tag{16}$$

which differs from the forced SIR model (1)–(3) in that deaths are assumed to occur only in the recovered stage R . In this model the variables S , I and R should be thought of as population sizes rather than proportions of the population, since their sum is not conserved. The parameter μ should be considered as the source of new susceptibles into the population and is the combined effect of both births and immigration. The parameter d is the death rate in the removed population. The equations are referred to as Bartlett’s model in the literature (e.g., [17,14]) but was also made use of by the pioneer epidemiological modelers Hamer and Soper in the early twentieth century.

The model assumes that the average age at infection is young and the infectious period of the disease is short compared to a person’s lifetime so that one can ignore deaths in the susceptible or infected stages. These assumptions may be reasonable, for example, for childhood infectious diseases such as measles in populations with low childhood death rate (see e.g. [12] where an SEIR version of the Bartlett model is employed). This simplification has the advantage of making the stochastic version of the model analytically tractable and thus far easier to study, yet the model’s behavior still resembles the more complex model in some respects, a fact that has been emphasized and taken advantage of more recently by Näsell [17] and Lindholm [14]. Nevertheless there are important differences between the two models. In particular the Bartlett model lacks an infection free equilibrium and therefore also lacks an epidemic threshold.

When there is no seasonal forcing ($\beta(t) = \beta_0$), the unforced model has an endemic equilibrium which is locally stable for all positive parameters. However seasonal forcing gives rise to complex dynamics qualitatively similar to that of the SIR model, including periodic behavior and chaos in regimes where the intensity of seasonality is relatively large. Consider now a recurrent epidemic having period T . Integrating (14) over $[0, T]$ and using periodicity, we obtain

$$A = \int_0^T \beta(t)S(t)I(t)dt = T\mu.$$

This has the interesting interpretation that the attack rate is exactly equal to the number of new susceptible individuals entering the population over a single year. Thus in the case of the Bartlett model the attack rate is independent of the intensity of the seasonal forcing, or in fact any other parameter except μ . Similarly, for n -year periodic solutions the average attack rate over n years is precisely equal to the annual number of births.

In the case of the standard SIR model (1)–(3), things are not so simple, and as we have noted the best that can be done is to obtain upper and lower bounds on the attack rate in terms of the systems’ parameters, to which we now turn.

2. Inequalities for the attack rate

It is known [16] that if $\mathcal{R}_0 \leq 1$, where \mathcal{R}_0 is given by (6), then all solutions of (1)–(3) converge to the disease free equilibrium $(S, I, R) = (1, 0, 0)$, and in particular there are no T -periodic solutions. We will therefore always assume, without further mention, that $\mathcal{R}_0 > 1$.

We shall prove two pairs of upper and lower bounds for the attack rate corresponding to a T -periodic solution (Theorems 3 and 5). The two sets of results are independent in the sense that neither of them implies the other, and each of them has its strengths and drawbacks.

To state the first result, we define a measure of seasonality s by

$$s = \frac{\frac{1}{T} \int_0^T |\beta_0(t)| dt}{\bar{\beta}}.$$

Note that $s = 0$ is equivalent to $\beta_0(t) \equiv 0$, $\beta(t) = \bar{\beta}$, so that the model reduces to the non-seasonal SIR model. Also it is easy to prove (see Section 3) that

Lemma 2. For any $\beta(t) \geq 0$ we have

$$0 \leq s < 2.$$

Theorem 3. For any T -periodic solution (S, I, R) of (1)–(3) we have the lower bound

$$A \geq \frac{T\mu}{1 + sT\mu} \left(1 - \frac{1}{\mathcal{R}_0}\right). \tag{17}$$

If

$$sT\mu < \frac{1}{\mathcal{R}_0} \tag{18}$$

then we have the upper bound

$$A \leq \frac{T\mu}{1 - sT\mu} \left(1 - \frac{1}{\mathcal{R}_0}\right). \tag{19}$$

We now make some remarks:

- (1) It is easily checked that (19), when valid, is stronger than (10). That is, the right hand side of (19) is smaller or equal to $T\mu$ when (18) holds.
- (2) As $\mathcal{R}_0 \rightarrow 1$, the right-hand side of (19) goes to 0, which implies that $A \rightarrow 0$, as expected.
- (3) As $s \rightarrow 0$, both the lower bound (17) and the upper bound (19) converge to A^* as given by (8), corresponding to the fact that when the seasonality is very weak, the attack rate will be very close to the non-seasonal case.
- (4) The necessity of imposing the condition (18) in order to obtain the upper bound (18) follows from the method used to prove Theorem 3. This condition represents a limitation of the above result, since it means that for parameter values violating it this theorem gives no upper bound. Theorem 5 below provides an upper bound that is valid for all parameter values, in terms of a different measure of seasonality.
- (5) Assume that we don’t know anything about the degree of seasonality, except for the mathematical fact that $0 \leq s < 2$ (Lemma 2). We can still know quite a lot about the possible attack rates. Theorem 3 provides lower and upper bounds for the attack rate, irrespective of the seasonality:

Corollary 4. For any T -periodic solution (S, I, R) of (1)–(3) we have

$$A \geq \frac{T\mu}{1 + 2T\mu} \left(1 - \frac{1}{\mathcal{R}_0}\right).$$

If $2T\mu < \frac{1}{\mathcal{R}_0}$ holds then

$$A \leq \frac{T\mu}{1 - 2T\mu} \left(1 - \frac{1}{\mathcal{R}_0}\right).$$

Our second result gives inequalities for the attack rates in terms of different measures of seasonality, defined by

$$\hat{\eta} = \frac{\sup_{t \in [0, T]} \beta_0(t)}{\bar{\beta}}, \quad \check{\eta} = -\frac{\inf_{t \in [0, T]} \beta_0(t)}{\bar{\beta}}. \tag{20}$$

