
Differences in time scales coupled with assortative mixing can lead to changes in the proportion of asymptomatic transmission and incidence over time

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Joshua S. Weitz: E-mail: jsweitz@gatech.edu [jdh: *The names and ordering can change if you prefer, but I think this is what we have talked about in the past. Of course, we should consult with Daniel and Jonathan.*]

Abstract

Asymptomatic transmission has made Covid-19 difficult to control and remains a key uncertain variable in the spread of the disease. The bulk of prior work has focused on estimating the prevalence of asymptomatic COVID-19 in a population at a certain time. However, the relative contribution of asymptomatic carriers with respect to transmission and incidence may change over time. Here, we find that if, (i) asymptomatic infections can transmit longer than symptomatic infections, and (ii) they are more likely to generate asymptomatic infections, then the proportion of asymptomatic incidence can increase as total new infections decrease. We also show find that differences in time scales coupled with assortative mixing by age can lead to changes in the average age of infection. These results show the importance of asymptomatic transmission on the overall disease dynamics of COVID-19.

1 Introduction

Asymptomatic carriers of infection pose challenges to epidemic control due to difficulties in identifying and isolating them [9, 13, 21]. They also affect inferences of disease severity by limiting our ability to estimate the total number of infections, as the number of reported cases typically represents symptomatic infections and is therefore biased. Estimating the contribution of asymptomatic carriers to disease dynamics may be important then for estimating the epidemic potential and for devising effective public health strategies (e.g., non-pharmaceutical interventions) [4, 6, 9, 15, 22]. Therefore, estimating the proportion of asymptomatic infection

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and transmission has remained a key question throughout the current COVID-19
pandemic [2, 5, 13, 14].

Although certain proportions with respect to asymptomatic infections—in particular, how
they vary with age—are characterized relatively well now [7, 22], there is still considerable
uncertainty in how well asymptomatic individuals can transmit. Documented cases of
asymptomatic transmission are rare due to difficulties in directly observing them. Comparisons
of viral load dynamics between asymptomatic and symptomatic infections indicate that both go
through similar courses of infection [10], but this does not necessarily imply that they are
equally transmissible. Another key uncertainty is their time scale of transmission, which is
characterized by the generation-interval distribution. The generation interval is defined as the
time between when a person is infected and when they infect another person [19]. The
generation interval distribution connects the “speed” (i.e., the exponential growth rate) and
“strength” (i.e., the basic reproduction number) of an epidemic [19]. Neglecting time scale
differences between asymptomatic and symptomatic transmission can lead to biases in
inferences about the strength of COVID-19 [15].

We hypothesize that behavioral effects and non-pharmaceutical interventions can cause
differences in the time scales of asymptomatic and symptomatic transmission. Asymptomatic
individuals are likely unaware of their infection and may not isolate as a result. In addition,
individual-based interventions, such as contact tracing, typically target symptomatic cases
which can shorten the time scale of symptomatic transmission [1]. Therefore, asymptomatic
infections may have longer generation intervals than symptomatic infections.

In addition to time scale differences of transmission, asymptomatic and symptomatic
infections may exhibit assortativity in their transmission patterns. That is, transmission from
asymptomatic infections may be more likely to cause asymptomatic infections, whereas
transmission from symptomatic infections may be more likely to cause symptomatic infections.
We refer to this effect as ‘assortative transmission.’ This effect may result from dose-dependent
responses in which a higher inoculum results in more severe illness. With respect to COVID-19
dynamics, the initial viral inoculum could differ between transmission from asymptomatic
versus symptomatic, if, for instance, asymptomatic individuals produce fewer infectious viral
particles than symptomatic individuals. Assortative transmission between asymptomatic and
symptomatic infections could also result from age demographic patterns in a population,
particularly in the context of COVID-19: since younger individuals are more likely to be
asymptomatic and mix with younger individuals, transmission from asymptomatic infections
will on average be more likely to cause asymptomatic infections than symptomatic infections.

Coupling time scale differences with assortative transmission of asymptomatic and
symptomatic infections can have important impacts on epidemic dynamics. If asymptomatic
infections have longer generation intervals, the proportion of asymptomatic transmission
increases over time. Since faster transmission is favored during the growth phase, a higher
proportion of transmission is attributable to symptomatic transmission during the growth phase
compared to during the decay phase. Thus, transmission from symptomatic infections
predominates during growth, while transmission from asymptomatic infections predominates
during decay. The addition of assortative transmission imparts an asymmetry between infection
and transmission with respect to the two infection types, resulting in changes in the proportion
of asymptomatic incidence over time. In this case, the proportion of asymptomatic incidence
will be higher during the decay phase than during the growth phase.

Finally, we explore the impact of coupling longer time scales of asymptomatic transmission

with age-dependent disease estimates and demographic mixing. We show that this coupling can
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lead to changes in the age distribution of newly infected individuals throughout an epidemic,
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depending on the growth or decay of new infections. Specifically, the average age of infection
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decreases as the number of new infections decreases. We study how differences in time scales
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and the degree of age-dependent assortativity impact the changes in age of newly infected
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individuals. If new infections decrease due to depletion of the susceptible population, the
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average age of infection decreases between 18-20 years. If instead new infections decrease due to
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public health interventions (i.e., decreasing contact rates), the average age of infection decreases
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by about 4 years assuming increased assortative mixing by age. We found evidence of changes
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in the age distribution of incident infections – from older to younger individuals – reported in
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both the US and the UK over summer 2020 [3,16] (see Figure S1).
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2 Results

2.1 Differences in time scales between asymptomatic and symptomatic transmission

First, we show that differences in generation intervals between asymptomatic and symptomatic
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infections can lead to changes in the proportion of asymptomatic transmission (i.e. the relative
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number of infections caused by transmission from asymptomatic vs. symptomatic infections)
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over the course of the epidemic. To do so, we model the spread of asymptomatic and
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symptomatic infections using an SEIR model that includes both asymptomatic and
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symptomatic infections (Methods). We consider when the mean infectious period of
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asymptomatic infections is longer than that of symptomatic infections, reflecting the potential
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impacts of behavioral and non-pharmaceutical interventions.
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To parametrise the SEIR model, we assume that both asymptomatic and symptomatic
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individuals have equal reproduction rates, irrespective of differences in their infectious periods.
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We set the probability that a new infection is asymptomatic ($p = 0.4$) and match the observed
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epidemic growth rate ($r = 0.14/\text{day}$). We assume that the exposed period, $\tau_e = 3 \text{ days}$ [4], is
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the same between asymptomatic and symptomatic infections. We then consider two scenarios:
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(1) when the epidemic is allowed to spread without any mitigation and (2) when intervention is
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introduced by reducing contact rates of asymptomatic and symptomatic infections equally
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(Methods).
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To illustrate the impact of time scale differences between asymptomatic and symptomatic
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infections on the proportion of asymptomatic transmission, we increase the average generation
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interval of asymptomatic infections by increasing the infectious period of asymptomatic
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infections from $T_a = 5, 6, 8 \text{ days}$ relative to symptomatic infections $T_s = 5 \text{ days}$. Because the
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exponential growth rate is fixed, the incidence curves start off identically across all simulations
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(Figure 1A,E). Longer generation intervals cause the epidemics to decay more slowly
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(Figure 1A,E). We see that the proportion of asymptomatic incidence (i.e., proportion of new
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infections that are asymptomatic) remains constant over time (Figure 1B,F). However, the
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proportion of asymptomatic transmission does change over the course of the epidemic; the
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proportion increases over time because a greater proportion of infections are caused by shorter
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generation intervals (i.e., symptomatic infections) during the growth phase, while a greater
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proportion of infections are caused by longer generation intervals (i.e., asymptomatic infections)
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during the decay phase (Figure 1C,G).
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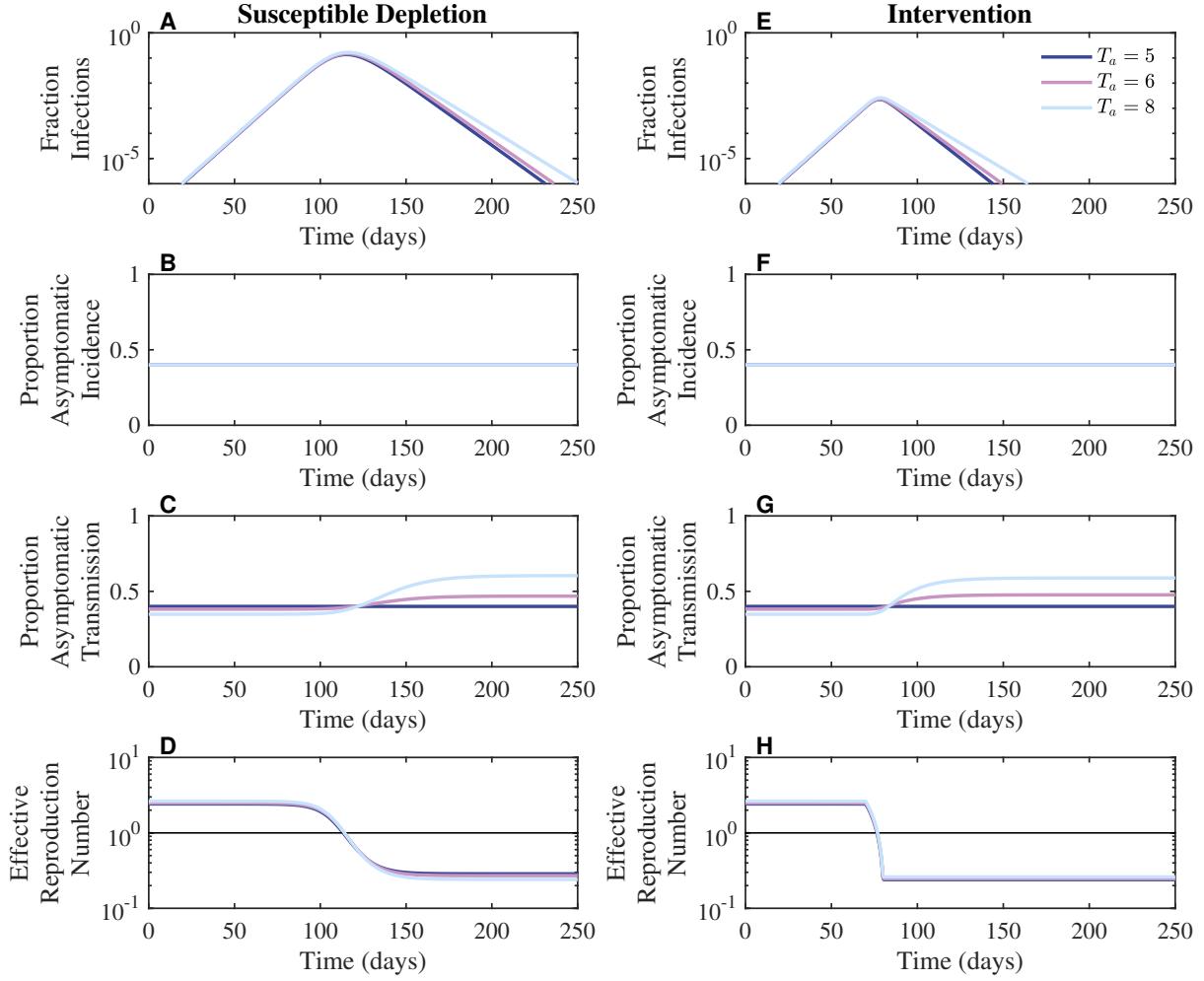


Figure 1. The proportion of asymptomatic transmission increases as new infections decrease over time. Setting the infectious period of symptomatic individuals, $T_s = 5$ days and increasing the infectious period of asymptomatic carriers from $T_a = 5$ days (dark blue), $T_a = 6$ days (purple), $T_a = 8$ days (light blue). (A-D) Without intervention the susceptible population is depleted. As infections decrease, the proportion of asymptomatic transmission increases when the asymptomatic infectious period is longer. (E-H) Effects on the changes in the proportion of asymptomatic transmission are comparable with intervention when the reproduction number is reduced to similar levels as with susceptible depletion. Across all simulations, the fixed proportion of new cases that are asymptomatic is $p = 0.4$ and the exponential growth rate is $r = 0.14/\text{day}$ (Methods). See Table 2 for parameter values.

