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Frequency-dependent incidence in models of sexually transmitted diseases: portrayal of pair-based transmission and effects of illness on contact behaviour

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We explore the transmission process for sexually transmitted diseases (STDs). We derive the classical frequency-dependent incidence mechanistically from a pair-formation model, using an approximation that applies to populations with rapid pairing dynamics (such as core groups or non-pair-bonding animals). This mechanistic derivation provides a framework to assess how accurately frequency-dependent incidence portrays the pair-based transmission known to underlie STD dynamics. This accuracy depends strongly on the disease being studied: frequency-dependent formulations are more suitable for chronic less-transmissible infections than for transient highly transmissible infections. Our results thus support earlier proposals to divide STDs into these two functional classes, and we suggest guidelines to help assess under what conditions each class can be appropriately modelled using frequency-dependent incidence. We then extend the derivation to include situations where infected individuals exhibit altered pairing behaviour. For four cases of increasing behavioural complexity, analytic expressions are presented for the generalized frequency-dependent incidence rate, basic reproductive number (R_0) and steady-state prevalence (i_∞) of an epidemic. The expression for R_0 is identical for all cases, giving refined insights into determinants of invasibility of STDs. Potentially significant effects of infection-induced changes in contact behaviour are illustrated by simulating epidemics of bacterial and viral STDs. We discuss the application of our results to STDs (in humans and animals) and other infectious diseases.

Keywords: sexually transmitted disease; epidemic models; incidence rate; pair formation; behavioural modification; HIV/AIDS

1. INTRODUCTION

Sexually transmitted diseases (STDs) are a significant and growing problem in public health worldwide (Piot *et al.* 2001; CDC 2002), and mathematical models have become an integral part of STD epidemiology (Hethcote & Yorke 1984; Castillo-Chavez 1989; Anderson & May 1991; Anderson & Garnett 2000; Garnett 2002*b*). The core of every infectious-disease model is its representation of the transmission process, and the fundamental question of how to formulate the transmission rate is the subject of active research (Antonovics *et al.* 1995; De Jong *et al.* 1995; McCallum *et al.* 2001, 2002; Fenton *et al.* 2002). Increasingly complex models have yielded important insights into STD dynamics, by incorporating details of heterogeneity in sexual behaviour (Hethcote & Yorke 1984; Anderson & May 1991), partnership dynamics (Dietz & Hadeler 1988; Waldstatter 1989; Diekmann *et al.* 1991; Kretzschmar & Dietz 1998; Kretzschmar 2000) and sexual-network structure (Kretzschmar & Morris 1996; Bauch & Rand 2000; Ferguson & Garnett 2000; Kretzschmar 2000; Eames & Keeling 2002). These gains

come at the expense of increasing mathematical and computational demands, however, so simple analytic formulations continue to play an important role. STD models based on frequency-dependent transmission—the classical analytic formulation—are published often and prominently, typically nested in models addressing larger topics such as drug resistance or competition between strains (e.g. Thrall & Antonovics 1997; Blower *et al.* 1998, 2000; Bowden & Garnett 2000; Sullivan *et al.* 2001; Boots & Knell 2002). In their review of STD modelling, Anderson & Garnett (2000) point out that simpler models are complementary to complex simulations and help to extract general principles and reach robust conclusions, which aid in policy development (though see Garnett *et al.* (1999) for a discussion of potential shortcomings). McCallum *et al.* (2002) observe that simple treatments of transmission will continue to be necessary, and that correspondence with more complex models is an important area for investigation.

In this spirit, we undertake to explore the transmission process for STDs and to relate complex dynamics to simple analytic expressions for the transmission rate. Using an approximation that applies to populations with rapid pairing dynamics (such as core groups or non-pair-bonding animals), we derive the classical frequency-dependent

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incidence mechanistically from a pair-formation model. We thus demonstrate a formal correspondence between the standard model of STD incidence and the pair-based contact process that is known to underlie STD dynamics. This mechanistic derivation clarifies the conditions required for the frequency-dependent model to represent pair-based transmission accurately, and provides a natural framework in which we assess the classical model's proper scope of application. We then extend the derivation to obtain generalized frequency-dependent transmission rates for situations where the pairing behaviour of individuals is influenced by their infection status.

Frequency-dependent transmission (also called the standard incidence or density-independent transmission) is the standard approach to modelling STD transmission in compartmental disease models (Getz & Pickering 1983; Antonovics *et al.* 1995; De Jong *et al.* 1995; Hethcote 2000; McCallum *et al.* 2001). In this formulation, the rate at which susceptible individuals become infected is proportional to the prevalence (or 'frequency') of the disease in the population. Let S and I represent the densities of susceptible and infectious individuals, respectively, and $N = S + I$ the total density; the prevalence is thus I/N. Also, let c_{FD} represent the average *per capita* rate of acquiring new sexual partners (assumed to be independent of population density) and p_{FD} represent the probability that transmission will occur over the course of an SI partnership (a partnership between a susceptible individual and an infectious individual). Then the frequency-dependent incidence rate, i.e. the rate at which new infections arise in the population, is (Anderson & May 1991; Hethcote 2000):

$$\varepsilon_{FD} = c_{FD}\, p_{FD}\left(\frac{I}{N}\right)S. \tag{1.1}$$

The frequency-dependent formulation does not explicitly model sexual partnerships: contacts have no temporal extent and the probability of transmission during a partnership is ill defined (Antonovics *et al.* 1995). Partnership dynamics have been recognized as a critical element of STD models since the seminal work of Dietz & Hadeler (1988) and are the basis for subsequent network models (Ferguson & Garnett 2000; Kretzschmar 2000). Pair-formation models account for the essential structure of STD epidemics, in that sexual contacts take place within partnerships (however short lived) and individuals in monogamous pairs are removed from mixing with the rest of the population. Modelling the finite duration of partnerships can have significant effects on both the transient and the steady-state properties of STD epidemics (Waldstatter 1989; Kretzschmar & Dietz 1998), and the resulting predictions for disease invasion or persistence can differ qualitatively from those of non-partnership models (Diekmann *et al.* 1991; Kretzschmar & Dietz 1998).

We seek to clarify the relationship of frequency-dependent incidence to the pairing processes underlying STD transmission. To do so, we construct a full model of partnership, disease and demographic dynamics and consider its behaviour in situations where pairing processes occur much faster than epidemic processes. In such situations we can separate the fast pair dynamics from the slower disease and demographic dynamics, and approximate that pair dynamics reach a quasi-steady state on epidemic

time-scales (i.e. that the pairing process constantly re-equilibrates as the epidemic progresses). We demonstrate numerically that solutions of the approximate system converge to those of the full system as the ratio of fast to slow time-scales tends to infinity. This approach follows Heesterbeek & Metz (1993; see also Diekmann & Heesterbeek 2000), who broke new ground by deriving a saturating transmission function from a pair-formation model. The mass-action formulation of their pairing process, however, may be suitable for non-STDs but is inappropriate for STDs (particularly among humans) for which rates of pair entry are generally thought to be density-independent (Dietz & Hadeler 1988; Waldstatter 1989; Diekmann *et al.* 1991). In this study, we derive analytic results from partnership models under the time-scale approximation, and use comparisons with a full pair-formation–epidemic model to test the approximation. We find that the accuracy of the approximation—and hence the accuracy with which frequency dependence portrays pair-based transmission—depends strongly on the natural history of the STD in question, as well as on the rates of partnership formation and break-up.