Since the average of $\beta_0(t)$ is 0, then if it is not identically 0 it must take both positive and negative values, so we have $\check{\eta}, \hat{\eta} \geq 0$. In the non-seasonal case, we have $\check{\eta} = \hat{\eta} = 0$. Note also that

$$1 + \frac{1}{\bar{\beta}} \inf_{t \in [0, T]} \beta_0(t) = \frac{1}{\bar{\beta}} \inf_{t \in [0, T]} \beta(t) \geq 0$$

implies that

$$\check{\eta} \leq 1.$$

Theorem 5. For any T -periodic solution (S, I, R) of (1)–(3) we have

$$T\mu \left(1 - \frac{1}{\mathcal{R}_0} \frac{1}{1 - \check{\eta}}\right) \leq A \leq T\mu \left(1 - \frac{1}{\mathcal{R}_0} \frac{1}{1 + \hat{\eta}}\right). \tag{21}$$

Some remarks:

- (1) The upper bound in Theorem 5 strictly improves the simple upper bound of Theorem 1.
- (2) For weak seasonality, that is as $\check{\eta}, \hat{\eta}$ converge to 0, the lower and upper bounds converge to the non-seasonal attack rate A^* given by (8).
- (3) For fixed seasonality and $\mathcal{R}_0 \rightarrow \infty$ (for example if $\beta_0(t)$ remains fixed while $\bar{\beta} \rightarrow \infty$), Theorem 5 shows that the attack rate converges to $T\mu$, the number of births.
- (4) In contrast with the result of Theorem 3, the upper bound in (21) does not approach 0 as $\mathcal{R}_0 \rightarrow 1$, which can be considered a defect of this result. On the other hand, while the upper bound in Theorem 3 requires the condition (18), Theorem 5 gives an upper bound that always holds.
- (5) The lower bound in (21) is non-trivial only if it is positive, that is only when $(1 - \check{\eta})\mathcal{R}_0 > 1$.
- (6) A major difference between Theorems 3 and 5 is that the measure of seasonality s used in Theorem 3 is based on the average size of $\beta_0(t)$, while the measures $\check{\eta}, \hat{\eta}$ are based on its extreme values.
- (7) A clear advantage of Theorem 5 over Theorem 3 is that it generalizes better to the case of subharmonic solutions, as will be shown below.

Let us now illustrate the above results with a numerical example. Consider a disease with an average infectious period of two weeks ($\frac{1}{\gamma} = \frac{14}{365}$ years) in a population with birth and death rate of 4% per year ($T = 1$ year, $\mu = 0.04$ year⁻¹).

Theorem 1 tells us that, whatever the reproduction number and the seasonality (as long as this seasonality leads to stable annual oscillations), the attack rate is bounded from above by

$$A < T\mu = 4\%.$$

To get a lower bound on A we have to know the basic reproduction number. Taking $\mathcal{R}_0 = 40$, we can use Corollary 4, which leads to

$$A \geq 3.61\%.$$

We stress that this lower bound holds for any seasonality $\beta_0(t)$, as long as it leads to stable annual oscillations. Note that the lower bound is close to the upper bound above.

More precise upper and lower bounds, using Theorems 3, and 5, are computed as part of the numerical example below.

In Fig. 2 we re-plot the attack rate as a function of δ for the same example as in Fig. 1, together with the upper and lower bounds for the attack rates given by Theorems 5 and 3. Note that in the case of a sinusoidal forcing $\beta(t) = \bar{\beta}(1 + \delta \cos(2\pi t))$, the seasonality measure s is given by

$$s = \delta \int_0^1 |\cos(2\pi t)| dt = \frac{2\delta}{\pi}.$$

Thus the maximal possible value of s , when $\delta = 1$, is $s = \frac{2}{\pi} = 0.6366$. The seasonality measures $\check{\eta}, \hat{\eta}$ are given by $\check{\eta} = \hat{\eta} = \delta$. The dashed lines in Fig. 2 (left) show the lower and upper bounds given by Theorem 3 (it can be checked that the condition (18) for the validity of the upper bound (19) holds when $\delta < 0.98$). The dotted lines show the lower and upper bounds given by Theorem 5. In this example, Theorem 3 gives a better lower bound, while Theorem 5 gives a better upper bound.

Note that the attack rate remains remarkably close to the attack rate of the non-seasonally forced case even for very strong seasonality, more so than is indicated by our analytic lower and upper bounds.

In the right part of Fig. 2 we focus on the range of values $0 < \delta < 0.15$ (weak seasonality). Here we see that for low strength of seasonality the attack rate dips slightly below its value for the non-seasonal case. This shows that the attack rate is not a monotone function of the forcing strength δ , so that both upper and lower bounds for the attack rate are indeed necessary.

Computations were carried out using MAPLE's rkf45 solver. To avoid numerical difficulties arising when solving (1)–(3) directly, we performed a log transform, setting $L(t) = \log(I(t))$ and re-writing the system (1)–(3) in terms of S, L, R .

3. Proofs

Proof of Lemma 2. Since $\int_0^T \beta_0(t) dt = 0$, we have

$$\int_{\beta_0(t) \geq 0} \beta_0(t) dt = - \int_{\beta_0(t) < 0} \beta_0(t) dt. \tag{22}$$

Since by the assumption $\beta(t) \geq 0$, we have

$$\beta_0(t) \geq -\bar{\beta}, \quad \forall t. \tag{23}$$

Using (22) and (23) we get

$$\begin{aligned} \int_0^T |\beta_0(t)| dt &= \int_{\beta_0(t) \geq 0} \beta_0(t) dt - \int_{\beta_0(t) < 0} \beta_0(t) dt \\ &= - \int_{\beta_0(t) < 0} \beta_0(t) dt - \int_{\beta_0(t) < 0} \beta_0(t) dt \\ &= -2 \int_{\beta_0(t) < 0} \beta_0(t) dt \leq 2 \int_{\beta_0(t) < 0} \bar{\beta} dt \leq 2 \int_0^T \bar{\beta} dt = 2T\bar{\beta}, \end{aligned}$$

so that $s \leq 2$. In fact the last inequality above is strict, since otherwise we would have $\beta_0(t) \leq 0$ everywhere, which is impossible, since the mean of $\beta_0(t)$ is 0. \square

The following example shows that the bound in Lemma 2 cannot be improved: Take $\beta(t) = 1$ for $0 \leq t \leq a$, $\beta(t) = 0$ for $a < t \leq T$. Then one computes that $s = 2(1 - \frac{a}{T})$, and by taking $a \rightarrow 0$ we can make s as close to 2 as we please.

