SUPPORTING INFORMATION Appendix S1: Mathematical development of the 'male resistance' mechanism

In this Supplementary Appendix, we develop the demography-based "male resistance" mechanism. We use it to characterize the effect of epidemics on male frequency in two ways, either over a gradient of epidemic size (like in survey, Fig. 2) or from a disease-free baseline (like in the experiment, Fig. 3). In this model, host recruitment, epidemiology, and male production are highly simplified. These simplifications are fairly striking, but they offer an analytically-tractable starting point.

Disease-free boundary case

Imagine that, without disease, males (m) and females (f) are produced from a constant reproductive flow, R. That big assumption means that disease does not influence overall population reproduction rate (R). However, a fraction s of that reproductive flow is allocated to females and the rest, (1-s), goes to males. Males die at rate d_m and females die at rate d_f, yielding a system (see also Table S1):

$$dm/dt = (1\text{-}s)\, R - d_m\, m \quad \text{(S1. a)}$$

$$df/dt = s\, R - d_f f. \quad \text{(S1. b)}$$

At equilibrium, male (m^*) and female (f^*) density reflect the ratio of gains to losses shown in each balance equation (equ. 1.a and 1.b, respectively), yielding:

$$m^* = \frac{(1-s)R}{d_m} \text{ and } f^* = \frac{sR}{d_f} \quad \text{(S2)}$$

and the frequency of males, $p_m^* = m^*/(m^*+f^*)$, is 1-s when death rates are equivalent. When they are not equivalent, p_m^* becomes:

$$p_m^* = \frac{1-s}{1-s(\gamma-1)} \quad \text{(S3)}$$

where γ is the ratio of background death rates of males to females ($\gamma = d_m/d_f$). This expression indicates that p_m^* would increase if males have lower background mortality rate than females, (i.e., if γ decreases, since $dp_m^*/d\gamma < 0$). Of course, males increase if allocation to males, (1-s), increases (or allocation to females, s, decreases: $dp_m^*/ds < 0$).

Only females become infected (complete male resistance, an extreme case)

If only females become infected, i.e., males completely resist disease, one can readily show that the frequency of males should increase with disease. Consider the system (Table S1):

$$dm/dt = (1\text{-}s)\, R - d_m\, m \quad \text{(S4. a)}$$

$$df/dt = s\, R - d_f f - \beta f \quad \text{(S4. b)}$$

$$df_I/dt = \beta f - v\, d_f f_I \quad \text{(S4. c)}$$

where β is a force of infection (labeled 'transmission rate' hereafter, but perhaps is best thought of as per capita transmission rate times a propagule rain of parasites). For simplification purposes, this force of infection is not a function of male and female dynamics. Then, f_I is

density of infected females, and v is a virulence multiplier (i.e., $v > 1$ indicates that the parasite exerts virulence on survival, increasing mortality from the background level). This system produces the equilibrium:

$$m^* = \frac{(1-s)R}{d_m}, f^* = \frac{sR}{\beta+d_f}, f_I^* = \frac{\beta f^*}{v d_f}. \quad \text{(S5)}$$

Thus, each term (equ. A5) is the ratio of gains and losses of each balance equation (equ. A4). At equilibrium, the proportion of females infected, $p_{f,I}^* = f_I^* / (f^* + f_I^*)$, is:

$$p_{f,I}^* = \frac{\beta}{\beta+vd_f} \quad \text{(S6)}$$

which is the ratio of gains of infection to the sum of gains and losses (i.e., the turnover of infected females). If background losses are equal between the sexes (i.e., $d = d_m = d_f$), then the proportion infected in the population, $p_I^* = f_I^* / (m^* + f^* + f_I^*)$, is:

$$p_I^* = \frac{s\beta}{s\beta+vd+v(1-s)\beta)} \quad \text{(S7)}$$

which, to little surprise, is lower than the proportion of females infected (if $s < 1$). The expression for proportion infected with unequal background mortality rates is more complicated:

$$p_I^* = \frac{s\beta\gamma}{s\beta\gamma+vd+v[(1-s)\beta+d(\gamma-1)s]} \quad \text{(S8)}$$

where γ is the ratio of background death rates of males to females ($\gamma = d_m / d_f$) and d denotes female death rate. Most importantly, both expressions increase with transmission rate, i.e., $dp_I^* / d\beta > 0$ (not displayed here but readily shown with some calculus). Proportion males, $p_m^* = m^* / (m^* + f^* + f_I^*)$, with equal ($\gamma = 1$) and unequal ($\gamma \neq 1$) background mortality are:

$$p_m^* = \frac{v(\beta+d)(1-s)}{vd+\beta[s+v(1-s)]} \quad \text{(for } d_m = d_f = d, \text{ or } \gamma = 1) \quad \text{(S9.a)}$$

$$p_m^* = \frac{v(\beta+d)(1-s)}{vd[1+s(\gamma-1)]+\beta[\gamma s+v(1-s)]} \quad \text{(for } d_m \neq d_f, \text{ so } \gamma \neq 1) \quad \text{(S9.b)}$$

and both expressions also increase with transmission rate, i.e., $dp_m^*/d\beta > 0$ (details not shown). Therefore, increases in transmission rate increase epidemic size (equilibrial infection prevalence of both females and the population) and also frequency of males. Additionally, one can readily show that, as long as $\beta > 0$ and $v > 1$, the proportion of males increases over the disease-free baseline in both cases (Equs. A9.a and A9b). Not that surprisingly, then, if males are completely resistant, they are guaranteed to increase in frequency over a disease-free baseline with higher β.

Both females and males become infected

Once males become infected, too, the relative resistance (θ) and the added virulence inflicted on male survival (ρ) must now both matter. Male frequency is not guaranteed to increase with transmission rate, β, now, but disease will likely increase male frequency from a disease-free baseline. To illustrate, consider this system (Table S1):

$$df/dt = s\,R - d\,f - \beta\,f \quad \text{(S10.a)}$$

$$dm/dt = (1\text{-}s)\,R - \gamma\,d\,m - \theta\,\beta\,m \quad \text{(S10.b)}$$

$$df_I/dt = \beta\,f - v\,d\,f_I \quad \text{(S10.c)}$$

$$dm_I/dt = \theta\,\beta\,m - \rho\,v\,(\gamma\,d)\,m_I \quad \text{(S10.d)}$$

where now transmission rate of females (β) can be greater than that of males ($\theta\,\beta$, assuming $0 < \theta < 1$ in equ. S4.a; males become more resistant with lower θ). Males also could have higher ($\gamma > 1$) or lower ($\gamma < 1$) background mortality rate than females without disease (where $\gamma = d_m / d_f$, and d is the background rate of females, without the 'f' subscript; equ. S4.b). Infection increases the mortality rate of infected females (f_I) to $v\,d$, assuming the virulence multiplier $v > 1$. Finally, this virulence on survival for males may differ from females (if $\rho \neq 1$; death rate of infected males is ($\rho\,v$) ($\gamma\,d$), which is their background death rate, $\gamma\,d$, times their virulence multiplier, $\rho\,v$, where we assume $\rho\,v \geq 1$ even if ρ might be less than one).

Equal background mortality and equal virulence case

Progress is best made with some simplifying scenarios. Imagine that males have the same background death rate as females ($\gamma = 1$) and suffer the same increase in mortality due to infection ($\rho = 1$). Now, the equilibrium becomes:

$$f^* = \frac{sR}{\beta+d},\ m^* = \frac{(1-s)R}{\theta\beta+d},\ f_I{}^* = \frac{\beta f^*}{vd},\ \text{and}\ m_I{}^* = \frac{\theta\beta m^*}{vd}. \quad \text{(S11)}$$