Finally, for situations where the time-scale approximation holds, we build on the foundation of pair-formation models to consider infection-induced changes in pairing behaviour. Previous work on behavioural change in STD epidemics has focused on population-level effects in humans, wherein education campaigns or community awareness of disease prevalence leads to reductions in risky behaviour or changes in partner selection (e.g. Hadeler & Castillo-Chavez 1995; Hyman & Li 1997; Hsieh & Sheu 2001). We consider a different class of behavioural change, applicable to humans and animals, in which individual contact behaviour is influenced by individual infection status (i.e. sick individuals behave differently from healthy ones). There is strong evidence for this phenomenon in the biological and behavioural literature, but it has not yet been incorporated into epidemiological theory.

The infection status of individuals (both human and animal) has been shown to affect their contact behaviour in STDs and other diseases (Kennedy *et al.* 1987; Loehle 1995; Able 1996; Beckage 1997; Garnett *et al.* 1999; Kiesecker *et al.* 1999; Webster *et al.* 2003), and evolutionary biologists have long speculated that parasites play a role in mating behaviour (Hamilton & Zuk 1982; Boots & Knell 2002). Proposed or observed mechanisms for lowered contact rates include debilitation and reduced vigour (e.g. Newshan *et al.* 1998; Schiltz & Sandfort 2000), social factors (Gold & Skinner 1996; Donovan 2000), scent cues (Penn & Potts 1998; Kavaliers *et al.* 1999) and secondary sexual characteristics (Hamilton & Zuk 1982; Loehle 1995; Able 1996). Pathogens can also modify host behaviour to increase the opportunity for transmission, as is commonly seen in macroparasitic infections (Beckage 1997); in sexual behaviour, such effects have been observed in mice (Kavaliers *et al.* 1999) and milkwood leaf beetles (Abbot & Dill 2001), and postulated in humans (Starks *et al.* 2000). In summary, ample evidence exists that the infection status of individuals may influence their partnering behaviour. In § 4, we generalize the theory of frequency-dependent transmission to incorporate this phenomenon in populations with rapid pairing dynamics.
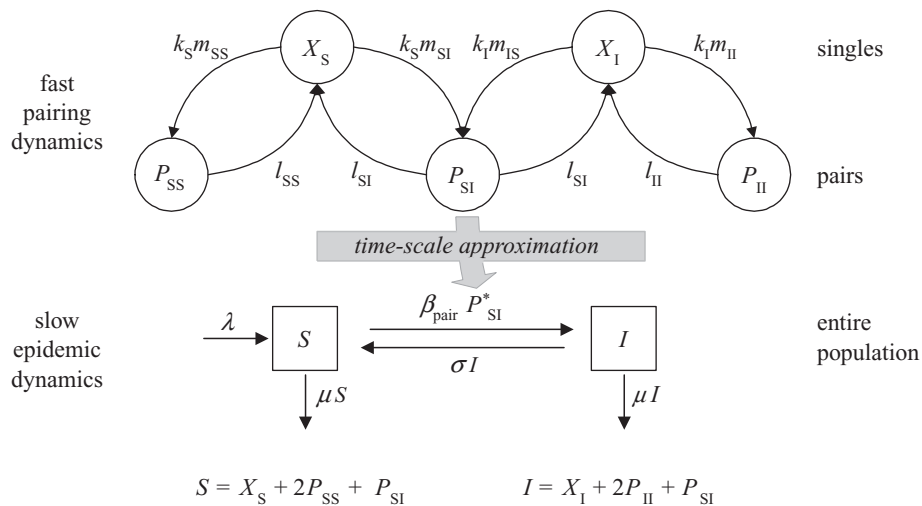
Figure 1. STD epidemic model. The fast pairing dynamics and slow epidemic dynamics are linked by a time-scale approximation, as described in § 2. *Fast pairing dynamics*: X_S and X_I are the densities of susceptible and infectious single individuals, respectively, while P_{SS}, P_{SI} and P_{II} represent partnerships between individuals of the disease states shown in the subscripts. Single individuals in the X_S and X_I pools enter partnerships at *per capita* rates k_S and k_I, respectively, independent of population density. Pairings of type P_{yz} break up at rate l_{yz} (for $y, z = S$ or I), and hence have lifetimes that are distributed exponentially with a mean of $1/l_{yz}$. For the simple case described in § 2, we set $k_S = k_I = k$ and $l_{SS} = l_{SI} = l_{II} = l$. When individuals of type y form partnerships, a proportion m_{yz} will be with individuals of type z (hence we always have $\Sigma_z m_{yz} = 1$). *Slow epidemic dynamics*: transmission occurs within SI pairs (at quasi-steady-state density P_{SI}^*) at rate β_{pair}, which is the product of the within-partnership rate of sex acts and the probability of transmission per sex act. Infected individuals recover at rate σ. There is a constant influx λ into the population, and individuals leave the population (by death, emigration or entering long-term relationships) at rate μ. We assume that the population density has reached an equilibrium value $N = S + I$, and hence $\lambda = \mu N$.

2. DERIVATION OF FREQUENCY-DEPENDENT TRANSMISSION FROM A PAIR-FORMATION MODEL

We consider a model for STD spread in a population of individuals engaging in short-lived sexual partnerships, such as a core group within an HIV/AIDS epidemic. Long-term relationships are outside the scope of this study, but have been examined elsewhere (Diekmann *et al.* 1991; Kretzschmar *et al.* 1994). In the model presented here, the defining characteristics of a partnership are that: (i) both individuals are removed from the mixing population for the duration of the pairing; and (ii) sexual contacts are occurring at some rate. We assume that sexual contacts do not occur outside partnerships and that concurrency is insignificant for these brief pairings. Hence, disease transmission takes place only in partnerships between infected and susceptible individuals. We describe pairing dynamics using the standard formulation of recent STD models (e.g. Dietz & Hadeler 1988; Waldstatter 1989; Diekmann *et al.* 1991; Kretzschmar *et al.* 1994; Kretzschmar & Dietz 1998; Bauch & Rand 2000), assuming that individuals enter partnerships at a constant *per capita* rate and choose partners according to a defined mixing pattern.

The model is explained in figure 1, and model equations are given in electronic Appendix A (available on The Royal Society's Publications Web site). The basic assumption is that pairing processes occur on a time-scale sufficiently faster than epidemic processes that the two systems can be separated, and pairing processes can be considered to be at quasi-steady state relative to the epidemic. (By contrast, the epidemic variables are assumed to be constant at the pairing time-scale.) This is the approach taken by Heesterbeek & Metz (1993; also Diekmann & Heesterbeek 2000), who use a singular perturbation method to separate time-scales that differ significantly. It is a quasi-steady state because the partnership equilibria will be responding continuously as the epidemic progresses.

When we consider the fast pairing dynamics, we divide the population into five groups according to relationship and disease status. When we consider the slower epidemic dynamics, we divide the population into just two groups, susceptible and infected individuals, with densities S and I, respectively. Each of these groups includes both single and partnered individuals, but on the epidemic time-scale we are concerned only with overall densities by disease state. The fast and slow dynamics are linked because new infections arise only in SI partnerships (at a constant rate β_{pair}), so the incidence rate derived from the rapid pairing model is

$$\varepsilon_{\text{rapid pairing}} = \beta_{pair} P_{SI}^*, \tag{2.1}$$

where P_{SI}^* is the steady-state density of SI partnerships.