We now turn to the proofs of Theorems 5 and 3, through a series of lemmas.

Given a T -periodic solution (S, I, R) of (1)–(3), we set

$$\bar{S} = \frac{1}{T} \int_0^T S(t) dt, \quad \bar{I} = \frac{1}{T} \int_0^T I(t) dt, \quad \bar{R} = \frac{1}{T} \int_0^T R(t) dt.$$

Lemma 6. If (S, I, R) is a T -periodic solution of (1)–(3), then

$$\frac{A}{T} = (\gamma + \mu)\bar{I} = \mu(1 - \bar{S}).$$

Proof. Since I is T -periodic we have

$$\int_0^T I(t)dt = I(T) - I(0) = 0,$$

hence, integrating (2) over $[0, T]$, we obtain

$$\frac{A}{T} = \frac{1}{T} \int_0^T \beta(t)S(t)I(t)dt = (\gamma + \mu) \frac{1}{T} \int_0^T I(t)dt = (\gamma + \mu)\bar{I}.$$

The other equality is obtained similarly, by integrating (1) over $[0, T]$, and exploiting the periodicity of $S(t)$. \square

Lemma 7. If (S, I, R) is a T -periodic solution of (1)–(3), then

$$\frac{1}{T} \int_0^T \beta(t)S(t)dt = \gamma + \mu.$$

Proof. Dividing both sides of (2) by I we get

$$[\log(I(t))]' = \beta(t)S(t) - (\gamma + \mu). \tag{24}$$

Integrating both sides over $[0, T]$, then by periodicity the left-hand side vanishes, and we get the result. \square

Proof of Theorem 5. Using Lemma 7 we have

$$\begin{aligned} \gamma + \mu &= \frac{1}{T} \int_0^T \beta(t)S(t)dt \geq \bar{S} \inf_{t \in [0, T]} \beta(t) = \bar{S}[\bar{\beta} + \inf_{t \in [0, T]} \beta_0(t)] \\ &= \bar{S}\bar{\beta}(1 - \hat{\eta}), \end{aligned}$$

so that

$$\bar{S} \leq \frac{\gamma + \mu}{\bar{\beta}(1 - \hat{\eta})} = \frac{1}{\mathcal{R}_0} \frac{1}{1 - \hat{\eta}}.$$

Hence, using Lemma 6 we have

$$A = T\mu(1 - \bar{S}) \geq T\mu \left(1 - \frac{1}{\mathcal{R}_0} \frac{1}{1 - \hat{\eta}}\right).$$

Similarly, we have

$$\begin{aligned} \gamma + \mu &= \frac{1}{T} \int_0^T \beta(t)S(t)dt \leq \bar{S} \sup_{t \in [0, T]} \beta(t) = \bar{S}[\bar{\beta} + \sup_{t \in [0, T]} \beta_0(t)] \\ &= \bar{S}\bar{\beta}(1 + \hat{\eta}), \end{aligned}$$

so that

$$\bar{S} \geq \frac{\gamma + \mu}{\bar{\beta}(1 + \hat{\eta})} = \frac{1}{\mathcal{R}_0} \frac{1}{1 + \hat{\eta}},$$

hence

$$A = T\mu(1 - \bar{S}) \leq T\mu \left(1 - \frac{1}{\mathcal{R}_0} \frac{1}{1 + \hat{\eta}}\right). \quad \square$$

We now prepare for the proof of Theorem 3.

Given a T -periodic solution (S, I, R) of (1)–(3), we set

$$S_{min} = \min_{t \in [0, T]} S(t), \quad S_{max} = \max_{t \in [0, T]} S(t).$$

Lemma 8. If (S, I, R) is a T -periodic solution of (1)–(3), then

$$S_{max} - S_{min} \leq \mu T(1 - \bar{S}).$$

Proof. Let $t_1 < t_2 < t_1 + T$ be such that $S(t_1) = S_{min}$, $S(t_2) = S_{max}$. Then, using (1),

$$\begin{aligned} S_{max} - S_{min} &= \int_{t_1}^{t_2} S'(t)dt = \int_{t_1}^{t_2} [\mu(1 - S(t)) - \beta(t)S(t)I(t)]dt \\ &\leq \int_{t_1}^{t_2} \mu(1 - S(t))dt \leq \mu \int_0^T (1 - S(t))dt \\ &= \mu T(1 - \bar{S}). \quad \square \end{aligned}$$

We set

$$S_0(t) = S(t) - \bar{S},$$

so that

$$\int_0^T S_0(t)dt = 0.$$

Lemma 9. If (S, I, R) is a T -periodic solution of (1)–(3), then

$$|S_0(t)| \leq \mu T(1 - \bar{S}). \tag{25}$$

Proof. Using Lemma 8,

$$\max_t S_0(t) = S_{max} - \bar{S} \leq S_{max} - S_{min} \leq \mu T(1 - \bar{S}),$$

$$\min_t S_0(t) = S_{min} - \bar{S} \geq S_{min} - S_{max} \geq -\mu T(1 - \bar{S}),$$

which give the result. \square

Lemma 10. If (S, I, R) is a T -periodic solution of (1)–(3), then

$$|\bar{S} - S^*| \leq sT\mu(1 - \bar{S}),$$

where S^* is given by (7).

