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Males can evolve lower resistance to sexually transmitted infections to infect their mates and thereby increase their own fitness

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Abstract
Sexually transmitted infections (STIs) often lower their host's future reproductive success by inducing sterility. Females can minimise the reproductive cost of infection by plastically increasing their current reproductive effort (i.e. terminal investment) before they become sterile. In polyandrous systems, long-term female survival or fecundity is often irrelevant to male fitness. Mating with an infected, terminally investing female potentially yields greater fitness gains for males than mating with an uninfected female. Males might consequently benefit from infecting females with an STI. We construct mathematical models of the evolutionary consequences of a sterilising STI. We show that females should terminally invest in response to an STI when immune investment is relatively ineffective at delaying STI-induced sterility. Cost-effective immune responses may conversely select for reduced reproductive effort after infection ('terminal divestment'). Crucially, we then show that female terminal investment can select for lower STI resistance in males. This selection is driven by fitness gains to males that acquire the STI and subsequently infect their mates, which offset any costs of infection (e.g. male sterility). This type of adaptive mate harm generates sexual conflict over the optimal level of resistance to STIs. It could partly explain why immune reactions to new infections are weaker in males than females of many species.

Keywords Life history · Model · Sexual conflict · Sexual dimorphism · Sexually antagonistic · Terminal investment

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Introduction

Sex differences in the harmful effects of sexually transmitted infections (STIs) can lead to intra-locus sexual conflict over disease resistance, where optimal immune investment is higher for the sex that suffers greater STI harm (Forman et al. 2012). More intriguing, however, is the idea that sexual conflict over immunity can arise because males benefit from transferring an STI to their mates (see Haaland et al. 2017, who discuss this idea in the framework of differential allocation). Specifically, this could occur if STI-infected females increase investment into their current offspring as an adaptive response to their reduced long-term fitness prospects (a form of 'terminal investment': Clutton-Brock 1984; note that, despite the name, terminal investment need not lead to the death of the female). This female response provides a fitness benefit to the sires of her current offspring. Consequently, males might be under selection to reduce their own immune resistance in order to acquire an STI and then infect their mates. This unusual mechanism would create sexual conflict over disease resistance, which might help to explain why males of many species have weaker immune responses to initial infections (Tschirren et al. 2003; Cordoba-Aguilar et al. 2006) and higher infection rates (Strandberg and Tucker 1974; Zuk and McKean 1996) than females (although patterns of sexual dimorphism in immunity are heterogeneous across species: Kelly et al. 2018; see also Cousineau and Alizon 2014; Gipson and Hall 2016).

Sexual conflict and mate harm

The evolutionary interests of male and female mating partners are never perfectly aligned (Chapman et al. 2003). Reproductive investment is a prime battleground for sexual conflict, with each sex generally preferring that their mates invest more in offspring. In many species, this conflict leads to inter-locus sexual conflict and selection for direct manipulation of partner behavior (Perry and Rowe 2015). For example, male *Drosophila* influence female egg laying rate via seminal fluid proteins (Rice 1996; Wolfner 1997, 2002; Yapici et al. 2008; Wilburn and Swanson 2016). Male traits that elevate egg production (Chapman et al. 1998; Lessells 2005; Bonduriansky 2014) are often accompanied by female traits to resist such manipulation (Wigby and Chapman 2004; Nandy et al. 2013). Parental investment decisions can also be manipulated indirectly by changing the conditions under which they are made. For instance, some studies suggest that males could evolve to harm their partners' future fitness prospects to induce an increase in current egg production (Lessells 2005; Bonduriansky 2014).

Terminal investment: going out with a bang

Terminal investment is an increase in current reproductive effort due to a decreased expectation of breeding in the future (e.g. due to elevated intrinsic or extrinsic mortality: Clutton-Brock 1984; Hansen et al. 2013; Travers et al. 2015; Duffield et al. 2017). Iteroparous species always trade off current and future reproduction, with selection favouring investment that maximises the sum of current and future expected fitness when population size is stable (Lack 1947; Williams 1966; Stearns 1976). The optimal balance is sensitive to an individual's prospects. An individual with lowered expectations for future fitness gain (e.g. due to high mortality risk) should terminally invest by increasing its investment in current reproduction (although such investment need not literally lead to the individual's death).

Terminal investment is often discussed in the context of senescence (Creighton et al. 2009), but many other factors can reduce future fitness prospects, including an increase in predation risk (Tyson et al. 2010), lower food availability (Kruuk and Parish 1982), and infection by pathogens (Knell and Webberley 2004). For example, female pea aphids *Acyrthosiphon pisum* injected with *Escherichia coli* produce more offspring than control females (Altincicek et al. 2008).

STIs as a manipulatable trigger for terminal investment

Female terminal investment potentially provides a mechanism that males can exploit to increase female investment in shared offspring. Males need only manipulate the 'cue' that triggers greater female investment. We see three reasons why STIs might be a plausible mechanism of adaptive mate harm, especially relative to other infectious diseases. First, STIs often cause sterility (Lockhart et al. 1996; Antonovics et al. 2011; Gimenes et al. 2014), which ends a host's reproductive lifespan and may consequently select for terminal investment. Indeed, terminally investing females have been shown to increase both egg quantity (Strandberg and Tucker 1974; Simmons and Rodgers 1994; Snook and Markow 2002; Rittschof et al. 2013; Staudacher et al. 2015) and quality (Bowers et al. 2012). Second, unlike many other forms of mate harm, such as physical injury, delayed sterility is unlikely to lower the fitness of the offspring of a current mate (Hurst et al. 1995). Consequently, a male may not suffer a fitness loss from infecting his mate. Third, many STIs are detrimental to females but cause minimal direct harm to males.

Terminal 'divestment': when it's better to just hang on in there

In contrast to our arguments above, in some cases infection may trigger an *increase* in immune defense, at the expense of reproductive investment (Ilmonen et al. 2000). We call such a strategy 'terminal divestment' if it leads to reduced overall investment in current offspring: i.e., the opposite of terminal investment. Since STIs are often life-long infections, additional immune investment might be insufficient to clear an infection, but it could delay sterility and extend an individual's reproductive lifespan. If selection favours reduced female reproductive investment upon acquiring an STI, this will increase the costs of infection for males, and thereby select for greater male STI resistance.

Our modelling approach

Terminal investment and divestment by females generate sex differences in the costs and benefits of STI infection. This should drive evolution of sex-specific patterns of immunity and resistance to STIs. When females terminally invest, infected (but fertile) males gain an immediate fitness benefit from transmitting the STI to their partners. Consequently, even if an STI is harmful to net male fitness, the potential to increase their mate's reproductive investment could reduce the fitness costs of infection relative to that experienced by a female, and therefore lead to sexual conflict over the optimal level of resistance.

Here we build a combined epidemiological and evolutionary model to determine: (1) how STIs affect female parental investment under different scenarios for the effectiveness of immune resistance; and (2) whether males can be under selection to infect their mates and therefore to be more susceptible to the STI. Our model predicts the coevolution of STI

Table 1 Summary of variables and parameters

Symbol	Description
w	Lifetime fitness
x	Reproductive effort
y	Immune effort
μ	Mortality rate
$\mu_{\min}$	Minimum mortality rate (for individuals that invest neither in reproduction nor immunity)
C	Steepness with which mortality increases with increasing total effort $x + y$
p	Probability of becoming infected at any particular mating (when partner infection status is unknown)
α	Probability of becoming infected when mating with an infected partner
$\alpha_{\max}$	Maximum value for α, occurring when an individual does not invest in STI resistance (i.e. $y_U = 0$)
A	Effectiveness of immune effort y_U in preventing STI acquisition
β	Rate at which an infected individual becomes sterile
$\beta_{\max}$	Maximum value for β, occurring when an individual does not invest in immunity after infection (i.e. $y_I = 0$)
B	Effectiveness of immune effort y_I in delaying the onset of sterility
U, I, S	Proportion of uninfected, infected-but-fertile, and sterile females in the population
R	Rate at which newly mature females are recruited into the population
r_M	Rate at which any female mates with males of infection status M
$\tilde{r}_{M,F}$	Rate at which a male of infection status M mates with females of infection status F

Unmarked symbols pertain to females, whereas the corresponding symbols for males are marked with a sperm-like tilde (like this: $\tilde{a}$). Subscripts U, I, or S indicate that the symbol applies to uninfected, infected-but-fertile, or sterile individuals, respectively

resistance and reproductive investment in both sexes. Our goal was not to explore all possible factors that could moderate these effects, but rather to confirm that the basic verbal argument is sound, and to establish a framework for more detailed models that could be parameterized and tested using empirical data.