Our goal is to express P_{SI}^* in terms of the basic quantities S and I, and thus to translate our complex model of partnership dynamics into the standard framework of compartmental epidemic models (SIS, SIR, SEIR, etc.) (Anderson & May 1991; Hethcote 2000). The time-scale approximation makes this possible—in electronic Appendix A we derive exact solutions for P_{SI}^* in terms of S, I and the pair formation and dissolution rate constants. In the simplest behavioural case, where single individuals of all types enter partnerships at rate k and partnerships of all types break up at rate l, we obtain:

$$P_{SI}^* = \left(\frac{k}{k + l}\right)\frac{SI}{N}.\tag{2.2}$$

This result can be understood intuitively. When the disease does not affect pairing behaviour the total steady-state density of partnerships is $(k/(k + l))N/2$, and the proportion of those that are SI pairs is $2SI/N^2$. (The former expression is derived in electronic Appendix A. The latter follows from the second term in the binomial expansion, $(S/N + I/N)^2 = S^2/N^2 + 2SI/N^2 + I^2/N^2$, which gives the relative proportions of SS, SI and II pairs assuming random mixing.) Equation (2.2) is simply the product of these two expressions.

Substituting our solution for P_{SI}^* into equation (2.1), we obtain a total incidence rate of $\beta_{pair} (k/(k + l))SI/N$. This expression is equivalent to equation (1.1), the classical frequency-dependent transmission function, if $c_{FD} p_{FD} = \beta_{pair} (k/(k + l))$. We seek to understand this equality by viewing c_{FD} and p_{FD} from the perspective of our pair-formation model. The mean duration of a partnership is $1/l$, and the mean period between partnerships is $1/k$. Assuming sequential monogamy, on average each individual will have one new sexual partner every $(1/l + 1/k)$ units of time. The mean number of partners per unit time is thus $c_{FD} = 1/(1/l + 1/k) = kl/(k + l)$. Also, the susceptible individual in an SI partnership has a constant risk of infection per unit time (or hazard rate) of β_{pair}. For a relationship of average duration $(1/l)$, the probability that transmission occurs is then $p_{FD} = 1 - \exp(-\beta_{pair}/l) \approx \beta_{pair}/l$ (the latter follows because we have assumed that disease dynamics are much slower than pair dynamics, implying $\beta_{pair} \ll l$). Expressing c_{FD} and p_{FD} in terms of our model parameters, therefore, we find that $c_{FD} p_{FD} \approx (kl/(k + l)) \times (\beta_{pair}/l) = \beta_{pair} (k/(k + l))$. This is precisely the equality obtained above by setting $\varepsilon_{rapid\ pairing} = \varepsilon_{FD}$. In summary, we have derived both the functional form of the classical frequency-dependent incidence ($\varepsilon \propto SI/N$) and its conventional coefficient ($c_{FD} p_{FD}$) from a mechanistic model of partnership dynamics.

3. VALIDITY OF FREQUENCY-DEPENDENT MODELS OF SEXUALLY TRANSMITTED DISEASE INCIDENCE

The assumption that pairing processes reach a steady state on epidemic time-scales allows us to link frequency-dependent incidence to pair-based transmission. To assess when our separation of fast and slow time-scales is valid, we compare epidemics simulated with classical frequency-dependent transmission (i.e. using the time-scale approximation) with those generated from a full pair-formation–epidemic system (i.e. without the approximation). The latter model closely matches those used in previous studies of pair formation and STDs (e.g. Dietz & Hadeler 1988) and includes processes that are missed under the time-scale approximation (namely the loss of SI partnerships owing to recovery of the infected individual, the gain of SI partnerships owing to recovery of one individual in an II pair, and partnerships ending owing to the death of one partner). Thus, we can assess the accuracy with which frequency-dependent models represent pair-based transmission, for given sets of parameters, by the similarity of the simulated epidemics. To

reach general conclusions, we compare epidemics of different types of STD in populations with pair dynamics occurring at a range of rates.

STDs have been divided into two groups according to their natural history: those with high transmission probability and short duration (chiefly bacterial pathogens) and those with low transmission probability and long duration (chiefly viruses) (Blanchard 2002; Garnett 2002a). We simulated epidemics for these two main classes of STD. To represent bacterial STDs, we drew parameter values from the literature on gonorrhoea, chlamydia and trichomoniasis (Kretzschmar *et al.* 1996; Garnett *et al.* 1999; Bowden & Garnett 2000): transmission rates are high, and infected individuals recover without immunity in roughly one month. To represent viral STDs, we chose parameters in the range appropriate for HIV and HSV-2 (Anderson *et al.* 1989; Castillo-Chavez 1989; Mertz *et al.* 1992; Blower *et al.* 1998, 2000): transmission is relatively slower, but there is no recovery. Parameter values for the two model diseases are specified in the legend to figure 2, as are basic reproductive numbers R_0 (calculated as described in § 4). In both cases, individuals are assumed to remain in the population for 10 years. Pairing parameters were chosen such that healthy individuals divide their time approximately equally between single and partnered states, and we follow Kretzschmar *et al.* (1996) in assuming a mean of one sex act per day in casual partnerships. Asymptomatic cases and variable infectivity are not treated explicitly, but can be considered to be averaged into the relevant rate constants. Admittedly, these are caricatures of the actual diseases, but they serve to illustrate the behaviour of two important classes of STDs (and of diseases acting on two different time-scales).

For bacterial and viral STDs, we assessed the accuracy with which frequency-dependent incidence represents pairing at different time-scales (figure 2), in the simplest case when all pairing and unpairing rates have the same value $k = l = 1/D$. We describe the time-scale of pair dynamics in terms of the mean partnership duration D, which in this case is also the mean time between partnerships. In all cases, recall that durations are exponentially distributed with mean D, so that many partnerships would last considerably more (or less) than D time-units. For both classes of STD the full-system simulation approaches the time-scale-approximated solution as pairing and unpairing rates $(1/D)$ increase to infinity. Thus, exact correspondence with frequency-dependent transmission is obtained only for instantaneous contact. For finite partnership (and between-partnership) durations, the epidemic always proceeds more slowly, since opportunities to transmit infection are more limited (Kretzschmar 2000).