The decays rates of new infections during intervention were matched with the susceptible depletion scenario. This yields similar changes in the proportion of asymptomatic transmission with beginning and end levels similar for corresponding curves Figure 1. Changes in proportion asymptomatic transmission can be modified by the speed of intervention. When intervention is faster, the proportion of asymptomatic transmission increases to higher levels Figure S2.

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2.2 Differences in time scales coupled with assortative transmission

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In the previous section, we showed that the proportion of asymptomatic transmission can increase as number of new infections decay in the population due to longer generation intervals of asymptomatic infections. Next, we show that longer generation intervals coupled with assortative transmission can change not only the proportion of asymptomatic transmission but also the proportion of asymptomatic incidence. To increase the assortativity in transmission between asymptomatic and symptomatic infections, we assume that the probability that asymptomatic transmission results in a new asymptomatic infection, $p_{a|a}$, is higher than the probability that symptomatic transmission results in a new asymptomatic infection, $p_{a|s}$. When assortative transmission is increased we keep the initial proportion of asymptomatic incidence (p_e) fixed. We match the initial proportion of asymptomatic incidence ($p_e = 0.4$) and the exponential growth rate ($r = 0.14$) across simulations (Methods). When $p_{a|a} = p_{a|s}$ the model collapses to the previous model, and we can use results of the previous section as a reference point.

We consider assortative transmission when the generation intervals of asymptomatic and symptomatic infections are equal and when they differ (Figure 2). When the generation intervals equal, both the proportion of asymptomatic transmission (Figure 2B,F, dark blue dashed lines) and the proportion of asymptomatic incidence (Figure 2C,G, dark blue dashed) remain constant over time. When the generation intervals of asymptomatic infections are longer than symptomatic infections, however, the proportion of asymptomatic incidence increases over time as total incident infections decrease (Figure 2B,F, light blue dashed lines). This increase in incidence then causes further increases in the proportion of asymptomatic transmission over the course of the epidemic (Figure 2C,G, comparing light blue solid and dashed lines).

2.3 Differences in time scales coupled with assortative mixing by age

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In the previous section, we showed that the proportion of incident infections that are asymptomatic can change over the course of the disease due to time scales differences coupled with assortative transmission of asymptomatic and symptomatic infections. Time scale differences alone are not sufficient to change the proportion of asymptomatic incidence. Rather, it is the additional assumption of assortative transmission that leads to such changes. We next consider how assortative transmission driven by age-dependent mixing patterns affect the mean age of infection. To do so, we consider an age-dependent SEIR model with asymptomatic and symptomatic infections. We allow the contact rates, the susceptibility to infection, and the probability of being asymptomatic (vs. symptomatic) to vary across age groups (Methods). We consider two scenarios: baseline (solid curves) vs. increased assortativity by age (dashed curves) (Figure 3).

With susceptible depletion, new infections decrease over time with longer generation intervals leading to slower decay (Figure 3A). The proportion of asymptomatic incidence increases over time similarly across all simulations (Figure 3B). The proportion of asymptomatic transmission increases more when the generation intervals of asymptomatic infections are longer (light blue) than when they are the same length (dark blue); increased assortative mixing by age shifts the initial proportion down (Figure 3C). As new infections decrease, the average age of infection also decreases (Figure 3D). The average age of infection falls between 18-22 years. Changes in the average age of infection are similar irrespective of time scale differences. The increases in asymptomatic incidence over time in the susceptible depletion case are thus due to differences

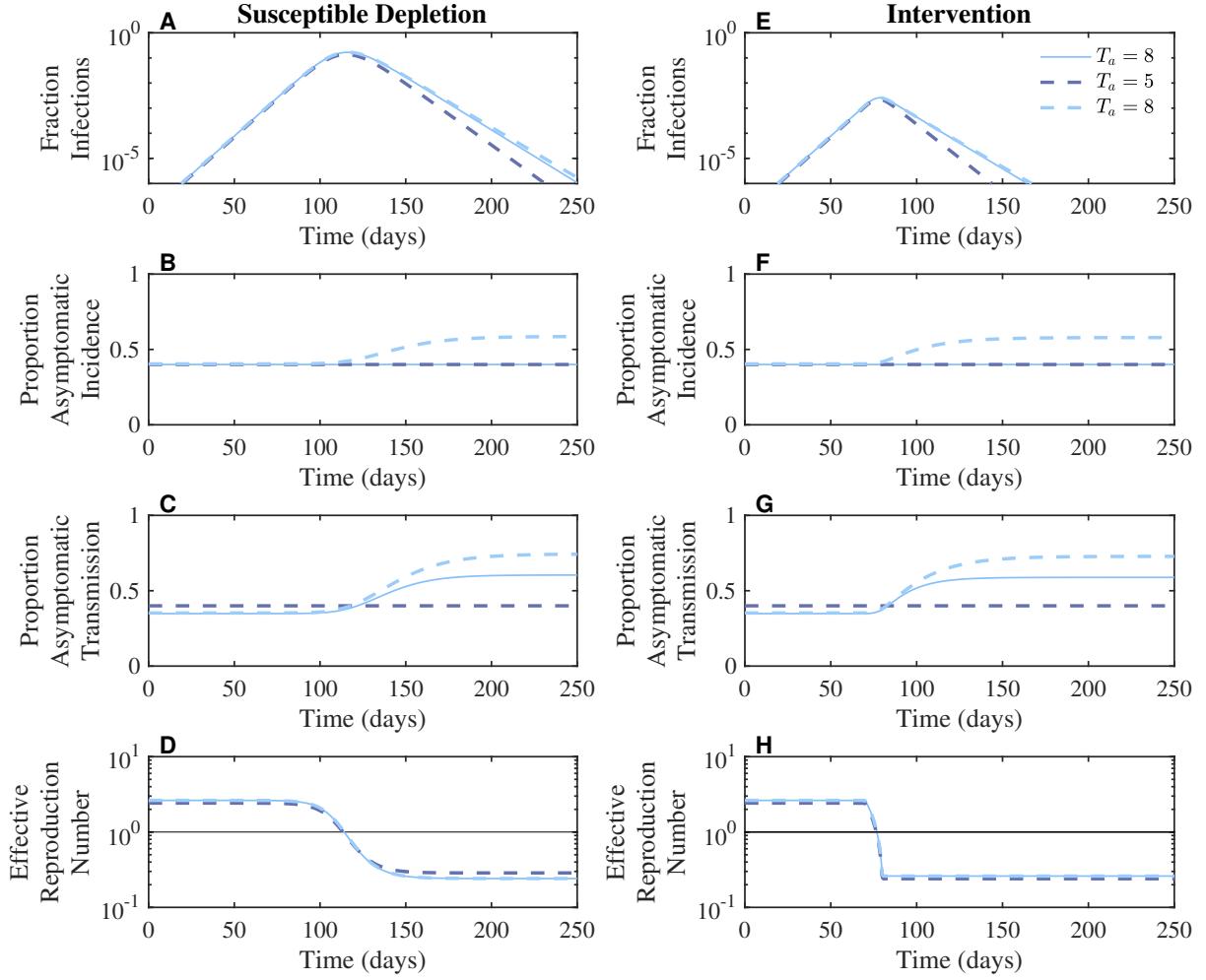


Figure 2. The proportion of asymptomatic transmission and incidence increase as new infections decrease over time. Setting the infectious period of symptomatic infections to $T_s = 5$ days, the dashed lines correspond to increased assortative transmission with $p(a|a) = 0.7$ when the infectious period of asymptomatic infections is $T_a = 5$ days (dark blue) and $T_a = 8$ days (light blue). For comparison, solid light blue curve is $T_a = 8$ without assortative transmission (same as in Figure 1). (A-D) With susceptible depletion. (E-H) Effects on changes in the proportion of asymptomatic transmission and incidence over time are comparable with intervention when the reproduction number is reduced to similar levels as with susceptible depletion. Both the initial proportion incidence, $p = 0.4$, and the exponential growth rate, $r = 0.14/\text{day}$, are fixed across simulations (Methods). See Table 3 for parameter values.

in susceptibility rates between younger and older individuals. The effective reproduction numbers are comparable between baseline and increased assortativity (Figure 3E).