Mate harm via STI infection

We first provide a simple continuous-time model of female reproductive effort under STI infection. The model serves both to recap previous sexual conflict theory (e.g. Lessells 2005; Johnstone and Keller 2000) and to set the stage for a full epidemiological model in the next section. We show that females infected with an STI should invest more in their current offspring than uninfected females, and that males may consequently benefit by infecting their mates. We assume that the STI leads to delayed female sterility, but does not directly affect mortality, nor the ability to produce offspring prior to sterilization (see "Discussion" section). However, changes in female reproductive effort after infection may affect both her offspring production and mortality. We initially ignore any detrimental effects of the STI on males: these costs are examined in our full epidemiological model (next section).

We assume that mature females follow the following breeding cycle: (1) mate with a single male; (2) fertilise eggs immediately after mating; (3) invest in eggs or offspring as they

develop. Once a female's offspring are fully developed, she remates immediately and the breeding cycle is repeated until she either dies or becomes sterile (note that the onset of sterility has no effect on already-fertilised offspring). Sterility (for infected females) and mortality may occur at any stage during the breeding cycle. For simplicity, we assume that females mate exactly once per batch of eggs, which are always fertilised by her last mate (i.e. no sperm storage or multiple paternity). Note that such 'serial monogamy' is predicted as an evolutionary result of STI infection under some circumstances (McLeod and Day 2017). We also assume that no offspring survive if the mother dies before they are fully developed. This means that a female's short-term survival is in her mate's evolutionary interest, but her long-term prospects are irrelevant to males.

The fitness value of a set of offspring is proportional to a female's reproductive effort x after her most recent mating, which may depend on her infection status (variables and parameters are summarised in Table 1). Our assumption of substantial post-mating investment in offspring is plausible if, for example, eggs are provisioned after mating (Staudacher et al. 2015; Giehr et al. 2017) or there is post-zygotic parental care (Hanssen 2006; Bowers et al. 2015; Amininasab et al. 2017). A female's instantaneous rate of mortality $\mu(x)$ increases with her reproductive effort during her current reproductive bout. We assume that offspring development takes an average of one unit time; this means that all time measurements are given in units of the mean offspring development time. For mathematical convenience we assume that the development times of individual broods follow an exponential distribution.

Let us write x_U for the reproductive effort of an uninfected female and x_I for that of an infected female. The mortality rates of these females are respectively $\mu_U = \mu(x_U)$ and $\mu_I = \mu(x_I)$. We first consider the average number of times an unmated female will mate without becoming infected. Suppose that at each mating, her probability of becoming infected is p. After her first mating, the female remains uninfected with probability $1-p$. Since she experiences mortality at a constant rate of μ_U and her offspring mature at a rate of 1, she survives until her offspring mature with probability $\frac{1}{1+\mu_U}$. She then remates immediately, after which she remains uninfected with probability $1-p$. Elaborating this pattern, the expected number of matings after which the female remains uninfected is given by a geometric series:

$$n_U = (1-p)\left[1 + \frac{1-p}{1+\mu_U} + \left(\frac{1-p}{1+\mu_U}\right)^2 + \cdots\right] = (1-p)\left(\frac{\mu_U+1}{\mu_U+p}\right) \tag{1}$$

By similar logic, the probability that the female survives to become infected is given by $p\left(\frac{\mu_U+1}{\mu_U+p}\right)$.

Once infected, we assume that females risk becoming sterile. Sterility does not occur immediately upon infection. Rather, the onset of sterility occurs at a constant rate of β per unit time, regardless of a female's behavior (we lift the latter restriction in the full model). The STI does not directly affect a female's mortality or offspring production, although changes in her reproductive effort could influence both traits. After infection, a female's expected number of matings is $1 + \frac{1}{\mu_I+\beta}$, including the mating in which she became infected. Consequently, the expected number of matings while infected but still fertile is:

$$n_I = p\left(\frac{\mu_U+1}{\mu_U+p}\right)\left(1 + \frac{1}{\mu_I+\beta}\right) \tag{2}$$

The expected fitness gain from mating equals the female's reproductive effort times the probability of surviving to produce offspring. This is $v_U = \frac{x_U}{1+\mu_U}$ for uninfected females and $v_I = \frac{x_I}{1+\mu_I}$ for infected females. A female's expected lifetime fitness is then:

$$w(x_U, x_I) = n_U v_U + n_I v_I \tag{3}$$

For a given choice of the parameters, optimal reproductive effort (x_U and x_I) is found by maximizing this expression numerically (Fig. 1).

Now consider a male who mates with the focal female. His fitness gain $\Delta\tilde{w}$ from mating is equal to the female's reproductive effort x multiplied by the probability $\frac{1}{1+\mu(x)}$ that she survives to produce offspring:

$$\Delta\tilde{w}(x) = \frac{x}{1+\mu(x)} \tag{4}$$

As above, this expression can be maximised numerically to obtain the *female* behavior that maximises *male* fitness. All else being equal, a male should prefer to mate with an uninfected female over an infected female if

$$\frac{x_U}{1+\mu_U} > \frac{x_I}{1+\mu_I} \tag{5}$$

If the reverse inequality holds, then males should prefer to mate with an infected female (all else being equal). Note that males do not want their mates to invest maximally in offspring, because we assume that offspring only survive if their mother remains alive until they mature (Lessells 2005).

The risk of sterility due to STI infection reduces the reproductive value of all females, but more so for those that are already infected (i.e. uninfected females have a probability,

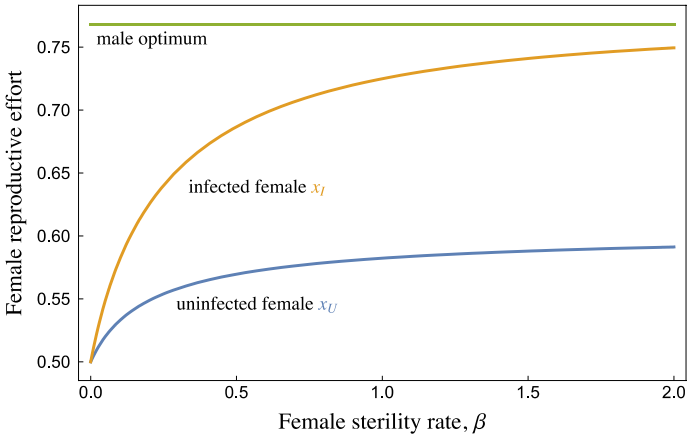


Fig. 1 Optimal reproductive effort of infected females (yellow, x_I) and uninfected females (blue, x_U) increases with female sterility rate (β, i.e. the rate at which infected females become sterile). Males always prefer greater reproductive effort by their mating partners (green) than females provide; but infected females approach the male optimum at very high sterility rates. This outcome is based on a simplified model where female infection and sterility rates are fixed and do not depend on their investment decisions (see 'Mate harm via STI infection' section). Shown with mortality rate function $\mu(x) = 0.1 + \frac{0.1x}{1-x}$ and a probability $p = 0.2$ that an uninfected female becomes infected by any given mating. (Color figure online)

but not a certainty, of being infected). Our model predicts that infected females should increase reproductive effort if the risk of sterility β is high ('terminal investment'). Their reproductive effort approaches the optimum for their male partners as β increases, reflecting the shift of resources towards current, over future, reproduction (Fig. 1). Uninfected females also increase their reproductive effort as β increases, but more modestly. Males consequently gain greater fitness from mating with females that are infected. This creates an incentive for males to infect their own partners.

