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The dynamics of scarlet fever epidemics in England and Wales in the 19th century

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SUMMARY

There was a marked rise in scarlet fever mortality in England and Wales in the mid-nineteenth century and spectral analysis of the registration details, 1847–80, shows that the interepidemic interval was 5–6 years, but after 1880 the endemic level fell and the fatal epidemics disappeared. The dynamics of the scarlet fever epidemics can be represented by a linearized mathematical model and because the system is lightly damped, it could be driven by an oscillation in susceptibility. Epidemics were significantly correlated with dry conditions in spring/summer ($P < 0{\cdot}001$), suggesting that these produced a low amplitude oscillation in susceptibility which drove the system. Epidemics also correlated ($P < 0{\cdot}001$) with an oscillation in wheat prices but at a lag of 3 years, suggesting that malnutrition during pregnancy caused increased susceptibility in the subsequent children which interacted synergistically with seasonal dry conditions. Scarlet fever mortality was sharply reduced after 1880 in parallel with falling wheat prices suggesting that the remarkable period of high scarlet fever mortality (1840–80) was dependent on poor nutritive levels during that time.

INTRODUCTION

Standard epidemiological (SEIR) models have been used to study the dynamics of viral infectious diseases [1] and in particular the detailed data series for measles in the UK in the 20th century [2]. Mathematical modelling suggests that the epidemics would decay unless they were maintained [3] and the study of nonlinear dynamics of measles epidemics has allowed the development of elegant deterministic [4] and stochastic [5, 6] models which incorporate spatial dynamics, seasonal forcing and age structure to describe the pattern of these epidemics and it has been suggested that measles dynamics in developed countries may exhibit low dimensional chaos [2, 4, 7–9]. We have shown, using a nonlinear model, how 2-yearly smallpox epidemics could be maintained by driving the system with an annual cycle of susceptibility [10].

In this communication we describe the epidemics of a bacterial disease, scarlet fever, in England during the 19th century and suggest that the dynamics of the disease changed markedly after 1875 because of markedly improved levels of nutrition. There were an enormous number of deaths from scarlet fever in England and Wales during 40 years in the middle of the 19th century; this period was preceded and followed by periods with very much lower levels of annual mortality from the disease. This period with a high mortality from scarlet fever is regarded as remarkable by historical epidemiologists [11]. The disease can be described by a linearized model which,

we suggest, can be used to explain the characteristics of the epidemics and the biology of scarlet fever in the 19th century. We have used conventional time series analysis to determine the periodicity of the epidemics and suggest that these were driven by a low amplitude oscillation in susceptibility.

METHODS

Scarlet fever deaths for England and Wales were taken from registration details 1847–93 as given by Creighton [11]. Deaths from the disease give a biased view of the epidemiology, but no comparable data series for infections exists for this interesting period for the biology of scarlet fever epidemics. The annual wheat price series for England was taken from the data given by Stratton [12]. Mean seasonal temperatures were taken from Manley [13] and mean seasonal rainfall was taken from Wales-Smith [14]. The seasons were defined as follows, winter: December (of the preceding year), January and February; spring: March, April and May; summer: June, July and August, autumn: September, October and November. Time-series analysis was carried out by the computing method of Shumway [15] with an IBM PC AT, as previously described [10, 16]. Multivariate analysis was run in Minitab.