With intervention, reduced transmission rates cause new infections to decay earlier and faster (Figure 3F). There is very little change in the proportion of asymptomatic incidence, although with time scale differences and increased assortative mixing the proportion increase over time (Figure 3G). When the generation intervals equal, there is no change in the

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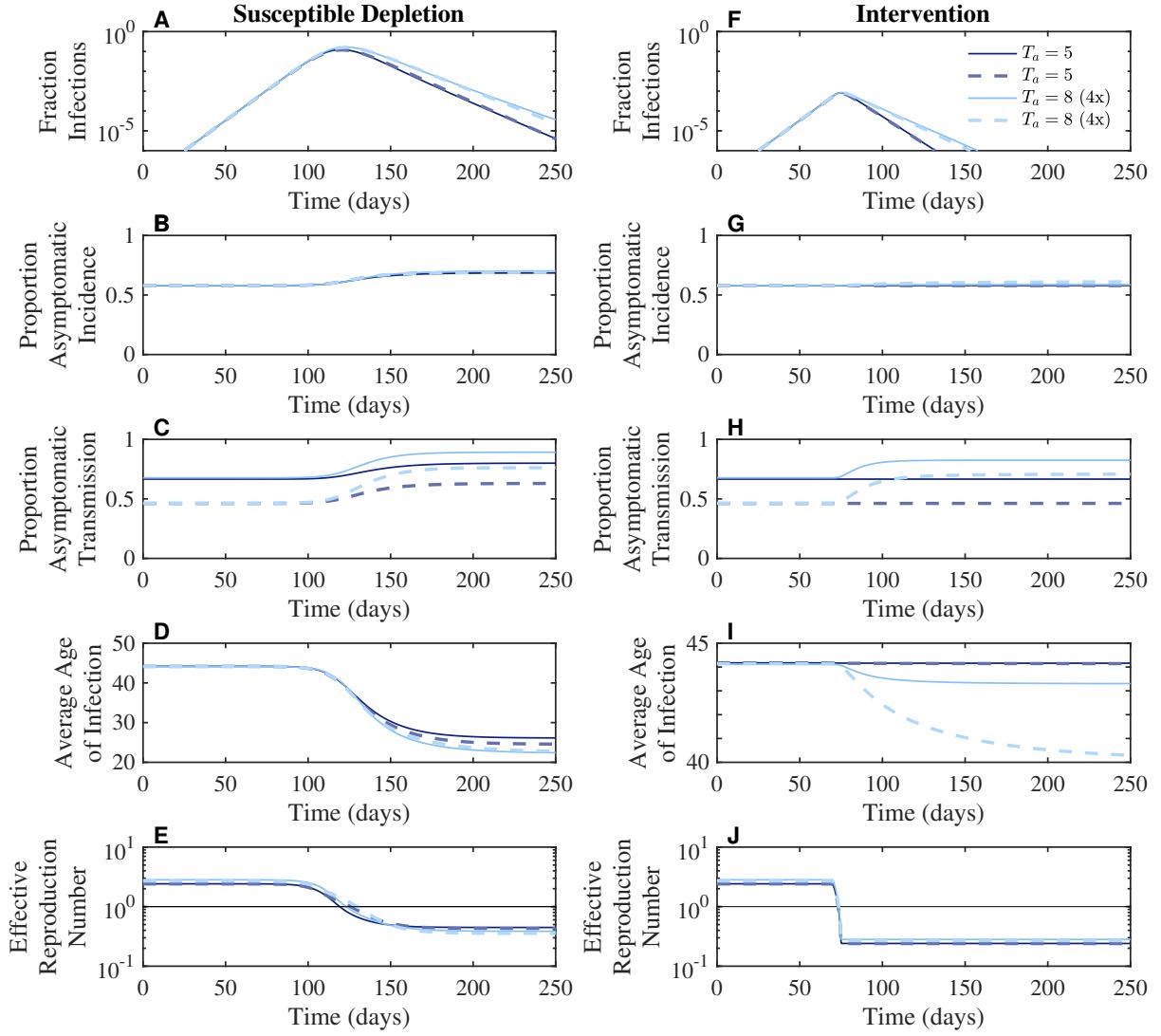


Figure 3. The average age of infection decreases as new infections decrease over time. Solid lines indicate baseline contact rates. Dashed lines indicate 4 times the assortative mixing by age from baseline contacts. We compare when the infectious periods of asymptomatic and symptomatic infections equal ($T_a = T_s = 5$ days) and when the infectious period of asymptomatic infections is longer ($T_a = 8, T_s = 5$). Across all four scenarios, the initial proportion of new infections that are asymptomatic is $p_e = 0.58$, and the exponential growth rate is $r = 0.14/\text{day}$ (Methods). See Table 5 for parameter values.

proportion of asymptomatic transmission. When the generation intervals of asymptomatic infections are longer on average than symptomatic infections, however, there is an increase in the proportion of asymptomatic transmission over time (Figure 3H). With baseline contact rates, the average age of infection remains relatively constant when intervention is introduced. With increased assortativity by age, though, the average age of infection decreases by about 4 years when asymptomatic generation intervals are longer (Figure 3I). This is still much less than with susceptible depletion though. (Compare Figure 3D and Figure 3I, noting the different

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age ranges on the y -axes.)

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3 Discussion

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The strength and time scale of asymptomatic transmission of COVID-19 remains a key
162 uncertainty. Here, we show that differences in asymptomatic and symptomatic transmission
163 time scale—characterized by generation intervals—can lead to changes in their relative
164 transmission over the course of an epidemic. In particular, longer generation intervals of
165 asymptomatic transmission can cause the proportion of asymptomatic transmission to increase
166 as total incident infections decrease. Furthermore, assortative transmission leads to increases in
167 the proportion of asymptomatic incidence over time. When assortativity is driven by
168 age-dependent mixing patterns, the mean age of infection increases as total incident infections
169 decrease.

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We considered differences in time scales with assortative transmission driven by possible
179 biological differences between asymptomatic and symptomatic infections, e.g., dose-dependent
180 responses to infection. Recent animal model studies of COVID-19 have shown dose-dependent
181 responses with respect to viral shedding and clinical severity [12, 18]. Data from animal model
182 studies of other human coronaviruses, including SARS-CoV, indicate that a higher initial viral
183 inoculum results in more severe outcomes [20]. If symptomatic infections typically shed more
184 infectious virus than asymptomatic infections, then the initial viral dose from symptomatic
185 transmission would be higher than from asymptomatic transmission.

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We considered differences in time scales coupled with assortative transmission driven by
196 age-dependent contacts and susceptibility to infection. The proportion of asymptomatic
197 transmission and incidence increase as total infections decrease. This is mainly due to
198 differences in susceptibility to infection by age. We do find, however, that increased
199 assortativity in contacts by age can cause changes in the age distribution of infection when
200 transmission rates are decreased due to, e.g., non-pharmaceutical interventions.

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important quantity that connects the epidemic growth rate to the basic reproduction number [19]. Here, we introduce and describe the SEIR models used in simulations.

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4.1 Model of asymptomatic transmission with fixed proportion of asymptomatic incidence

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Let $p \in [0, 1]$ be the intrinsic proportion of incident infections that are asymptomatic, and let $\mathcal{R}_{0,a}$ and $\mathcal{R}_{0,s}$ be the basic reproduction numbers of asymptomatic and symptomatic infections, respectively. The basic reproduction number of the model is $\mathcal{R}_0 = p\mathcal{R}_{0,a} + (1-p)\mathcal{R}_{0,s}$, and the intrinsic proportion of asymptomatic transmission is $z = p \frac{\mathcal{R}_{0,a}}{\mathcal{R}_0}$ [15]. We explored the impact of time scales on disease dynamics, using the following SEIR model with asymptomatic and symptomatic infections: S is the susceptible population, E is the exposed population, I is the infected population, and R denotes the recovered population. The model equations are given by

$$\begin{aligned}\dot{S} &= - \overbrace{\beta_a S I_a}^{\text{asymp. transmission}} - \overbrace{\beta_s S I_s}^{\text{symp. transmission}} \\ \dot{E}_a &= \overbrace{p (\beta_a S I_a + \beta_s S I_s)}^{\text{asymp. incidence}} - E_a/\tau \\ \dot{E}_s &= \overbrace{(1-p) (\beta_a S I_a + \beta_s S I_s)}^{\text{symp. incidence}} - E_s/\tau \\ \dot{I}_a &= E_a/\tau - I_a/T_a \\ \dot{I}_s &= E_s/\tau - I_s/T_s \\ \dot{R}_a &= I_a/T_a \\ \dot{R}_s &= I_s/T_s .\end{aligned}\tag{1}$$

Here, the subscripts, a for asymptomatic and s for symptomatic, separate the population according to asymptomatic and symptomatic infections at the time of exposure to an infected individual. In equation (1), we have assumed that the exposed period, τ , is the same for both asymptomatic and symptomatic infections. See Table S1 for parameter descriptions and Figure S3 for a schematic of model equations. We write the infectious period of asymptomatic individuals, T_a and the infectious period of symptomatic individuals, T_s . The mean of the generation interval is the sum of the exposed and infectious period. Hence, the average generation interval of asymptomatic infections is $\bar{G}_a = 1/\tau + 1/T_a$ and the average generation interval of symptomatic infections is $\bar{G}_s = 1/\tau + 1/T_s$. For the set of differential equations in equation (1), the generation interval distributions for asymptomatic and symptomatic transmission are, respectively,

$$\begin{aligned}g_a(t) &= \frac{1}{T_a - \tau} (\exp(-t/T_a) - \exp(-t/\tau)) \\ g_s(t) &= \frac{1}{T_s - \tau} (\exp(-t/T_s) - \exp(-t/\tau)) .\end{aligned}\tag{2}$$

See Figure S4 for the shape of these distributions with different mean generation intervals.

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For the set of differential equations in (1), the realized proportion of asymptomatic transmission is

$$q(t) = \frac{\beta_a I_a}{\beta_a I_a + \beta_s I_s} .\tag{3}$$

We parametrised the SEIR model given in (1) as follows: we let the exponential growth rate (208)
 $(r = 0.14)$, the initial proportion of asymptomatic incidence ($p_e = 0.4$), and the exposed period (209)
 $(\tau = 3$ days for both asymptomatic and symptomatic infections) be the same across simulations. (210)
We then consider when the infectious period of asymptomatic infections is longer than the (211)
infectious period of symptomatic infections. We fix $T_s = 5$ days and increase the infectious (212)
period of asymptomatic infections from $T_a = 5, 6, 8$ days. For simplicity, we assume that (213)
asymptomatic infections transmit to the same number of individuals in the population. That is, (214)
the basic reproduction numbers of asymptomatic vs. symptomatic infections are equal, (215)
 $\mathcal{R}_{0,a} = \mathcal{R}_{0,s} = \mathcal{R}_0$ (Figure S5A). We calculated \mathcal{R}_0 using the next generation matrix [8,17]. See (216)
also Table 2 for parameter values used in the simulation shown in Figure 1. We also (217)
parametrised the model assuming transmission rates are equal, i.e., $\beta_a = \beta_s = \beta$ (Figure S5B). (218)
Similar changes in the intrinsic proportion of asymptomatic transmission occur (Figure S6). (219)

4.2 Model of asymptomatic transmission with assortative mixing

In this section, we consider a model with assortative transmission from asymptomatic and (220)
symptomatic infections. We define the parameters: $p_{a|a}$ is the probability that an (221)
asymptomatic infection results from contact with an asymptotically infected individual, (222)
whereas $p_{a|s}$ is the probability that an asymptomatic infection results from contact with a (223)
symptomatically infected individual. Then $p_{s|a} = 1 - p_{a|a}$ and $p_{s|s} = 1 - p_{a|s}$ by the law of total (224)
probability, giving the model one more parameter than the model considered in equation (1). (225)
We write the model equations,

$$\begin{aligned} \dot{S} &= -\overbrace{\beta_a S I_a}^{\text{asym. transmission}} - \overbrace{\beta_s S I_s}^{\text{symp. transmission}} \\ \dot{E}_a &= \underbrace{p_{a|a} \beta_a S I_a + p_{a|s} \beta_s S I_s}_{\text{asym. incidence}} - E_a / \tau \\ \dot{E}_s &= \underbrace{(1 - p_{a|a}) \beta_a S I_a + (1 - p_{a|s}) \beta_s S I_s}_{\text{symp. incidence}} - E_s / \tau \\ \dot{I}_a &= E_a / \tau - I_a / T_a \\ \dot{I}_s &= E_s / \tau - I_s / T_s \\ \dot{R}_a &= I_a / T_a \\ \dot{R}_s &= I_s / T_s . \end{aligned} \tag{4}$$

See Table 1 for parameter descriptions and Figure S7 for model diagram. In the first SEIR (221)
model explored (equation (1)), we found that the realized asymptomatic transmission can differ (222)
from the intrinsic and change over time when the infectious period of asymptomatic infections, (223)
 T_a , is different from that of symptomatic infections, T_s . For each set of time scales, T_a and T_s , (224)
we break symmetry (i.e. $p_{a|a} = p_{a|s}$) by increasing $p_{a|a}$ and decreasing $p_{a|s}$, while keeping the (225)
initial proportion of asymptomatic incidence fixed (See Supplemental Information and (226)
Figure S8).