Epidemiological model

The above model, while illustrative, is simplified in two important ways. First, reproductive effort may trade off against investment in immune function (Hosken 2001; McNamara and Simmons 2017; Keller et al. 2018). Stronger immunity decreases the likelihood of acquiring an STI and lowers the rate at which an acquired STI results in sterilization. If females plastically increase their immune effort in response to STI infection, they might reduce (rather than increase) their reproductive effort in order to free up resources (i.e. terminal divestment). If so, males would lose fitness by infecting their mates.

Second, we have ignored direct effects of the STI on males. In our simplified model, the STI only affected a male's fitness by changing the reproductive output of his mates. Under this assumption, female terminal investment following STI infection should select for males with no resistance to the STI. On the other hand, female terminal divestment might select for male resistance to avoid acquiring the STI and infecting his mates. If, however, the STI causes sterility in males, then there is a direct reason to invest in resistance. A male's optimal strategy will then balance the risk of sterility against the costs of immune effort, and the gains or losses of infecting his mates.

Equilibrium strategies for reproductive and immune effort depend on several interacting factors. The prevalence of the STI in the population, as well as its sex-specific effects, determine the optimal behavior of each sex. However, this behavior also feeds back to determine STI prevalence (Ashby and Gupta 2013). To predict the coevolution of these traits, we require a full game-theoretic model that incorporates the epidemiology of the STI.

We now consider the evolution of reproductive effort and immunity in both sexes in a population with an endemic STI. All individuals are either uninfected (U), infected but still fertile (I), or sterile (S). Sterile individuals can still mate with and infect others, but they do not produce viable offspring. We assume that the STI is cryptic so that it is not possible to seek out or otherwise favour mates with a particular infection status. We first construct an epidemiological model to derive the stable demographic structure of a population, assuming that rates of mortality, STI transmission and sterility onset are fixed for each sex. We then describe how reproductive and immune effort are assumed to affect STI transmission and mortality. Lastly, we calculate sex-specific behavior and demographic structure in a population at evolutionary equilibrium.

Epidemiology: make-up of a demographically stable population

We begin by calculating the proportion of each type of individual in a population at demographic equilibrium (i.e. we find the proportions U, I and S for females and $\tilde{U}$, $\tilde{I}$ and $\tilde{S}$ for males, where $U + I + S + \tilde{U} + \tilde{I} + \tilde{S} = 1$). We assume that demographic processes proceed

much more quickly than evolution, so that the sex-specific rates of mortality, STI transmission and sterility onset can be treated as fixed. All demographic processes (recruitment, mating, sterility, and mortality) occur continuously at constant rates (Fig. 2).

We assume that population size has reached a stable equilibrium, so that newly mature individuals enter the population at the same rate as older individuals die (Úbeda and Jansen 2016). The total rate of recruitment (R for females and $\tilde{R}$ for males) is then:

$$R + \tilde{R} = \mu_U U + \mu_I (I + S) + \tilde{\mu}_U \tilde{U} + \tilde{\mu}_I \left(\tilde{I} + \tilde{S}\right) \tag{6}$$

Note that we do not consider population size dynamics explicitly in our model. We assume an even sex ratio at maturity (i.e. $R = \tilde{R}$), but sex differences in mortality can nonetheless lead to biased adult sex ratios.

We first derive the rates of change in the proportion of males and females of each infection status (Fig. 2), and then equate these to zero to find the stable demographic structure. Three processes affect the proportion of uninfected females U. First, virgin females arrive in the population at a rate of R. With probability p, these females are infected during their first mating; the remaining $(1 - p)R$ females join the uninfected population (note that p is not a constant but depends on both the female's immune investment and the proportion of infected males in the population: see below). Second, non-virgin uninfected females become infected at a total rate of pU. Third, uninfected females die at a rate of $\mu_U U$. The total rate of change in U is then:

$$\frac{dU}{dt} = (1 - p)R - pU - \mu_U U \tag{7}$$

Similarly, newly infected females arrive at a total rate of $p(R + U)$. Infected females become sterile at a rate of βI and die at a rate of $\mu_I I$. The rate of change in I is consequently:

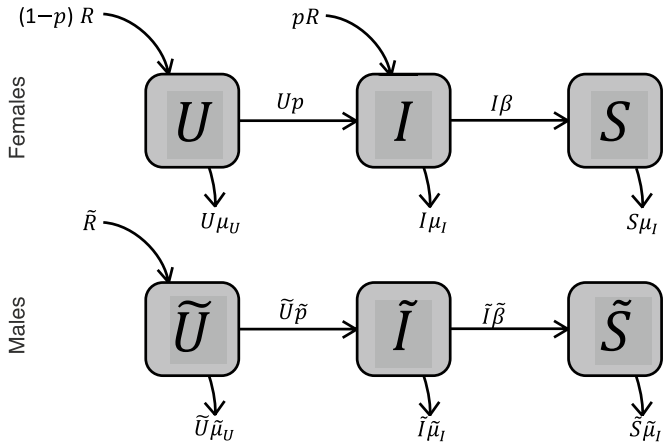


Fig. 2 Epidemiological flow-diagram with uninfected (U for females, $\tilde{U}$ for males), infected (I for females, $\tilde{I}$ for males), and sterile (S for females, $\tilde{S}$ for males) classes separated by sex. The sex ratio at maturation is equal ($R = \tilde{R}$). Females mate immediately upon reaching maturity and randomly thereafter, whereas males mate randomly throughout their adult lives. Matings with opposite-sex individuals lead to infection with probability p, which depends on both individual immune investment and the proportion of infected individuals. Infected individuals become sterile at a constant rate (β for females and $\tilde{\beta}$ for males). Mortality rates (μ) may differ by sex and infection status, although sterile and infected individuals have the same mortality rate (see text)

$$\frac{dI}{dt} = p(R+U) - \beta I - \mu_I I \tag{8}$$

Last, sterile females arrive at a rate of βI and die at a rate of $\mu_I S$ (remember that sterile individuals share the same strategies, hence mortality rates, as infected ones). This gives us:

$$\frac{dS}{dt} = \beta I - \mu_I S \tag{9}$$

The equations for males are similar, except that males do not generally mate immediately on maturity, as their mating opportunities are limited by female availability (see below). We write $\tilde{p}$ for the rate at which uninfected males become infected, and $\tilde{\beta}$ for the rate of sterility onset in infected males (note that $\tilde{p}$ depends on both male immune investment and the proportion of infected females: see below). The rates of change in males of each type are then given by:

$$\frac{d\tilde{U}}{dt} = \tilde{R} - \tilde{p}\tilde{U} - \tilde{\mu}_U \tilde{U} \tag{10}$$

$$\frac{d\tilde{I}}{dt} = \tilde{p}\tilde{U} - \tilde{\beta}\tilde{I} - \tilde{\mu}_I \tilde{I} \tag{11}$$

$$\frac{d\tilde{S}}{dt} = \tilde{\beta}\tilde{I} - \tilde{\mu}_I \tilde{S} \tag{12}$$

To find the composition of the population at equilibrium, we set the derivatives in Eqs. (7)–(12) to zero and solve numerically, subject to the constraint that $U + I + S + \tilde{U} + \tilde{I} + \tilde{S} = 1$. For some parameter values, there is no equilibrium where the STI persists (i.e. the only equilibrium is with $U + \tilde{U} = 1$).

