Intermediate levels of asymptomaticit transmission can lead to the worst population-level outcomes

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SARS-CoV-2 has had devastating effects at the population level. However, many individuals experienced mild cases, making it harder to estimate the magnitude of spread and fatality rate [1]. The ratio of fatalities to documented cases (the case-fatality rate, CFR) is typically between 1%–4%, varying across population because of testing patterns, treatment practice, case definitions, and other factors [2, 3, 4]. But many infections were never documented; the ratio of fatalities to total infections (the infection fatality rate, IFR) has been estimated to be closer to 0.5%–1% for pre-vaccinated populations whose demographics are similar to that of the United States [5]. This means that more than 99% of individuals infected with COVID-19 will survive. Moreover, at least half of the infections are sufficiently mild that they could be classified as subclinical or even asymptomatic.

Individuals infected asymptomatically with SARS-CoV-2 can still transmit to others. This means that the presence of asymptomatic infections may have countervailing effects at the population level. On one hand, an asymptomatic infection means that the individual infected avoids hospitalization and fatality. On the other hand, asymptomatic infections are less likely to be detected [6], meaning that they are less likely to take precautions and more likely to infect others. Altogether, the prevalence of asymptomatic infections can paradoxically make population-level outcomes worse than if SARS-CoV-2 was more dangerous at the individual level.

To explore this idea, we propose a simple epidemic model, in which infected individuals can be asymptomatically or symptomatically infected, with probabilities p and $1-p$, respectively (Fig. 1). Asymptomatically infected individuals always recover, whereas a fraction f of symptomatically infected individuals die. Asymptomatically and symptomatically infected individuals can also have different infection characteristics, including their transmission rates (β_a and β_s) and recovery rates

(γ_a and γ_s). Our key assumption is that symptomatically infected individuals take greater precautions than do asymptomatically infected individuals (e.g., via reducing contacts or increased mask-wearing) and therefore reduce their transmission rate by a fraction δ; we note that the parameter δ may also capture intervention measures that target symptomatically infected individuals, such as symptom-based isolation. For our main simulations, we assume that asymptomatically infected individuals have a lower reproduction number—this is modeled by assuming lower transmission rates for asymptomatically infected individuals ($\beta_a = 0.75\beta_s$) and equal recovery rates ($\gamma_a = \gamma_s$). We assume that asymptomatic individuals do not die, and evaluate the effects on population-level mortality of changing the asymptomatic proportion p while holding the fatality rate for *symptomatic* cases, f, constant (the IFR $(1-p)f$ thus decreases as p increases).

Fig. 1 shows simulated epidemic outcomes using parameters similar to those of the originating strain of SARS-CoV-2, without any mitigation other than that individuals who are symptomatic reduce their transmission rate by δ. In the absence of the behavioral effect ($\delta = 0$), the final size decreases with the asymptomatic proportion p because more symptomatic infections leads to a higher basic reproduction number:

$$\mathcal{R}_0 = (1-p)(1-\delta)\mathcal{R}_s + p\mathcal{R}_a, \tag{1}$$

where $\mathcal{R}_s = \beta_s/\gamma_s$ and $\mathcal{R}_a = \beta_a/\gamma_a$ represent the reproduction numbers of asymptomatic and symptomatic individuals. This relationship changes as δ increases. In particular, when $\delta > 1 - \mathcal{R}_a/\mathcal{R}_s$ (in this case, $\delta > 0.25$), the basic reproduction number (and thus epidemic size) increases with p because the effective symptomatic transmission rate (including behavioral response) is less than that the asymptomatic rate. For δ in this range, we can find a critical level of asymptomatic proportion, p_c:

$$p_c = \frac{1-(1-\delta)\mathcal{R}_s}{\mathcal{R}_a - (1-\delta)\mathcal{R}_s} \tag{2}$$

such that $p > p_c$ is required for an outbreak.

When behavioral protection is high, the effect of asymptomatic proportion on fatalities shows countervailing effects of individual-level protection and population-level risk. For high values of δ, the peak fatality occurs at intermediate levels of asymptomatic spread: although less individuals die per infection for higher values of p, the increase in total infections also leads to an increase in total fatalities. In contrast, when δ is small enough such that $\mathcal{R}_s \geq \mathcal{R}_a$, then total fatalities decrease with p because because both the number of infections and the IFR ($(1-p)f$) decrease with increasing p.

High values of δ required for the nonlinear effects of asymptomaticity on deaths may seem unrealistic—in practice, δ cannot be greater than the amount of post-symptomatic transmission. While several studies have estimated the proportion of pre-symptomatic transmission to be around 30%–60% for the SARS-CoV-2 wildtype strain, many of them were likely subject to intervention and behavioral effects already as they were conducted after SARS-CoV-2 awareness became widespread [7]. Instead,