Proof. Using Lemma 7, we have

$$\begin{aligned} \gamma + \mu &= \frac{1}{T} \int_0^T \beta(t)S(t)dt = \frac{1}{T} \int_0^T (\beta_0(t) + \bar{\beta})(S_0(t) + \bar{S})dt \\ &= \frac{1}{T} \int_0^T \beta_0(t)S_0(t)dt + \bar{\beta}\bar{S}. \end{aligned} \tag{26}$$

From (26) and Lemma 9 we get

$$\begin{aligned} |\gamma + \mu - \bar{\beta}\bar{S}| &\leq \frac{1}{T} \int_0^T |\beta_0(t)S_0(t)|dt \\ &\leq \frac{1}{T} [\max_{t \in [0, T]} |S_0(t)|] \int_0^T |\beta_0(t)|dt \leq \mu(1 - \bar{S}) \int_0^T |\beta_0(t)|dt, \end{aligned}$$

and dividing both sides by $\bar{\beta}$, we get the result. \square

Lemma 11. For any T -periodic solution (S, I, R) of (1)–(3) we have

$$\bar{S} \leq \frac{S^* + sT\mu}{1 + sT\mu}. \tag{27}$$

Assuming that

$$sT\mu < 1, \tag{28}$$

we have

$$\bar{S} \geq \frac{S^* - sT\mu}{1 - sT\mu}. \tag{29}$$

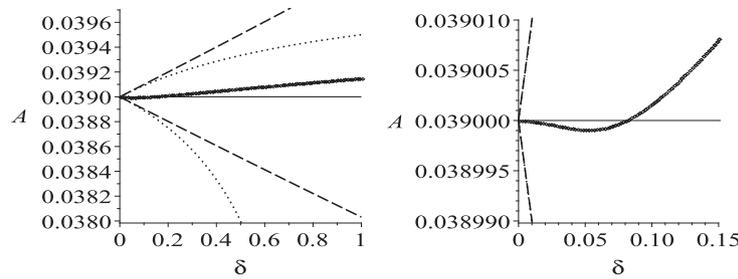


Fig. 2. Attack rates for sinusoidal forcing, $T = 1$, $\mu = 0.04$, $\gamma = \frac{365}{14}$, $\mathcal{R}_0 = 40$, as a function of the seasonality parameter δ . Also shown are the upper and lower bounds for the attack rates given by our inequalities (see text). The left part shows the graph for the entire range $0 < \delta < 1$, and the right part focuses on the range $0 < \delta < 0.15$.

Proof. Using Lemma 10 we have

$$\bar{S} - S^* \leq sT\mu(1 - \bar{S})$$

or, equivalently,

$$\bar{S} \leq \frac{S^* + sT\mu}{1 + sT\mu}$$

and we get the upper bound on \bar{S} .

Using Lemma 10 we have

$$S^* - \bar{S} \leq sT\mu(1 - \bar{S})$$

so that

$$S^* - T\mu s \leq (1 - T\mu s)\bar{S}. \tag{30}$$

By assumption (28) we can divide both sides of (30) by $1 - T\mu s$, and obtain the lower bound on \bar{S} . \square

Proof of Theorem 3. From Lemma 6 and (27) we have

$$A = \mu T(1 - \bar{S}) \geq \mu T \left(1 - \frac{S^* + sT\mu}{1 + sT\mu}\right) = \frac{T\mu}{1 + sT\mu} \left(1 - \frac{1}{\mathcal{R}_0}\right).$$

If (28) holds, then Lemma 6 and (29) give:

$$A = \mu T(1 - \bar{S}) \leq T\mu \left(1 - \frac{S^* - sT\mu}{1 - sT\mu}\right) = \frac{T\mu}{1 - sT\mu} \left(1 - \frac{1}{\mathcal{R}_0}\right). \tag{31}$$

Note, however, that in order for (31) to be nontrivial in the sense that the upper bound given by this inequality is better than the upper bound given by Theorem 1, we need that

$$\frac{T\mu}{1 - sT\mu} \left(1 - \frac{1}{\mathcal{R}_0}\right) < T\mu,$$

which is equivalent to (18). \square

4. Average attack rates for subharmonic and chaotic solutions

We now turn to the case when an nT -periodic solution ($n \geq 2$) $S(t), I(t), R(t)$ exists. Such a solution has n different attack rates $A^{(k)}$ ($1 \leq k \leq n$) associated to it, given by (12), and assuming this periodic solution is globally stable, these numbers describe the attack rates on consecutive years for any solution of the system (1)–(3), after transients have died down.

In Fig. 3 (top left) we plot the attack rate for the sinusoidally forced equations, with the same parameters as those used in Figs. 1, 2, except for β which was reduced so that $\mathcal{R}_0 = 20$. For each value of δ we plotted the attack rates in each of 60 consecutive years (starting from year 50 to avoid transients). We note that there is no guarantee that in our numerical calculations we obtained all possible subharmonic or chaotic oscillations due to the possibility of multi-stability in some parameter ranges.

For low values of δ we have stable annual oscillations, and we see that their attack rates are very close to the attack rate for the non-seasonal case, a fact which is at least partially explained by Theorems 3 and 5. For higher values of δ , a period-doubling bifurcation occurs, leading to two-year periodic solutions (see also Fig. 4). The attack rates in each of the two years no longer satisfies our inequalities. Indeed, even the rougher upper bound $A \leq T\mu$

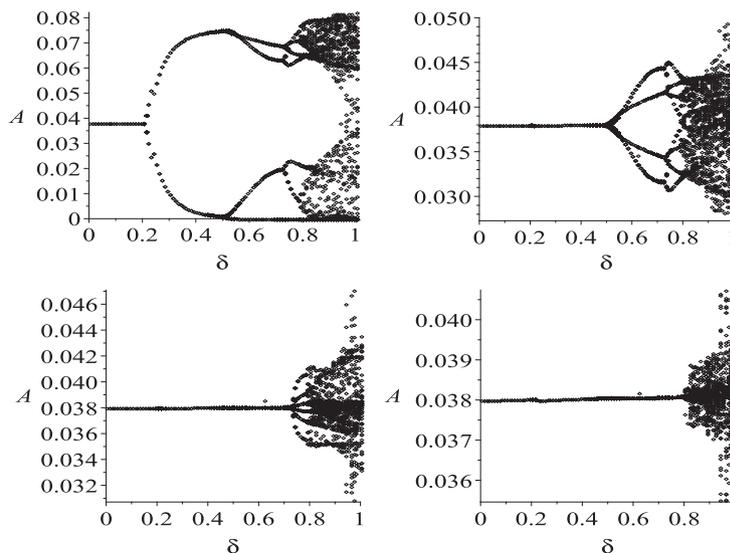


Fig. 3. Attack rates for sinusoidal forcing, $T = 1$, $\mu = 0.04$, $\gamma = \frac{365}{14}$, $\mathcal{R}_0 = 20$, as a function of the seasonality parameter δ (top left), and the attack rate averaged over 2 years (top right), over 4 years (bottom left) and over 16 years (bottom right). Note the differences of scales on the A axis in the different plots.