Strategies: reproductive and immune effort

We now consider how immunity, mortality and mating rates are determined by sex-specific investment strategies. Each individual allocates resources to both reproduction (x for females and $\tilde{x}$ for males) and immune function (y and $\tilde{y}$), both of which impose survival costs. For females, the total fitness value of a brood of offspring is proportional to her reproductive effort x (see earlier). For males, the expected mating rate is proportional to $\tilde{x}$ (see below). Males do not affect the fitness value of a brood, except indirectly by infecting their mating partner. An individual's investment strategy may depend on its infection status. There are consequently 8 strategy variables: x_U, y_U, x_I and y_I for females and $\tilde{x}_U$, $\tilde{y}_U$, $\tilde{x}_I$ and $\tilde{y}_I$ for males.

The behaviour of sterile individuals is not under direct selection, as they produce no offspring. We consequently assume that they use the same strategies as infected-but-fertile individuals. Note, however, that sterile individuals still interact with fertile individuals via mating and mortality (which affects the rate of new recruitment). The unselected behavior of sterile individuals therefore affects the ESS strategies for both uninfected and infected individuals.

Immune effort has two possible benefits. First, for uninfected individuals, it decreases the probability (α or $\tilde{\alpha}$) of acquiring the STI when mating with an infected partner. The

risk of infection upon mating with an infected individual is described by the following relationships:

$$\alpha(y_U) = \alpha_{\max} \exp(-Ay_U), \quad \tilde{\alpha}(\tilde{y}_U) = \tilde{\alpha}_{\max} \exp(-\tilde{A}\tilde{y}_U) \tag{13}$$

The parameters $\alpha_{\max}$ and $\tilde{\alpha}_{\max}$ determine the infection probability for individuals who invest nothing in immune function. The slope parameters A and $\tilde{A}$ determine how effectively infection risk is reduced by immune effort. The exponential function prevents infection probability from going to zero, which would result in STI extinction.

Second, once infected, immune effort determines the rate (β or $\tilde{\beta}$) at which the STI leads to sterility:

$$\beta(y_I) = \beta_{\max} \exp(-By_I), \quad \tilde{\beta}(\tilde{y}_I) = \tilde{\beta}_{\max} \exp(-\tilde{B}\tilde{y}_I) \tag{14}$$

The parameters $\beta_{\max}$ and $\tilde{\beta}_{\max}$ are the maximum rates at which infected individuals become sterile, whereas B and $\tilde{B}$ determine how effectively sterility is delayed by immune effort. The model allows for sex differences in both the infectivity and virulence of the STI [Eqs. (13) and (14) respectively], even when males and females invest equally in immune function.

We assume that both reproductive and immune effort are costly and increase an individual's instantaneous rate of mortality μ. We model mortality as an accelerating function of the total investment $x + y$ in reproduction and immunity:

$$\mu(x + y) = \mu_{\min} + \frac{C(x + y)}{1 - (x + y)} \tag{15}$$

The minimum mortality $\mu_{\min}$ applies to individuals who invest in neither immunity nor reproduction. The slope C determines how steeply mortality increases with total effort. The total investment $x + y$ must be less than one, because $x + y = 1$ implies instant death. Consequently, we can think of $1 - x - y$ as the resources invested in survival (e.g. somatic maintenance or predator avoidance). We write, for example, $\mu_U = \mu(x_U + y_U)$ for the mortality rate of an uninfected female, $\tilde{\mu}_I = \mu(\tilde{x}_I + \tilde{y}_I)$ for an infected male, and so on.

Female mating rates are not determined by their investment strategies: all females mate immediately upon reaching maturity and then re-mate immediately each time their offspring mature. The total rate of matings in the population is consequently $(R + U + I + S)P$, where P is the equilibrium female population size (note that the average number of matings per individual per unit time is greater than $U + I + S = 1$, because a female's initial mating must also be accounted for). For males, on the other hand, mating rate is determined by their reproductive effort relative to other males in the population, which may depend on their infection status (U, I or S, noting that U includes both virgin and non-virgin uninfected males). The share of matings obtained by males of a given infection status consequently depends on both the frequency and the average reproductive effort of these males. The probability that any given mating is with a male of status M (where $M = U, I$ or S) is given by:

$$r_M = \frac{\tilde{x}_M \tilde{M}}{\tilde{x}_U \tilde{U} + \tilde{x}_I (\tilde{I} + \tilde{S})} \tag{16}$$

Note that $r_U + r_I + r_S = 1$. The probability that a female becomes infected from any given mating is $p = \alpha(r_I + r_S)$.

Similarly, a male of infection status M mates with females of status F at a rate of:

$$\tilde{r}_{M,F} = \left(\frac{\tilde{x}_M}{\tilde{x}_U \tilde{U} + \tilde{x}_I \left(\tilde{I} + \tilde{S} \right)} \right) F \tag{17}$$

Here we allow $F = R, U, I, S$, so that $\tilde{r}_{M,R}$ represents the rate of matings with newly mature virgin females, and $\tilde{r}_{M,U}$ represents the rate of matings with non-virgin uninfected females. Note that the Fisher condition is fulfilled because $r_M F = \tilde{r}_{M,F} \tilde{M}$ for all types M and F (i.e. the total mating rate of type F females with type M males equals that of type M males with type F females, which is a logical necessity: Houston and McNamara 2005; Jennions and Fromhage 2017). The rate at which an uninfected male becomes infected is $\tilde{p} = \tilde{\alpha} \left(\tilde{r}_{U,I} + \tilde{r}_{U,S} \right)$.

Reproductive and immune effort in a population at evolutionary equilibrium

In the previous section, we derived the demographic make-up of a stable population, assuming that all individuals play the same fixed (although sex-specific) strategies for reproductive and immune effort. We can now calculate the fitness of mutant individuals that diverge from the population strategies (details in "Appendix"). We assume that demographic change happens much faster than evolutionary change, so that we can calculate fitness against the background of a demographically stable population.

We write population strategies in vector form as $X = \left(x_U, y_U, x_I, y_I \right)$ for females and $\tilde{X} = \left(\tilde{x}_U, \tilde{y}_U, \tilde{x}_I, \tilde{y}_I \right)$ for males. Female or male mutants play strategies $X^* = \left(x_U^*, y_U^*, x_I^*, y_I^* \right)$ or $\tilde{X}^* = \left(\tilde{x}_U^*, \tilde{y}_U^*, \tilde{x}_I^*, \tilde{y}_I^* \right)$ respectively. We write $w(X^*)$ for the fitness of a mutant female playing X^* in a population where all other females play X and all males play $\tilde{X}$. For male mutants, we define $\tilde{w}\left(\tilde{X}^* \right)$ analagously. The selection differentials for males and females are then approximately proportional to (Taylor 1996):

$$S(X) = \left. \frac{\partial w(X^*)}{\partial X^*} \right|_{X^* = X}, \quad \tilde{S}\left(\tilde{X} \right) = \left. \frac{\partial \tilde{w}\left(\tilde{X}^* \right)}{\partial \tilde{X}^*} \right|_{\tilde{X}^* = \tilde{X}} \tag{18}$$

This relies on the simplifying assumption that additive genetic variance is approximately equal for all traits. We found evolutionarily equilibria by starting with arbitrary initial strategies X_0 and $\tilde{X}_0$ and following the selection trajectories defined by $S(X)$ and $\tilde{S}\left(\tilde{X} \right)$ until the strategies converged to an equilibrium. This was done by iterating the equation:

$$\begin{pmatrix} X_{t+1} \\ \tilde{X}_{t+1} \end{pmatrix} = \begin{pmatrix} X_t + \Delta S\left(X_t \right) \\ \tilde{X}_t + \Delta \tilde{S}\left(\tilde{X}_t \right) \end{pmatrix} \tag{19}$$

with Δ a small positive constant (we found $\Delta = 0.01$ suitable). In other words, in each time step, the strategies move a small step in the direction of selection, with the step size equal to Δ times the intensity of selection. Stable population structure was found using Eqs. (7)–(12) for each iteration. Different choices of initial strategies always led to the same equilibria, except for choices that led to STI extinction.