The proportion of infected females still exceeds that of males as long as males are more resistant, i.e., $p_{f,I}{}^* > p_{m,I}{}^*$ if $\theta < 1$, where:

$$p^*_{f,I} = \frac{\beta}{\beta+vd} \quad \text{and}\ p^*_{m,I} = \frac{\theta\beta}{\theta\beta+vd} \quad \text{(S12)}$$

but both quantities increase with transmission rate (i.e. $dp_{f,I}{}^*/d\beta > 0$ and $dp_{m,I}{}^*/d\beta > 0$). The expression for proportion males, $p_m{}^*$, becomes more complicated. However, it increases with transmission rate (i.e., epidemic size, $dp_m{}^*/d\beta > 0$) as long as:

$$\theta < v(d/\beta)^2 \quad \text{(S13)}$$

Assuming males are more resistant ($\theta < 1$), this condition is more readily met with much stronger resistance of males ($\theta << 1$), at higher added virulence on mortality (v), but at lower transmission rate for females (β).

Equal background mortality ($\gamma = 1$) but unequal virulence ($\rho \neq 1$) case

If males suffer higher mortality from infection than females ($\rho > 1$), the frequency of males could go up or down with infection prevalence. The analytical expressions for these conditions become less transparent than those above, but one can readily visualize them given parameters chosen (Fig. S1). But before proceeding, we should first note that once the virulence multiplier can change ($\rho \neq 1$), proportion of infected females may not exceed that of males, even when males are more resistant ($\theta < 1$), since now:

$$p^*_{f,I} = \frac{\beta}{\beta+vd} \quad \text{and} \quad p^*_{m,I} = \frac{\theta\beta}{\theta\beta+\rho vd}. \quad \text{(S14)}$$

Female frequency exceeds male frequency of infection, $p_{f,I}{}^* > p_{m,I}{}^*$, as long as $\theta < \rho$. This condition means that if males are more resistant ($\theta < 1$) but also suffer lower virulence once infected ($\rho < 1$), it is possible for infection prevalence in males to exceed those in females. In those cases, females simply pass through the infection stage too quickly (with turnover rate $\beta + vd$) to accumulate much, relative to infected males (which have turnover rate $\theta\beta + \rho vd$). On the

other hand, if males are more resistant ($\theta < 1$) but suffer high virulence ($\rho > 1$), prevalence of female infection is guaranteed to exceed that of males. Note also that, if males are not resistant ($\theta = 1$) but males suffer higher virulence from infection ($\rho>1$), prevalence of infection in females can exceed that in males – this point ultimately speaks to one interpretation offered concerning results presented (involving two tests of male resistance [Fig. 5B] vs. [Fig. 5C and 6]).

As discussed above, there are two different ways to think about the male resistance mechanism. The first version proves most stringent: when does male frequency increase with epidemic size, i.e., when is $dp_m^*/d\beta > 0$? Does it always increase with epidemic size? To answer version one, realize that over a gradient of (now female) transmission rate (β), infection prevalence at the entire population level always increases (with biologically resistant parameters). However, the proportion of males, p_m^* can show a hump shape pattern with transmission rate (hence epidemic size). Imagine that males are somewhat resistant ($\theta = 0.5$; Fig. S1*a*) or highly resistant ($\theta = 0.2$; Fig. S1*b*). Male frequency starts at 0.3 without disease (since $s = 0.7$ here at zero transmission rate, $\beta = 0$, and equivalent background mortality rates, $\gamma = 1$ so baseline male frequency is 1-s). Then, consider different values of relative virulence of infection on male mortality ρ. This ρ parameter can range from a 'super male' scenario where more resistant males ($\theta < 1$) also suffer less virulence on mortality ($\rho= 0.75$), to equivalent virulence on mortality ($\rho = 1$), to increasingly higher virulence suffered by males ($\rho > 1$, indicating a resistance-virulence tradeoff). (These relative virulence levels, ρ, are the contours on Fig. S2). The proportion of males tends to first increase, then decrease at some transmission rate, β (epidemic size); that peak occurs at lower β with increasing relative virulence on males, ρ. The shapes of this these curves depend some on the parameters (here: $R = 0.1$, $d = 0.03$, $s = 0.7$, $v = 2$; $\theta = 0.5$ in panel A, but higher male resistance, $\theta = 0.2$, in panel B). However, the point is clear. Even when males resist infection more than females ($\theta < 1$), frequency of males during epidemics does not necessarily increase with β, a proxy for epidemic size. Male frequency is more likely to increase with infection prevalence if males are strongly resistant (higher θ; panel B) and/or and suffer lower mortality when sick (smaller ρ) than females.

