mathematics

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Supplementary Information for The Influence of Latent and Chronic Infection on Pathogen Persistence

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S1. Methodology

The deterministic model frameworks that include recovery, SIR, $SEIR$ and $SICR$ are shown in equations S1,S2 and S3. The SIR model framework is as follows:

$$\begin{aligned}\frac{dS}{dt} &= bN(1-qN) - \beta_F S\frac{I}{N} - \beta_D SI - dS,\\ \frac{dI}{dt} &= \beta_F S\frac{I}{N} + \beta_D SI - (\alpha+\gamma+d)I,\\ \frac{dR}{dt} &= \gamma I - dR.\end{aligned} \tag{S1}$$

Here, S represents total susceptible population density, I the infected density and R the recovered density, with $N = S + I + R$ the total population density. The maximum birth rate is given by b, which is modified due to intra-specific competition through the parameter, $q = (b-d)/bK$, where K denotes the carrying capacity of the population. The natural death rate is given by d. For the infection dynamics we denote β_F to be the frequency-dependent transmission rate, β_D the density-dependent transmission coefficient, γ the recovery rate and α the additional death rate from the disease for infected individuals.

The SIR model can be modified to include an exposed class, E, as follows:

$$\begin{aligned}\frac{dS}{dt} &= bN(1-qN) - \beta_F S\frac{I+\epsilon E}{N} - \beta_D S(I+\epsilon E) - dS,\\ \frac{dE}{dt} &= \beta_F S\frac{I+\epsilon E}{N} + \beta_D S(I+\epsilon E) - (\kappa+d)E,\\ \frac{dI}{dt} &= \kappa E - (\alpha+\gamma+d)I,\\ \frac{dR}{dt} &= \gamma I - dR.\end{aligned} \tag{S2}$$

In the $SEIR$ model infection leads to a susceptible individual entering the exposed class. Progression from the exposed class to the infected class occurs at rate κ. We also assume that individuals with the exposed form of the infection are infectious and can transmit the infection at a proportion ϵ of that of the infected class.

The SIR model can also be modified to include a chronically infected class, C, as follows:

Citation: O'Neill, X.; White, A.; Clancy, D.; Ruiz-Fons, F.; Gortázar, C. The Influence of Latent and Chronic Infection on Pathogen Persistence. *Mathematics* **2021**, *9*, 1007. https://doi.org/10.3390/math9091007

Received: 15 March 2021
Accepted: 26 April 2021
Published: 29 April 2021

$$\begin{aligned}
\frac{dS}{dt} &= bN(1-qN) - \beta_F S\frac{I+\epsilon C}{N} - \beta_D S(I+\epsilon C) - dS,\\
\frac{dI}{dt} &= \beta_F S\frac{I+\epsilon C}{N} + \beta_D S(I+\epsilon C) - (\alpha+\gamma+d)I,\\
\frac{dC}{dt} &= \gamma I - (\kappa+d+c\alpha)C,\\
\frac{dR}{dt} &= \kappa C - dR.
\end{aligned} \tag{S3}$$

In the $SICR$ model individuals enter a chronically infected class following infection from which they progress to a recovered and immune class at rate κ. Chronically infected individuals may incur disease-induced mortality at a fraction, c, of that of an infected individual and are also assumed to be infectious and transmit the infection at a proportion ϵ of that of the infected class.

The stochastic versions of the $SEIR$ and $SICR$ model frameworks can be constructed following the methods outlined in section 2 of the main paper.

S1.1. Reproductive Numbers

The basic reproductive number of the infection for the SIS and SIR model frameworks is shown in equation S4:

$$\mathcal{R}_0 = \frac{\beta_D K + \beta_F}{\alpha+\gamma+d} \tag{S4}$$

The basic reproductive number of the infection for the $SEIS$ and $SEIR$ model frameworks is shown in equation S5:

$$\mathcal{R}_0 = \frac{\beta_D K + \beta_F}{\kappa+d}\left(\epsilon + \frac{\kappa}{\alpha+\gamma+d}\right) \tag{S5}$$