Fig. 3 Behavioral strategies and demographic structure of a population at evolutionary and demographic equilibrium, shown as the effectiveness of female immune effort against sterility varies (B, horizontal axis): **a** Optimal reproductive effort (solid lines, x_U and x_I) and immune effort (dashed lines, y_U and y_I) of infected females (yellow) and uninfected females (blue). When female immune effort is ineffective at delaying sterility (small B), females increase reproductive effort after infection (i.e. terminal investment). In contrast, if immune effort is highly effective at delaying sterility (high B), females increase immune effort but reduce reproductive effort after infection (i.e. terminal divestment). **b** Optimal reproductive effort (solid lines, $\tilde{x}_U$ and $\tilde{x}_I$) and immune effort (dashed lines, $\tilde{y}_U$ and $\tilde{y}_I$) of infected males (yellow) and uninfected males (blue). **c** Proportions of the population made up by males (dashed lines) and females (solid lines) that are uninfected (blue), infected (yellow) and sterile (green). All panels are shown with $\alpha_{\max} = \tilde{\alpha}_{\max} = 1$, $A = \tilde{A} = 2$, $\beta_{\max} = \tilde{\beta}_{\max} = 1$, $\tilde{B} = 5$, and $\mu_{\min} = C = 0.1$. (Color figure online)

How does female terminal investment affect male resistance?

In our model, male resistance evolves under selection arising from two mechanisms: (1) STIs can induce male sterility, which selects for higher resistance; and (2) transferring an STI to a female partner can either elevate or lower her reproductive effort, which selects for lower or higher resistance respectively (see Results). But how can we disentangle these two selection pressures? How do we show that males evolve lower resistance *because* transferring the STI elevates female reproductive effort (Morrow et al. 2003)? We consider this question using a thought experiment that reveals the logic of our model.

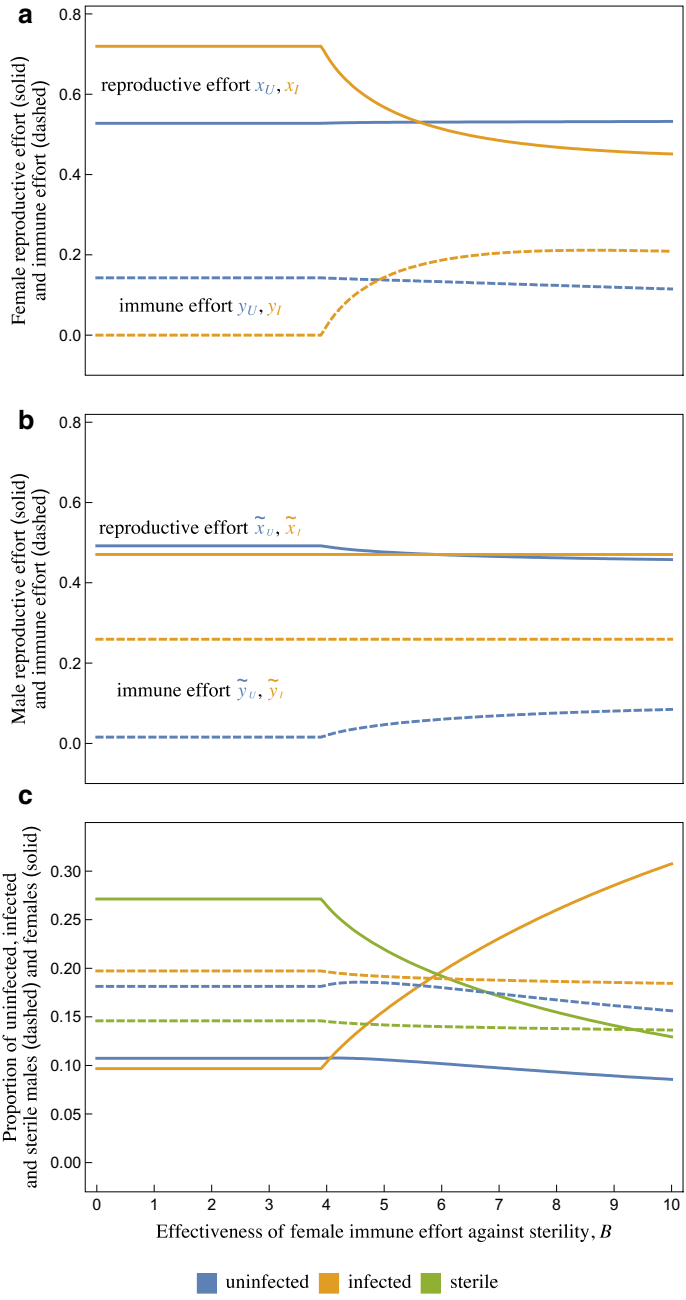
We consider a rare mutant male (a 'non-infector') who is susceptible to the STI, but cannot pass it on to his mates. A non-infector is therefore incapable of directly influencing a female's reproductive effort. Consequently, his immune effort affects his fitness exclusively by reducing his risk of sterility. If we compare the non-infector's optimal strategies to that of a typical male (i.e. everyone else), we can assess how strongly the evolution of male resistance is determined by its effect on female reproductive effort. We assume a large population so that the strategies of a rare mutant have a negligible effect on the infection rates of other individuals.

We begin by calculating evolutionarily stable strategies for the population exactly as above. We then calculate the mutant male's fitness $\tilde{w}$ as a function of his strategies $\tilde{X}^*$. His fitness function is identical to that of typical males [see Eqs. (23)–(27) in the "Appendix"], except that his fitness gain from mating does not depend on his own infection status (i.e. $\tilde{v}_I = \tilde{v}_U$). We then maximize $\tilde{w}$ numerically over all possible strategies $\tilde{X}^*$ to find the mutant's optimal strategies.

Results of the epidemiological model

Should a female terminally invest?

How a female should optimally allocate her resources to reproduction and immunity depends on two factors. First, what is her reproductive value? If her reproductive value declines (e.g. due to infection), this should, all else being equal, select for higher allocation to current reproduction. Second, how effective is her immune effort in preventing infection or delaying sterility after infection, and thereby increasing her reproductive value? If immune effort is highly effective, then she should direct resources away from reproduction toward immunity.