The proportion of asymptomatic incidence can be written in terms of the proportion of (227)
asymptomatic transmission, $q(t)$, such that (228)

$$p(t) = p_{a|a} q(t) + p_{a|s} (1 - q(t)) . \tag{5}$$

When generation intervals of asymptomatic infections are longer than symptomatic infections (e.g., $T_a > T_s$) and assortativity increased ($p_{a|a} > p_{a|s}$), $p(t)$ can increase as new infections decrease over time (Figure 2). See Table 3 for parameter values used in the simulation shown in Figure 2. We also parametrised the model assuming that the transmission rates equal, i.e., $\beta_a = \beta_s = \beta$ (Figure S9). Similar changes in the intrinsic proportion of asymptomatic transmission occur (Figure S10).

4.3 Age-dependent SEIR Model with asymptomatic transmission

Here, we consider an age-dependent SEIR model parametrised with empirical estimates of contact rates, susceptibility, and symptomaticity by age. For each age group n , we let S_n represent the number of susceptible individuals; $E_{n,a}$ ($E_{n,s}$) be the number of individuals exposed who will become asymptomatic (symptomatic); $I_{n,a}$ and ($I_{n,s}$) be the number of asymptomatic (symptomatic) infections; R_n be the number of recovered individuals. For each age group n , the compartments satisfy, $S_n + E_{n,a} + E_{n,s} + I_{n,a} + I_{n,s} + R_n = P_n$, where P_n is the population size of age group n . The age groups span intervals of 10 years, going from 0-9 ($n = 1$) up to 60-69 ($n = 7$) with the last group being 70+ ($n = 8$); the model has a total of $N = 8$ age groups.

Following Zhang et al., we model the contact patterns between the age groups by including an empirically estimated fixed contact matrix, $(C_{n,m})_{n,m=1}^N$, where $C_{n,m}$ is the average number of contacts (per day) individuals in age group n make with individuals in age group m . In our simulations, we used baseline contact estimates from the population of Wuhan, which estimate baseline contact rates (prior to COVID-19) between individuals in different age groups [23]. (See Figure S12A for heatmap of the 8×8 contact matrix used.) We also used age-dependent estimates of disease with respect to the probability of infection (α_n) and the probability of the infection being symptomatic (u_n) (as opposed to asymptomatic) from [7] (Figure S12B). Then we define $\sigma_{s,n} = \alpha_n u_n$, the probability that individuals in age group n , who come in contact with infected individuals, will acquire symptomatic infections and $\sigma_{a,n} = \alpha_n (1 - u_n)$, the probability that individuals in age group n , who come in contact with infected individuals, will acquire asymptomatic infections. The last ingredient we need is the age distribution of the population in Wuhan, i.e. the number of individuals that fall within 10 year intervals; we used the population sizes, P_n , from Wuhan and plotted as fractions of the population in Figure S12C.

With the age-dependent contact matrix and disease estimates defined, we write the incident infections (i.e., the rate of new infections) for each age group n that are asymptomatic and symptomatic, respectively:

$$i_{a,n}(t) = \beta_a \sigma_{a,n} S_n(t) \left(\sum_{m=1}^N C_{n,m} \frac{I_{a,m}(t)}{P_m} \right) + \beta_s \sigma_{s,n} S_n(t) \left(\sum_{m=1}^N C_{n,m} \frac{I_{s,m}(t)}{P_m} \right) \quad (6)$$

$$i_{s,n}(t) = \beta_a \sigma_{s,n} S_n(t) \left(\sum_{j=1}^N C_{n,j} \frac{I_{a,j}(t)}{P_m} \right) + \beta_s \sigma_{s,n} S_n(t) \left(\sum_{m=1}^N C_{n,m} \frac{I_{s,m}(t)}{P_m} \right). \quad (7)$$

Note that total incident infections in each age group n is

$$\begin{aligned} i_n(t) &= i_{a,n}(t) + i_{s,n}(t) \\ &= \beta_a \alpha_n S_n(t) \left(\sum_{m=1}^N C_{n,m} \frac{I_{a,m}(t)}{P_m} \right) + \beta_s \alpha_n S_n(t) \left(\sum_{m=1}^N C_{n,m} \frac{I_{s,m}(t)}{P_m} \right). \end{aligned} \quad (8)$$

The total incident infections, $i(t)$, is given by

$$i(t) = \sum_{n=1}^N i_n(t). \quad (9)$$

Then we write the age-dependent SEIR model with asymptomatic and symptomatic infections as

$$\begin{aligned} \dot{S} &= -i(t) \\ \dot{E}_{a,n} &= i_{a,n}(t) - E_{a,n}/\tau \\ \dot{E}_{s,n} &= i_{s,n}(t) - E_{s,n}/\tau \\ \dot{I}_{a,n} &= E_{a,n}/\tau - I_{a,n}/T_a \\ \dot{I}_{s,n} &= E_{s,n}/\tau - I_{s,n}/T_s \\ \dot{R}_n &= I_{a,n}/T_a + I_{s,n}/T_s. \end{aligned} \quad (10)$$

Note that the total number of incident infections that are caused by asymptomatic and symptomatic transmission are given by, respectively,

$$w_a(t) = \sum_{n=1}^N \beta_a \alpha_n S_n(t) \left(\sum_{m=1}^N C_{n,m} \frac{I_{a,m}(t)}{P_m} \right) \quad (11)$$

$$w_s(t) = \sum_{n=1}^N \beta_s \alpha_n S_n(t) \left(\sum_{m=1}^N C_{n,m} \frac{I_{s,m}(t)}{P_m} \right). \quad (12)$$

Then the proportion of asymptomatic transmission is

$$q(t) = \frac{w_a(t)}{w_a(t) + w_s(t)}. \quad (13)$$

The proportion of asymptomatic incident infections is

$$p(t) = \frac{\sum_{n=1}^N i_{a,n}(t)}{i(t)}. \quad (14)$$

The average age of incident infections is given by

$$\bar{a}(t) = \sum_{n=1}^N M_n \left(\frac{i_n(t)}{i(t)} \right). \quad (15)$$

where M_n is the midpoint of age group n .

We also calculated the probabilities $p_{a|a}(t)$ and $p_{a|s}(t)$ for the age-dependent model. For
 $p_{a|a}(t)$, let $K_{a,a}$ denote the number of asymptomatic incident infections caused by
asymptomatic transmission. Then

$$K_{a,a}(t) = \beta_a \left(\sum_{n=1}^N \sigma_{a,n} S_n(t) \sum_{m=1}^N C_{n,m} \left(\frac{I_{a,m}(t)}{P_m} \right) \right), \quad (16)$$

where $I_a(t)$ is the total number of asymptomatic infections at time t . We have

$$p_{a|a}(t) = \frac{K_{a,a}(t)}{w_a(t)}, \quad (17)$$

where $w_a(t)$ is the total number of incident infections caused by asymptomatic transmission,
given in equation (11). Analogously, for $p_{a|s}(t)$, let

$$K_{a,s}(t) = \left(\sum_{n=1}^N \sigma_{a,n} S_n(t) \sum_{m=1}^N C_{n,m} \left(\frac{I_{s,m}(t)}{P_m} \right) \right), \quad (18)$$

where $I_s(t)$ is the total number of symptomatic infections at time t . Then

$$p_{a|s}(t) = \frac{K_{a,s}(t)}{w_s(t)}, \quad (19)$$

where $w_s(t)$ is the number of incident infections caused by symptomatic transmission, given in
equation (12). We plot the conditionals, $p_{a|a}(t)$ and $p_{a|s}(t)$, in Figure S13 for the simulations
shown in Figure 3.

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up to JSW ?]

References

1. S. T. Ali, L. Wang, E. H. Lau, X.-K. Xu, Z. Du, Y. Wu, G. M. Leung, and B. J. Cowling. Serial interval of sars-cov-2 was shortened over time by nonpharmaceutical interventions. *Science*, 369(6507):1106–1109, 2020.
2. Y. Bai, L. Yao, T. Wei, F. Tian, D.-Y. Jin, L. Chen, and M. Wang. Presumed asymptomatic carrier transmission of covid-19. *Jama*, 323(14):1406–1407, 2020.
3. T. K. Boehmer, J. DeVies, E. Caruso, K. L. van Santen, S. Tang, C. L. Black, K. P. Hartnett, A. Kite-Powell, S. Dietz, M. Lozier, et al. Changing age distribution of the covid-19 pandemic—united states, may–august 2020. *Morbidity and Mortality Weekly Report*, 69(39):1404, 2020.

-
4. T. S. Brett and P. Rohani. Transmission dynamics reveal the impracticality of covid-19
herd immunity strategies. *Proceedings of the National Academy of Sciences*,
117(41):25897–25903, 2020. 290
291
292
5. J. F.-W. Chan, S. Yuan, K.-H. Kok, K. K.-W. To, H. Chu, J. Yang, F. Xing, J. Liu,
C. C.-Y. Yip, R. W.-S. Poon, et al. A familial cluster of pneumonia associated with the
2019 novel coronavirus indicating person-to-person transmission: a study of a family
cluster. *The lancet*, 395(10223):514–523, 2020. 293
294
295
296
6. M. Chinazzi, J. T. Davis, M. Ajelli, C. Gioannini, M. Litvinova, S. Merler, A. P.
y Piontti, K. Mu, L. Rossi, K. Sun, et al. The effect of travel restrictions on the spread of
the 2019 novel coronavirus (covid-19) outbreak. *Science*, 368(6489):395–400, 2020. 297
298
299
7. N. G. Davies, P. Klepac, Y. Liu, K. Prem, M. Jit, and R. M. Eggo. Age-dependent
effects in the transmission and control of covid-19 epidemics. *Nature medicine*,
26(8):1205–1211, 2020. 300
301
302
8. O. Diekmann, J. Heesterbeek, and M. G. Roberts. The construction of next-generation
matrices for compartmental epidemic models. *Journal of the Royal Society Interface*,
7(47):873–885, 2010. 303
304
305
9. C. Fraser, S. Riley, R. M. Anderson, and N. M. Ferguson. Factors that make an
infectious disease outbreak controllable. *Proceedings of the National Academy of Sciences*,
101(16):6146–6151, 2004. 306
307
308
10. X. He, E. H. Lau, P. Wu, X. Deng, J. Wang, X. Hao, Y. C. Lau, J. Y. Wong, Y. Guan,
X. Tan, et al. Temporal dynamics in viral shedding and transmissibility of COVID-19.
Nature medicine, 26(5):672–675, 2020. 309
310
311
11. J. Heesterbeek and K. Dietz. The concept of ro in epidemic theory. *Statistica neerlandica*,
50(1):89–110, 1996. 312
313
12. M. Imai, K. Iwatsuki-Horimoto, M. Hatta, S. Loeber, P. J. Halfmann, N. Nakajima,
T. Watanabe, M. Ujie, K. Takahashi, M. Ito, et al. Syrian hamsters as a small animal
model for sars-cov-2 infection and countermeasure development. *Proceedings of the
National Academy of Sciences*, 117(28):16587–16595, 2020. 314
315
316
317
13. M. A. Johansson, T. M. Quandelacy, S. Kada, P. V. Prasad, M. Steele, J. T. Brooks,
R. B. Slayton, M. Biggerstaff, and J. C. Butler. Sars-cov-2 transmission from people
without covid-19 symptoms. *JAMA network open*, 4(1):e2035057–e2035057, 2021. 318
319
320
14. X. Pan, D. Chen, Y. Xia, X. Wu, T. Li, X. Ou, L. Zhou, and J. Liu. Asymptomatic cases
in a family cluster with sars-cov-2 infection. *The Lancet Infectious Diseases*,
20(4):410–411, 2020. 321
322
323
15. S. W. Park, D. M. Cornforth, J. Dushoff, and J. S. Weitz. The time scale of
asymptomatic transmission affects estimates of epidemic potential in the covid-19
outbreak. *Epidemics*, 31:100392, 2020. 324
325
326
16. S. Riley, K. E. Ainslie, O. Eales, C. E. Walters, H. Wang, C. Atchison, C. Fronterre, P. J.
Diggle, D. Ashby, C. A. Donnelly, et al. Resurgence of sars-cov-2: detection by
community viral surveillance. *Science*, 2021. 327
328
329