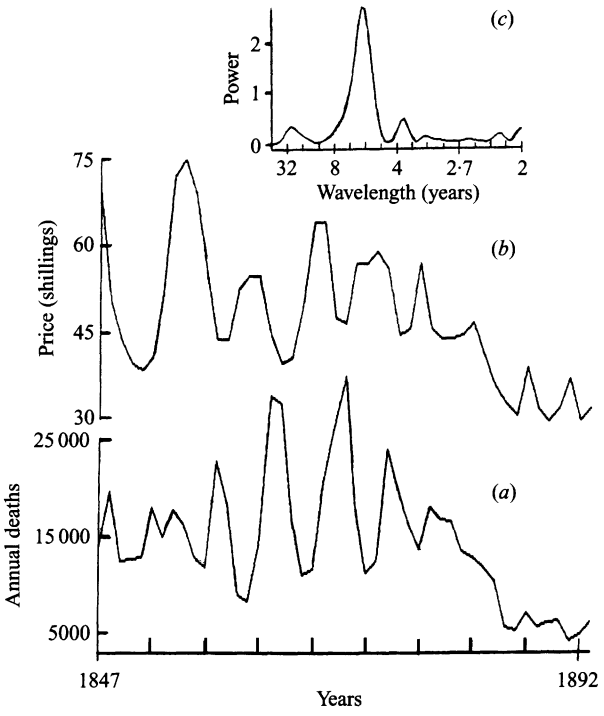

Fig. 1. (*a*) Annual scarlet fever deaths in England and Wales, 1847–92. The abscissa is divided into 5-year intervals. Note disappearance of epidemics and rapid fall in the endemic level of lethal cases after 1880. (*b*) Annual wheat price (shillings). Note the marked fall in average prices after 1880 which parallels the reduced lethality of scarlet fever at that time. (*c*) Spectral analysis of scarlet fever deaths during the epidemics, 1847–1881. Note major peaks at 5–6 years.

RESULTS

Annual scarlet fever deaths in England and Wales are shown in Figure 1*a*; there are clear epidemics from 1847–80 but thereafter the endemic level of deaths falls rapidly and the fatal epidemics virtually disappear. Spectral analysis of the series for the period 1847–80 shows a peak at wavelength 5·3–5·6 years (Fig. 1*c*) showing that the interepidemic interval (T) was 5–6 years.

The annual wheat price series, 1847–93, is shown in Figure 1*b*; it closely mirrors the scarlet fever deaths series with clear oscillations up to 1880 and a sharp fall in the index thereafter. Spectral analysis of the wheat price series shows a dominant peak at 6·7 years. The cross-correlation between scarlet fever deaths and wheat price series during the period of the epidemics 1847–80 was studied by the following techniques: (i) Cross-correlation function which is illustrated in Figure 2*a* (filter window = 4–9 years). There is a strong correlation between the two series (c.c.f. = 0·87), but with a clear lag of 2–3 years. (ii) Squared coherence programme which tests statistically the correlation between the oscillations in two series shows that wheat prices and scarlet fever deaths are significantly correlated in the 5–6 year waveband ($P < 0{\cdot}001$), again with a lag of 3 years.

No significant correlation was found between seasonal temperatures and the epidemics of scarlet fever, unlike the dynamics of whooping cough where the epidemics were correlated significantly with low temperatures in autumn and winter [17].

However, during the epidemics, 1847–80, the scarlet fever deaths series was significantly correlated with low mean spring and low mean summer rainfall (i.e. dry conditions). Analysis was carried out with the following tests (i) Squared coherence relations: scarlet fever deaths correlated significantly with low summer rainfall ($P < 0{\cdot}001$) in the 5–6 year waveband and with low spring rainfall ($P < 0{\cdot}01$) in the 5-year waveband, both series at zero lag. (ii) Cross-correlation function (filter window = 4–9 years) shows that scarlet fever deaths in the epidemics correlated

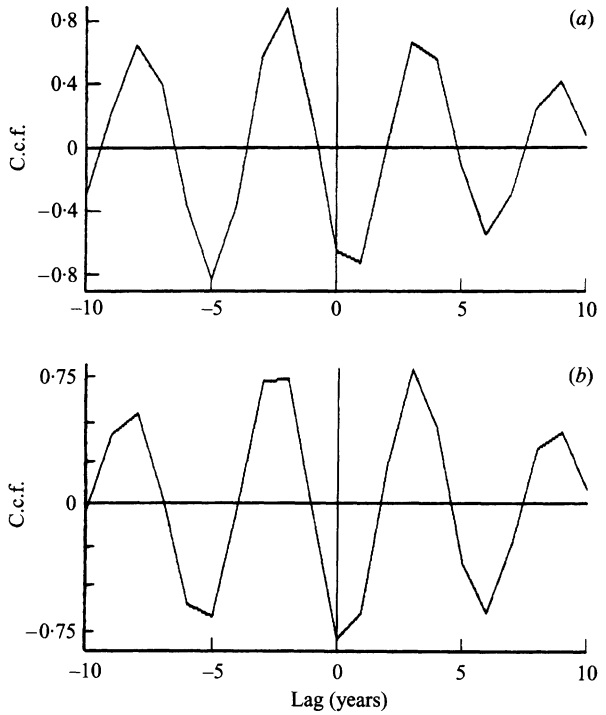

Fig. 2. Cross-correlation functions, 1847–80. Filter window = 4–9 years. (*a*) Wheat prices versus annual scarlet fever deaths. Note that high wheat prices are negatively correlated with mortality which lags by 2–3 years. (*b*) Scarlet fever deaths *vs.* summer rainfall. Note correlation between low rainfall and mortality.

with low summer rainfall (c.c.f. = −0·8, Fig. 2*b*) and with low spring rainfall (c.c.f. = −0·51), both seasons at zero lag.