Differences in the effectiveness of immune effort before and after STI infection can alter the pattern of terminal investment that we saw in our initial, simplified model (see 'Mate harm via STI infection' section and Fig. 1). If immune effort is more effective at preventing infection than at delaying sterility (e.g. A is high relative to B), then uninfected females

Fig. 4 Effect of female reproductive strategies on optimal male resistance, shown as the effectiveness of female immune effort against sterility varies (B, horizontal axis): **a** Optimal reproductive effort of infected females (yellow, x_U) and uninfected females (blue, x_I). **b** The expected fitness benefit to males of mating with an infected female (yellow, $\frac{x_U}{1+\mu_U}$) or an uninfected female (blue, $\frac{x_I}{1+\mu_I}$). The dashed and solid vertical lines, which indicate where the curves in panels **a** and **b** cross, do not coincide because fitness benefits to males depend not only on a female's reproductive effort, but also on her short-term mortality (which depends on both reproductive and immune effort). **c** Optimal immune effort prior to infection ($\tilde{y}_U$) for both typical males (blue) and mutant males that cannot infect their partners with the STI (red). When infected females provide higher fitness benefits than uninfected females (left of the vertical solid line), typical males reduce their STI resistance due to the fitness benefits of infecting their partners (i.e. the blue line lies below the red line). Conversely, if uninfected females provide higher fitness benefits (right of the vertical solid line), then males increase their resistance to the STI (i.e. the red line lies above the blue line). All panels are shown with $\alpha_{\max} = \tilde{\alpha}_{\max} = 1$, $A = \tilde{A} = 2$, $\beta_{\max} = \tilde{\beta}_{\max} = 1$, $\tilde{B} = 5$, and $\mu_{\min} = C = 0.1$. (Color figure online)

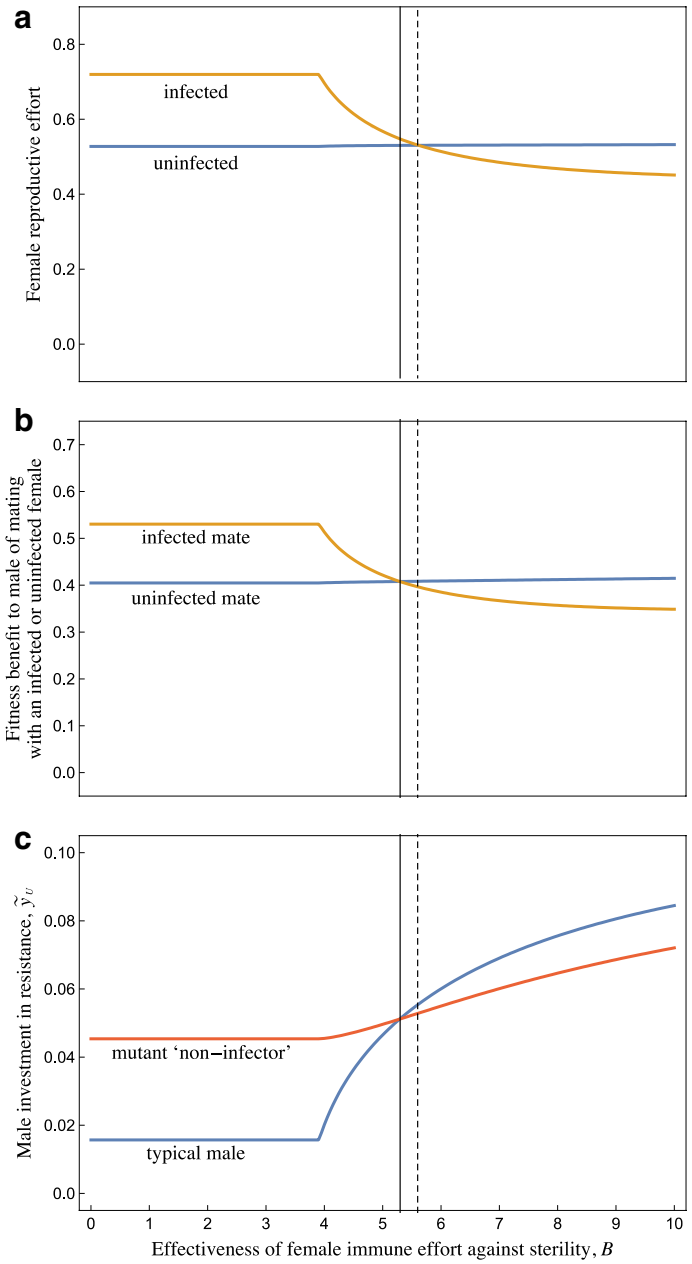
might increase immune effort and reduce reproductive effort relative to infected females. This will strengthen the magnitude of terminal investment following infection. On the other hand, if immune effort is more effective at delaying sterility (e.g. B is high relative to A), then infected females might show increased immunity and reduced reproductive effort. A large increase in immunity post infection could potentially reduce an infected female's reproductive effort below that of uninfected females (i.e. terminal divestment).

We illustrate this argument by varying the effectiveness of female immune effort against sterility (B), while holding all other parameters, including A, constant (Fig. 3). Females invest more in immunity y_I after becoming infected as B increases, and this is accompanied by a decline in their reproductive effort x_I (Fig. 3a). For low values of B, infected females invest more in reproduction than do uninfected females ($x_I > x_U$, terminal investment), but this trend reverses at high values of B because infected females instead direct investment toward immune function ($x_I < x_U$, terminal divestment). Due to increasing immune effort after infection, the proportion of sterile females in the population decreases with increasing B, while the proportion of infected-but-fertile females increases (Fig. 3c).

How do female reproductive strategies affect optimal male resistance?

A male's expected fitness gain from mating depends on his mate's reproductive effort and mortality rate. Both of these parameters, in turn, depend on her infection status (from above, $\Delta\tilde{w} = \frac{x_U}{1+\mu_U}$ or $\frac{x_I}{1+\mu_I}$ for mating with an uninfected or infected female respectively). Consequently, depending on the circumstances, males may gain more (or less) by mating with an infected rather than an uninfected female (Fig. 4b). Our model excludes direct mate choice (as infection status is cryptic) so males cannot choose to mate with infected females. Males can, however, influence the likelihood that their mate is infected: namely, by transferring the STI to their mate. This means that, in some circumstances, the STI provides a fitness benefit to males, which partially or fully offsets any costs. The only way in which a male can increase the chances that he acquires an STI is to have a lower resistance $\tilde{y}_U$ (see below).

Males generally gain more from females with the infection status that has a higher reproductive effort x (e.g. infected females at low B, where $x_I > x_U$, or uninfected female at high B, where $x_U > x_I$: Fig. 4b). In borderline cases where the reproductive effort of the two types is similar (i.e. $x_U \approx x_I$), males can, however, gain more by mating with a female of the type with lower immune effort (even if she has a slightly lower reproductive effort).



This is because males only benefit from a mating *if* the female survives long enough to produce offspring. Female immune effort increases her mortality without providing any fitness benefit to the male. In Fig. 4, for instance, the vertical dashed line indicates the value of B at which there is equal reproductive effort by infected and uninfected females (i.e. $x_U = x_I$). The vertical solid line indicates where males gain the same fitness returns from both types

of females (i.e. $\frac{x_U}{1+\mu_U} = \frac{x_I}{1+\mu_I}$). In the space between these two lines, infected females terminally invest, but males nonetheless gain more from mating with uninfected females. This is because infected females also have higher mortality (due to greater total investment in reproduction and immunity). When a male infects his partner, the small increase in her reproductive effort is not enough to offset the reduction in her probability of surviving to produce his offspring.

We have argued that if females increase their reproductive effort after infection (terminal investment), then males should reduce their investment in STI resistance ($\tilde{y}_U$) because they benefit by infecting their mates. Indeed, males tend to have lower STI resistance when females engage in terminal investment rather than divestment (i.e. lower to the left than the right of the vertical dotted line in Fig. 4c). But is this because males reduce their resistance in order to benefit from their partners' terminal investment? Apparently so, as the optimal resistance of a typical male is lower than that of a mutant non-infector male whenever infected females are more profitable mates (Fig. 4c, left of the vertical solid line).

On the other hand, if infected females reduce their reproductive effort (terminal divestment), thereby becoming less profitable for males than uninfected females, then males should increase their STI resistance, despite the mortality cost, to avoid infecting their mates. Indeed, typical males have higher resistance than non-infector males under such conditions (Fig. 4c, right of the vertical solid line). The comparison with non-infector males shows that selection to infect females can have substantial effects on the evolution of male immunity. For example, a 36% increase in female reproductive effort after infection corresponds to a 65% reduction in male resistance effort for our parameter values (Fig. 4a, c; for B values less than 4).