On the other hand, if males die quickly once they get sick (e.g., $\rho = 2$, or mortality is twice as high for males), male frequency can drop with increasing β. In this scenario, males cycle out of the population quickly during epidemics due to infection, lowering their frequency. Thus, the prediction that male frequency always increases with increasing epidemic size has some bounds (see Fig. S2*a,b* for combinations of transmission rate, β, and relative virulence, ρ, below which males increase in frequency with β, i.e., $dp_m^* / d\beta > 0$). If males are more resistant ($\theta < 1$) but suffer even more from virulence than females (i.e., $\rho > 1$), they can only increase in frequency at lower β (smaller epidemics).

However, these conditions are too stringent for a second version of the male resistance mechanism. Consider this alternative: under what conditions would an epidemic of any size increase male frequency from disease-free conditions (a mathematical analogue to the experiment in Fig. 3)? Male frequency without disease, assuming equal mortality rates ($d = d_f =$

d_m, so $\gamma = 1$), is $1 - s$. During epidemics, male frequency exceeds this background level when:

$$\rho < \frac{\theta(\beta+d)}{\theta(\beta+vd)-d(v-1)} \quad \text{(S15)}$$

This condition makes it much easier to get an increase in males (Appendix S1, Figs. S1, S2*c,d*). Now, if males are more resistant ($\theta > 1$), they can also suffer more from infection than females ($\rho > 1$) and still increase from a disease-free baseline. Therefore, even large epidemics will likely catalyze an increase in male frequency over the disease-free baseline (i.e., keeping male frequency in the white area in Fig. S1 and below the contours in Fig. S2.*c.d*, and ensuring equ. S15 is met), so as long as males do not suffer too much when infected (putting male frequency into the grey area of Fig. S1, or above the contours in Fig. S2.*c,d*).

Unequal background mortality: $d_m > d_f$, so $\gamma > 1$, but equal virulence ($\rho = 1$)

It turns out that differing background mortality rates between the sexes do not matter much. Imagine that males die at a higher background rate, i.e., $d_m > d_f$, so $\gamma > 1$. Now, proportion males infected, $p_{m,I}^*$, and proportion females infected, $p_{f,I}^*$, are both:

$$p_{f,I}^* = \frac{\beta}{\beta+vd} \quad \text{and } p_{m,I}^* = \frac{\theta\beta}{\theta\beta+\rho\gamma vd} \quad \text{(S16)}$$

(where the proportion of females infected hasn't changed from equ. S10, but the proportion of males has dropped if $\gamma > 1$). Additionally, the frequency of male infections is lower than that of females, $p_{m,I}^* < p_{f,I}^*$, if $\gamma < \theta / \rho$. While not guaranteed, this condition states that resistant males ($\theta < 1$) cannot suffer too high a background mortality (γ), especially if males experience higher virulence than females ($\rho>1$). Still, with higher male resistance, it remains likely that $p_{m,I}^* < p_{f,I}^*$.

In this scenario, the less restrictive version of the male resistance mechanism is readily met. Without disease, male frequency changes from 1- *s* to:

$$p_m^* = \frac{1-s}{1+s(\gamma-1)} \quad \text{(S17)}$$

(as noted already in equ. S3), which decreases as γ increases. Males increase from this baseline frequency (equ. S17) as long as:

$$\gamma > \frac{\theta(\beta+d)(\rho-1)}{\rho d(v-1)} \quad \text{(S18)}$$

which simplifies to $\gamma > \theta$ when males and females experience the same proportional, virulent increase in mortality from infection ($\rho = 1$). In that case, resistant males ($\theta < 1$) suffering higher background mortality rate ($\gamma > 1$) are sure to increase from baseline. If males survive relatively better than females when infected ($\rho < 1$), males suffering higher background mortality are likely to increase in frequency with any disease over baseline, unless they survive too well (not shown).

