Modeling asymptomatic transmission in COVID-19 dynamics

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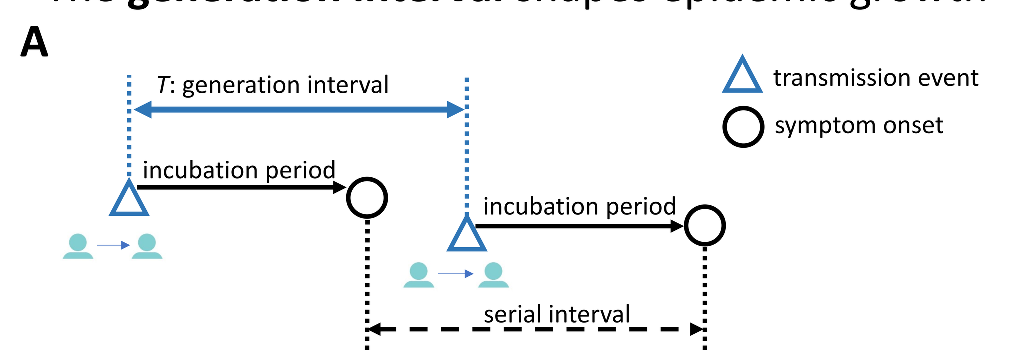
1. Overview

➤ The **generation interval** shapes epidemic growth



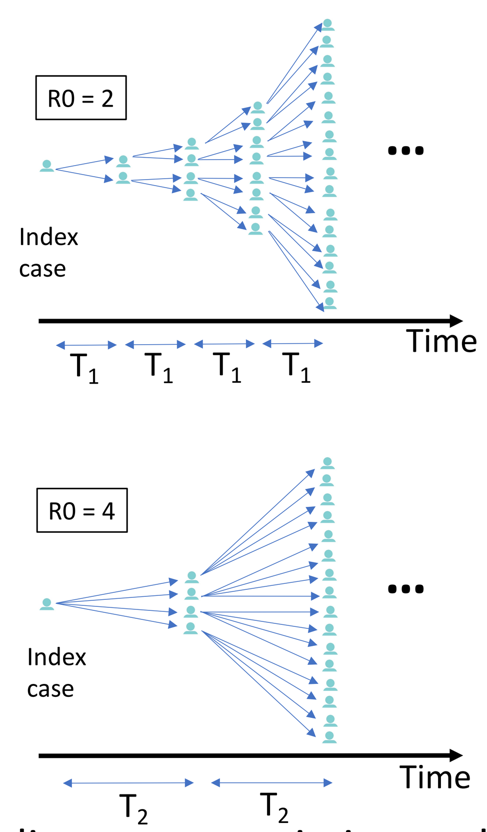


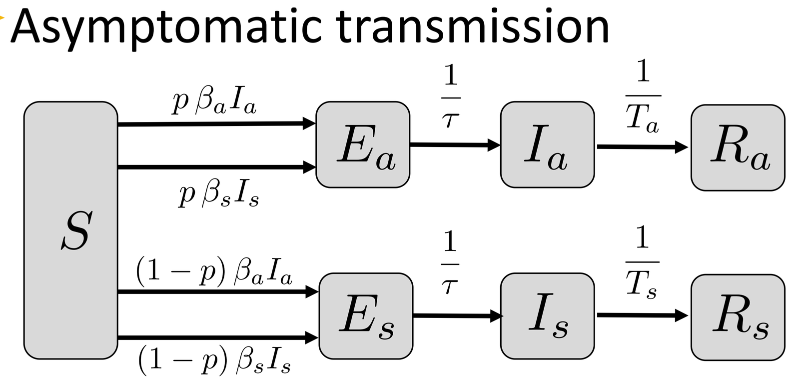
Figure 1. **(A)** The **generation interval (*T*)** is the time between when an individual is infected and when that individual infects another person. **(B)** *T* connects the reproduction number R_0 (an individual-level quantity measuring the "strength" of the epidemic) to the exponential growth rate *r* (a population-level quantity measuring the "speed" of the epidemic) [1]. Two scenarios in which the *r's* are the same but the R_0's differ: $R_0 = 2$ with T_1 *(top) vs.* $R_0 = 4$ with $T_2 = 2T_1$ *(bottom).* (Adapted from [2].)