STI extinction

For certain choices of parameters, the STI was predicted not to persist in the population. In particular, STI extinction occurs when a small investment of resources is sufficient to ensure strong STI resistance (i.e. $\alpha_{\max}$ is small and/or A is large). Higher population turnover (e.g. a high minimum mortality rate $\mu_{\min}$) can also contribute to STI extinction because, in the absence of vertical transmission, new arrivals in the population are always uninfected. In our model, sterile individuals continue to mate and infect their mating partners, which facilitates the persistence of the STI. However, even if sterile individuals do not mate, the STI can still persist over a broad parameter space (data not shown).

Discussion

Our model determines how STI infection affects the optimal allocation of resources to immunity and reproduction in both sexes. It confirms that (1) there are biologically plausible scenarios where females should increase reproductive effort upon becoming infected, and (2) this form of terminal investment can, in principle, select for reduced male resistance to the STI. Reduced resistance increases a male's likelihood of acquiring an STI and passing it on to his mates, thereby allowing him to benefit from their terminal investment. This is a form of 'adaptive mate harm', where males benefit in fitness terms by harming their mates (Johnstone and Keller 2000; Lessells 2005; McLeod and Day 2017). Female

terminal investment selects for reduced male resistance in our model regardless of any other factor, including the choice of parameter values. However, net selection on male resistance, and hence its ESS value, depends on the costs to males of acquiring the STI.

Reproduction and immunity draw on common resources (Schwenke et al. 2016), and are consequently constrained in their joint responses to STI infection. In a model where immune effort is assumed to be fixed (i.e. it cannot respond plastically to STI infection), females should always terminally invest in response to infection (see 'Mate harm via STI infection' section). However, plastic adjustments in immunity complicate this picture. When immune effort is highly effective in delaying STI-induced sterility, females might increase their immune effort after infection at the expense of reduced reproductive effort. This 'terminal divestment' selects for increased, rather than reduced, male resistance, as in this case males lose fitness by infecting a mating partner.

Key assumptions of the model

Our model makes several key life-history assumptions that must be met for the predictions to be plausible. First, and most importantly, females must be able to respond to STI infection by plastically adjusting reproductive effort into current offspring (i.e. those potentially sired by the STI-transmitting male). This is only possible if females continue to provide parental investment after mating, e.g. because eggs are provisioned after mating, as occurs in some insects (Staudacher et al. 2015), or there is post-zygotic parental care, as in many birds and mammals (e.g. Amininasab et al. 2017; Bowers et al. 2015). Females must also be able to detect STI acquisition quickly enough to adjust effort in the current reproductive bout.

Second, we assume that there is no vertical or non-sexual horizontal transmission of the STI. However, at least in insects (Knell and Webberley 2004), many STIs have at least one additional transmission pathway. How the addition of vertical transmission would influence our results is likely to depend on the relative fitness costs and benefits of being born infected for sons and daughters. It seems probable that the infection costs for daughters (who will probably become sterile before they can breed) will far outweigh the gains for sons. As such, the reproductive value of the offspring of infected females would probably be lower than that of uninfected females. This would reduce selection on males to acquire and transfer an STI. This effect could, however, be reduced or reversed if infected females produce a male-biased offspring sex ratio (analogous to females adjusting the offspring sex ratio in response to sex-specific fitness effects associated with their partner's genotype: e.g. Booksmythe et al. 2017). The addition of non-sexual horizontal transmission could have another major consequence. It would presumably reduce the benefit to males of becoming infected so as to infect their own partners by weakening the link between STI transmission and female reproductive effort.

Third, terminal divestment can only evolve in our model if greater immune effort delays STI-induced sterility, thereby extending the female's reproductive lifespan. If females cannot increase their fertile lifespan, then all females should terminally invest. The effect of immune effort on STI-induced sterility has received minimal empirical study. In principle, it would be straightforward to measure an individual's immunocompetence (Norris 2000; Brown et al. 2011; Kelly et al. 2018) then experimentally infect it with an STI and measure the rate of onset of sterility. This approach assumes, however, that the chosen immunity assay is correlated with immune effort that specifically targets the focal STI.

Fourth, we assume that the STI induces sterility but does not directly affect host mortality. A mortality-inducing STI would reduce female reproductive value and could potentially select for terminal investment, as in our model. Alternatively, terminal divestment might be adaptive if increasing investment in immunity or somatic maintenance after infection helps to reduce STI-related mortality. However, two major differences make it hard to transfer our model's predictions to this scenario. First, if host mortality increases rapidly after STI acquisition, then males have less incentive to infect their mates, because infected females might die before they can produce offspring (Lessells 2005). Second, STI-induced mortality will reduce the proportion of sterile individuals in the population, which feeds back to affect both the epidemiological and evolutionary dynamics. The behavioural consequences of these differences are hard to predict without an appropriate model.

Lastly, our model is designed to predict the behaviour of a host-STI system at equilibrium. Consequently, we do not model evolutionary change in parameter values, which is expected to occur due to coevolutionary feedback between host strategies and the STI. Accounting for this coevolution would cause some parameters that are assumed fixed in our model to vary, changing the location of evolutionary equilibria. We also do not explicitly model changes in host population size due to the STI. Some previous models predict host extinction when an STI causes complete host sterility (see e.g. Thrall et al. 1993; Ryder et al. 2007), although the delayed onset of sterility in our model reduces this risk. Negative density-dependence of offspring production or recruitment may also reduce the probability of host extinction (Holman and Kokko 2013). Further, our model assumes that there is no feedback from population size to demographic parameters like individual mating rates (e.g. there are no Allee effects: Courchamp et al. 1999). Considering these factors would likely require stochastic simulations to estimate host and STI extinction probabilities.

Empirical evidence for terminal investment and divestment

There is good evidence that females plastically alter their reproductive effort in response to an immune challenge (e.g. Reaney and Knell 2010; Reavey et al. 2014; Bowers et al. 2015). Our model allowed for a continuum of female responses to infection, ranging from terminal divestment (increased immune effort and decreased reproductive effort) to terminal investment (increased reproductive effort and decreased immune effort). Empirical studies of communicable diseases and parasites similarly indicate the full range of possible female responses, from terminal divestment (sometimes known as 'self-maintenance') (e.g. *Euoniticellus intermedius*, Reaney and Knell 2010; *Tenebrio molitor*, Krams et al. 2016: *Aedes aegypti*, Sylvestre et al. 2013; *Culex pipiens*, Vézilier et al. 2012), to no response (e.g. Armitage et al. 2003), to terminal investment (sometimes referred to as 'fecundity compensation') (e.g. *Aedes aegypti*, Ruiz-Guzmán et al. 2016; *Acyrthosiphon pisum* Altincicek et al. 2008; *Passer domesticus*, Bonneaud et al. 2004). Unfortunately, very few studies have specifically measured the initial reproductive response of females to STIs. Webberley et al. (2004) performed one such experiment, comparing the egg laying rate of two spot ladybirds, *Adalia decempunctata,* that were either infected or uninfected with *Coccipolipus hippodamiae*. In the first 15 days following infection, infected females had a larger variance in egg laying rate than uninfected controls, with terminal investment and divestment both apparently occurring. It is unclear if this variation in response to STIs is common, or whether a uniform response is generally favoured.

Immunity and sexual conflict

Females often show greater immunocompetence than males (Grossman 1989; Marriott and Huet-Hudson 2006; although see Vincent and Sharp 2014). Explanations for this phenomenon include: (1) vertical transmission of diseases, which disproportionately increases female infection cost (as infected females always risk passing an infection on to their offspring, whereas infected males avoid this cost when mating with healthy females); (2) a trade-off with investment into reproduction under 'winner-takes-all' mating competition, which can cause males to invest more heavily in sexually selected traits than females do in offspring production, leaving males with fewer resources to allocate to immunity (Rolff 2002); and (3) higher mating skew for males than females means that fewer males are exposed to the infection (Thrall et al. 2000) (although these tend to be males with higher than average fitness, who are consequently more visible to selection).