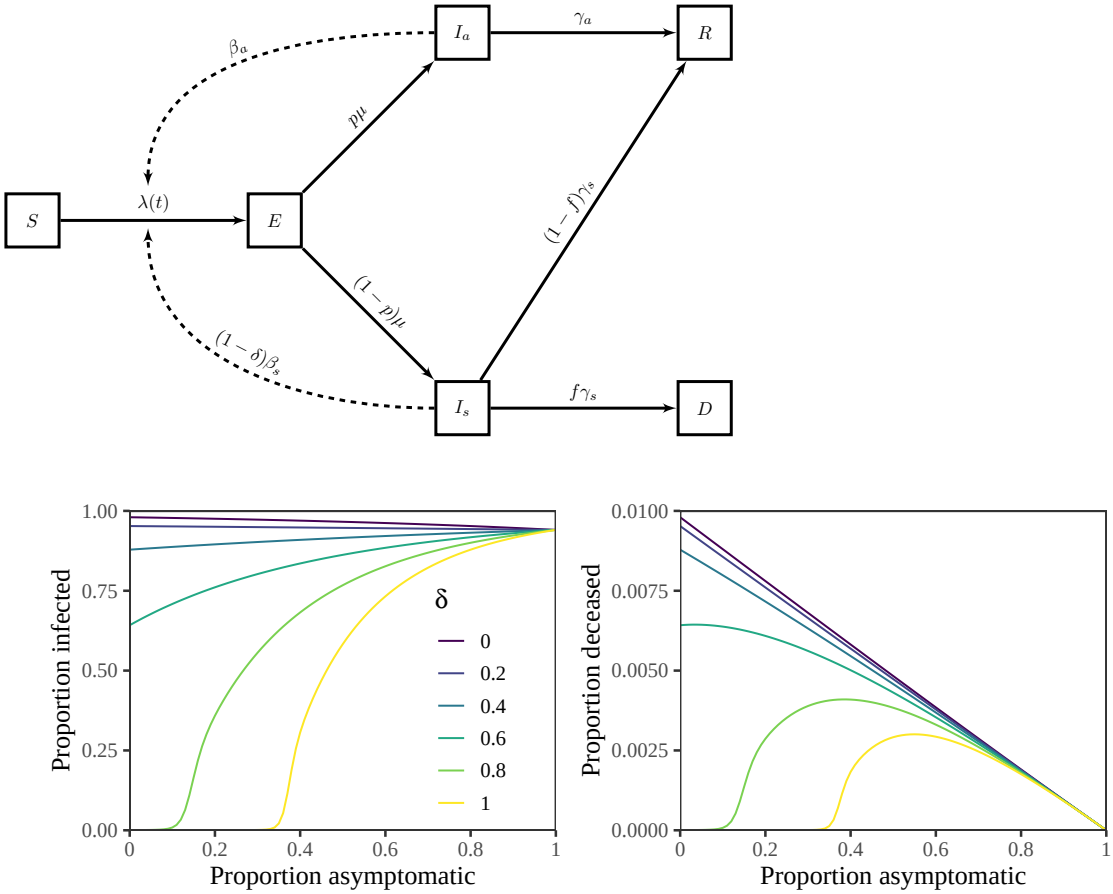

Figure 1: **Schematic diagram and simulations of a model with asymptomatic transmission and symptom-responsive transmission reduction.** (Top) S represents susceptible individuals; E represents exposed individuals; I_a represents asymptomatically infected individuals; I_s represents symptomatically infected individuals; R represents recovered individuals; and D represents deceased individuals. See Methods for model details. (Bottom left) Total infections as a function of the proportion of asymptomatic infections p across a wide range scenarios for δ. (Bottom right) Total deaths as a function of the proportion of asymptomatic infections p across a wide range scenarios for δ. We simulate the model for 365 days, assuming $\beta_s = 0.8$/day, $\beta_a = 0.75\beta_s$, $\mu = 0.5$/day, $\gamma_s = \gamma_a = 0.2$/day, and $f = 0.01$. We assume that 10^{-4} proportion of individuals are initially infected.

[8] recently estimated that the proportion of pre-symptomatic transmission can be as low as 20% (95%CI: 6%–32%) during the first few weeks of the pandemic when the pandemic-awareness and intervention measures were minimal. There are two implications for the discrepancy in the estimates of the proportion of presymptomatic transmission—first, a low proportion of presymptomatic transmission suggests that high δ values are feasible (although not necessarily likely) during the initial pandemic

phase; and second, intermediate levels of behavioral effects ($\delta > 0$) would have been already present early in the pandemic to reduce the proportion of presymptomatic transmission from 20% to 60%.