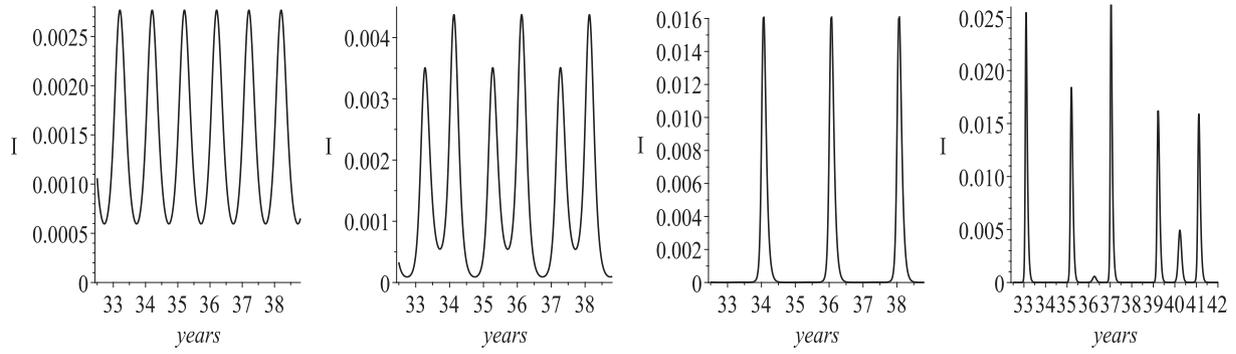


Fig. 4. Solutions curves $I(t)$ for sinusoidal forcing, $T = 1$, $\mu = 0.04$, $\gamma = \frac{365}{14}$, $\mathcal{R}_0 = 20$, and four values of the seasonality. From left to right: $\delta = 0.1$, $\delta = 0.21$, $\delta = 0.3$, $\delta = 0.9$.

(Theorem 1) does not hold in the ‘strong’ years, when the attack rate is significantly larger than the birth rate.

However, if we consider the average attack rate \tilde{A} over two years, as computed in Fig. 3 (top right), we see that, in the parameter range for which the $2T$ -periodic solution is stable, this average attack is very close to the attack rate in the non-seasonal case. Similarly, in Fig. 3 (bottom left) we average the attack rates over 4 years. We see that the average attack rate of the 4-year-periodic solutions (see Fig. 3) is also very close to that of the attack rate in the unforced case. When we average the attack rate over 16 years, even the average attack rates corresponding to chaotic oscillations become very close to the attack rate of the unforced case.

One would like to derive inequalities that would rigorously justify these numerical observations, for subharmonic solutions of any order, as well as for chaotic solutions. We now show that the results proven above for the case of T -periodic solutions can be applied, in a simple way, to gain some information on the average attack rate for subharmonic solutions.

Suppose (S, I, R) is a periodic solution of (1)–(3) with period nT ($n \geq 2$). Since the forcing $\beta(t)$ is T -periodic, it is also nT -periodic. We can thus consider (S, I, R) to be a nT -periodic solution corresponding to a nT -periodic forcing, so that all the results of Section 2 can be applied. Note that:

- (1) The attack rate corresponding to (S, I, R) , when considered as an nT -periodic solution, is equal to n times the average of the n attack rates on intervals of length T (see (13)).
- (2) The seasonality measures s , $\hat{\eta}$, $\tilde{\eta}$ corresponding to $\beta(t)$, when considered as an nT -periodic forcing, are the same as its seasonality measure when considered as a T -periodic solution.

Thus applying Theorem 5 to (S, I, R) , considered as an nT -periodic solution to an equation with nT -periodic forcing we get

$$nT\mu \left(1 - \frac{1}{\mathcal{R}_0} \frac{1}{1 - \tilde{\eta}}\right) \leq n\tilde{A} \leq nT\mu \left(1 - \frac{1}{\mathcal{R}_0} \frac{1}{1 + \hat{\eta}}\right)$$

that is,

Theorem 12. Let (S, I, R) be an nT -periodic solution of (1)–(3). Let \tilde{A} be its average attack rate, as defined in (13).

Then we have

$$T\mu \left(1 - \frac{1}{\mathcal{R}_0} \frac{1}{1 - \tilde{\eta}}\right) \leq \tilde{A} \leq T\mu \left(1 - \frac{1}{\mathcal{R}_0} \frac{1}{1 + \hat{\eta}}\right).$$

In particular, the upper bound above shows that the average attack rate for any multi-year oscillation is bounded by the annual number of births $T\mu$. Although there can be years in which the attack rate will be much higher than the number of births, this will be compensated for by other years in which the attack rate will be nearly 0.

In a similar way, we can apply Theorem 3 to (S, I, R) , considered as an nT -periodic solution to an equation with nT -periodic forcing to get

Theorem 13. Let (S, I, R) be an nT -periodic solution of (1)–(3). Let \tilde{A} be its average attack rate, as defined in (13). Then we have the lower bound (32)

$$\tilde{A} \geq \frac{T\mu}{1 + nsT\mu} \left(1 - \frac{1}{\mathcal{R}_0}\right). \tag{32}$$

and if

$$nsT\mu < \frac{1}{\mathcal{R}_0} \tag{33}$$

then we have the upper bound

$$\tilde{A} \leq \frac{\mu T}{1 - nsT\mu} \left(1 - \frac{1}{\mathcal{R}_0}\right). \tag{34}$$

We note, however, that the result of Theorem 13 is less satisfactory than that of Theorem 12. The dependence on n in the right-hand side of (32) implies that when n is large the lower bound approaches 0. Similarly, for fixed $\beta(t)$ and μ the condition (33) for the validity of (34) fails when n is sufficiently large. In Theorem 12, by contrast, the upper and lower bounds are both independent of n , and thus give information on the average attack rates of all subharmonic solutions, of whatever order.