Our study highlights a fourth, non-mutually exclusive, explanation, which is that males can benefit from infecting females with a disease. This form of adaptive male harm is unusual in that it potentially involves both *inter-locus* sexual conflict over the transmission of the STI, and *intra-locus* conflict over optimal investment in resistance. Our model assumes that immunity evolves independently in males and females (i.e. we do not consider intra-locus conflict). However, immune alleles are commonly shared between the sexes (Rolff et al. 2005), which leads to intra-locus sexual conflict when male and female optima differ (Pennell and Morrow 2013). Naively, correlated evolution of immunity between the sexes should simply cause male and female resistance to be more similar than predicted by our model. Feedbacks between the epidemiology of an STI and individual host strategies are, however, complex (Ashby and Gupta 2013). For instance, female-driven evolution towards higher resistance in both sexes might dramatically reduce or even eliminate the prevalence of the STI in a population (Thrall et al. 1993; Ryder et al. 2007). Explicit genetic models are necessary to understand how constraints on the evolution of sex-specific immune response affect the evolution of terminal investment and adaptive mate harm. The relative importance of these four competing explanations can potentially be tested using a comparative approach to determine the relationship between sex differences in immune response and aspects of a population's mating system.

In sum, our model shows that sexually transmitted diseases could, in principle, be harnessed by males to manipulate the behaviour of females for the male's own benefit. Empirical studies are now needed to determine whether or not this mechanism of male manipulation of females has evolved in nature.

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Compliance with ethical standards

Conflict of interest The authors declare no conflicts of interest.

Appendix

Calculating fitness for the epidemiological model

Here we calculate the fitness of mutant individuals for the epidemiological model. We assume all other individuals in the population play the same sex-specific strategies. Demographic change is assumed to happen much faster than evolutionary change, so that we can calculate

fitness against the background of a stable population as described in the main text. We mark variables that depend on the mutant's strategies with a star.

Consider first a mutant female. As in our initial simple model, we can partition her lifetime fitness w as the sum of fitness gained while uninfected and while infected [cf. Eq. (3)]. Each term equals her expected number of matings (n_U or n_I) times the expected fitness gain per mating (v_U or v_I):

$$w\left(x_U^*, y_U^*, x_I^*, y_I^*\right) = n_U v_U + n_I v_I \tag{20}$$

As before, the expected fitness gain from mating is $v_U = \frac{x_U^*}{1+\mu_U^*}$ for an uninfected female and $v_I = \frac{x_I^*}{1+\mu_I^*}$ for an infected female. However, the numbers of matings must be adjusted for two reasons. First, they now depend on both reproductive and immune effort. Second, matings with sterile males do not yield viable offspring, so it is more convenient to only tally matings with fertile mates (i.e. the expected numbers of matings n_U and n_I are defined to only include matings with fertile males). Note that matings with sterile males are still costly, as they consume the same time and reproductive resources as matings with fertile males.

The probability that a female becomes infected during any given mating is $p^* = \alpha^*\left(r_I + r_S\right)$. The probability that her mate is fertile, given that she remains uninfected after mating, is $\frac{r_U+(1-\alpha^*)r_I}{r_U+(1-\alpha^*)\left(r_I+r_S\right)}$. The expected number of matings while uninfected is then [cf. Eq. (1)]:

$$n_U = (1-p^*)\left(\frac{\mu_U^*+1}{\mu_U^*+p^*}\right)\left(\frac{r_U+(1-\alpha^*)r_I}{r_U+(1-\alpha^*)\left(r_I+r_S\right)}\right) \tag{21}$$

Similarly, when a female is newly infected by her mate, the probability that her mate is fertile is $\frac{r_I}{r_I+r_S}$. For all subsequent matings while infected, the mate is fertile with probability $r_U + r_I$. The expected number of matings while infected is consequently [cf. Eq. (2)]:

$$n_I = p^*\left(\frac{\mu_U^*+1}{\mu_U^*+p^*}\right)\left(\frac{r_I}{r_I+r_S} + \frac{r_U+r_I}{\mu_U^*+\beta^*}\right) \tag{22}$$

Male lifetime fitness can be partitioned similarly as:

$$\tilde{w}\left(\tilde{x}_U^*, \tilde{y}_U^*, \tilde{x}_I^*, \tilde{y}^*\right) = \tilde{n}_U \tilde{v}_U + \tilde{n}_I \tilde{v}_I \tag{23}$$

Unlike the case for females, we count the mating in which a male becomes infected under $\tilde{n}_U$ rather than $\tilde{n}_I$, because his expected fitness gain from that mating does not change due to his becoming infected (infection only influences his future mating rate). A mutant male can leave the uninfected state in two ways: by dying, which occurs at a rate of $\tilde{\mu}_U^*$, or by becoming infected, at a rate of $\tilde{p}^* = \tilde{\alpha}^*\left(\tilde{r}_{U,I}^* + \tilde{r}_{U,S}^*\right)$. While uninfected, he mates with fertile females at a total rate of $\tilde{r}_{U,R}^* + \tilde{r}_{U,U}^* + \tilde{r}_{U,I}^*$. The expected number of matings while uninfected is then:

$$\tilde{n}_U = \frac{\tilde{r}_{U,R}^* + \tilde{r}_{U,U}^* + \tilde{r}_{U,I}^*}{\tilde{p}^* + \tilde{\mu}_U^*} \tag{24}$$

The probability that the male becomes infected at some point in his lifetime is $\frac{\tilde{p}^*}{\tilde{p}^*+\tilde{\mu}_U^*}$. Once infected, he mates with fertile females at a rate of $\tilde{r}_{I,R}^* + \tilde{r}_{I,U}^* + \tilde{r}_{I,I}^*$. His reproductive life ends when he becomes sterile, at a rate of $\tilde{\beta}^*$, or dies, at a rate of $\tilde{\mu}_I^*$. His expected number of matings while infected is then:

$$\tilde{n}_I = \left(\frac{\tilde{p}^*}{\tilde{p}^* + \tilde{\mu}_U^*}\right)\left(\frac{\tilde{r}_{I,R}^* + \tilde{r}_{I,U}^* + \tilde{r}_{I,I}^*}{\tilde{\beta}^* + \tilde{\mu}_I^*}\right) \tag{25}$$

Matings with uninfected females have fitness value $\frac{x_U}{1+\mu_U}$, whereas those with infected females have fitness value $\frac{x_I}{1+\mu_I}$. The average fitness value of mating while uninfected is given by weighting each of these by the proportion of matings with uninfected females (R or U) or infected females (I) out of all matings with fertile females:

$$\tilde{v}_U = \left(\frac{R+U}{R+U+I}\right)\left(\frac{x_U}{1+\mu_U}\right) + \left(\frac{I}{R+U+I}\right)\left(\frac{x_I}{1+\mu_I}\right) \tag{26}$$

If an infected male mates with an uninfected female, he will infect her with probability α, after which his expected fitness gain is $\frac{x_I}{1+\mu_I}$. If he does not infect her, or if she was already infected, then the situation is unchanged from Eq. (26). The average fitness value of mating while infected is consequently:

$$\tilde{v}_I = \left(\frac{(1-\alpha)(R+U)}{R+U+I}\right)\left(\frac{x_U}{1+\mu_U}\right) + \left(\frac{\alpha(R+U)+I}{R+U+I}\right)\left(\frac{x_I}{1+\mu_I}\right) \tag{27}$$

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