The results are radically different for the two disease classes, owing to their distinct intrinsic time-scales. For the faster bacterial STDs, the epidemics predicted by the full-system simulation and by frequency-dependent transmission diverge rapidly as D increases (figure 2a). For mean durations of 1 day or less (extremely fast partner change) the epidemics are roughly equivalent—differing by less than 10% in final prevalence and 25% in time to half-maximum prevalence. When D increases to just one week the full-system curve is hardly recognizable. The viral STD (figure 2b), with its slower disease processes and higher reproductive number, is more forgiving of
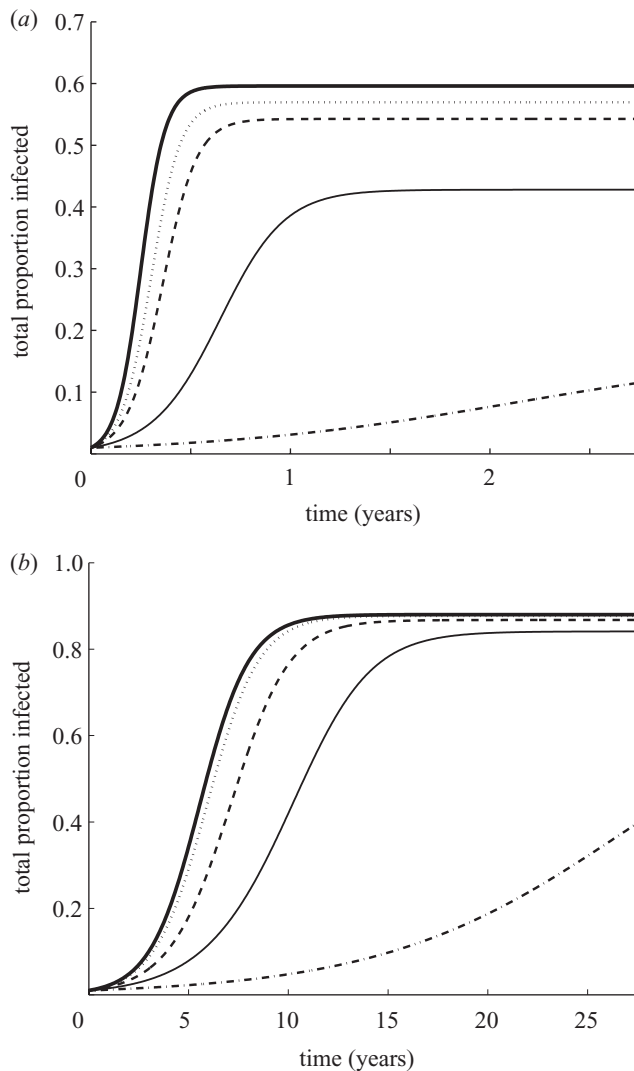
Figure 2. Accuracy of time-scale approximation pair dynamics on different time-scales. (*a*) Epidemic of bacterial STD. The heavy line shows the time-course predicted using the frequency-dependent incidence rate derived with the time-scale approximation (equations (2.2) and (A 4)); the lighter lines show the results of simulating the full system (equation (A 1)). Pairing time-scales are described by D (dotted line, $D = 0.5$ days; dashed line, $D = 1$ day; solid line, $D = 3$ days; dot–dashed line, $D = 1$ week), which represents the mean duration of partnerships and between-partnership periods. Disease parameters: $\beta_{\text{pair}} = 0.15$ day^{-1}, $\sigma = 0.03$ day^{-1}. $R_0 = 2.48$ under the time-scale approximation. (*b*) Epidemic of viral STD. As in (*a*), except $\beta_{\text{pair}} = 0.005$ day^{-1} and $\sigma = 0$, and therefore $R_0 = 8.33$. (Thick line, frequency dependent; dotted line, $D = 1$ week; dashed line, $D = 1$ month; solid line, $D = 3$ months; dot–dashed line, $D = 1$ year.) Results were obtained using a second-order modified Rosenbrock method for stiff ordinary differential equations (algorithm ode23s in MATLAB v. 6.1 (Mathworks, Natick, MA, USA)). In (*a*) and (*b*) $\mu = 0.0003$ day^{-1}, and at $t = 0$, $S_0 = 0.99$ and $I_0 = 0.01$.

slower pair dynamics. For mean partnership durations of up to one month the full-system epidemic is roughly equivalent (as defined above) to the frequency-dependent approximation, and even with $D = 3$ months the epidemics are qualitatively similar (though their rates of growth differ considerably). As a general rule, we have found that the

agreement between the full-system and frequency-dependent models depends both on the relative time-scales of disease and pairing dynamics and on the reproductive number of the disease: slower disease dynamics and higher values of R_0 permit longer-term partnerships to be modelled accurately by frequency dependence.

4. INFECTION-INDUCED CHANGES IN PAIRING BEHAVIOUR

For scenarios where the time-scale approximation is reasonable (discussed in § 5), we now extend our analysis in keeping with strong evidence that the infection status of individuals influences their contact behaviour. We introduce different rates, k_S and k_I, at which susceptible and infected individuals enter partnerships, and different rates, l_{SS}, l_{SI} and l_{II}, at which the three types of partnerships dissolve (see equation (A 2) in electronic Appendix A for implementation details). In electronic Appendix A, we derive analytic solutions for the steady-state SI pair density, P_{SI}^*, from the resulting equations. As in § 2 we can use these in conjunction with equation (2.1) to express the total incidence rate in closed-form expressions. By defining the dimensionless proportions $s = S/N$ and $i = I/N$ and representing our contact parameters by the vector $\kappa = (k_S, k_I, l_{SS}, l_{SI}, l_{II})$, we find that all resulting incidence rates share a generalized frequency-dependent form:

$$\varepsilon_{\text{rapid pairing}} = \beta_{\text{pair}} \phi_\kappa(s,i) \frac{SI}{N}, \tag{4.1}$$

where $\phi_\kappa(s,i)$ is a function of time-varying values of s and i (though note that $s + i = 1$ for all time) and the pair formation and dissolution rates κ. The $\phi_\kappa(s,i)$ for four different behavioural scenarios are shown in table 1, encompassing situations where individual infection status influences either pair-formation rates or partnership durations or both, as well as the baseline case of no behavioural shifts.

The $\phi_\kappa(s,i)$ are independent of total density N, as expected since the pairing process can be described entirely in terms of frequencies (by dividing both sides of equation (A 2) by N). Hence, as for the simple case in § 2, we find that $\varepsilon_{\text{rapid pairing}} \propto SI/N \propto N$, i.e. that the total incidence increases linearly with N. Therefore the *per capita* disease risk (the force of infection) is not influenced by N, so even these behaviourally complex models exhibit the density-independence characteristic of the frequency-dependent formulation.

Incorporating infection-induced changes in pairing behaviour leads to nonlinearities in the dependence of the incidence rate on the relative proportions of susceptible and infectious individuals (s and i, respectively). The incidence rate will thus vary from the standard frequency-dependent pattern ($\varepsilon_{\text{FD}} \propto siN$) during the course of an epidemic. As an example consider case 2 in table 1: if infected individuals have reduced pairing rates (i.e. $k_I < k_S$, and hence $\pi_I < \pi_S$), the value of $\phi_\kappa(s,i)$ increases as i gets larger. The incidence rate will accelerate as the epidemic progresses, relative to that expected based on homogeneous pairing behaviour (case 1). This somewhat counterintuitive finding arises because the less numerous type limits the rate of SI pair formation, so k_S has increasing

Table 1. Results for epidemics with infection-induced changes in behaviour.