➤ **Asymptomatic carriers** are important to consider for disease transmission and estimates of epidemic burden [3]

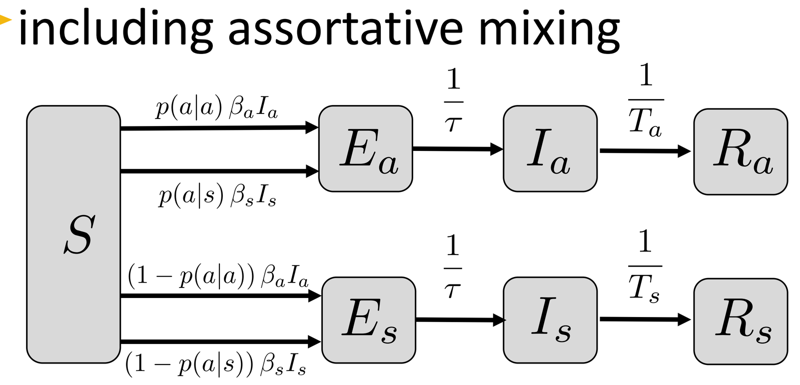
- Asymptomatic carriers may have similar potential to transmit [4], but are not aware and do not isolate → longer generation intervals
- Symptomatic individuals isolate shortly after the onset of symptoms → shorter generation intervals
- If asymptomatic carriers have longer generation intervals relative to symptomatic individuals, what is their impact on disease dynamics at the population level? How do the relative amounts of asymptomatic *transmission* and *incidence* change with total new infections?

2. SEIR models with asymptomatic/symptomatic infections

➤ Asymptomatic transmission



➤ including assortative mixing



variables:
- S : susceptible individuals
- E : exposed individuals
- I : infected individuals
- R : recovered individuals

parameters:
- β : transmission rate
- τ : exposed period
- T : infectious period

subscripts:
- a : asymptomatic individuals
- s : symptomatic individuals

➤ The SEIR model with age-dependent contacts and susceptibility

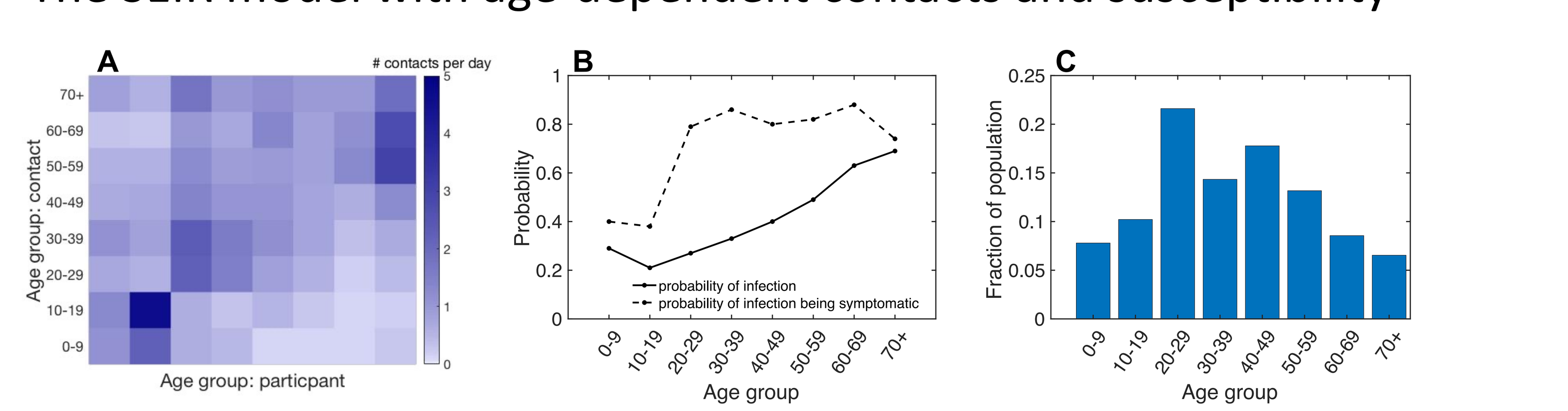


Figure 2. **Parametrization of the age-dependent SEIR model. (A)** Contact matrix from Wuhan [5] by age, showing the average number of contacts one age group makes with another age group. **(B)** Probability of being susceptible to infection by age (solid) and probability of having a symptomatic infection by age (dashed) [6]. **(C)** Age distribution of Wuhan.

