Partnership dynamics and strain competition

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Abstract

Models of epidemic spread that include partnership dynamics within the host population have demonstrated that finite length partnerships can limit the spread of pathogens. Here the influence of partnerships on strain competition is investigated. A simple epidemic and partnership formation model is used to demonstrate that, in contrast to standard epidemiological models, the constraint introduced by partnerships can influence the success of pathogen strains. When partnership turnover is slow, strains must have a long infectious period in order to persist, a requirement of much less importance when partnership turnover is rapid. By introducing a trade-off between transmission rate and infectious period it is shown that populations with different behaviours can favour different strains. Implications for control measures based on behavioural modifications are discussed, with such measures perhaps leading to the emergence of new strains.

Keywords: Epidemiology; Strain competition; Partnership model; Basic reproductive ratio

1. Introduction

Understanding the spread of infectious diseases is a complicated business, with the characteristics of both host and pathogen being variable and uncertain. A wide range of mathematical models has been developed to investigate key parameters and make usable predictions about epidemic spread and control (Anderson and May, 1991; Ferguson et al., 2003, 2005; Keeling et al., 1997, 2001; Longini et al., 2005); by their nature such models simplify reality, by ignoring aspects of differences between individuals, variation between pathogens, and so on. One common assumption is that host individuals interact at random—this greatly simplifies the model and is often, given a paucity of data, the only reasonable approach. However, it has been recognized that the common assumption of instantaneous interactions between members of a population is inappropriate in many situations (Dietz and Hadeler, 1988; Keeling et al., 1997, Kretzschmar and Morris, 1996). It is often the case that contacts between individuals exist for some non-negligible duration, and this has particularly been considered in the context of sexually transmitted diseases (STDs), for which the relevant sexual partnerships may be of considerable length (Johnson et al., 2001; Kretzschmar et al., 1996; Wellings et al., 1994). A number of models have been developed that include the partnership status of individuals (Dietz and Hadeler, 1988; Kretzschmar et al., 1996; Kretzschmar and Dietz, 1998; Kretzschmar and Morris, 1996). In such models, it is only between individuals within a sexual partnership that infection can be transmitted.

The inclusion of serially monogamous partnerships within models of epidemic spread has a number of effects on the dynamics of infection. Disease spreads through the population much less quickly, since each individual is only capable of passing infection to one contact at a time; for infection to travel further the current partnership has to break up and a new partnership form between an infectious and a susceptible individual. The speed at which infection moves through the population depends to a large extent on the partnership behaviour observed; if partnerships are too
This paper presents a partnership model of simple STDs and investigates how competition between pathogen strains is affected by finite partnerships. The additional time-scale introduced to the system by the consideration of partnerships means that there are additional pressures on any pathogen. For an infection to persist it must be sufficiently infectious to be transmitted during a partnership and sufficiently long-lived to endure the periods between partnerships. Therefore, effect of partnership considerations on the evolutionary pressures experienced by pathogens is considered. In particular, it is shown that the behaviour of the population determines the success of a pathogen and the characteristics of the optimal pathogen strain. This effect is not seen in models that do not consider partnerships. By introducing a trade-off function constraining the relationship between transmission rate and infectious period it is shown that changes in population behaviour can result in changes in pathogen properties and that interventions based on modifying population behaviour may be less successful than might be hoped.

2. The model

A model for the spread of a relatively simple infection, based on that developed in Dietz and Hadeler (1988) is presented. Individuals can be in one of two infection states: susceptible or infected. On recovery, individuals become susceptible once more, leading to susceptible–infected–susceptible (SIS) dynamics (Hethcote and Yorke, 1984). Furthermore, we assume that individuals can only become infected when in a partnership, and that individuals are serially monogamous: that is, they have at most one partner at any time. Existing partnerships can break up and partnerships can form between any two single individuals. We model these processes (infection, recovery, and partnership dynamics) with a series of differential equations. We define the variables as follows: $S$ and $I$ are the numbers of unpartnered (single) susceptible and infected individuals. The numbers of partnerships of different types are denoted $PSS$, $PSI$ and $PHI$, with pairs counted once in each direction (this means that a partnership between two susceptible individuals contributes two to $PSS$ and that $PSI = PNI$). The variables satisfy

\[ S + I + PSS + 2PSI + PHI = N, \]

\[ \text{the fixed population size.} \tag{1} \]

Formulation of a model requires some assumptions about the process of pair formation: following Kretzschmar and Dietz (1998) we assume that partnerships break up at rate $\rho$ and that the rate of formation of new partnerships is proportional to the number of single individuals. This allows partnership formation to take place at a rate determined by the preferences of the individual rather than through chance interactions within the population; thus the rate with which a single individual forms a new partnership does not depend on the number of single individuals in the population; partnership behaviour is independent of the population size.