It might be suggested that this correlation between the epidemics of scarlet fever mortality and low seasonal rainfall was indirect and that climatic conditions were directly affecting crop yields and thereby driving the epidemics. However, we have studied the annual wheat price series by time series analysis and have shown that the regular 5–6 year oscillation is not significantly correlated with seasonal weather; we suggest that it is driven by economic factors, the short-term effects of a good or bad harvest (autoregressive effects) and possibly by regular epidemics of fungal pathogens of grains (Scott and colleagues, personal observation).

The possible interacting effects of scarlet fever mortality of the three variables, spring rainfall, summer rainfall and wheat prices were further studied by multivariate analysis which confirmed these findings. The overall regression was highly significant ($P = 0{\cdot}002$), with the correlations for low spring rainfall and low summer rainfall at $P = 0{\cdot}038$ and $P = 0{\cdot}004$ respectively. Scarlet fever mortality was negatively correlated with wheat prices ($P = 0{\cdot}039$) as would be expected from Figure 1*a*, i.e. the oscillation in wheat prices and scarlet fever mortality are 180° out of phase and consequently mortality lags prices by 2–3 years.

DISCUSSION

Scarlet fever has been regarded as becoming relatively benign over the last 150 years [18] but the disease is not mild everywhere and no one can forecast what its epidemic future may be [19]. A recent, unexplained increase in severe streptococcal diseases in the USA and UK has been compared to the 1825–85 pandemic of fatal scarlet fever. Although scarlet fever may not be representative of all severe streptococcal diseases, it was the only one that was reliably identified in the 19th century [20]. These authors suggest that the 19th century data show that efforts to prevent severe streptococcal diseases should begin with a better characterization of the epidemiology of the disease.

The theory of the dynamics of scarlet fever epidemics is described in the Appendix; the linearized model is derived from a susceptible exposed-infective-recovered (SEIR) model [2] which is driven by a periodic variation in susceptibility. The system is shown to be oscillatory, i.e. there are epidemics of the disease superimposed on the endemic level and the interepidemic interval is determined by the product of population size (N) and susceptibility (β), see equation (12). The epidemics would die out unless the system were driven in some way and it is suggested that a periodic variation in susceptibility ($\delta\beta$) acts to maintain the epidemics [10]. Equations (1)–(12) represent a linearized model of what is clearly a nonlinear system. However, the linearized model has been shown to give an almost identical output when compared with the fully nonlinear model (see Appendix) and it is concluded that it provides a satisfactory description of the behaviour of the system.

The system is also characterized by its damping factor (ζ; see equation (9)) which determines the rate of decay of the epidemics. It is a dimensional ratio which is a measure of the degree of damping within the system, i.e. the attenuation of the amplitude of the oscillation at its resonant frequency. The modelling used to describe the 5/6 yearly scarlet fever epidemics shows that the system is lightly damped so that the periodicity of the driving fluctuation in susceptibility must be close to the natural frequency of the epidemics if they are to be maintained.