Let us consider now the case of chaotic solutions, that is solutions which are not periodic and do not approach any periodic solution as $t \rightarrow \infty$. It is natural to define an average attack rate for such solutions, and attempt to obtain inequalities on it. Naturally, the averaging in this case will have to be over an infinite interval. For any solution of (1)–(3), let us define

$$\tilde{A} = T \lim_{\tau \rightarrow \infty} \frac{1}{\tau} \int_0^\tau \beta(t)S(t)I(t)dt,$$

provided that this limit exists. One can easily check that if our solution approaches a T -periodic solution, then \tilde{A} as defined above is equal to the attack rate A of the limiting periodic solution, and more generally if our solution approaches an nT -periodic solution then \tilde{A} as defined above is equal to the averaged attack rate of the limiting subharmonic solution. Thus the average attack rate defined above indeed generalizes the notions considered before. However, it is not at all clear that this limit indeed exists in cases where the solution does not approach a periodic one. This is an interesting question which we leave open. Whatever the answer to this questions turns out to be, we can always define upper and lower average attack rates by

$$\hat{A} = T \limsup_{\tau \rightarrow \infty} \frac{1}{\tau} \int_0^\tau \beta(t)S(t)I(t)dt,$$

$$\check{A} = T \liminf_{\tau \rightarrow \infty} \frac{1}{\tau} \int_0^\tau \beta(t)S(t)I(t)dt.$$

These two quantities are equal to each other if and only if the limit \hat{A} exists.

We now show that Theorem 12 generalizes to

Theorem 14. For any solution (S, I, R) of (1)–(3),

$$T\mu \left(1 - \frac{1}{\mathcal{R}_0} \frac{1}{1 - \hat{\eta}}\right) \leq \check{A} \leq \hat{A} \leq T\mu \left(1 - \frac{1}{\mathcal{R}_0} \frac{1}{1 + \hat{\eta}}\right).$$

Proof. Integrating (2) over $[0, \tau]$, and dividing by τ we get

$$\frac{1}{\tau} [S(\tau) - S(0)] = \mu \frac{1}{\tau} \int_0^\tau (1 - S(t))dt - \frac{1}{\tau} \int_0^\tau \beta(t)S(t)I(t)dt.$$

Since $S(\tau)$ is bounded by 1, the left-hand side of the above goes to 0 as $\tau \rightarrow \infty$, and we get

$$\begin{aligned} \hat{A} &= T\mu \limsup_{\tau \rightarrow \infty} \frac{1}{\tau} \int_0^\tau (1 - S(t))dt \\ &= T\mu \left[1 - \liminf_{\tau \rightarrow \infty} \frac{1}{\tau} \int_0^\tau S(t)dt\right], \end{aligned} \tag{35}$$

$$\begin{aligned} \check{A} &= T\mu \liminf_{\tau \rightarrow \infty} \frac{1}{\tau} \int_0^\tau (1 - S(t))dt \\ &= T\mu \left[1 - \limsup_{\tau \rightarrow \infty} \frac{1}{\tau} \int_0^\tau S(t)dt\right]. \end{aligned} \tag{36}$$

Integrating the equality (24) over $[0, \tau]$ and dividing by τ we get

$$\frac{1}{\tau} [I(\tau) - I(0)] = \frac{1}{\tau} \int_0^\tau \beta(t)S(t)dt - (\gamma + \mu),$$

and by the boundedness of $I(t)$ we get

$$\lim_{\tau \rightarrow \infty} \frac{1}{\tau} \int_0^\tau \beta(t)S(t)dt = \gamma + \mu. \tag{37}$$

Noting that

$$\left(\inf_{t \in [0, T]} \beta(t)\right) \frac{1}{\tau} \int_0^\tau S(t)dt \leq \frac{1}{\tau} \int_0^\tau \beta(t)S(t)dt \leq \left(\sup_{t \in [0, T]} \beta(t)\right) \frac{1}{\tau} \int_0^\tau S(t)dt,$$

and taking the limit $\tau \rightarrow \infty$ and using (37) we have

$$\begin{aligned} &\left(\inf_{t \in [0, T]} \beta(t)\right) \limsup_{\tau \rightarrow \infty} \frac{1}{\tau} \int_0^\tau S(t)dt \leq \gamma + \mu \\ &\leq \left(\sup_{t \in [0, T]} \beta(t)\right) \liminf_{\tau \rightarrow \infty} \frac{1}{\tau} \int_0^\tau S(t)dt. \end{aligned}$$

Together with (35), (36) we have

$$\begin{aligned} \hat{A} &= T\mu \left[1 - \liminf_{\tau \rightarrow \infty} \frac{1}{\tau} \int_0^\tau S(t)dt\right] \leq T\mu \left[1 - \frac{\gamma + \mu}{\sup_{t \in [0, T]} \beta(t)}\right] \\ &= T\mu \left(1 - \frac{1}{\mathcal{R}_0} \frac{1}{1 + \hat{\eta}}\right), \\ \check{A} &= T\mu \left[1 - \limsup_{\tau \rightarrow \infty} \frac{1}{\tau} \int_0^\tau S(t)dt\right] \geq T\mu \left[1 - \frac{\gamma + \mu}{\inf_{t \in [0, T]} \beta(t)}\right] \\ &= T\mu \left(1 - \frac{1}{\mathcal{R}_0} \frac{1}{1 - \hat{\eta}}\right). \quad \square \end{aligned}$$

We note that Theorem 5 (hence also Theorem 12) is a consequence of Theorem 14, but we chose to give a separate proof of Theorem 5 for expository purposes.