We can now write down the following system of equations:

\[
\begin{align*}
\dot{S} &= gI - \alpha S + \rho (PSS + PSI), \\
\dot{I} &= -gI + \alpha I + \rho (PSI + PHI), \\
PSS' &= 2gPSI - \rho PSS + \alpha \frac{S^2}{S + I}, \\
PHI' &= a(PHI - PSI) - \tau PSI - \rho PSI + \alpha \frac{SI}{S + I}, \\
PSI' &= -2gPSI + 2\tau PSI - \rho PSI + \alpha \frac{I^2}{S + I}.
\end{align*}
\]

where $\tau$ is the transmission rate within a partnership, $g$ the recovery rate, $\rho$ the rate of partnership break-up and $\alpha$ the rate of partnership formation.

3. Analysis

Considering a disease-free population, the equations are reduced to

\[
\begin{align*}
\dot{S} &= -\alpha S + \rho PSS, \\
\dot{PSS} &= -\rho PSS + \alpha S, \\
\end{align*}
\]

with $S + PSS = N$. At equilibrium, this means that a proportion $\alpha/(\alpha + \rho)$ of the population is in a partnership. Since infection can only be transmitted by individuals within the context of a partnership one might expect that by maximizing this proportion prevalence of infection might also be maximized. This is not so, however; although increasing $\alpha$ does indeed increase prevalence, the effect of the partnership break-up rate $\rho$ is somewhat different (Fig. 1(a)); prevalence is maximized at some intermediate value. When partnerships break up too rapidly too few individuals are paired up to allow infection to be transmitted; conversely, when partnership turnover is too slow infection is trapped within a few pairs and cannot spread further. In the limit $\rho \to \infty$ or $\rho \to 0$ the population reaches a disease-free equilibrium.

3.1. Strain competition

The equations above can easily be adapted to allow for multiple strains of infection. If an individual can only be infected with one strain at any one time then within a homogeneous population only a single strain will persist. In this section we examine how the identity of the
dominant strain can be determined and how this strain depends on the characteristics of the population. We show
that neither $R_0$ nor equilibrium prevalence can be used reliably to predict the dominant strain (an effect previously
observed when concurrent infection with several strains is permitted (May and Nowak, 1994; Nowak and May,
1994)), and demonstrate an alternative means of directly
determining the outcome of strain competition.

One way of assessing the competitive ability of a strain is by considering the basic reproductive ratio of the infection,
$R_0$, defined as the number of new cases produced by an infectious individual in an otherwise susceptible population (Anderson and May, 1991). In non-partnership models, the strain with the highest value of $R_0$ will dominate, and we might expect the same effect to be shown here (Bremer-
mann and Thieme, 1989; Nowak and May, 1994; Turner and Garnett, 2002). Calculation of this vital epidemiolog-
ical quantity is less straightforward in a partnership model than in the more familiar random-mixing approaches; a
new infectious individual must form partnerships before being able to generate new infections. However, an
expression for $R_0$ can be derived by calculating the expected number of new cases that will be generated by a
newly infectious index case in an otherwise susceptible population (Diekmann and Heesterbeek, 2000). Following
the methods of Diekmann and Heesterbeek (2000, Section 5.6) we note that a new infection must be in a partnership
with another infected individual (the source case) and that to generate subsequent cases either this partnership must
break up or the source case must recover and thus be available for re-infection by the index case.

We define $R_1$ to be the number of distinct secondary cases generated by an infected index case currently not in a partnership. $R_2$ is defined to be the number of distinct secondary cases generated by an infected index case currently in a partnership with a susceptible that has not been previously infected by the index case. We can then write

$$R_0 = \frac{\rho}{\rho + 2g} R_1 + \frac{g}{\rho + 2g} R_2,$$

where $\rho/(\rho + 2g)$ is the probability that the initial infected–infected partnership breaks up before either individual recovers, and $g/(\rho + 2g)$ is the probability that the source case recovers before the index case and before partnership break-up.