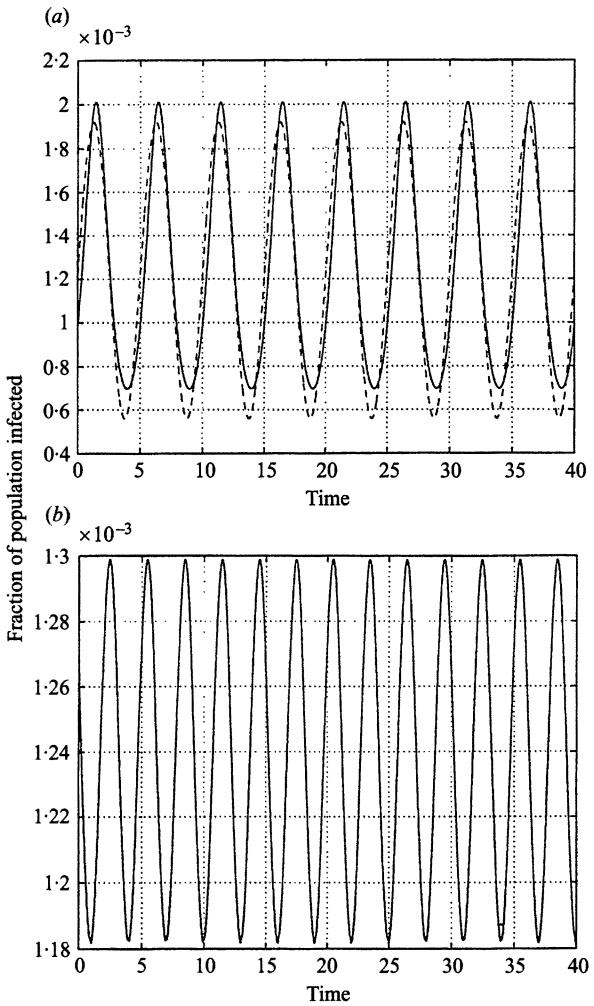

Fig. 3. Models of scarlet fever epidemics, where $N\beta = 60{\cdot}5$, $\mu = 0{\cdot}04$ year^{-1}, $\nu = 21$ year^{-1}, $\omega_r = 5$ years, $\delta\beta = 0{\cdot}003$. Solid line = nonlinear model; dashed line = linear model. (*a*) wavelength of input ($\delta\beta$) = 5 years. Note the similarity between the two models. (*b*) wavelength of input ($\delta\beta$) = 3 years. The nonlinear and linearized models give identical results in both *a* and *b*. However, the amplitude of the epidemics in *b* is reduced compared with *a* (note scale on ordinate) because the system is not oscillating at ω_r. Abscissa: years.

Spectral analysis of scarlet fever deaths in England and Wales (Fig. 1 *c*) during the period of the pandemic, 1847–80, shows that the interepidemic interval was 5–6 years. Nβ = 60·5 (calculated from equation (12)), so that the damping factor, $\zeta = 0{\cdot}046$ (where ζ lies between 0 and 1; equation (9)). Because the system is so lightly damped, it will oscillate, and large amplitude epidemics will be maintained, in response to an oscillation in susceptibility ($\delta\beta$) of very small amplitude (0·003) (see Appendix; Fig. 3) if this is at the resonant frequency of the system (equation (9)).

The scarlet fever epidemics were significantly correlated with dry conditions in spring and summer suggesting that these periodic seasonal effects were sufficient to produce a low amplitude oscillation in susceptibility which drove the system and maintained the epidemics. Creighton [11], had noted that high mortality from scarlatina was apparently associated with a rainfall below average and it is difficult to suggest why dry conditions should cause an increase in susceptibility, although this oscillation in susceptibility need be of only very small amplitude (see above). Waddy [21] has shown that the infectivity of certain respiratory diseases is increased in air of low absolute humidity in both Ghana and England and Wales and suggests that such air also dries the nasopharyngeal mucosa more rapidly and may thereby lower its resistance. We have shown that smallpox epidemics correlated significantly with dry conditions, suggesting that, in this disease also, the epidemics were maintained by a comparable oscillation in $\delta\beta$.

We have shown previously from historical epidemiological studies that the national wheat price index in earlier centuries provided a good measure of the fluctuating nutritional standards [22]. Excellent cross-correlation is found between the oscillations in grain prices and mortality cycles [16] and neonatal mortality [11, 22]. Similarly the high mortality rate from measles in underdeveloped countries today is linked to poor nutrition and inadequate medical services. Malnutrition may interfere with the immune response to the measles virus: giant cells persist in nasal secretions and the illness is prolonged. Protein deficiency seems to be associated with a much higher incidence of complications, especially bronchopneumonia [19].