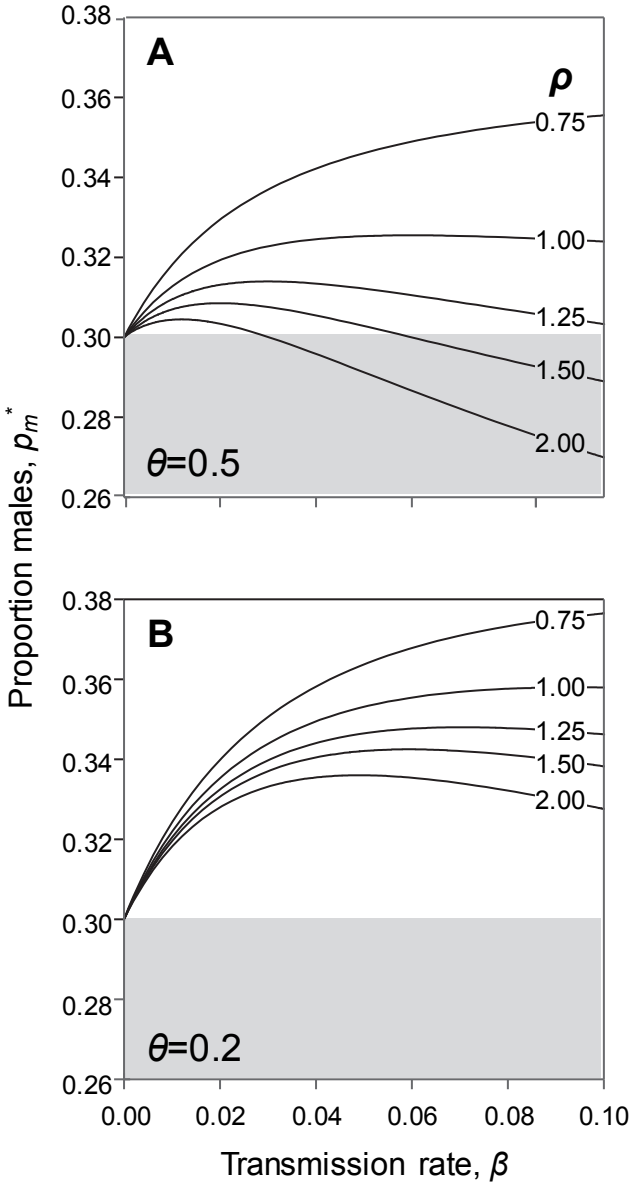

Figure S1. Proportion males over a gradient of (female) transmission rate, when background death rates are equivalent between males and females (γ=1). Contours denote relative virulence of infection to males, ρ, from less harm on mortality experienced by females (ρ = 0.75) to twice the harm to mortality (ρ = 2.0), compared to females. (A) Somewhat resistant males (θ = 0.5, i.e., females have twice the transmission rate as males) to (B) highly resistant males (θ = 0.2). Grey boxes denote scenarios in which male frequency drops below baseline, disease free levels (1-s). Other parameters: R = 0.2, d = 0.03, s = 0.7.