Similarly, we can write $R_1 = \tau/(\alpha + g) R_2$, the multiplier here being the probability that the index case forms a partnership before recovering; likewise, $R_2 = (\rho + \tau + g) R_1 + \tau/(\rho + \tau + g) R_1 (1 + \rho/(\rho + g) R_1)$, where the first part of the expression considers the case when break-up is the next event to occur and the second part of the expression considers the case when the next event is infection: the ‘$+1$’ accounts for the new case generated and the final term allows for further secondary cases should the partnership break up before the index case recovers. Combining these expressions gives

$$R_0 = \frac{\tau (\rho + g)(\alpha + g^2 + \rho \alpha)}{g(\rho + 2g)(\rho + \tau + g)(\rho + g + \alpha)},$$

Fig. 1(b) shows how $R_0$ varies with the partnership turnover parameters; like prevalence, it is maximized by an intermediate break-up rate.

Alternatively, we can look for the strain that maximizes equilibrium prevalence. Prevalence is not easy to calculate directly but can be determined as follows: the number of infected individuals is given by $I = I + P_{SI} + P_{II}$, and Eq. (3) shows that at equilibrium $P_{SI} + P_{II} = (\alpha + g)/\rho I^*$ (asterisks represent equilibrium values), and thus that $I^* = ((\alpha + \rho + g)/\rho) I^*$. Hence all that remains is to determine $I^*$, the equilibrium number of unpartnered infected individuals. Since we already know the equilibrium proportion of the population that is single, it suffices to calculate the equilibrium fraction of the unpartnered population that is infected, which we denote by $\tilde{I} = I^*/(I^* + S^*)$; similarly, $\tilde{S} = 1 - \tilde{I}$. 

![Equilibrium prevalence as a function of partnership parameters, determined using the analytical method developed in the analysis section.](image)

![Formation rate](image)
Thus, we have
\[
\frac{I}{N} = \frac{(x + \rho + g)}{x + \rho} \hat{I},
\] (11)

\(\hat{I}\) can be calculated as follows: in a population at equilibrium, consider an unpartnered infected individual. In order to maintain the equilibrium the first partnership it is involved in must result in on average the same number of emergent single infected individuals as enter the partnership. Let \(r_{SI}\) and \(r_{II}\) be the number of infected single individuals that emerge from an \(SI\) and an \(II\) partnership respectively. Thus, we require
\[
1 = \frac{x}{x + g} \hat{S} r_{SI} + \frac{1}{2} \frac{x}{x + g} \hat{I} r_{II}.
\] (12)

The first term on the right-hand side is the product of the probability that the index case is still infectious when it forms its first partnership, the probability that this partnership is with a susceptible individual, and the resulting number of single infected individuals that emerge; the second term is similar, concerning partnerships formed with infected individuals, the factor of \(\frac{1}{2}\) present since these partnerships require an input of two infected individuals.

Within the partnership infection or recovery can occur, and the partnership can break up (Fig. 2). These transitions allow us to relate \(r_{SI}\) and \(r_{II}\) via
\[
r_{SI} = \frac{\tau}{\rho + \tau + g} r_{II} + \frac{\rho}{\rho + \tau + g},
\] (13)

\[
r_{II} = \frac{2g}{\rho + 2g} r_{SI} + 2 \times \frac{\rho}{\rho + 2g},
\] (14)

the factor of two in the final term being present because an \(II\) pair produces two infecteds on break-up. We can therefore calculate \(r_{SI}\) and \(r_{II}\) explicitly and use these to determine \(\hat{I}\), thus giving, after some manipulation, an analytical expression for the equilibrium prevalence:
\[
\frac{I}{N} = \frac{(x + \rho + g)}{\rho \tau (x + \rho)} \left\{ \rho \tau - \rho g - 2g^2 - \frac{q}{\alpha} (\rho^2 + 3\rho g + \rho \tau + 2g^2) \right\}.
\] (15)

A third, direct, method for determining the outcome of competition uses similar reasoning to that which gave us this expression for prevalence: consider now an endemic population of strain \(J\), with parameters \(\tau_J, g_J\) (for which \(\hat{J}\) can be determined as above) and an invading population of strain \(I\) with parameters \(\tau_I, g_I\). To determine whether strain \(I\) can invade we consider an unpartnered strain \(I\) individual and examine the outcome of the first partnership this individual is involved in; if the partnership results in, on average, more than one unpartnered strain \(I\) infection then the strain can persist; if not, then it will die out. We denote by \(R_I\) the number of emergent unpartnered strain \(I\) individuals; invasion is possible if \(R_I > 1\). By the same reasoning as above
\[
R_I = \frac{x}{x + g_J} \hat{S} r_{SI} + \frac{x}{x + g_J} \hat{I} r_{II},
\] (16)

where \(r_{II}\) is the number of unpartnered strain \(J\) individuals emerging from an \(IJ\) partnership. The number of possible transitions within the partnership is larger than above, since an \(II\) partnership can be produced if the strain \(J\) individual recovers and the strain \(I\) individual transmits before partnership break-up; transitions and transition probabilities are shown in Fig. 3. Again, these transitions