Considering the example of sinusoidal forcing with $\mu = 0.04$, $\gamma = \frac{365}{14}$, $\mathcal{R}_0 = 20$ as in Fig. 3, the above Theorem implies that for any solution we have

$$0.04 \left(1 - 0.05 \frac{1}{1 - \delta}\right) \leq \check{A} \leq \hat{A} \leq 0.04 \left(1 - 0.05 \frac{1}{1 + \delta}\right).$$

In particular the upper bound gives $\hat{A} \leq 3.9\%$ for all $0 \leq \delta \leq 1$. Note, however that the lower bound above is non-trivial only if $\delta \leq 0.95$, and approaches 0 as $\delta \rightarrow 0.95$. Although such high seasonalities are probably unlikely in reality, this still points to the fact that an improvement to our theoretical results is called for. We thus leave it as an open problem to find a lower bound for the average attack rate of a general solution that will hold for all seasonalities, or to show that such a bound does not exist.

5. Discussion

This paper contains both rigorously proved results and descriptions of phenomena observed in numerical simulations. The import of both these types of results is that the attack rates of seasonally-forced epidemics which are periodic with a period of one year, or the average attack rates for epidemics with a period of several years, and even chaotic epidemics, are very close to the attack rate in the non-seasonal model with the same average transmissibility (that is, with the same reproduction number), as given by (8). This is not to be taken to imply that seasonal forcing is unimportant: as we have seen, varying the seasonal forcing changes the shape of the epidemic curve dramatically, as well as causing the bifurcation from annual-periodic to subharmonic and chaotic behavior. Indeed, it is against the background fact that seasonality has enormous impact on the behavior of the SIR model that the finding that the attack rate (or average attack rate in the case of subharmonic and chaotic solutions) is nearly independent of seasonality is interesting. These considerations imply a ‘negative’ result which should be taken into account by those studying epidemics: since knowledge of the yearly attack rate gives little information on the strength of seasonality, but the strength of seasonality is an important determinant of the shape of the epidemic curve, attack rate is a limited measure for understanding the epidemic process of seasonal infections. Thus, although attack rates can be estimated in a relatively precise way through seroepidemiological studies, they cannot replace the information provided by time series describing the entire course of epidemics, gathered through continuous surveillance.

The fact that seasonality has a minor effect on attack rates means that some simple epidemiological considerations derived from the non-seasonal model through formula (8) carry over without change to the case of seasonal forcing. For example:

- (1) Consider the dependence of the attack rate on the birth rate μ . Since, for realistic values, we have $\mu \ll \gamma$, the dependence of \mathcal{R}_0 on μ is nearly negligible, so (8) shows that the attack rate depends linearly on the birth rate μ . In view of our results, this will hold, to a good approximation, also in the seasonal case.
- (2) We can use the fact that (8) gives an excellent approximation to the average attack rate in the seasonally forced case to study the effect of vaccination. If a fraction ϕ of the population is vaccinated at birth, the model (1)–(3) changes to

$$S' = \mu(1 - \phi - S) - \beta(t)SI, \tag{38}$$

$$I' = \beta(t)SI - (\gamma + \mu)I, \tag{39}$$

$$R' = \mu\phi + \gamma I - \mu R. \tag{40}$$

Following the observation of Earn et al. [8], we can set

$$\check{S} = (1 - \phi)^{-1}S, \quad \check{I} = (1 - \phi)^{-1}I, \quad \check{\beta}(t) = (1 - \phi)\beta(t) \tag{41}$$

and re-write (38) and (39) as

$$\dot{S} = \mu(1 - \check{S}) - \check{\beta}(t)\check{S}\check{I} \quad (42)$$

$$\dot{I} = \check{\beta}(t)\check{S}\check{I} - (\gamma + \mu)\check{I} \quad (43)$$

(the third equation can be ignored, as it does not couple back to the first two). This is a system of the same form as (1) and (2), so that, by our results, its average attack rate is given to a very good approximation by the attack rate for the corresponding non-seasonal system, that is

$$\check{A} \approx T\mu \left(1 - \frac{1}{\mathcal{R}_0}\right) = \mu T \left(1 - \frac{\gamma + \mu}{(1 - \phi)\beta}\right),$$

and since by (41) we have that the average attack rate of (38)–(40) is $\bar{A} = (1 - \phi)\check{A}$, we obtain the approximate formula

$$\bar{A} \approx \mu T \left(1 - \phi - \frac{1}{\mathcal{R}_0}\right). \quad (44)$$

More precise formulations can be given using our upper and lower bounds. For example, applying Theorem 12 to the system (42) and (43) (assuming now the behavior of the system is periodic or subharmonic), we obtain

$$T\mu \left(1 - \phi - \frac{1}{\mathcal{R}_0} \frac{1}{1 - \hat{\eta}(1 - \phi)}\right) \leq \bar{A} \\ \leq T\mu \left(1 - \phi - \frac{1}{\mathcal{R}_0} \frac{1}{1 + \hat{\eta}(1 - \phi)}\right),$$

where $\hat{\eta}$, $\check{\eta}$ are given by (20). In the chaotic case we obtain similar inequalities for the upper and lower average attack rates after vaccination, by applying Theorem 14.

As a numerical example of (44), consider the case $\mu = 0.04$, $\gamma = \frac{365}{14}$, $\mathcal{R}_0 = 20$ and sinusoidal seasonality with $\delta = 0.25$. Without vaccination ($\phi = 0$), numerical simulation gives two year oscillations with alternating attack rates $A^{(1)} = 2.17348\%$ and $A^{(2)} = 5.42716\%$, so the average attack rate is $\bar{A} = 3.80032\%$, while the approximate formula (44) gives $\bar{A} \approx 3.80000\%$. Suppose now that we vaccinate 60% of newborns. Simulation then shows that we get two-year oscillations with attack rates $A^{(1)} = 2.12881\%$, $A^{(2)} = 0.67367\%$, so the average attack rate is $\bar{A} = 1.40124\%$, while the approximate formula (44) gives $\bar{A} \approx 1.40000\%$.