(Here, $s = S/N$, $i = I/N$, $\pi_S = k_S/(k_S + l_{SI})$ and $\pi_I = k_I/(k_I + l_{SI})$, and $a = (l_{SI}/k_I)(1 - (l_{SI}/l_{SS})) + (l_{SI}/k_S)(1 - (l_{SI}/l_{II})) + (1 - (l_{SI}^2/l_{SS}l_{II}))$. If $k_S = k_I$, then $\pi_S = \pi_I \equiv \pi$. R_0 is given by equation (4.2).)

case	pairing rates (κ)	$\phi_\kappa(s,i)$	i_∞
1	$k_S = k_I = k$; $l_{SS} = l_{SI} = l_{II} = l$	$\dfrac{k}{k+l}$	$1 - \dfrac{1}{R_0}$
2	$k_S \neq k_I$; $l_{SS} = l_{SI} = l_{II} = l$	$\dfrac{\pi_S\pi_I}{\pi_S s + \pi_I i}$	$1 - \dfrac{1}{R_0\dfrac{\pi_S}{\pi_I} + \left(1 - \dfrac{\pi_S}{\pi_I}\right)}$
3	$k_S = k_I = k$; $l_{SS} \neq l_{SI} \neq l_{II}$	$\dfrac{\pi}{\frac{1}{2} + \frac{1}{2}\sqrt{1 - 4a\pi^2 si}}$	$1 - \dfrac{1 - a\pi^2/R_0}{R_0 - a\pi^2/R_0}$
4	$k_S \neq k_I$; $l_{SS} \neq l_{SI} \neq l_{II}$	$\dfrac{\pi_S\pi_I}{\frac{1}{2}\left(\pi_S s + \pi_I i + \sqrt{(\pi_S s + \pi_I i)^2 - 4a(\pi_S\pi_I)^2 si}\right)}$	$1 - \dfrac{1 - a\pi_S\pi_I/R_0}{R_0\dfrac{\pi_S}{\pi_I} + \left(1 - \dfrac{\pi_S}{\pi_I}\right) - a\pi_S\pi_I/R_0}$

influence as i approaches 1. Such dynamics could be significant for the current discussion of the effect of epidemic phase on epidemiological studies of STDs (Blanchard 2002; Garnett 2002a). Note that this effect is the opposite of that usually considered in models of behavioural change at the population level, in which higher prevalence is assumed to lower transmission rates via reduced contacts or greater precautions (Hadeler & Castillo-Chavez 1995; Hyman & Li 1997; Hsieh & Sheu 2001).

To understand the effects of pairing behaviour being influenced by illness, we derive the fundamental epidemiological quantities for the SIS model with constant recruitment shown in figure 1 (see also equation (A 4) in electronic Appendix A). The basic reproductive number, R_0, is the expected number of secondary cases caused by an infectious individual in a wholly susceptible population (Diekmann & Heesterbeek 2000). The threshold condition for disease invasion is $R_0 > 1$, since the first infection must more than replace itself for the disease to become established. The calculation of R_0 is described in electronic Appendix A—remarkably, for all four behavioural cases, we obtain the same result:

$$R_0 = \frac{\beta_{\text{pair}}}{\sigma + \mu}\left(\frac{k_I}{k_I + l_{SI}}\right), \qquad (4.2)$$

provided that $k_S > 0$ (and k_I and l_{SI} are replaced by k and l in the appropriate cases). Recall that σ and μ are, respectively, the *per capita* rates of recovery and of leaving the rapidly pairing population, so $1/(\sigma + \mu)$ is the mean period that an infectious individual spends in the population. The factor $k_I/(k_I + l_{SI})$ is the proportion of this period that an infectious individual spends in SI pairs, when the population is wholly susceptible.

This outcome is surprising for several reasons. First, we note that equation (4.2) is identical to the standard result for frequency-dependent transmission, $R_0 = c_{\text{FD}}p_{\text{FD}}/(\sigma + \mu)$, if we equate $c_{\text{FD}}p_{\text{FD}} = \beta_{\text{pair}}(k_I/(k_I + l_{SI}))$ (Hethcote 2000). From the arguments in § 2, this equivalence requires that c_{FD} be interpreted as the rate at which infected individuals acquire new sexual partners. Some authors use this

convention (e.g. McCallum *et al.* 2001) but many do not (e.g. Anderson *et al.* 1989; Hethcote 2000).

Second, R_0 is independent of several key parameters of the model. The rate at which susceptible individuals enter contact partnerships, k_S, does not affect the ability of the disease to invade a population (provided that $k_S > 0$). While not obvious, this can be understood by noting that the early rate of formation of SI pairs will be limited by the supply of infectious individuals. R_0 is also independent of l_{SS} and l_{II}, and hence of the durations of SS and II partnerships. Again, this is unexpected, since individuals in SS (or II) partnerships are effectively vaccinated (or case isolated) owing to their removal from the mixing population, and the existence of such partnerships is expected to counter the spread of an STD (Dietz & Hadeler 1988; Kretzschmar 2000). The number of II pairs at the time of invasion is negligibly small, however, and furthermore the time-scale approximation precludes the existence of long-lived SS (or II) pairs, and hence eliminates their potential vaccinating (or isolating) effect.

When $R_0 > 1$, the disease is able to invade, and we are interested in its equilibrium properties. The calculation of i_∞, the steady-state endemic prevalence, is described in electronic Appendix A. Results are shown in table 1, where we see that even the heterogeneous-behaviour cases are modifications of the classical solution $i_\infty = 1 - 1/R_0$ (Anderson & May 1991). The dependence of i_∞ on the pair formation and dissolution rates is shown in figure 3a, and, in contrast to the R_0 result, these trends immediately match our expectations. As k_S or k_I is increased (and hence susceptible or infectious individuals enter partnerships more quickly) the steady-state prevalence rises. The infected proportion drops as l_{SI} is raised, since SI pairs break up more quickly and the window for transmission grows shorter. As l_{SS} or l_{II} is increased, i_∞ increases owing to the briefer protection offered by the effective vaccine or isolation of SS or II partnerships, respectively. We see i_∞ go to zero—failure of the disease to persist—only as k_I and l_{SI} change, because these are the only pairing parameters that influence R_0.
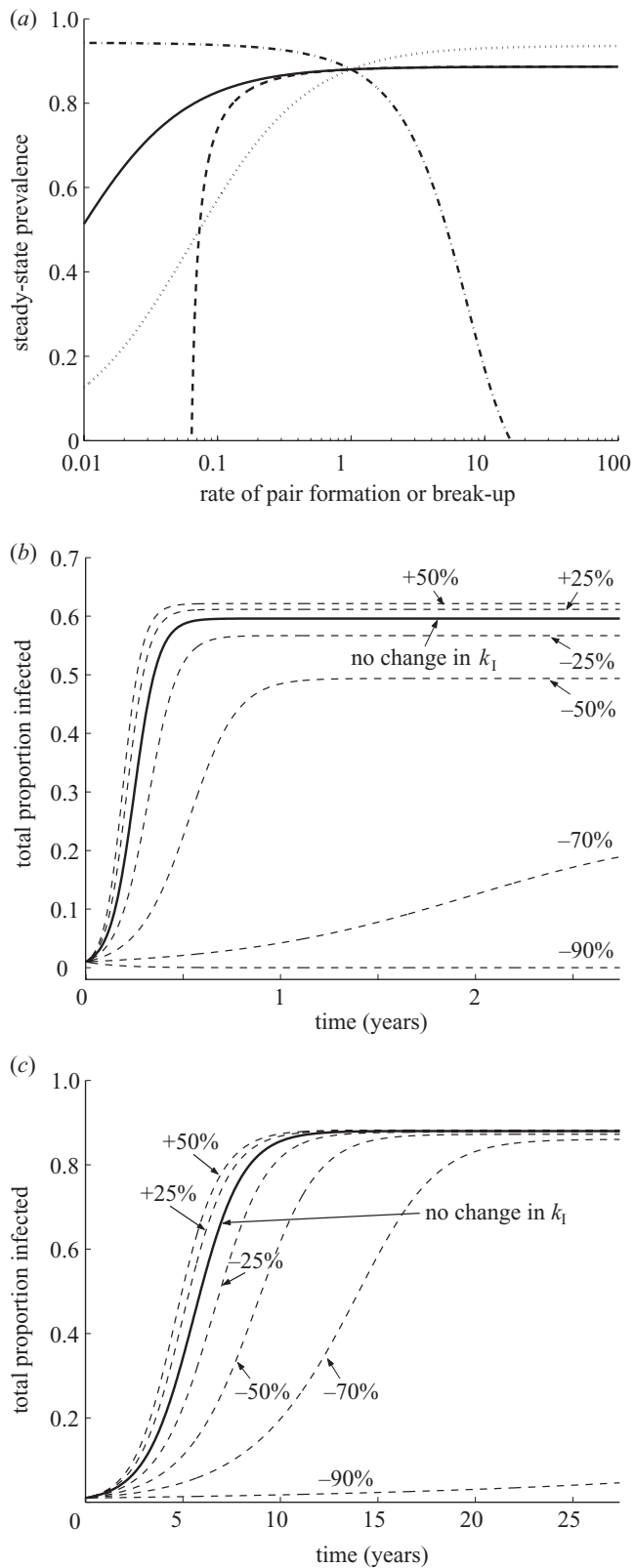
(a)