We therefore consider two additional of mathematical models with increasing complexities to answer a more general question: does intermediate amount of subclinical (including both asymptomatic and presymptomatic) transmission lead to a peak in fatalities? First, we analyze a modelin which there is a fraction θ of transmission occurs presymptomatically and all individuals eventually transition to a symptomatic phase (Supplementary Figure S1). When the reproduction number is fixed, increasing the proportion of presymptomatic transmission θ causes larger outbreaks, and therefore more deaths, in the presence of symptom-responsive transmission reduction ($\delta > 0$). However, standard compartmental models implicitly assume that the fatality rate f is independent of the amount of presymptomatic transmission—in the extreme case where all transmission happens presymptomatically, we assume that the case fatality rate is far lower than in the limit when none of the transmission is in the presymptomatic phase. [**JD:** *We need a bit more detail here. I have no idea what proportion of COVID deaths are post-viral. Maybe I'm COVID-ignorant, but I want more info: many flu deaths are post-viral, and it's not super-clear how much of a role viral replication (or escape from deep lungs?) plays in fatality.*] We therefore assume a tradeoff between the amount of presymptomatic transmission θ and the fatality rate f: $f(\theta) = f_0(1 - \theta^a)$, which monotonically decreases from f_0 to 0; the nonlinearity of the tradeoff is characterized by the power law exponent a. In the simple case where the fatality rate decreases linearly with θ, the relationship between the amount of presymptomatic transmission θ and total fatalities is equivalent to that between the amount of asymptomatic transmission and total fatalities in the original model (Fig. 1). As we increase the exponent a, we obtain a nonlinear tradeoff curve where fatality rate f remains roughly constant for low to intermediate values of θ and suddenly decreases to 0 as θ approaches 1; in these cases, peak fatalities occur at intermediate levels of presymptomatic transmission for even lower values of $\delta = 0.6$, which now represents reduction in transmission after symptom onset.

We then extend our model to consider the effects of generalized *subclinical* transmission, which includes both presymptomatic and asymptomatic transmission (Supplementary Figure S2). In particular, we fix the reproduction number of symptomatic individuals and calculate the proportion of fatalities as a function of the proportion of total subclinical transmission and the proportion of subclinical transmission that is caused by presymptomatic transmission. This generalized model extends the models proposed in Fig. 1, where all subclinical transmission is caused by asymptomatic transmission, and the model shown in Supplementary Figure S1 where all subclinical transmission is caused by presymptomatic transmission. Using the generalized subclinical transmission model, we find a wide variety of scenarios for which peak fatalities occur at intermediate levels of subclinical transmission in the presence of moderate to strong behavioral effects, $\delta > 0.6$ (Supplementary Figure S2); this pattern is robust even to the absence of a tradeoff between the amount

of presymptomatic transmission and the fatality rate. One exception is the case discussed earlier in which all subclinical transmission is caused by presymptomatic transmission. Hereafter, we focus on asymptomatic infections for simplicity, but our conclusions have implications for the more general case of subclinical transmission.

We now apply our framework to understand the impact of immunity on total fatalities at the population scale by dividing the population into two groups: immunologically naive and protected. The dynamics of immunologically naive individuals are equivalent to our original model (Fig. 1). The dynamics of protected individuals include three additional parameters, which characterize the amount of protection against infection ϵ_i, symptoms ϵ_s, and deaths ϵ_d (Fig. 2). For simplicity, we assume that the population is exactly split in half (50% naive and 50% protected) and mixes homogeneously. We also do not consider the separate effect of immunity on transmission (beyond the effect on infection). In other words, we assume that asymptomatic infections in protected and unprotected people have the same reproduction numbers (and likewise for the symptomatic infections). In practice, both asymptomatic and symptomatic infections in protected people are less likey to transmit than their unprotected counterparts: asymptomatic infections in protected people may indicate limited viral replication or even immune boosting, in which case an exposed individual may successfully fight off the pathogen early in infection before it can be transmitted; and symptomatic infections in protected people may reflect a strong immune response (rather than high viral laod), in which case symptomaticity can be a poor proxy for transmission. We assume a relatively strong behavioral effect $\delta = 0.8$ for illustration. [**SWP:** *JD: see if you like what I did in this P, esp in terms of boosting.*]

The impact of protection against infection ϵ_i is analogous to changing $\mathcal{R}_0$ in the original model: as immunity provides stronger protection against infection (higher ϵ_i), the number of deaths decreases and a higher asymptomatic fraction p is required for the infection to spread (Fig. 2A). We note that protection against infection scales the fatality curve nonlinearly, reflecting the nonlinear relationship between $\mathcal{R}_0$ and the final size. The impact of protection against symptoms ϵ_s is equivalent to changing the asymptomatic fraction p for the protected population: the peaks of the fatality curves move to lower values of p as we increase the degree of protection ϵ_s (Fig. 2B). Therefore, for low values of p, protection against symptoms can increase the total number of fatalities at the population level by increasing the proportion (and number) of asymptomatically infected individuals, who can readily transmit infections to other individuals. This also means that the critical level of asymptomatic proportion decreases, allowing more dangerous infections (with lower p) to invade, which would not have been able to spread in an otherwise immunologically naive population. We note that the equivalence between protection against symptoms ϵ_s and fraction asymptomatic p relies on our assumption that immunity does not provide protection against transmission. Protection against deaths ϵ_d directly modulates the fatality rate for symptomatic cases and therefore linearly scales the fatality curves (Fig. 2C).