(3) From (8) we see that once \mathcal{R}_0 is sufficiently large, further increase leads to very small increase in the attack rate. Thus the average attack rate corresponding to $\mathcal{R}_0 = 20$ will only be 1.06 times as large as the attack rate corresponding to $\mathcal{R}_0 = 10$. Considering evolution to higher transmissibility, we hence see that while in the short term a more transmissible mutant will spread faster and thus has a chance of becoming dominant, in the longer term this increased transmissibility will have little effect on the ‘success’ of the pathogen, measured by its attack rate. However, an increase in the reproductive number does have important consequences with regard to the dynamical behavior when transmissibility is seasonal. When the reproductive number is smaller, the transition from annual epidemics to subharmonic behavior or chaotic occurs at a lower value of the seasonality (in the case $\mathcal{R}_0 = 40$ that was considered in the Introduction, such a transition did not occur at all).

For all practical purposes, for parameter ranges relevant to real epidemics, the results of the theorems that we have proven are sufficiently precise to bound the attack rate (or average attack rates) in a narrow interval around the attack rate in the non-forced case. However, the numerical simulations have revealed that the attack rates (or average attack rates) are several orders of magnitude

closer to the non-seasonal attack rates than is implied by our theorems. In our simulations the differences between (average) attack rates in the seasonal and non-seasonal cases were fractions of percentages, regardless of the strength of the seasonality. We stress that while in our presentation above we demonstrated this effect using particular parameter values, we carried out extensive experimentation and found that it holds for the wide range parameter values $(\mathcal{R}_0, \mu, \gamma)$ that we have tested, without exception, including the range of \mathcal{R}_0 values (1–50) that have been estimated for infectious diseases in humans.

One possible explanation for this gap between what we can prove and what we observe in simulations could be that the inequalities we find apply to *arbitrary* forcing functions $\beta(t)$, while the numerical experiments are carried out with specific forcing functions. It could be that for some different forcing, the differences in attack rates in the seasonal and non-seasonal cases will be larger than for the sinusoidal forcing used above. However, numerical experiments with piecewise-constant forcing, as often used to model school-term periods [18,19], have given results very similar to the sinusoidally-forced case in terms of the near-independence of the attack rate (or average attack rate) on seasonality. It is therefore also possible that there exist sharper inequalities for bounding the attack rates, which will more fully explain the numerical results. We leave this as an open question.

Acknowledgments

We thank Asher Uziel for pointing out to us the unusual constancy of the attack rate.

Funding: The authors acknowledge support of EU-FP7 grant Epiwork, Israel Science Foundation, and Israeli Ministry of Health.

References

- [1] S. Altizer, A. Dobson, P. Hosseini, P. Hudson, M. Pascual, P. Rohani, Seasonality and the dynamics of infectious diseases, *Ecol. Lett.* 9 (2006) 467.
- [2] J.L. Aron, I.B. Schwartz, Seasonality and period-doubling bifurcations in an epidemic model, *J. Theor. Biol.* 110 (1984) 665.
- [3] N. Bacaer, M.G.M. Gomes, On the final size of epidemics with seasonality, *Bull. Math. Biol.* 71 (2009) 1954.
- [4] M.S. Bartlett, Deterministic and stochastic models for recurrent epidemics, *Proceedings of the 3rd Berkeley Symposium on Mathematical Statistics and Probability*, vol. 4, University of California Press, Berkeley, 1956, p. 81.
- [5] M.S. Bartlett, Measles periodicity and community size (with discussion), *J. R. Stat. Soc. A* 120 (1957) 48.
- [6] M.S. Bartlett, The critical community size for measles in the United States, *J. R. Stat. Soc. A* 123 (1960) 37.
- [7] K. Dietz, The Incidence of Infectious Diseases under the Influence of Seasonal Fluctuations, *Lecture Notes in Biomathematics*, vol. 11, Springer Verlag, New York, 1976, p. 1.
- [8] D.J.D. Earn, P. Rohani, B.M. Bolker, B.T. Grenfell, A simple model for complex dynamical transitions in epidemics, *Science* 287 (2000) 667.
- [9] N.C. Grassly, C. Fraser, Seasonal infectious disease epidemiology, *Proc. R. Soc. B* 273 (2006) 2541.
- [10] J. Greenman, M. Kamo, M. Boots, External forcing of ecological and epidemiological systems: a resonance approach, *Physica D* 190 (2004) 136.
- [11] D. He, E.L. Ionides, A.A. King, Plug-and-play inference for disease dynamics: measles in large and small populations as a case study, *J. R. Soc. Interf.* 7 (2010) 271.
- [12] G. Hooker, S.P. Ellner, L. De Vargas Roditi, D.J.D. Earn, Parameterizing state-space models for infectious disease dynamics by generalized profiling: measles in Ontario, *J. R. Soc. Interf.* 8 (2011) 961.
- [13] M. Keeling, P. Rohani, B.T. Grenfell, Seasonally forced disease dynamics explored as switching between attractors, *Physica D* 148 (2001) 317.
- [14] M. Lindholm, On the time to extinction for a two-type version of Bartlett’s epidemic model, *Math. Biosci.* 212 (2008) 99.
- [15] W. London, J.A. Yorke, Recurrent outbreaks of measles, chickenpox and mumps. i. Seasonal variation in contact rates, *Am. J. Epidemiol.* 98 (1973) 453.
- [16] J. Ma, Z. Ma, Epidemic threshold conditions for seasonally forced SEIR models, *MBE* 3 (2006) 161.
- [17] I. Näsell, On the time to extinction in recurrent epidemics, *J. R. Stat. Soc. B* 66 (1999) 309.
- [18] R. Olinky, A. Huppert, L. Stone, Seasonal dynamics and thresholds governing recurrent epidemics, *J. Math. Biol.* 56 (2008) 827.
- [19] L. Stone, R. Olinky, A. Huppert, Seasonal dynamics of recurrent epidemics, *Nature* 446 (2007) 533.