Figure 3. Effect of infection-induced changes in behaviour. (a) Dependence of the steady-state endemic prevalence, i_{∞}, on pairing-rate parameters, calculated using the expressions shown in table 1. The parameters were varied one at a time, while the non-varying parameter values were as for (b,c), below. Dotted line, k_S; dashed line, k_I; dot–dashed line, l_{SI}; solid line, l_{SS} or l_{II}. (b,c) Epidemic time-courses for (b) a bacterial STD and (c) a viral STD. In the base case (solid line) $k_S = k_I = 1$ day^{-1}, while in other cases (dashed lines) the pairing rate for infectious individuals (k_I) is reduced or increased by the proportion shown. Disease parameters and initial conditions as in figure 2, and $l_{SS} = l_{SI} = l_{II} = 1$ day^{-1}.

(b)

(c)

To demonstrate the potential dynamic effects of contact behaviour varying with infection status, we simulated epidemics of bacterial and viral STDs for varying values of k_I (figure 3b,c). (Note that to apply the time-scale approximation for a bacterial STD, we model an extremely promiscuous population with a mean partnership duration of 1 day.) The solid curves show the base case where disease does not influence behaviour, while the broken lines show

the outcomes when infection causes individuals to decrease (or increase) their pair-formation rate by the proportions shown. For the bacterial STD (figure 3b), diminished values of k_I lead to drastically altered epidemics, since they bring R_0 close to, and even below, the threshold value of one. In the base case, $R_0 = 2.48$. When k_I is diminished by 50% (yielding $R_0 = 1.65$) the epidemic increases roughly half as fast (as measured by the time to half-maximum prevalence), but a 70% decrease ($R_0 = 1.14$) slows it by more than 10-fold. A 90% reduction causes the disease to die out, since $R_0 < 1$. For the viral STD (figure 3c), $R_0 = 8.33$ in the base case (considerably further from the threshold range), so reductions in k_I have much weaker effects than for the bacterial disease. Even when the pairing activity of infected individuals is reduced by 70%, R_0 is still nearly 4 and the epidemic progresses at almost half its speed in the base case. Only when k_I is reduced 10-fold, yielding $R_0 \sim 1.5$, do dramatically slower dynamics result. For both diseases increases in k_I cause only incremental changes, since R_0 is already significantly greater than one.

5. DISCUSSION

We have analysed the dynamics of pair-based disease transmission for populations with rapid partner exchange. Beginning with a pair-formation model, we presented a mechanistic derivation of the classical frequency-dependent incidence. We used this derivation in two ways: first as a formal framework to assess how accurately frequency-dependent incidence portrays the pair-based transmission known to underlie STD dynamics, and second as a platform from which to derive extensions of classical epidemiological theory that include the effects of illness on contact behaviour.

Many assumptions were required in our derivation. Unless another mechanistic link between frequency-dependent incidence and pair-based transmission can be found, it seems that all of these assumptions are made implicitly whenever STD dynamics are modelled using frequency-dependent transmission. Some of these assumptions are widely recognized: partnerships form by random mixing, with no memory of past contacts or consideration of social clustering. Individuals are sequentially monogamous, and mixing is proportionate with respect to disease status. For mathematical simplicity, we did not subdivide the population by sex, age or sexual-activity class, but such structure is often included in frequency-dependent STD models.

The most challenging assumption, however, is the time-scale approximation, wherein we assert that pairing processes are sufficiently faster than epidemic dynamics that we can assume that they are at equilibrium. From our simulation results (figure 2), we see that predictions obtained using this approximation equal those from a full pair-dynamic–epidemic model only in the limit of instantaneous partnerships. When partnerships have a finite duration, the approximated (frequency-dependent) epidemic always grows faster and reaches a higher final prevalence than the full system. The range of pairing time-scales for which the two epidemics are similar, though, depends strongly on the disease in question, and our findings support Garnett's division of STDs into two functional groups according to their natural history (Garnett 2002a). Suppose we say that the time-scale approximation is satisfied when the solutions differ by less than 10% in final prevalence and 25% in time to half-maximum prevalence. For relatively fast transient STDs such as chlamydia (figure 2a), only very promiscuous populations change partners rapidly enough for the approximation to be satisfied—$D = 1$ day implies roughly 180 sexual partners per year. (Note that a model specific to gonorrhoea would have a value of β_{pair} approximately twice as high as that used in figure 2a, and thus even faster partner change would be required.) For slower-moving chronic STDs such as HIV, the approximation is satisfied for partnerships with a mean duration of a month or more.

Results derived from the time-scale approximation—including the classical frequency-dependent incidence and our results for infection-induced behavioural changes—must therefore be used advisedly. For fast-moving bacterial STDs, the results will be accurate for only a small subset of human populations. Failure to recognize this can lead to catastrophically poor predictions, as shown in figure 2a where partnerships more than a few days long generate a simulated epidemic that differs drastically from that predicted by the classical model. For chronic viral STDs, expressions derived from the time-scale approximation are more widely applicable (see relationship data in Anderson *et al.* 1989), but great caution is required in extending models beyond core groups to general human populations. Note that concurrent sexual relationships, not considered here, effectively increase the rate of partner change and would soften these restrictions somewhat. Also, our simulations assumed a mean of one sex act per day within partnerships—a lower contact rate would allow proportionately longer partnership durations to be modelled accurately. Clearly, the frequency-dependent models could also be applied to STDs in animal populations (Lockhart *et al.* 1996) and are particularly suitable for species whose mating systems feature short-lived monogamous pairings.

For situations where the time-scale approximation is reasonable, we extend our mechanistic derivation to develop new tools for disease modelling. There is rich evidence in humans and animals that sickness influences contact behaviour, yet this phenomenon is largely overlooked in the theory of disease spread. We provide expressions for the incidence rate, basic reproductive number (R_0) and endemic prevalence (i_∞) for four cases in which pairing behaviour is influenced increasingly by infection. These expressions can be incorporated directly into SI or SIS epidemic models, and can be generalized readily to any SEIR-type model when only infectious (I) individuals display altered behaviour.