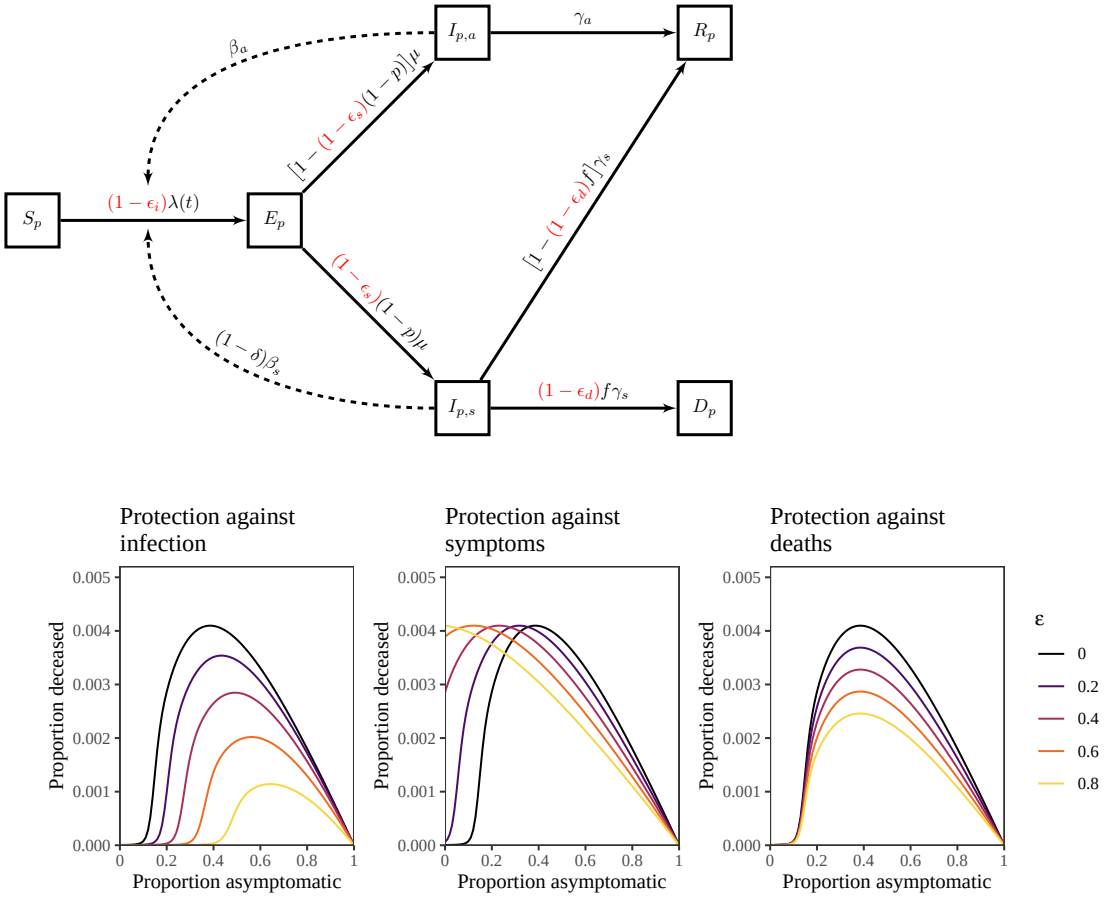

Figure 2: **Schematic diagram and simulations of a model with symptom-responsive transmission reduction and immunity.** (Top) The subscript p represents protected individuals. Immunity may provide protection against infection, symptoms, or deaths. The dynamics of immunologically naive individuals are described in Fig. 1. (Bottom) Total deaths as a function of the proportion of asymptomatic infections p across a wide range scenarios for protection against infection ϵ_i, symptoms ϵ_s, and deaths ϵ_d. We simulate the model for 365 days, assuming $\beta_s = 4/5/\text{day}$, $\beta_a = 0.75\beta_s$, $\mu = 1/2/\text{day}$, $\gamma_s = \gamma_a = 1/5/\text{day}$, $f = 0.01$, and $\delta = 0.8$. We assume that 10^{-4} proportion of individuals are initially infected.

Finally, we use our framework to understand the impact of behavioral effects on invading variants (Fig. 3). In doing so, we first simulate the dynamics of a wildtype variant for 1 year using our base model (Fig. 1). We then simulate a new variant invading a partially immune population using our extended model (Fig. 2), where the immunity is solely derived from natural infections caused by the wildtype variant. We consider two types of variants (which are simulated separately): one with the same severity p (variant 1, orange) and a milder one with higher p (variant 2, purple).