The basic reproductive number of the infection for the $SICS$ and $SICR$ model frameworks is shown in equation S6:

$$\mathcal{R}_0 = \frac{\beta_D K + \beta_F}{\alpha+\gamma+d}\left(1 + \frac{\epsilon\gamma}{\kappa+d}\right) \tag{S6}$$

S2. Analytical Derivation of the Mean Time to Pathogen Extinction

To validate the simulation based methods that we employ in the main paper to determine the mean time to pathogen extinction, we derive the exact time to pathogen extinction for the SIS model framework. We consider a continuous-time Markov chain on a finite state space and define all possible states, $1,\ldots,n$, of the system with the possible pathogen free states (states $1,...,n_0$) as follows: $((S,I) = 1:(0,0), 2:(1,0), 3:(2,0)\ldots n_0:(K,0))$. We denote Q as the transition rate matrix, where each entry, q_{ij} for $i \neq j$ represents the rate of transition from state i to state j and with $q_{ii} = -\sum_{j\neq i} q_{ij}$. Then the expected time to reach the set of pathogen extinction states $1,\ldots,n_0$ from a starting state i, can be given by e_i and can be obtained by noting that $e_i = 0$ for $i = 1,2,\ldots,n_0$ and solving the following linear system for $\{e_i : n_0+1 \leq i \leq n\}$:

$$\sum_{j=n_0+1}^{n} q_{ij}e_j = -1, \qquad \text{for } i = n_0+1, n_0+2, \ldots n. \tag{S7}$$

Markov chain theory dictates that these equations have a unique solution [1], and as the states labelled $1,\ldots n_0$ represent the pathogen free states, by finding e_i we find the expected time to pathogen extinction from an initial starting state i.

For our model frameworks, we use a carrying capacity, $K = 1000$, and so this gives a high number of possible states. For the SIS model framework, where the set of possible states is given by $\{S \in (0, K), I \in (0, K); S + I < K\}$, there are 501501 possible states and therefore computing the transition rate matrix Q, and deriving the mean time to extinction e_i requires considerable computational effort. As we are considering a continuous Markov chain on finite space, any transition rate corresponding to a transition which requires more than one event to take place, (for example, going from one susceptible individual to three susceptible individuals) will be zero. As a result the transition rate matrix Q can be considered sparse and this helps reduce the computational effort. We restrict the use of this method to the SIS model framework as the introduction of additional classes (such as an immune, latent or chronically infected class) greatly increase the computational effort required.

The comparison between this analytical derivation and the simulation method adopted in the main paper for calculating the mean time to pathogen extinction for the SIS model is shown in Figure S1 and there is good agreement between the two methods.

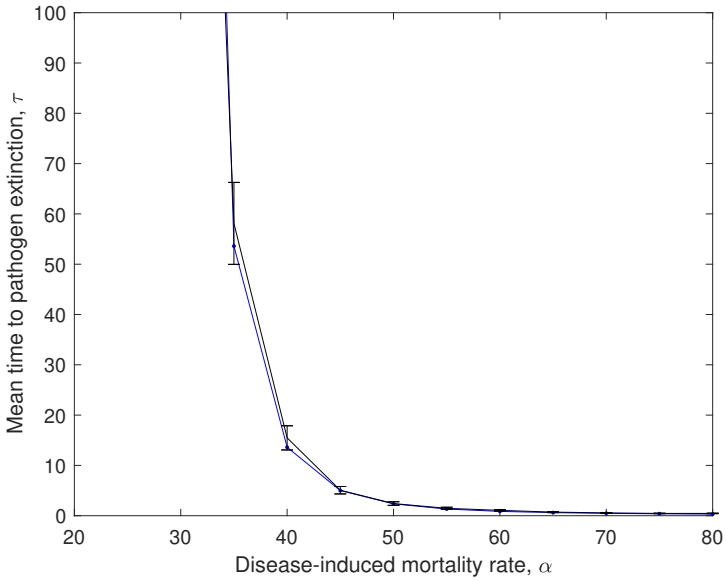

Figure S1. The mean time to extinction of the infection in the SIS model framework against disease-induced mortality for the simulation method used in this study (black) and the exact time to pathogen extinction from analysis of a continuous-time Markov chain on a finite state space (blue).