We found a common expression for R_0 in all of the cases we considered, revealing that the invasion ability of a disease depends on the rate at which infectious individuals enter partnerships (k_I) and the duration of SI pairs ($1/l_{SI}$), but not on other pairing parameters. Concordant SS and II partnerships do not influence the disease's threshold properties—despite their expected roles as effective vaccine and case isolation, respectively—though they do influence i_∞ as expected. Our general expression for R_0 is identical to the classical result for frequency-dependent epidemics, subject to careful interpretation of the contact rate (c_{FD}) as the rate at which infected individuals acquire sexual partners. This finding corresponds with those of the one previous study (that we are aware of) that explicitly linked pair formation and break-up to the infection status of the individuals involved. Dietz & Hadeler (1988) presented a threshold analysis of a pair-formation model with parameters that differ according to infection status, and found (as we did) that the classical result appears in the limit of fast pair dynamics.

It is important to distinguish our findings from those of previous models of 'behaviour change' in STD epidemics (Hadeler & Castillo-Chavez 1995; Hyman & Li 1997; Hsieh & Sheu 2001). In these studies, susceptible individuals may choose to change their rate of acquiring new sexual partners (c_{FD}) or the probability of transmission per partnership (p_{FD}), typically as a result of public-education campaigns or community awareness of disease risk. This is certainly an important topic in current STD epidemiology, but it is fundamentally different from the infection-induced behavioural effects addressed here. Our treatment considers the direct effects of individual infection status on individual contact behaviour: we allow *per capita* pair-entry rates to differ between susceptible and infected individuals, and break-up rates to differ among SS, SI and II pairs. This approach hinges on considering the distinct contributions of each individual in forming a pair, and leads to nonlinear dependence of the transmission rate on the proportions of S and I individuals (beyond the usual bilinear *SI* form). A recent study found such nonlinearity to be a common feature of incidence data (Fenton *et al.* 2002); disease effects on contact behaviour are an unexplored mechanism for this trend. Simulations in which individual pairing rates were reduced (or increased) by infection demonstrated that these behavioural effects could have striking impacts on epidemic progression (figure 3b,c).

These results may also be applicable to diseases transmitted by non-sexual contact (the results of Heesterbeek & Metz (1993) also apply to this problem). Diseases of casual contact are increasingly being modelled using frequency-dependent incidence, and it is reasonable to speculate on the effect of disease symptoms on casual-contact behaviour. The time-scale approximation (of rapid contact dynamics) is likely to be valid for such diseases, but the assumption that partnerships are exclusive breaks down—higher-order groupings and simultaneous contacts may play a significant role. This question merits additional investigation, which would also be relevant to concurrent partnerships in STD models.

Links between analytic theory and complex simulation models are of vital importance, serving to distil insights and unify rapidly growing fields of research. This point has been emphasized in the context of epidemiology (Anderson & Garnett 2000; McCallum *et al.* 2002), and a similar goal is being pursued using correlation techniques for network models of disease (Bauch & Rand 2000; Ferguson & Garnett 2000; Eames & Keeling 2002). In exploring the relation between partnership dynamics and the classical frequency-dependent treatment of transmission, we have understood more clearly both the meaning of the classical model and the proper limits of its application. We have also extended the theoretical results to include changes in contact behaviour caused by illness, so that this well-recognized effect can be incorporated into simple analytic models when biological evidence requires it.

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This is an electronic appendix to the paper by Lloyd-Smith *et al.* 2004 Frequency-dependent incidence in models of sexually transmitted diseases: portrayal of pair-based transmission and effects of illness on contact behaviour. *Proc. R. Soc. Lond.* B **271,** 625–634. (DOI 10.1098/ rspb.2003.2632.)

Electronic appendices are refereed with the text. However, no attempt is made to impose a uniform editorial style on the electronic appendices.

Electronic Appendix A. Derivations

Derivation of SI pair density, P_{SI}^*

Here we present a general derivation of the steady-state SI pair density P_{SI}^*, including the results shown in sections 2 and 4. We begin with the standard one-sex formulation of a pair-formation/epidemic model, extended such that pair-entry rates k_y and break-up rates l_{yz} (where y,z=S or I) can vary as a function of infection status (c.f. Dietz & Hadeler 1988):

$$\frac{dX_S}{dt} = -k_S X_S + 2l_{SS}P_{SS} + l_{SI}P_{SI} + \sigma X_I + \lambda - \mu X_S + \mu(2P_{SS} + P_{SI})$$

$$\frac{dX_I}{dt} = -k_I X_I + 2l_{II}P_{II} + l_{SI}P_{SI} - \sigma X_I - \mu X_I + \mu(2P_{II} + P_{SI})$$

$$\frac{dP_{SS}}{dt} = \tfrac{1}{2}k_S m_{SS} X_S - l_{SS}P_{SS} + \sigma P_{SI} - 2\mu P_{SS} \qquad\qquad (A1)$$

$$\frac{dP_{SI}}{dt} = \tfrac{1}{2}k_S m_{SI} X_S + \tfrac{1}{2}k_I m_{IS} X_I - l_{SI}P_{SI} - \beta_{pair}P_{SI} - \sigma P_{SI} + 2\sigma P_{II} - 2\mu P_{SI}$$

$$\frac{dP_{II}}{dt} = \tfrac{1}{2}k_I m_{II} X_I - l_{II}P_{II} + \beta_{pair}P_{SI} - 2\sigma P_{II} - 2\mu P_{II}$$

Parameters and variables are defined in the caption to figure 1. The factors of ½ reflect that it takes two individuals to make a partnership (i.e. one unit of P_{yz} is equivalent to two units of X_S or X_I), and the factors of 2 in μ and σ terms reflect events that arise from transitions undergone by either member of a pair. Note that mixed partnerships (P_{SI}) are formed both by X_S individuals "choosing" X_I individuals and vice versa; the two separate terms are essential to maintaining constant population size. We assume that population density has reached equilibrium, and set $\lambda=\mu N$.

This derivation pertains to populations where pair formation and dissolution occur on faster timescales than disease and demographic processes (i.e. pairing rate parameters k_y and l_{yz} are significantly greater than epidemic rates β_{pair}, σ and μ). We therefore approximate that disease states are constant on the timescale of pairing processes, and separate the fast pairing dynamics from the slow epidemic dynamics as described in the main text and shown in figure 1. The pairing dynamics are then described by:

$$\begin{cases} \dfrac{dX_S}{dt} = -k_S X_S + 2l_{SS} P_{SS} + l_{SI} P_{SI} \\[2ex] \dfrac{dX_I}{dt} = -k_I X_I + 2l_{II} P_{II} + l_{SI} P_{SI} \\[2ex] \dfrac{dP_{SS}}{dt} = \tfrac{1}{2} k_S m_{SS} X_S - l_{SS} P_{SS} \\[2ex] \dfrac{dP_{SI}}{dt} = \tfrac{1}{2} k_S m_{SI} X_S + \tfrac{1}{2} k_I m_{IS} X_I - l_{SI} P_{SI} \\[2ex] \dfrac{dP_{II}}{dt} = \tfrac{1}{2} k_I m_{II} X_I - l_{II} P_{II} \end{cases} \qquad (A2)$$

Fast pairing dynamics

We consider the slower dynamics of disease transmission and demographic processes at the whole-population scale. First we collect the total densities (in and out of partnerships) of susceptible and infectious individuals into variables S and I:

$$\begin{aligned} S &= X_S + 2P_{SS} + P_{SI} \\ I &= X_I + 2P_{II} + P_{SI} \end{aligned} \qquad (A3)$$