First, we consider a scenario in which immunity only provides protection against

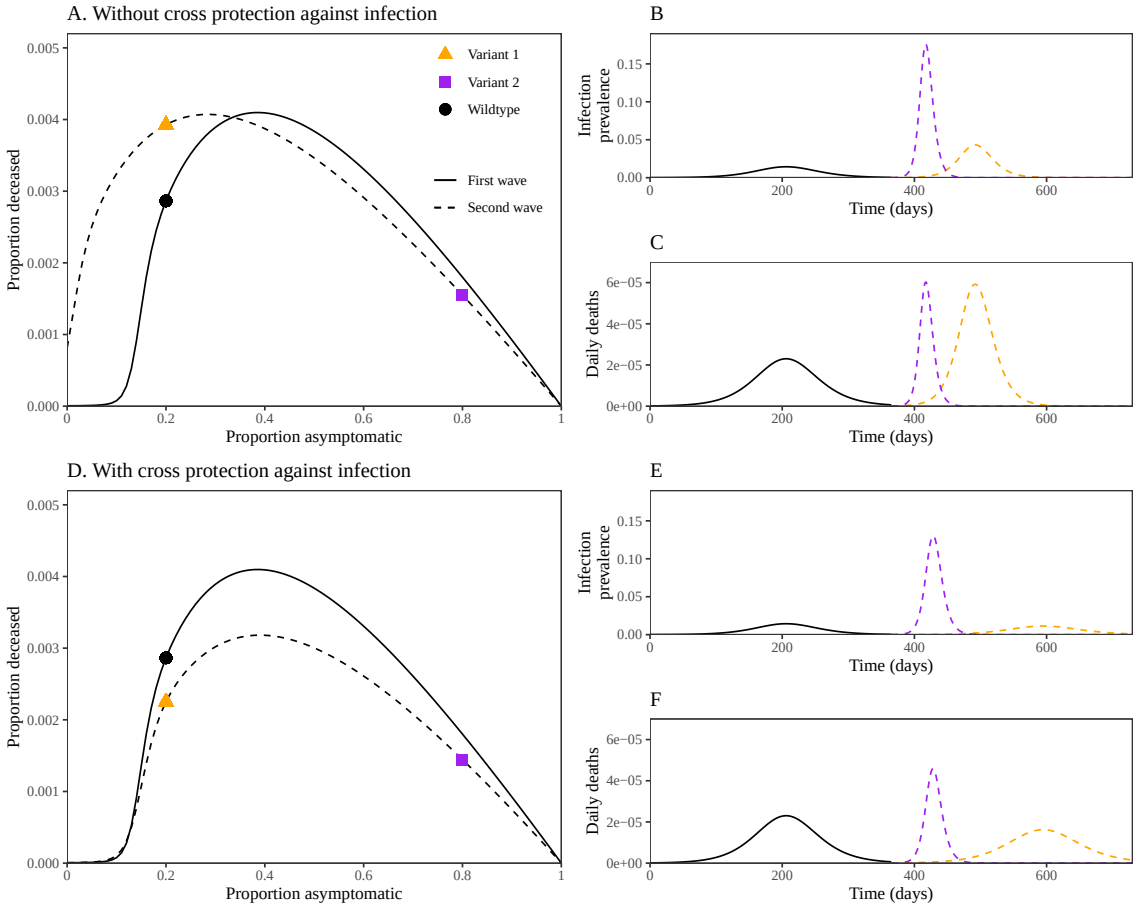

Figure 3: **Dynamics of invading variants under symptom-responsive transmission reduction and immunity.** (A, D) Asymptomaticity–fatality curves for the first (solid lines) and second waves (dashed lines). Points represent specific scenarios we assume for the first and second waves. Fatality curves for the first wave are calculated by simulating an epidemic for 1 year using parameters from Fig. 1 with $\delta = 0.8$. Fatality curves for the second wave are calculated by first simulating the first wave assuming $p = 0.2$ for 1 year to calculate the proportion immune and then simulating the extended model presented in Fig. 2 for two different values of p as shown. (B, E) Dynamics of infection prevalence for the wildtype variant (black, solid line) and two possible invading variants (colored, dashed line). (C, F) Dynamics of daily deaths for the wildtype variant (black, solid line) and two possible invading variants (colored, dashed line).

symptoms, $\epsilon_s = 0.4$ (Fig. 3A–C). In this case, protection against symptoms allows new variants to spread faster, resulting in larger outbreaks (Fig. 3B). Although the milder (purple) variant exhibits a faster epidemic growth rate and reaches a higher peak (Fig. 3B), it reaches similar peak fatality as the more severe (orange) variant (Fig. 3C). The asymptomaticity–fatality curve provides additional insight (Fig. 3A):

even though a milder, invading variant (purple square) gives higher peak fatality than the original, wildtype variant (black circle), it leads to lower fatalities overall because deaths are concentrated over a shorter period of time. In general, when δ is large, invading variants with similar asymptomaticity p will spread better and result in worse population-level outcomes if immunity (either from vaccination or natural infection) provides protection against symptoms.

Next, we consider a more realistic scenario in which immunity provides protection against both symptoms, $\epsilon_s = 0.4$, and infection, $\epsilon_i = 0.4$ (Fig. 3D–F). In this case, cross protection against infection has a large effect on the more severe (orange) variant, causing its peak infection prevalence (Fig. 3E) and fatality (Fig. 3F) to be lower than that of the original, wildtype variant. Across a wide range of asymptomatic proportion p, we find that this immunity profile is sufficient to prevent worse outcomes at the population level.

In summary, using a simplified model we have shown that asymptomatic infections can represent a double-edged sword by providing a better outcome for some individuals while facilitating onward transmission that leads to a worse outcome for the population as a whole. Extending our framework further shows that the immunity profile plays a critical role in determining the dynamics of future variants: while protection against symptoms protects health at the individual level, it can lead to more infections, and potentially more deaths, at the population level.

Our simulations of invading variants resemble the dynamics of the SARS-CoV-2 Omicron variant. Despite moderate levels of vaccine effectiveness against symptomatic and severe cases caused by the Omicron variant, especially after booster shots [9], both vaccine- and infection-derived immunity provided limited protection against infections [10]. This immune evasion helped the Omicron variant to cause more infections in South Africa than previous variants [11]; even though the Omicron variant is probably milder than XXX [12, 13], the number of hospitalizations and deaths caused by the Omicron variant was high [14, 15, 16].