![Fig. 2. Transitions and transition probabilities used to calculate equilibrium prevalence.](image)

![Fig. 3. Transitions and transition probabilities used to determine the outcome of strain competition.](image)
allow us to relate \( r_{SI} \), \( r_{IJ} \), and \( r_{II} \) using

\[
r_{SI} = \frac{\tau_f}{\rho + \tau_f + g_f} r_{II} + \frac{\rho}{\rho + \tau_f + g_f},
\]

(17)

\[
r_{IJ} = \frac{g_f}{\rho + g_f + g_f} r_{SI} + \frac{\rho}{\rho + g_f + g_f},
\]

(18)

\[
r_{II} = \frac{2g_f}{\rho + 2g_f} r_{SI} + 2 \times \frac{\rho}{\rho + 2g_f}.
\]

(19)

Although the equations become algebraically messy, as above we can solve for \( r_{SI} \) and \( r_{IJ} \). This allows us to evaluate \( R_f \), and thence determine whether or not strain \( f \) can invade strain \( i \).

We now have three methods of investigating strain competition; we will use and compare these methods in the following section.

4. Pathogen optimization

We consider the possibility of pathogen evolution; that is to say the transmission and recovery rates are allowed to vary. We would not expect these rates to vary independently—if this were possible then every pathogen would become infinitely infectious over an infinite infectious period. Instead, we expect there to be a trade-off between infectious period and infectiousness (Bremermann and Thieme, 1989; Boots and Sasaki, 1999; Turner and Garnett, 2002; van Baalen, 2002). The precise form such a trade-off will take is unknown, so following van Baalen (2002) we apply a trade-off of the form \( g = a + b\tau^c \), with \( c > 1 \). This function assumes that the recovery rate increases more than linearly with transmission rate because of an increased immune response to more detrimental infections. In a non-partnership model the dominant strain would be the one with the highest value of \( \tau/g \) (Bremermann and Thieme, 1989; van Baalen, 2002)—such a strain maximizes both \( R_0 \) and equilibrium prevalence; however, partnership models are more complex and we would expect “fast” strains (those with a high transmission rate and short infectious period) to be at a comparative disadvantage when partnership turnover is slow. Fig. 4 shows equilibrium prevalence and \( R_0 \) as functions of \( \tau \) for several trade-off curves; both prevalence and \( R_0 \) have a single maximum but this does not occur at the same value of \( \tau \). Indeed, neither of these two quantities can accurately predict the dominant strain. Fig. 5 shows the relationship between the partnership turnover rate and the dominant pathogen strain. In Fig. 5 the partnership formation rate is assumed to be proportional to the break-up rate. As anticipated, faster partnership behaviour favours faster strains. Neither \( R_0 \) nor equilibrium prevalence accurately predicts the outcome of competition, whereas the direct competition method agrees almost exactly with the results obtained by running competing-strain simulations.

When partnerships are included the properties of the host population determine the effectiveness and identity of pathogen strains, a result not apparent in standard models. This result has further implications. For example, if a host population consists of more than one behavioural subgroup, for instance one in which partnership turnover is rapid and one in which it is slow, then it is possible for two strains to coexist, each strain dominating within one sub-population. If the sub-populations are sufficiently segregated it may be the case that different evolutionary pressures will lead to divergence of strain properties. Thus, population diversity can result in strain diversity. Shown in Fig. 6 is the dominant strain in two behaviourally distinct populations and the range of strains within each population that would out-compete the dominant strain from the other population. We...
see that in a heterogeneous population a range of pathogen parameters allows strain coexistence.

A common tactic for the control of infectious diseases is to persuade the population to modify its behaviour—changes in partnership behaviour can have a large effect on $R_0$ and prevalence (Fig. 1). If we suppose the infection to be well-adapted to its host population, then a reduction in the rate of partnership turnover will in general act to reduce $R_0$ and prevalence. However, if different strains can emerge it may be that altering partnership turnover rates will result in the pathogen adapting to its new host environment, with the outcome that the effect on $R_0$ and on equilibrium prevalence is smaller than expected (Fig. 7). Therefore, care needs to be taken both in estimating the effects of behavioural interventions and in evaluating the success of the message: a low reduction in the impact of the pathogen may not be the result of a failure to persuade individuals to change their behaviour but may arise because of the pathogen’s inherent mutability.