-
17. M. G. Roberts and J. Heesterbeek. Characterizing the next-generation matrix and basic reproduction number in ecological epidemiology. *Journal of mathematical biology*, 66(4):1045–1064, 2013. 330
331
332
18. K. A. Ryan, K. R. Bewley, S. A. Fotheringham, G. S. Slack, P. Brown, Y. Hall, N. I. Wand, A. C. Marriott, B. E. Cavell, J. A. Tree, et al. Dose-dependent response to infection with sars-cov-2 in the ferret model and evidence of protective immunity. *Nature communications*, 12(1):1–13, 2021. 333
334
335
336
19. J. Wallinga and M. Lipsitch. How generation intervals shape the relationship between growth rates and reproductive numbers. *Proceedings of the Royal Society B: Biological Sciences*, 274(1609):599–604, 2007. 337
338
339
20. T. Watanabe, T. A. Bartrand, M. H. Weir, T. Omura, and C. N. Haas. Development of a dose-response model for sars coronavirus. *Risk Analysis: An International Journal*, 30(7):1129–1138, 2010. 340
341
342
21. W. E. Wei, Z. Li, C. J. Chiew, S. E. Yong, M. P. Toh, and V. J. Lee. Presymptomatic transmission of sars-cov-2—singapore, january 23–march 16, 2020. *Morbidity and Mortality Weekly Report*, 69(14):411, 2020. 343
344
345
22. J. T. Wu, K. Leung, M. Bushman, N. Kishore, R. Niehus, P. M. de Salazar, B. J. Cowling, M. Lipsitch, and G. M. Leung. Estimating clinical severity of covid-19 from the transmission dynamics in wuhan, china. *Nature medicine*, 26(4):506–510, 2020. 346
347
348
23. J. Zhang, M. Litvinova, Y. Liang, Y. Wang, W. Wang, S. Zhao, Q. Wu, S. Merler, C. Viboud, A. Vespignani, et al. Changes in contact patterns shape the dynamics of the covid-19 outbreak in china. *Science*, 368(6498):1481–1486, 2020. 349
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Supplemental Information

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Supplemental Tables

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Table 1. Parameters and their descriptions. SEIR models with asymptomatic and symptomatic infections (without age-dependence).

Parameter	Description
β_a, β_s	Transmission rates of asymptomatic and symptomatic infections (days^{-1})
T_a, T_s	Infectious periods of asymptomatic and symptomatic infections (days)
τ	Exposed period (days)
r	Exponential growth rate (days^{-1})
\mathcal{R}_0	Basic reproduction number
p	Proportion of new infections that are asymptomatic
$p_{a a}$	Probability that an asymptomatic infection causes an asymptomatic infection
$p_{a s}$	Probability that a symptomatic infection causes an asymptomatic infection

Table 2. Parameter values used in Figure 1. Across simulations, we fixed the following parameters: $T_s = 5$, $\tau = 3$, $r = 0.14$, $p = 0.4$.

Curve description	Parameter values
Dark blue	$T_a = 5, \beta_a = \beta_s = 0.48, \mathcal{R}_0 = 2.42$
Purple	$T_a = 6, \beta_a = 0.42, \beta_s = 0.50, \mathcal{R}_0 = 2.50$
Light blue	$T_a = 8, \beta_a = 0.33, \beta_s = 0.53, \mathcal{R}_0 = 2.63$

Table 3. Parameter values used in Figure 2. Across simulations, we fixed the following parameters: $T_s = 5$, $\tau = 3$, $r = 0.14$.

Curve description	Parameter values
Solid light blue	$T_a = 8, \beta_a = 0.33, \beta_s = 0.53, \mathcal{R}_0 = 2.63, p = 0.4$
Dashed dark blue	$T_a = 5, \beta_a = \beta_s = 0.48, \mathcal{R}_0 = 2.42, r = 0.14, p_{a a} = 0.7, p_{a s} = 0.2$
Dashed light blue	$T_a = 8, \beta_a = 0.33, \beta_s = 0.53, \mathcal{R}_0 = 2.63, p_{a a} = 0.7, p_{a s} = 0.24$

Table 4. Parameter descriptions. Age-dependent SEIR model with asymptomatic and symptomatic infections.

Parameter	Description
β_a, β_s	Transmission rates of asymptomatic and symptomatic infections (days $^{-1}$)
T_a, T_s	Infectious periods of asymptomatic and symptomatic infections (days)
τ	Exposed period (days)
r	Exponential growth rate (days $^{-1}$)
\mathcal{R}_0	Basic reproduction number
α_n	Susceptibility to infection for age group n
u_n	Probability of an infection being symptomatic for age group n
P_n	Population age distribution
$C_{n,m}$	Average number of contacts between individuals in age group n with individuals in age group m .

Table 5. Parameter values used in Figure 3. Across simulations, we fixed the following parameters: $T_s = 5$, $\tau = 3$, $r = 0.14$, and $p = 0.58$. Here, $4 \times C_{n,n}$ indicates increased assortativity 4 times the baseline within group contact rates $C_{n,n}$. Note, however, the transmission rates are rescaled from baseline, so the 4 times is an increase in diagonal elements relative to nondiagonal of the contact matrix.

Curve description	Parameter values
Solid dark blue	$T_a = 5, \beta_a = 0.10, \beta_s = 0.062, \mathcal{R}_0 = 2.42$
Solid light blue	$T_a = 8, \beta_a = 0.079, \beta_s = 0.060, \mathcal{R}_0 = 2.82$
Dashed dark blue	$T_a = 5, \beta_a = 0.040, \beta_s = 0.060, \mathcal{R}_0 = 2.42, 4 \times C_{n,n}$
Dashed light blue	$T_a = 8, \beta_a = 0.031, \beta_s = 0.061, \mathcal{R}_0 = 2.72, 4 \times C_{n,n}$

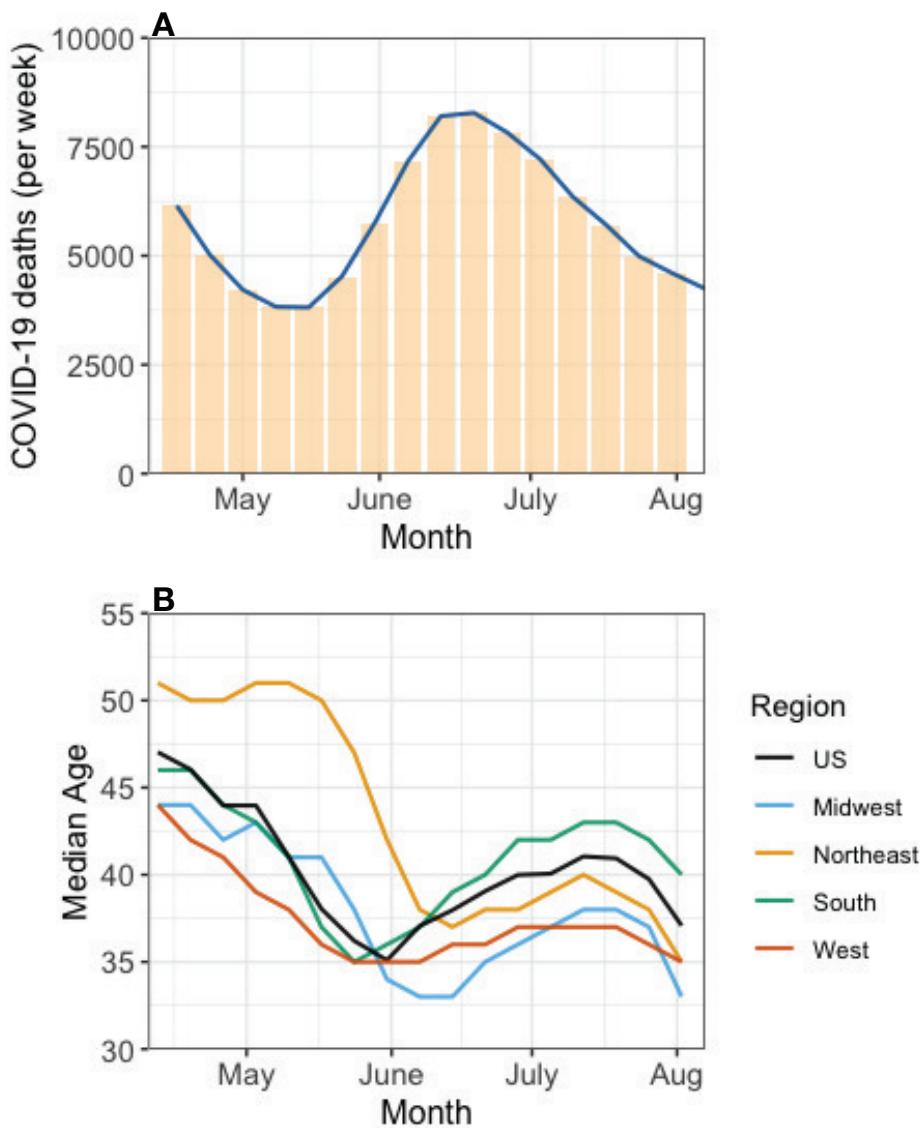


Figure S1. Changes in Median age of COVID-19 infections in US (May-Aug. 2020) as epidemic burden changes over time. (A) End of week deaths due to COVID-19 (bars) from 30 May 2020 to 12 Sept. 2020 from CDC surveillance data. Data are shifted by 21 days to estimate the shape of incident infections. **(B)** Positive RT-PCR tests reported to the CDC by median age from 1 May 2020 to 28 August 2020 from overall US and four US census regions. Tick marks are at 22nd day of the month. Data from October 2020 MMWR [3].