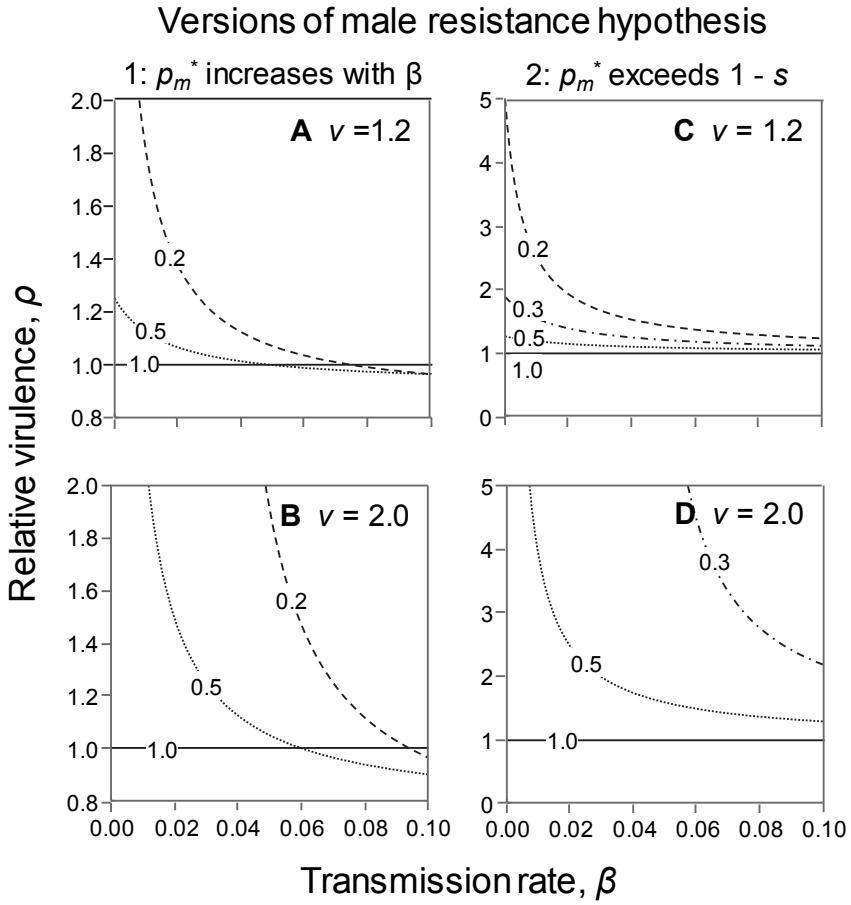

Figure S2. Conditions where male frequency increases with transmission, left column, or increases over disease-free baseline, right column. (A) – (B): For a given value of female transmission rate, β, male frequency, p_m^*, increases with β, i.e., $dp_m^*/d\beta > 0$ for values of relative virulence of infection on males, ρ, below the line given female virulence multiplier (A) $v = 1.2$ (i.e., the parasite is not highly virulent) and (B) $v = 2.0$ (i.e. the parasite doubles female mortality rate). (C) – (D): For values of ρ below the lines, male frequency exceeds background infection levels, $1 - s$ (assuming that males and females have the same background mortality here, $\gamma = 1$). (C) Lower ($v = 1.2$) and (D) higher ($v = 2.0$) female virulence multipliers are shown. The contours denote different levels of male resistance, where lower θ drops transmission rate of males ($\theta\beta$) below that of females, β. Other parameters: $R = 0.2$, $d = 0.03$, $s = 0.7$.

Table S1. List of state variables and parameters in the model of male frequency and disease.

Symbol	Description/Meaning
f	Female density, uninfected
f_I	Female density, infected
m	Male density, uninfected
m_I	Male density, infected
t	Time
d	Background death rate (d_f for females, d_m for males)
R	Reproductive flux (rate of reproduction)
s	Fraction of reproductive flux allocated to females
v	Virulence multiplier on females ($v > 1$: infection increases death rate of infected, $v\,d$)
β	Force of infection, i.e., transmission rate; becomes female transmission rate
γ	Relative background death, males/females ($\gamma = d_m / d_f$)
θ	Transmission multiplier of males – $\theta < 1$ indicates male resistance
ρ	Virulence on males relative to females, i.e., $\rho < 1$ means males survive better than females, $\rho > 1$ means males suffer higher virulence than females
$p_{f,I}^*$	Proportion of female population that is infected (at equilibrium)
$p_{m,I}^*$	Proportion of male population that is infected (at equilibrium)
p_I^*	Proportion of total host population that is infected (at equilibrium)
p_m^*	Proportion of total host population that is male (at equilibrium)