If the only difference between pre- and post-intervention populations is the length of partnerships (i.e. $\rho$ differs but $\alpha$ does not) then it may even be the case that the impact of the infection is increased by the intervention. As shown in Fig. 8, if the original break-up rate is large a moderate reduction can increase prevalence and $R_0$ and a large reduction is required in order to substantially reduce the impact of the pathogen. Therefore, when pathogen evolution is possible a change in partnership behaviour might be unexpectedly detrimental to the population.

5. Discussion

This paper has examined the effect of partnership turnover on disease spread, a relevant issue for any
infection that passes through interactions of a finite duration. Partnership considerations are most readily applied to STDs, which is the context in which they have been looked at here.

Following previous work, a model of disease spread through a system of partnerships has been developed, and it is immediately clear that the rate of partnership turnover influences the impact of a pathogen. For an infection to persist partnerships must last sufficiently long to allow transmission to take place and must break up sufficiently quickly to allow further partnerships to form before recovery occurs. Therefore, both prevalence and $R_0$ are maximized by an intermediate value of the partnership break-up rate.

The interaction between partnership and infection dynamics has implications for strain competition. When there is a trade-off between transmission rate and infectious period, such that rapidly transmitted strains tend to be rapidly recovered from, it is seen that “fast” strains are best suited to “fast” populations. If the host population consists of several self-contained behavioural subgroups, with differing partnership behaviour, we would expect different strains to dominate in each subgroup. The extent to which subgroups are self-contained is not clear, but assortative (like-with-like) mixing has been observed (Garnett et al., 1996) and this behavioural clustering may suffice to allow strains to coexist. The degree to which strain characteristics and partnership behaviours correlate is yet to be quantified and may be a fruitful area for further epidemiological investigation.

The possibility of strain evolution affects intervention measures; by altering partnership behaviour conditions may be made less favourable for the current strain but other strains may emerge that spread better in the new

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**Fig. 7.** (a) Equilibrium prevalence of the dominant strain as a function of partnership break-up rate. (b) $R_0$ of the dominant strain as a function of partnership break-up rate. Partnership formation rate is fixed at $a = 75$ throughout.

**Fig. 8.** (a) Equilibrium prevalence of the dominant strain as a function of partnership break-up rate. (b) $R_0$ of the dominant strain as a function of partnership break-up rate. Partnership formation rate is fixed at $a = 75$ throughout.
conditions. As a general rule a slowing of the partnership processes (formation and break-up) will result in a reduction in the impact of the prevalent strain—both its prevalence and its speed of spread—although the identity of this infection might change. However, a reduction in the partnership break-up rate that is not accompanied by a similar change in the formation rate may lead to increased infection prevalence and $R_0$.

The model presented here is at best a caricature of the interactions taking place in real populations; to be able to be used as a predictive tool it would require numerous additions, including such factors as male/female differences, asymptomatic infections and behavioural heterogeneities. Partnership formation and break-up are complex processes arising from a wide range of social and behavioural influences that have not been included. All interactions have been assumed to be serially monogamous; this appears to be the norm for the majority of most populations but concurrent or overlapping partnerships have also been shown to be an important influence on disease spread (Garnett and Johnson, 1997; Johnson et al., 2001; Kretzschmar and Morris, 1996). Although the monogamous paradigm is unlikely to be universally applicable, it is often possible to view concurrent partnerships as several rapidly changing monogamous interactions, each lasting for only a short period; for instance, a week of overlapping partnerships could be represented as seven day-long monogamous partnerships alternating between two partners. Even when partnerships are best viewed as concurrent, the conclusions presented here regarding the influence of partnership turnover rates and inter-partner periods are still expected to hold. The simple approach taken both permits analysis and helps to illustrate the importance of partnership dynamics in epidemic behaviour, something that might be less apparent in a more detailed model.

There is a vast difference between models that include partnerships and those that do not; the former are capable of displaying much more complex behaviour, even when the infection dynamics are extremely simple; the extra time-scale introduced by the formation and break-up of partnerships constrains the spread of infection and gives an advantage to long-lasting infections. It is no surprise therefore that many sexually transmitted infections are particularly long-lived (Kretzschmar et al., 1996). It may be the case that ideas of partnership turnover are applicable to other types of infectious disease, particularly if transmission tends to occur between long-term social contacts (such as within families); the existence of long-lasting partnerships can both facilitate and constrain transmission and the non-random nature of many social interactions has implications for understanding epidemic dynamics (Ferguson et al., 2005; Keeling et al., 1997).

Differences in community structure within different parts of a population including factors such as the length and frequency of interactions and the likelihood of interacting with novel individuals will all affect the way infection spreads and may result in different strains dominating in differing sub-populations.

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References