It is clear that after 1880 both the scarlet fever fatalities (Fig. 1 *a*) and the wheat price series (Fig. 1 *b*) fall sharply and progressively. The two data series correlate closely ($P < 0{\cdot}001$) during this period when scarlet fever eventually ceased to be a lethal disease. Dietary standards in the UK improved in the second half of the 19th century, with real wages rising particularly after 1870. Imported food supplemented and improved the diets of many sections of the population [23]. The findings in the present study suggest that the greatly improved general nutrition associated with low wheat prices in the last quarter of the 19th century contributed to the steady fall in the lethality of the disease. Records for scarlet fever deaths are incomplete before 1847 but it is clear that mortality doubled in 1839 from the preceding year and was particularly severe in 1840 (20000 deaths). The endemic level of annual deaths then continued at

a high rate until 1880. Inspection of the annual wheat price series shows that the index rose in 1838 and the mean level remained high until 1880 (see Fig. 1*b*), suggesting that the remarkable 40 years of scarlet fever mortality [11] was initiated and was dependent on the poor nutritive levels at that time.

The scarlet fever epidemics during 1847–80 were also significantly correlated ($P < 0{\cdot}001$) with the oscillation in wheat prices which is clearly seen in Fig. 1*b*. However, there was a lag of 2–3 years between the two series. We suggest that high wheat prices and inadequate nutrition of the mother during pregnancy caused greater susceptibility to the disease in the subsequent children who contracted it and died in the next epidemic. Neonatal mortality has been shown to be associated with malnutrition in pregnancy, whereas post-neonatal mortality was primarily directly dependent on exogenous causes in the first year of life, both in England in the 17th century [22] and in the Dutch hunger winter between September 1944 and May 1945 [24, 25]. Malnutrition during pregnancy has also been suggested to increase the susceptibility of the progeny to measles (Duncan and colleagues, personal observation). The critical importance of a good diet during pregnancy has been elucidated by Barker in his studies of historical epidemiology [26]. Although correlation does not prove causality, we suggest that oscillations of malnutrition, in this way, produced oscillations of susceptibility to scarlet fever in children which interacted synergistically with periods of low rainfall in spring and/or summer to produce an oscillation in $\delta\beta$ which drove the system and maintained the epidemics at its resonant frequency.

During the period of the 5-year epidemics in scarlet fever, it can be predicted from equation (13) that the mean age of contracting scarlet fever was approximately 13 years, much higher than for the 2-year epidemics of smallpox and measles (Duncan and colleagues, personal observation). However, Creighton [11] reports that in the last half of the 19th century in England and Wales two-thirds of the deaths from scarlet fever occurred in children under the age of 5 years; the attacks were much more likely to be fatal in the first years of life and the lethality decreased rapidly after 5 years old. The results presented here (Fig. 1*a*) are for scarlet fever deaths which therefore will be predominantly of young children. Possibly, in each epidemic those dying in age groups 0–2 years within one inter-epidemic interval of 5 years were mainly born to undernourished mothers whilst those in age groups 2–5 years may have suffered from increased susceptibility associated with periodic seasonal dry conditions.

APPENDIX

Theory of the dynamics of infectious diseases

The dynamics of the scarlet fever epidemics can be described by a standard SIR model [2] which is driven by periodic variations in susceptibility [2, 7, 10]. This has the form

$$\frac{dx}{dt} = \mu - \mu x - N\beta xy(1 + \delta\beta \sin \omega t), \tag{1}$$

$$\frac{dy}{dt} = N\beta xy(1 + \delta\beta \sin \omega t) - (\mu + \nu)\, y, \tag{2}$$

where

N = number in the population;

x = endemic level of susceptibles expressed as a fraction of N;

y = endemic level of infectives expressed as a fraction of N;

μ = death rate = 1/life expectancy ($\mathring{e}_0$) = 0·04 years^{-1};

β = transmission coefficient (susceptibility to disease);

$\delta\beta$ = fractional variation in susceptibility;

ν = rate of recovery from disease = 1/infectious period (17 days) = 24 years^{-1};

ω = angular frequency of oscillation in susceptibility = 2π/period of oscillation.

This model ignores both the latent period of the infection and the mortality because of the disease. These factors can be included in the model, but they do not substantially alter the results. It is assumed that infectives who survived an attack of scarlet fever did not suffer again because of antitoxic and antibacterial immunity [19].