There are several limitations to our analysis. First of all, behavioral and intervention effects must be large in order for the fatality to peak at intermediate levels of asymptomaticity. While we are able to generalize our results using more realistic models, incorporating both presymptomatic and asymptomatic transmission, the transmission rate needs to be reduced by at least 60% after symptom onset for us to see the nonlinear effects of subclinical transmission on population-level outcomes. [**SWP:** *what are some other limitations we should address?*] [**JD:** *Something about estimating protection against different endpoints. We should also highlight the importance of doing this estimation.*]

SARS-CoV-2 has proven hard to control in large part because transmission is often decoupled from symptoms. Although mitigation efforts have often prioritized responding to symptoms—including symptom-based testing, fever checks, mask-wearing for infectious individuals—a different approach that strives to reduce the chance of asymptomatic transmission while increasing treatment of symptomatically infected individuals could both reduce infection risk at the source and in the event

that individuals are at risk for severe outcomes. As more variants continue to emerge, updating vaccines to prevent infections, and not just diseases, will be critical to controlling the course of the pandemic. [**JD:** *This is complicated. Maybe regular waves of mild SC2 are a good way to control morbidity in the medium term. There is also an argument to make about symptom-focused responses and evolution toward mildness.*]

Supplementary Materials

Methods

Models without immunity

First, we consider a simple, compartmental model with asymptomatic and symptomatic infections in a homogeneously mixing population. The model dynamics are as follows:

$$\dot{S} = -\beta_a S I_a - (1-\delta)\beta_s S I_s \tag{3}$$
$$\dot{E} = \beta_a S I_a + (1-\delta)\beta_s S I_s - \mu E \tag{4}$$
$$\dot{I}_a = p\mu E - \gamma_a I_a \tag{5}$$
$$\dot{I}_s = (1-p)\mu E - \gamma_s I_s \tag{6}$$
$$\dot{R} = \gamma_a I_a + (1-f)\gamma_s I_s \tag{7}$$
$$\dot{D} = f\gamma_s I_s \tag{8}$$

where the transmission rate β and recovery rate γ can be potentially differ between asymptomatic and symptomatically infected individuals. Here, δ denotes the reduction in transmissibility due to responsive measures taken by symptomatically infected individuals. Throughout the paper, we use parameters that are broadly consistent with the dynamics of the originating strain of SARS-CoV-2: $\beta_s = 0.8/\text{day}$, $\beta_a = 0.75\beta_s$, $1/\mu = 2\,\text{days}$, $1/\gamma_s = 1/\gamma_a = 5\,\text{days}$, and $f = 0.01$.

We then consider a model with presymptomatic transmission (and without asymptomatic transmission), where all infected individuals eventually develop symptoms:

$$\dot{S} = -\beta_a S I_a - (1-\delta)\beta_s S I_s \tag{9}$$
$$\dot{E} = \beta_a S I_a + (1-\delta)\beta_s S I_s - \mu E \tag{10}$$
$$\dot{I}_p = \mu E - \sigma I_p \tag{11}$$
$$\dot{I}_s = \sigma I_p - \gamma_s I_s \tag{12}$$
$$\dot{R} = (1-f)\gamma_s I_s \tag{13}$$
$$\dot{D} = f\gamma_s I_s \tag{14}$$

For this model, the presymptomatic $\mathcal{R}_p$ and symptomatic $\mathcal{R}_s$ reproduction numbers are given by $\mathcal{R}_p = \beta_p/\sigma$ and $\mathcal{R}_s = \beta_s/\gamma_s$ in the absence of the behavioral effect; and the basic reproduction number is equal to the sum of the two. Then, the intrinsic proportion of presymptomatic transmission is given by:

$$\theta = \frac{\mathcal{R}_p}{\mathcal{R}_p + \mathcal{R}_s}. \tag{15}$$

We assume there is a tradeoff between the proportion of presymptomatic transmission and fatality rate:

$$f(\theta) = f_0(1-\theta^a), \tag{16}$$

where $f_0 = 0.01$ represents the baseline fatality rate and the exponent a is varied between 1 and 5. Throughout simulations, we assume $\mathcal{R}_0 = 4$, $1/\sigma = 2$ days, and $1/\gamma_s = 3$ days. All other parameters are same as before.