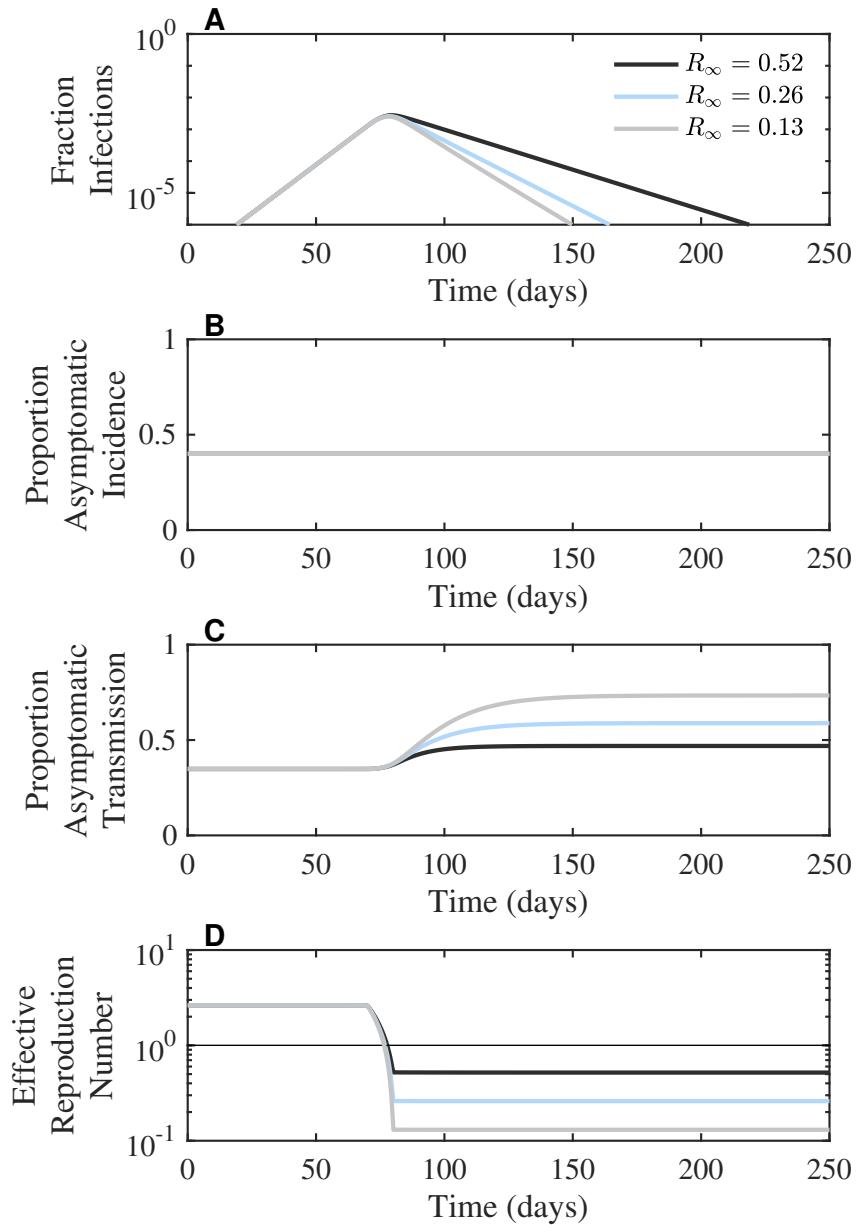


Figure S2. Effects of varying the speed of intervention on the changes in the proportion asymptomatic transmission. Light blue is the same as in Figure 1. Decreasing the final mitigation level and fixing the time period through which the effective reproduction number is reduced (10 days). Black line is twice the final effective reproduction and gray line is half the final effective reproduction number of light blue curve.

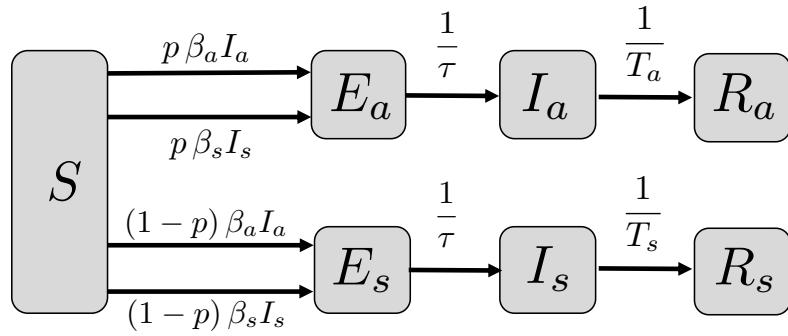


Figure S3. Model structure of SEIR model with fixed proportion asymptomatic incidence. The parameter p sets the proportion of incident cases that are asymptomatic infections. Here, T_a (T_s) is the asymptomatic (symptomatic) infectious period, and τ is the exposed period, assumed to be the same for the both asymptomatic and symptomatic infections.

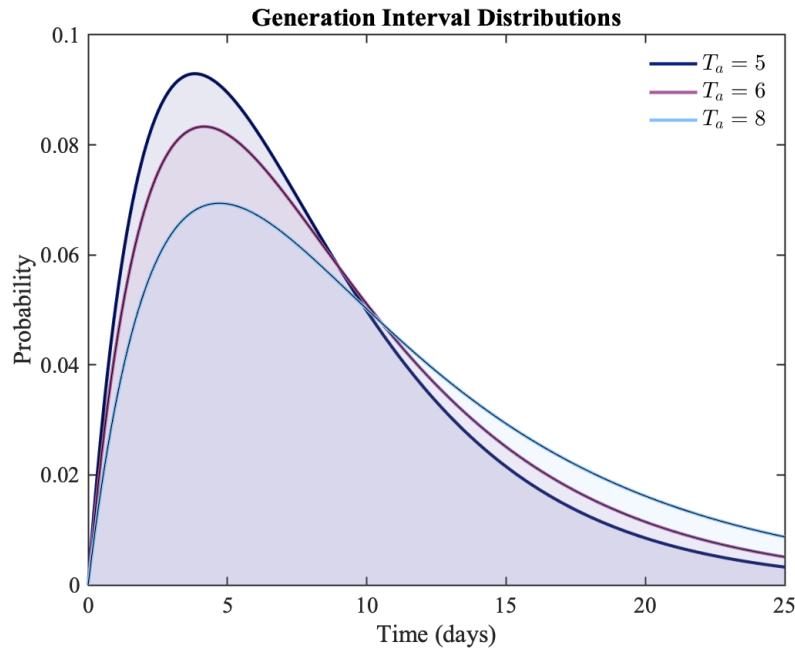


Figure S4. Generation interval distributions of the SEIR model increasing the mean generation time. Increasing the infectious period, $T_a = 5, 6, 8$ days, with fixed exposed period of $\tau = 3$ days. See Equation (2).

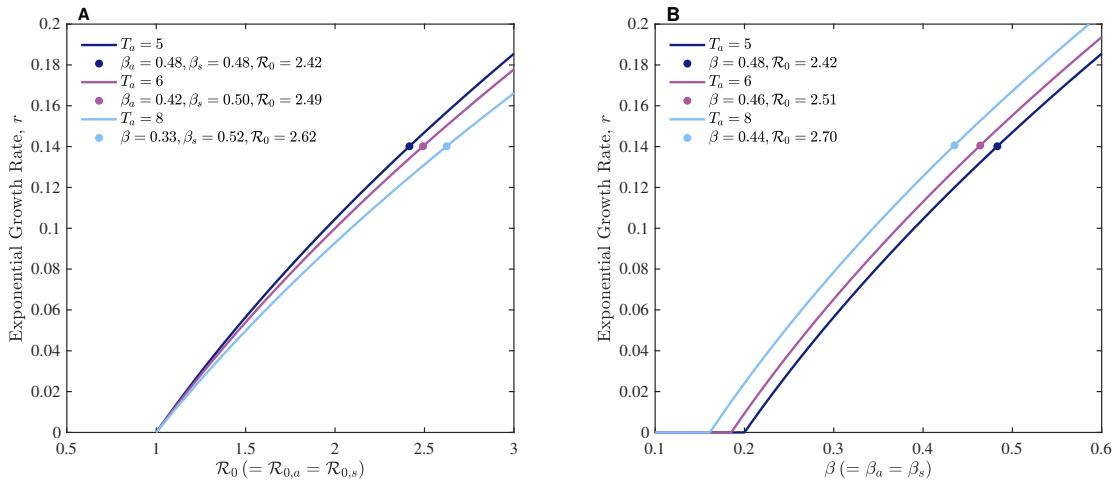


Figure S5. Two ways to parametrise of SEIR model with fixed proportion asymptomatic incidence. We set $p = 0.4$ the proportion of new infections that are asymptomatic to find parameters such that the exponential growth is $r = 0.14$. (A) Assuming the basic reproduction numbers between asymptomatic and symptomatic individuals are the same, i.e., $\mathcal{R}_0 = \mathcal{R}_{0,a} = \mathcal{R}_{0,s}$. Dots correspond to parameter values used in Figure 1 and given in Table 2. (B) Assuming the transmission rates between asymptomatic and symptomatic individuals are the same, i.e., $\beta = \beta_a = \beta_s$. Dots correspond to parameter values used in Figure S6.