The epidemic can now be represented with a standard SEIR-type compartmental model; as an example we treat an SIS epidemic with constant recruitment rate λ. The total incidence rate is $\beta_{\text{pair}} P_{SI}^*$ (equation 2.1), the mortality rate μ is independent of disease status, and the recovery rate is σ. Thus:

Slow epidemic dynamics

$$\begin{cases} \dfrac{dS}{dt} = \lambda - \beta_{\text{pair}} P_{SI}^* + \sigma I - \mu S \\[2ex] \dfrac{dI}{dt} = \beta_{\text{pair}} P_{SI}^* - (\sigma + \mu) I \end{cases} \qquad (A4)$$

As described in section 2, our goal is to find an expression for the steady-state density of mixed SI partnerships, P_{SI}^*, in terms of the population densities S and I. The first step is to specify the mixing matrix for pair formation. The matrix element m_{yz} is the proportion of partnerships formed by y-type individuals which will be with individuals of type z. In this study we assume proportionate mixing, hence the m_{yz} are simply the fractional contributions of each group to the total pair formation rate:

$$m_{SS} = m_{IS} = \frac{k_S X_S}{k_S X_S + k_I X_I}$$

$$m_{SI} = m_{II} = \frac{k_I X_I}{k_S X_S + k_I X_I}$$

(A5)

Note that $k_S\, m_{SI}\, X_S = k_I\, m_{IS}\, X_I$ under this assumption.

Substituting equations (A3) and (A5) into system (A2), we get:

$$\frac{dP_{SS}}{dt} = \frac{\frac{1}{2}k_S^2(S - 2P_{SS} - P_{SI})^2}{k_S(S - 2P_{SS} - P_{SI}) + k_I(I - 2P_{II} - P_{SI})} - l_{SS}P_{SS}$$

$$\frac{dP_{SI}}{dt} = \frac{k_S k_I(S - 2P_{SS} - P_{SI})(I - 2P_{II} - P_{SI})}{k_S(S - 2P_{SS} - P_{SI}) + k_I(I - 2P_{II} - P_{SI})} - l_{SI}P_{SI}$$

(A6)

$$\frac{dP_{II}}{dt} = \frac{\frac{1}{2}k_I^2(I - 2P_{II} - P_{SI})^2}{k_S(S - 2P_{SS} - P_{SI}) + k_I(I - 2P_{II} - P_{SI})} - l_{II}P_{II}$$

We let the pairing dynamics go to steady-state by setting the right-hand sides of (A6) equal to zero. This leads to a system of three quadratic equations in the three unknowns P_{SS}^*, P_{SI}^*, P_{II}^*, which we wish to solve for P_{SI}^*. This system was simplified using Mathematica (Wolfram Research, Champaign IL), yielding the following quadratic equation in P_{SI}^*:

$$a(P_{SI}^*)^2 + bP_{SI}^* + c = 0 \quad \text{where}$$

$$a = \frac{l_{SI}}{k_I}\left(1 - \frac{l_{SI}}{l_{SS}}\right) + \frac{l_{SI}}{k_S}\left(1 - \frac{l_{SI}}{l_{II}}\right) + \left(1 - \frac{l_{SI}^2}{l_{SS}l_{II}}\right)$$

$$b = -\left(\frac{\pi_S S + \pi_I I}{\pi_S \pi_I}\right)$$

(A7)

$$c = SI$$

and $\pi_S = \dfrac{k_S}{k_S + l_{SI}}$ and $\pi_I = \dfrac{k_I}{k_I + l_{SI}}$.

We consider four cases, in which infection status has varying influence on pairing behaviour (i.e. different sets of the pair formation and dissolution rates k_S, k_I, l_{SS}, l_{SI} and l_{II} have distinct values). When pair dissolution rates are equal ($l_{SS} = l_{SI} = l_{II} = l$), $a = 0$ in equation (A7) and $P_{SI}^* = -c/b$. Otherwise the quadratic formula was used to find P_{SI}^*. For $a < 0$ there is only one positive

solution, $P_{\mathrm{SI}}^* = \frac{1}{2a}\left(-b - \sqrt{b^2 - 4ac}\right)$. When $0 < a < b^2/4c$ both solutions are real and positive, but only $P_{\mathrm{SI}}^* = \frac{1}{2a}\left(-b - \sqrt{b^2 - 4ac}\right)$ remains bounded on the $(0,N/2)$ interval (for all numerical tests we have conducted). By reorganising terms in $b^2 - 4ac$ into a difference-of-terms squared plus some positive terms, it can be shown that $b^2 - 4ac > 0$ always (for $k_{\mathrm{S}}, k_{\mathrm{I}}, l_{\mathrm{SS}}, l_{\mathrm{SI}}, l_{\mathrm{II}} > 0$) so solutions are always real. Exact solutions for P_{SI}^* in all four cases lead to incidence rates as shown in equation (4.1), with full expressions shown in table 1. All solutions have been checked numerically to ensure their validity.

Calculation of R_0 and i_∞

The basic reproductive number, R_0, is the expected number of secondary cases caused by a typical infectious individual in a wholly susceptible population. As such, it can be calculated as the product of the total rate of transmission per I individual times the expected duration of infectiousness, in the limit $S \to N$ (Anderson & May 1991). From equation (A4), with $P_{\mathrm{SI}}^* = \phi_\kappa(s,i)\frac{SI}{N}$ as in equation (4.1), we find for our model:

$$
\begin{aligned}
R_0 &= \lim_{S \to N}\left(\text{transmission rate per I individual} \times \text{duration of infectiousness}\right) \\
&= \lim_{S \to N}\left(\beta_{\mathrm{pair}}\,\phi_\kappa(s,i)\frac{S}{N} \times \frac{1}{\sigma + \mu}\right) \\
&= \frac{\beta_{\mathrm{pair}}}{\sigma + \mu}\lim_{S \to N}\left(\phi_\kappa(s,i)\right)
\end{aligned}
\tag{A8}
$$

From the expressions $\phi_\kappa(s,i)$ in table 1, it is readily shown that $\lim_{S \to N}\left[\phi_\kappa(s,i)\right] = \pi_{\mathrm{I}} = \dfrac{k_{\mathrm{I}}}{k_{\mathrm{I}} + l_{\mathrm{SI}}}$ for all cases. Therefore R_0 takes the same form for all four levels of infection-induced behavioural shifts, as shown in equation (4.2).

We can also calculate the equilibrium density of infectives, I_∞, by finding the non-zero solution to $\left(\dfrac{dI}{dt}\right)_{I^* \neq 0} = 0$. From this we can calculate the steady-state endemic prevalence, $i_\infty = \dfrac{I_\infty}{N}$.
Results are shown in table 1.

Calculation of steady-state density of partnerships

When disease does not influence pair-formation dynamics, we can simply model the density of unpartnered individuals, X, and of partnerships, P:

$$\frac{dX}{dt} = -kX + 2lP$$

$$\frac{dP}{dt} = \tfrac{1}{2}kX - lP$$

(A9)

Since the total population density (N) is constant, one of these equations is redundant. The steady-state is found by setting the right-hand side equal to zero and substituting $X=N-2P$. We can then solve for the steady-state density of partnerships:

$$P^* = \left(\frac{k}{k+l}\right)\frac{N}{2}$$

(A10)