Finally, we combine both models to include both presymptomatic and asymptomatic transmission:

$$\dot{S} = -\beta_a S I_a - (1-\delta)\beta_s S I_s \tag{17}$$

$$\dot{E} = \beta_a S I_a + (1-\delta)\beta_s S I_s - \mu E \tag{18}$$

$$\dot{I}_p = \mu E - \sigma I_p \tag{19}$$

$$\dot{I}_a = p\sigma I_p - \gamma_a I_a \tag{20}$$

$$\dot{I}_s = (1-p)\sigma I_p - \gamma_s I_s \tag{21}$$

$$\dot{R} = \gamma_a I_a + (1-f)\gamma_s I_s \tag{22}$$

$$\dot{D} = f\gamma_s I_s \tag{23}$$

For this model, the reproduction number of individuals who will eventually develop symptoms is equal to: $\mathcal{R}_p + \mathcal{R}_s$; similarly, the reproduction number of individuals who remain asymptomatic is equal to: $\mathcal{R}_p + \mathcal{R}_a$. Since proportion p of all infections is asymptomatic, the basic reproduction number is given by the weighted average of these two reproduction numbers:

$$\mathcal{R}_0 = p(\mathcal{R}_p + \mathcal{R}_a) + (1-p)(\mathcal{R}_p + \mathcal{R}_s) = \mathcal{R}_p + p\mathcal{R}_a + (1-p)\mathcal{R}_s. \tag{24}$$

Then, the proportion of subclinical transmission ϕ is given by:

$$\phi = \frac{\mathcal{R}_p + p\mathcal{R}_a}{\mathcal{R}_0}. \tag{25}$$

For simulations of the combined model, we start by fixing the reproduction number of individuals who will eventually develop symptoms: $\mathcal{R}_{\text{symp}} = \mathcal{R}_p + \mathcal{R}_s = 4$. Consistent with previous assumptions, we also assume that asymptomatic reproduction number is lower than that of the symptomatic reproduction number: $\mathcal{R}_a = \rho\mathcal{R}_s$ where $\rho = 0.75$. Then, for a given value of the proportion of subclinical transmission ϕ and proportion of subclinical transmission caused by the presymptomatic transmission, $\eta = \mathcal{R}_p/(\mathcal{R}_p + p\mathcal{R}_a)$, we can solve for the transmission rate for each compartment β and the proportion asymptomatic p. More specifically:

$$\mathcal{R}_p = \frac{\mathcal{R}_{\text{symp}}}{1+y} \tag{26}$$

$$\mathcal{R}_s = \mathcal{R}_{\text{symp}} - \mathcal{R}_p \tag{27}$$

$$\mathcal{R}_a = \rho\mathcal{R}_s \tag{28}$$

$$p = \left(\frac{1}{\eta} - 1\right)\frac{\mathcal{R}_p}{\mathcal{R}_a}, \tag{29}$$

where $y = (1/\phi - 1)/\eta + (1/\eta - 1)/\rho$. All other parameters are same as before.

Model with immunity

We then model the spread of infection in a partially immune population. The model dynamics are as follows:

$$\dot{S} = -\lambda(t)S \tag{30}$$
$$\dot{E} = \lambda(t)S - \mu E \tag{31}$$
$$\dot{I}_a = p\mu E - \gamma_a I_a \tag{32}$$
$$\dot{I}_s = (1-p)\mu E - \gamma_s I_s \tag{33}$$
$$\dot{R} = \gamma_a I_a + (1-f)\gamma_s I_s \tag{34}$$
$$\dot{D} = f\gamma_s I_s \tag{35}$$
$$\dot{S}_p = -(1-\epsilon_i)\lambda(t)S_p \tag{36}$$
$$\dot{E}_p = (1-\epsilon_i)\lambda(t)S_p - \mu E_p \tag{37}$$
$$\dot{I}_{p,a} = (1-(1-\epsilon_s)(1-p))\mu E_p - \gamma_a I_{p,a} \tag{38}$$
$$\dot{I}_{p,s} = (1-\epsilon_s)(1-p)\mu E_p - \gamma_s I_{p,s} \tag{39}$$
$$\dot{R}_p = \gamma_a I_{p,a} + (1-(1-\epsilon_d)f)\gamma_s I_{p,s} \tag{40}$$
$$\dot{D}_p = (1-\epsilon_d)f\gamma_s I_{p,s} \tag{41}$$

where ϵ represents the degree of protection against infection, symptoms and death. The force of infection $\lambda(t)$ is given by:

$$\lambda(t) = \beta_a(I_a + I_{p,a}) + (1-\delta)\beta_s(I_s + I_{p,s}). \tag{42}$$

Here, subscripts p denote individuals who are immune and therefore are protected.