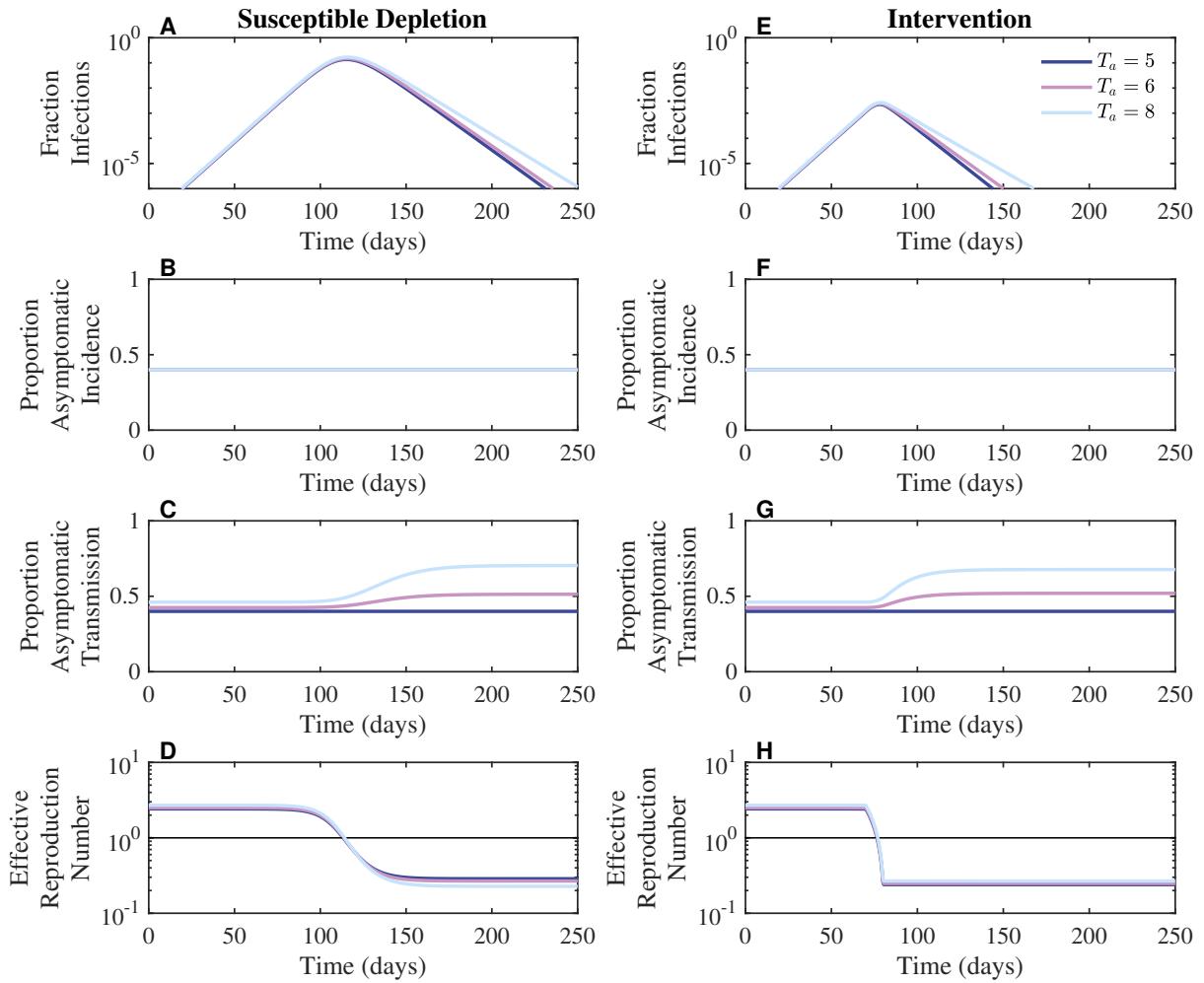


Figure S6. Similar to Figure 1 but assuming asymptomatic and symptomatic have the same transmission rates. With $T_s = 5$, increasing the infectious period of asymptomatic infections from $T_a = 5$ (dark blue), $T_a = 6$ (purple), $T_a = 8$ (light blue). Across all simulations, the fixed proportion of new cases that are asymptomatic is $p = 0.4$ and the exponential growth rate is $r = 0.14/\text{day}$ (Methods). See Figure S5B for parametrisation.

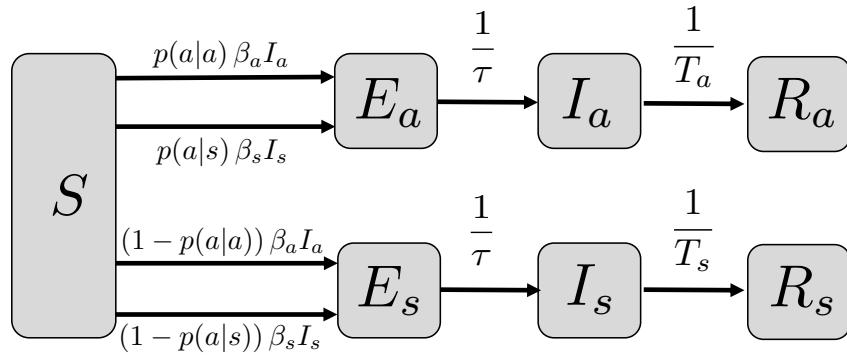


Figure S7. Model structure of SEIR model with assortative transmission. The parameters $p(a|a)$ ($p(a|s)$) indicate the fraction of asymptomatic infections from asymptomatic (symptomatic) transmission. Here, T_a (T_s) is the asymptomatic (symptomatic) infectious period, τ is the exposed period, the same for the both asymptomatic and symptomatic infections.

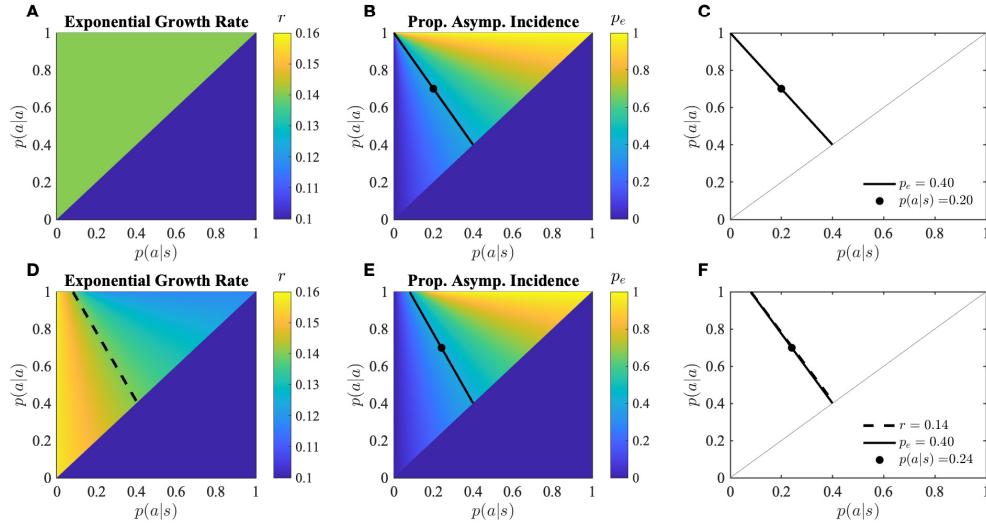


Figure S8. Finding parameters $p(a|a)$ and $p(a|s)$ when reproduction numbers equal. (A-C) $T_a = T_s = 5$ and (D-F) $T_a = 8, T_s = 5$. (A,D) Exponential growth rate as a function of parameters $p(a|a)$ and $p(a|s)$. When time scales equal the exponential growth rate is constant, $r = 0.14$. When time scales differ the exponential growth rate is constant along the dashed line in panel D. (B,E) The proportion of asymptomatic incidence. Solid lines indicate the level set, 0.4; dot is increased assortativity with $p(a|a) = 0.7$. Here, the basic reproduction numbers of the asymptomatic and symptomatic classes are equal, i.e., $\mathcal{R}_{0,a} = \mathcal{R}_{0,s} = \mathcal{R}_0$. (C,F) There is a line of parameters $p(a|a)$ and $p(a|s)$ such that the exponential growth rate is $r = 0.14$ and the proportion of asymptomatic incidence is 0.4. Simulations shown in Figure 2.

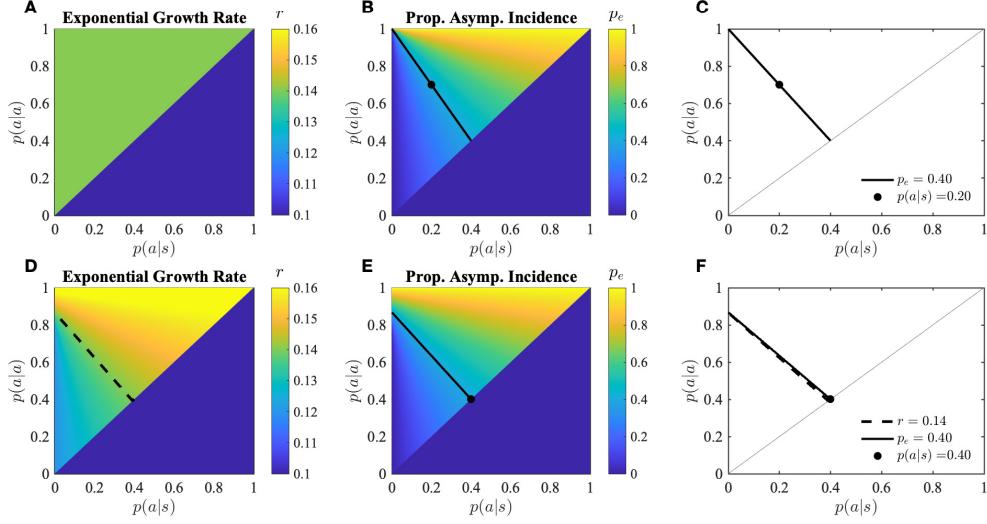


Figure S9. Finding parameters $p(a|a)$ and $p(a|s)$ when transmission rates equal. (A-C) $T_a = T_s = 5$ and (D-F) $T_a = 8, T_s = 5$. (A,D) Exponential growth rate as a function of parameters $p(a|a)$ and $p(a|s)$. When time scales equal the exponential growth rate is constant, $r = 0.14$. When time scales differ the exponential growth rate is constant along the dashed line in panel D. (B,E) The proportion of asymptomatic incidence. Solid lines indicate the level set, 0.4; dot is increased assortativity with $p(a|a) = 0.7$. Here, the asymptomatic and symptomatic transmission rates are equal, i.e., $\beta_a = \beta_s = \beta$. (C,F) There is a line of parameters $p(a|a)$ and $p(a|s)$ such that the exponential growth rate is $r = 0.14$ and the proportion of asymptomatic incidence is 0.4. Simulations shown in Figure S10.