S3. An SI and $SICI$ Model Framework

In the discussion of the main paper we consider the possibility of chronically infected individuals reverting back to the infected class ($SICI$) and assess how this process affects the time to pathogen extinction when compared to an SI model framework. The SI model is outlined in equations S8 as follows:

$$\begin{aligned} \frac{dS}{dt} &= bN(1 - qN) - \beta_F S\frac{I}{N} - \beta_D SI - dS, \\ \frac{dI}{dt} &= \beta_F S\frac{I}{N} + \beta_D SI - I(\alpha + d). \end{aligned} \tag{S8}$$

Here, S represents total susceptible population density and I the infected density, with $N = S + I$ the total population density. The maximum birth rate is given by b, which is modified due to intra-specific competition through the parameter, $q = (b - d)/bK$, where K denotes the carrying capacity of the population. The natural death rate is given by d. For the infection dynamics we denote β_F to be the frequency-dependent transmission rate, β_D the density-dependent transmission coefficient, γ the recovery rate and α the additional

death rate from the disease for infected individuals.

The SI model framework can be extended to form an $SICI$ model framework (see equations S9). In addition to a susceptible class, S, we assume two separate infected classes, I_1 & I_2, and a chronically infected class, C. Here, $I_T = I_1 + I_2$ denotes the total infected population density. Both infected populations can infect a susceptible individual, which then progresses to the initial infected state, I_1. An individual in this state can recover to a chronic state at rate, γ, and then progress to the secondary infected state, I_2 at rate, κ. Once in the I_2 class an individual will either die naturally or suffer disease-induced mortality at rate, α. The $SICI$ model is as follows:

$$\begin{aligned}
\frac{dS}{dt} &= bN(1-qN) - \beta_F S\frac{I_T}{N} - \beta_D S I_T - dS,\\
\frac{dI_1}{dt} &= \beta_F S\frac{I_T}{N} + \beta_D S I_T - I_1(\gamma + \alpha + d),\\
\frac{dC}{dt} &= \gamma I_1 - C(\kappa + d),\\
\frac{dI_2}{dt} &= \kappa C - I_2(\alpha_2 + d).
\end{aligned} \tag{S9}$$

The stochastic versions of the SI and $SICI$ model frameworks can be constructed following the methods outlined in section 2 of the main paper.

S3.1. Results

A comparison of the SI and $SICI$ frameworks indicates that the mean time to pathogen extinction is increased for all levels of disease-induced mortality under the $SICI$ framework compared to an SI framework (Figure S2).

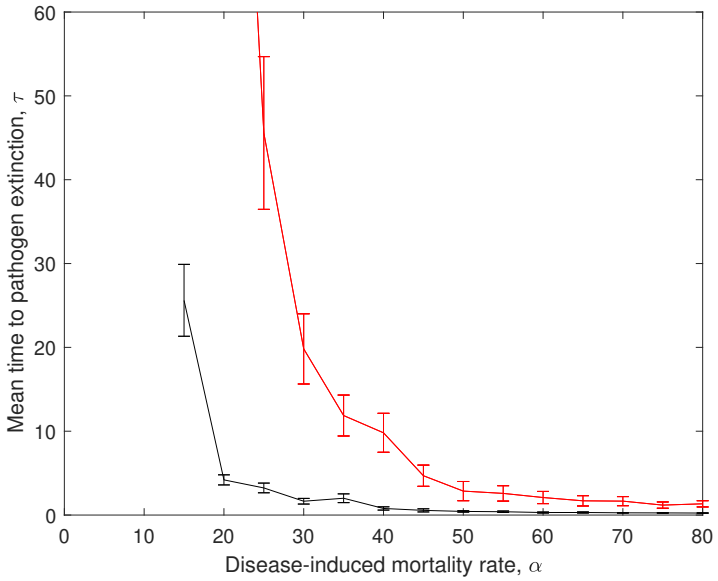

Figure S2. The mean times to pathogen extinction (with 95% confidence intervals) plotted against the disease-induced mortality rate, α, for SI (black) and $SICI$ (red) model frameworks. Results show the mean and 95% confidence intervals for 100 realisations of each model framework. When not changed in the figure baseline parameter values were used (see main paper, Table 2).

References

1. Norris, J., Markov Chains; Cambridge University Press, 1997; chapter 3.