Supplementary Figures

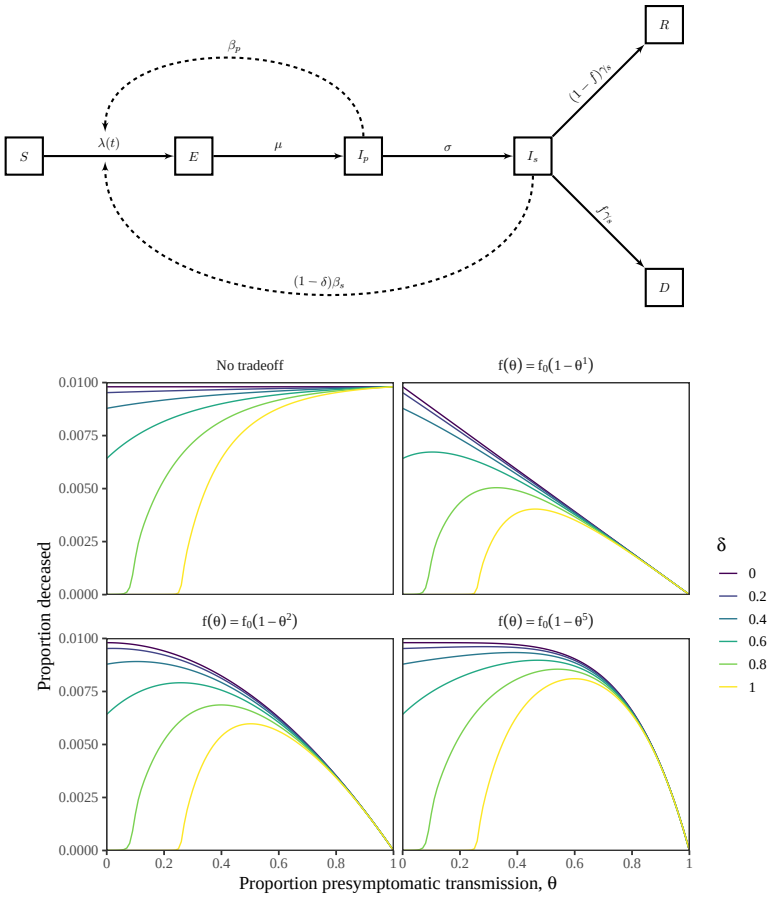

Figure S1: **Schematic diagram and simulations of a model with presymptomatic transmission and symptom-responsive transmission reduction.** (Top) S represents susceptible individuals; E represents exposed individuals; I_p represents presymptomatically infected individuals; I_s represents symptomatically infected individuals; R represents recovered individuals; and D represents deceased individuals. See Methods for model details. (Bottom) Total deaths as a function of the proportion of presymptomatic transmission θ across a wide range scenarios for δ and a tradeoff between the proportion of presymptomatic infections θ and fatality rates f.

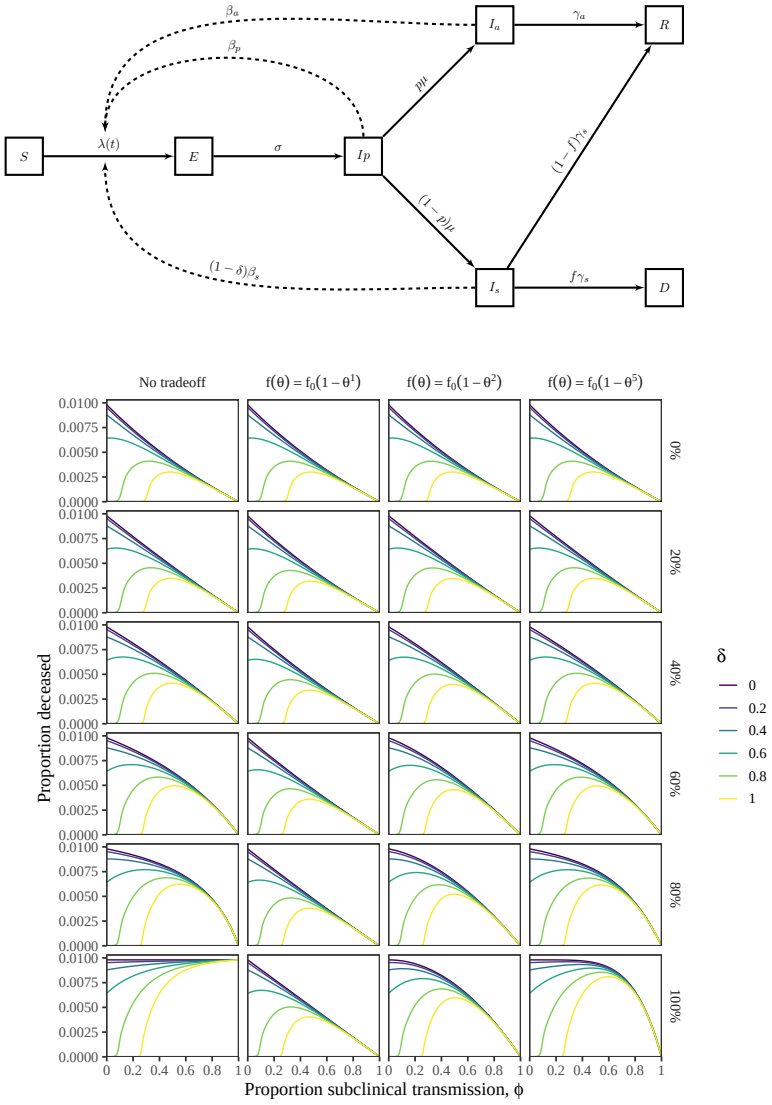

Figure S2: **Schematic diagram and simulations of a model with presymptomatic and asymptomatic transmission and symptom-responsive transmission reduction.** (Top) S represents susceptible individuals; E represents exposed individuals; I_p represents presymptomatically infected individuals; I_a represents symptomatically infected individuals; I_s represents symptomatically infected individuals; R represents recovered individuals; and D represents deceased individuals. See Methods for model details. (Bottom) Total deaths as a function of the proportion of subclinical transmission ϕ across a wide range scenarios for δ and a tradeoff between the proportion of presymptomatic infections θ and fatality rates f.

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