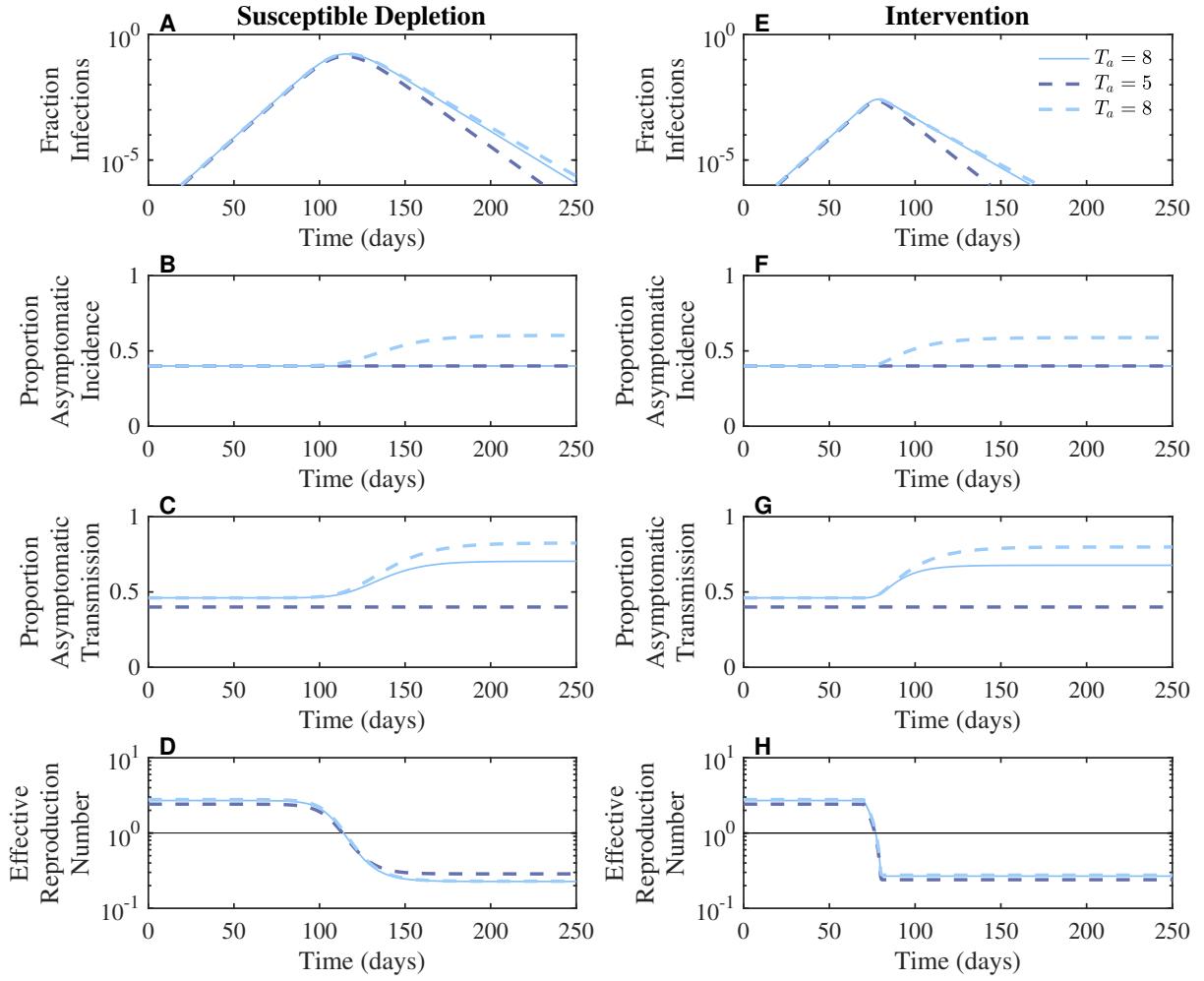


Figure S10. Similar to Figure 2 but assuming transmission rates of asymptomatic and symptomatic infections equal. Setting $T_s = 5$ and increasing the infectious period of asymptomatic carriers from $T_a = 5$ (dark blue) to $T_a = 8$ (light blue). Solid lines correspond to $p = 0.4$ (same as Figure S6) and dashed lines correspond to increased assortativity with $p(a|a) = 0.7$ (and $p(a|s)$ value shown in legend) such that the initial proportion incidence equals 0.4 and exponential growth rate $r = 0.14$. Symmetry breaking lines with respect to $p(a|a)$ and $p(a|s)$ are shown in Figure S9.

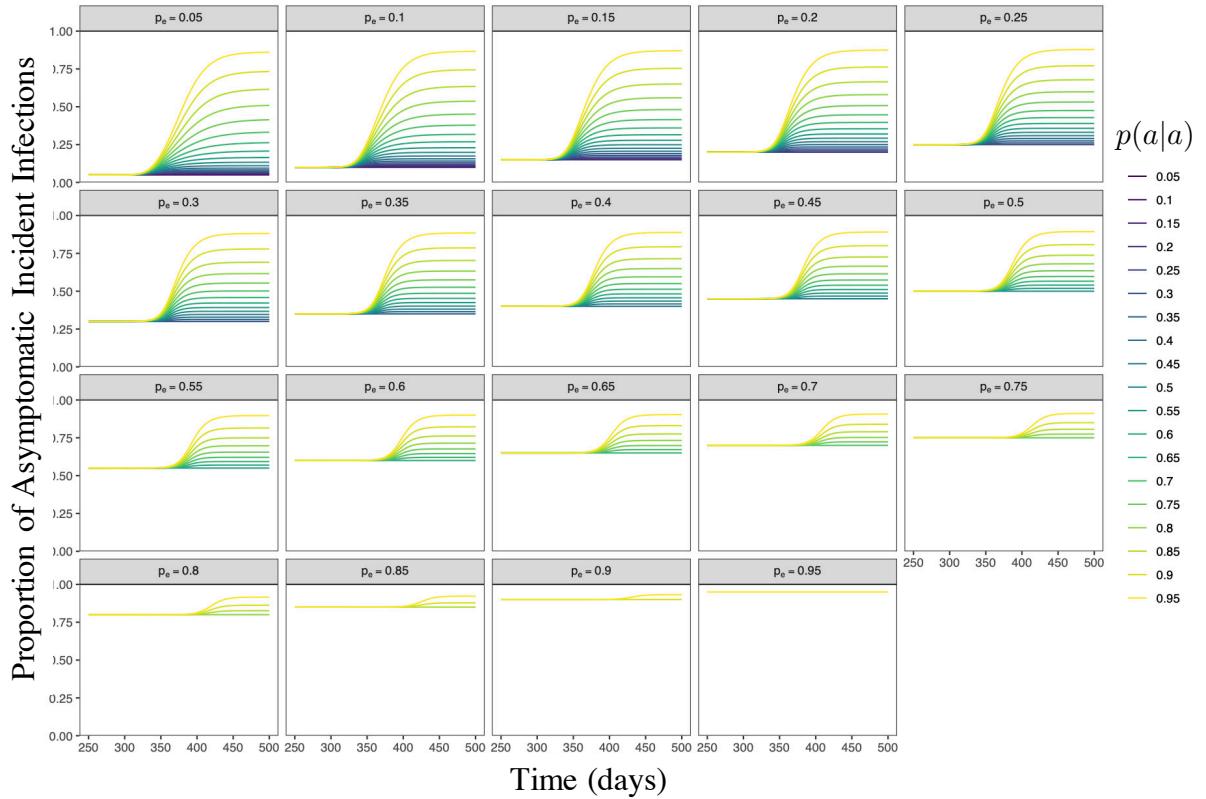


Figure S11. A continuum of trajectories for each initial proportion asymptomatic incident infections. For each initial proportion of asymptomatic incidence $p_e = 0.05, 0.1, \dots, 0.95$ (top of each panel), there is a line of $p(a|a)$ and $p(a|s)$ values such that the initial proportions of asymptomatic incidence are satisfied and the exponential growth rates are matched. Increasing $p_{a|a} = 0.05, 0.1, \dots, 0.95$ (colors go from blue to yellow), increases assortative mixing of asymptomatic and symptomatic infections.

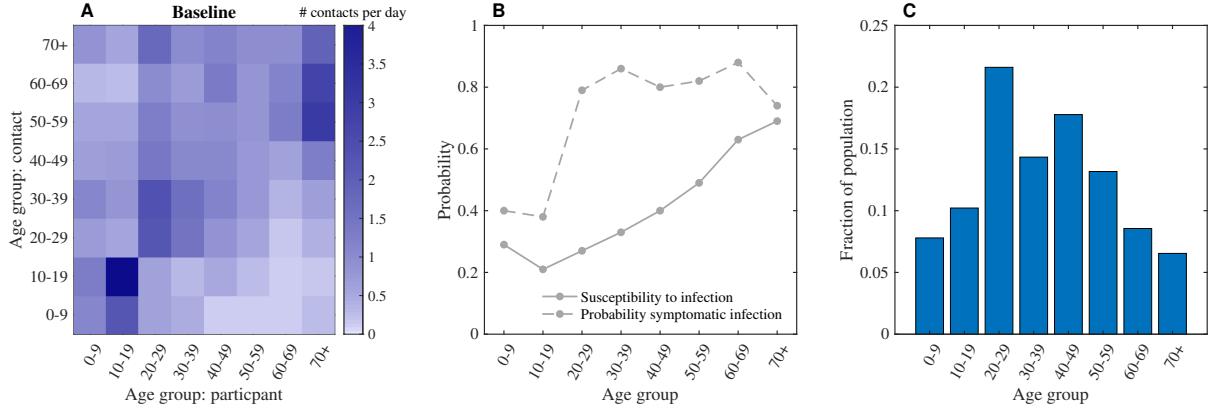


Figure S12. parametrisation of the age-dependent SEIR model. (A) 8×8 contact matrix by age from Wuhan [23]. The blue color gradient indicates the average number of contacts between individuals in different age groups. (B) Probability of being susceptible to infection by age (solid) and probability of the infection being symptomatic by age (dashed) [7]. (C) Age distribution of the population in Wuhan, China. (See Methods.)

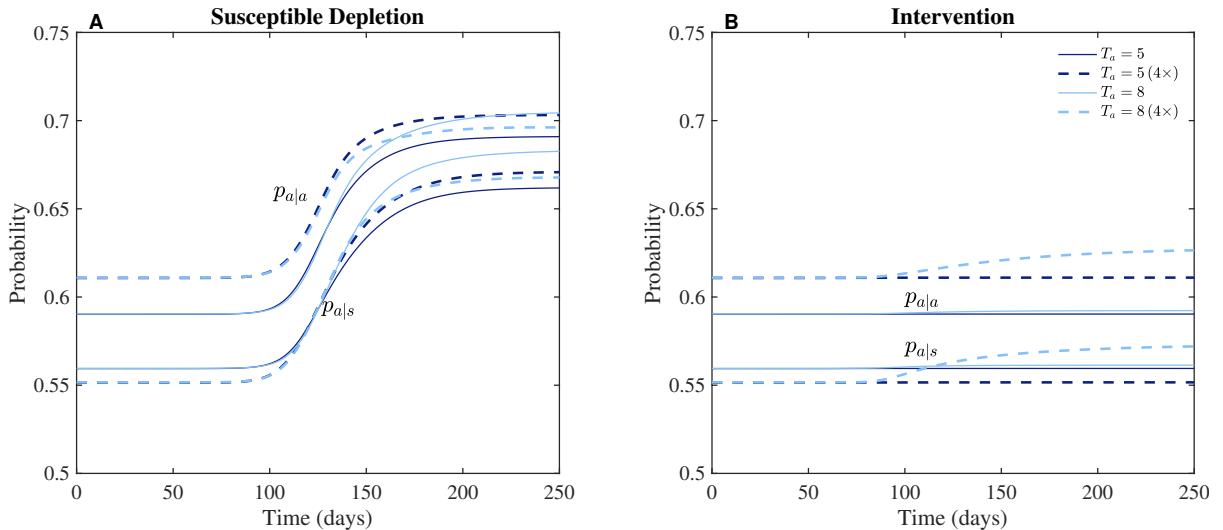


Figure S13. Changes in assortative transmission in the age-dependent model. For the simulations in Figure 3, we plot the conditional probabilities, $p_{a|a}(t)$ and $p_{a|s}(t)$ with susceptible depletion (A) or intervention (B). For each time point, all four $p_{a|a}(t)$ curves are greater than all four $p_{a|s}(t)$ curves.