In the absence of variations in susceptibility ($\delta\beta = 0$) the steady state values for the proportion of susceptibles and infectives are [1]

$$x_0 = \frac{\mu + \nu}{N\beta}, \tag{3}$$

$$y_0 = \frac{\mu}{\mu + \nu}(1 - x_0). \tag{4}$$

When $\delta\beta > 0$ is small, equations (1) and (2) can be approximated by a linearized model, by defining

$$x = x_0 + x_1, \tag{5}$$

$$y = y_0 + y_1, \tag{6}$$

where x_1 and y_1 represent the variations in x and y from their steady state values. Substituting equations (5) and (6) into equations (1) and (2) and ignoring higher order terms gives

$$\frac{dx_1}{dt} \approx -(N\beta y_0+\mu)x_1-(\mu+\nu)y_1-(\mu+\nu)y_0\,\delta\beta\sin\omega t, \tag{7}$$

$$\frac{dy_1}{dt} \approx N\beta y_0 x_1+(\mu+\nu)y_0\,\delta\beta\sin\omega t. \tag{8}$$

These equations describe a forced second order linear system where the forcing function is the periodic driving term $(\mu+\nu)y_0\,\delta\beta\sin\omega t$, i.e. oscillations in susceptibility ($\delta\beta$) can act as a driver for the system [4, 7, 9]. The system can be characterized by its natural, undamped frequency, ω_n and by its damping factor, ζ, which is a dimensionless ratio in the range 0–1 and is a measure of the degree of damping within the system, i.e. the attenuation of the amplitude of the oscillation at its resonant frequency. The damping factor is given by

$$\zeta = \frac{N\beta}{2(\mu+\nu)}\sqrt{\left(\frac{\mu}{N\beta-(\mu+\nu)}\right)}. \tag{9}$$

For the values of μ, ν and $N\beta$ used to describe the 5–6 year scarlet fever epidemics, 1847–80, ζ is small (much less than 1) indicating that the system is lightly damped. Since ζ is small, the system will amplify a driving term that has a frequency at the resonant frequency ω_r, where

$$\omega_r = \sqrt{(1-\zeta^2)}\,\omega_n \approx \omega_n \tag{10}$$

and

$$\omega_n = \sqrt{\{\mu[N\beta-(\mu+\nu)]\}}. \tag{11}$$

Because ζ is small, the frequency response of the system is very sharp, so that the amplification will be limited to driving terms that have a frequency close to this resonant frequency [27]. As a result, the oscillations in x_1 and y_1 will be dominated by frequency components close to ω_r. The period of the resonant frequency is

$$T = \frac{2\pi}{\sqrt{\{\mu[N\beta-(\mu+\nu)]\}}}. \tag{12}$$

Thus, the interepidemic interval is determined by $N\beta$.

If $\mu << \nu$, then this expression coincides with that given by Anderson and May [1].

$$T = 2\pi\sqrt{(AD)}, \tag{13}$$

where A = average age of contracting the disease; D = length of infectious period.

Strictly, equations (1) and (2) require that N, the total population, remains constant, but if N varies more slowly than the resonant frequency of the system, then equations (7) and (8) are still valid approximations to the dynamics of the underlying system.

The foregoing equations represent a linearized model of what is clearly a nonlinear system. The two models have been compared, using the same parameters, and the results are shown in Fig. 3, where $N\beta = 60{\cdot}5$ (for a resonant period = 5 years; equation (12)), $\mu = 0{\cdot}04$ year^{-1}, $\nu = 21$ year^{-1} and $\delta\beta = 0{\cdot}003$. The solid line in Fig. 3 represents the output from the full nonlinear model [10] and the dashed line the output from the linearized model (above). The period of the driver ($\delta\beta$) in Fig. 3*a* is 5 years (ω_r) and it can be seen that the two outputs are very similar, differing only slightly in the amplitude of the epidemics. It is, therefore, reasonable to use a linearized model for describing the oscillations in endemic systems where the magnitude of these oscillations is significantly smaller than the endemic level of the disease. It is noteworthy that large amplitude epidemics (where amplitude of oscillation/basal endemic level $\approx$ 50%) are produced by a very small $\delta\beta$ (0·003), i.e. only a low amplitude oscillation in susceptibility is necessary to maintain the epidemics.

Figure 3*b* illustrates the linear and non-linear models with the same characteristics, but the period of the driver is 3 years, i.e. not at ω_r. The responses of the linearized and nonlinear models are identical and we conclude that the former constitutes a satisfactory working model. Fig. 3*b* shows that, although ω_r remains at 5 years, the system oscillates at the frequency of the driver (3 years). Furthermore, the amplitude of the epidemics is reduced because the system is not oscillating at ω_r.

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