3. Longer time scales of asymptomatic transmission

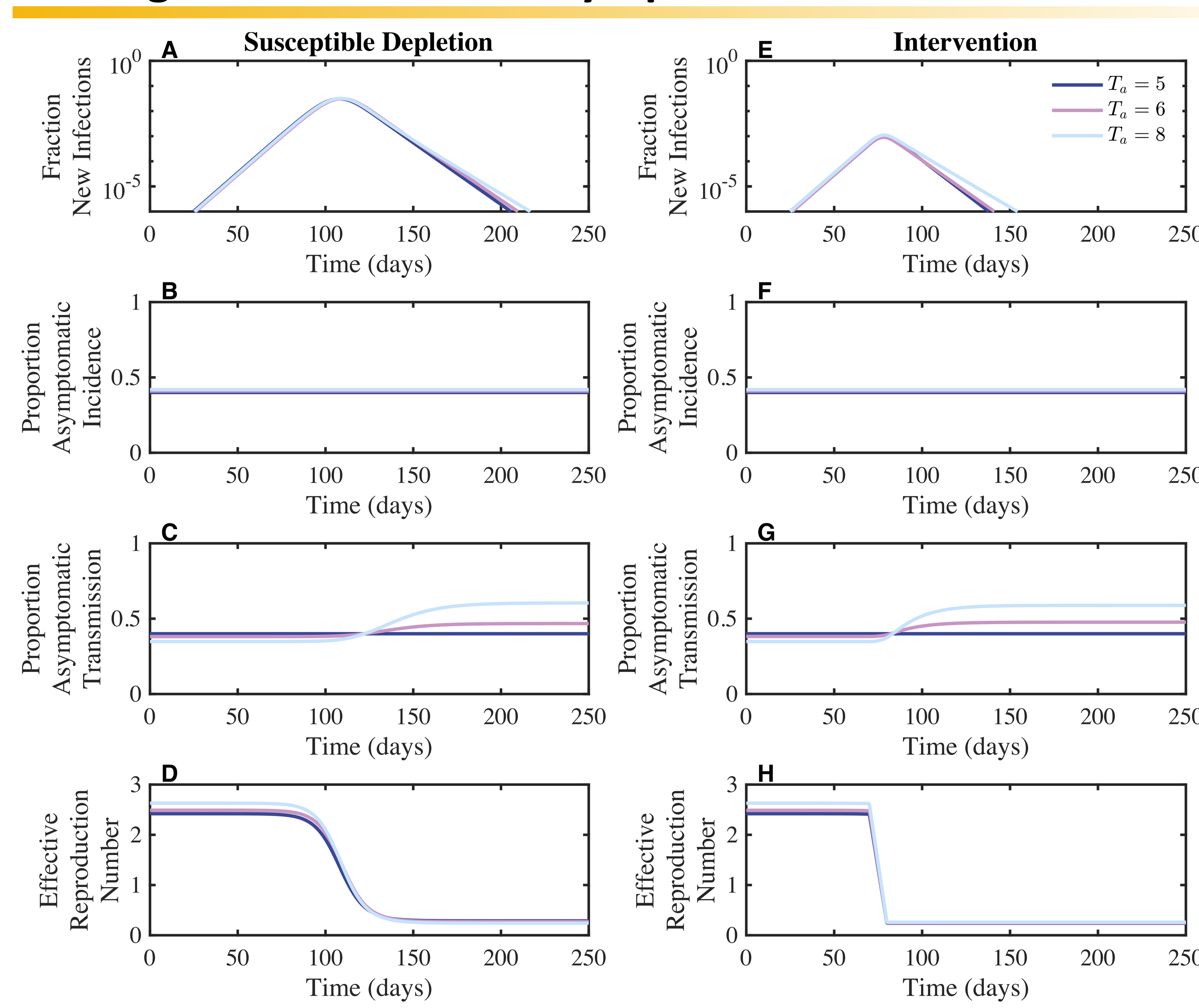


Figure 3. **Longer time sales of asymptomatic infections increase the proportion of asymptomatic transmission.** Setting the infectious period of symptomatic individuals to T_s = 5 days, we increase the infectious period of asymptomatic carriers from T_a = 5 days (dark blue), T_a = 6 days (purple), T_a = 8 days (light blue). **(A-D)** Without intervention the susceptible population is depleted. As new infections decrease, the proportion of asymptomatic transmission increases when the asymptomatic infectious period is longer. **(E-H)** Changes in the proportion of asymptomatic transmission are comparable with intervention when the reproduction number is reduced to similar levels as with susceptible depletion.

4. Longer time scales & assortative transmission

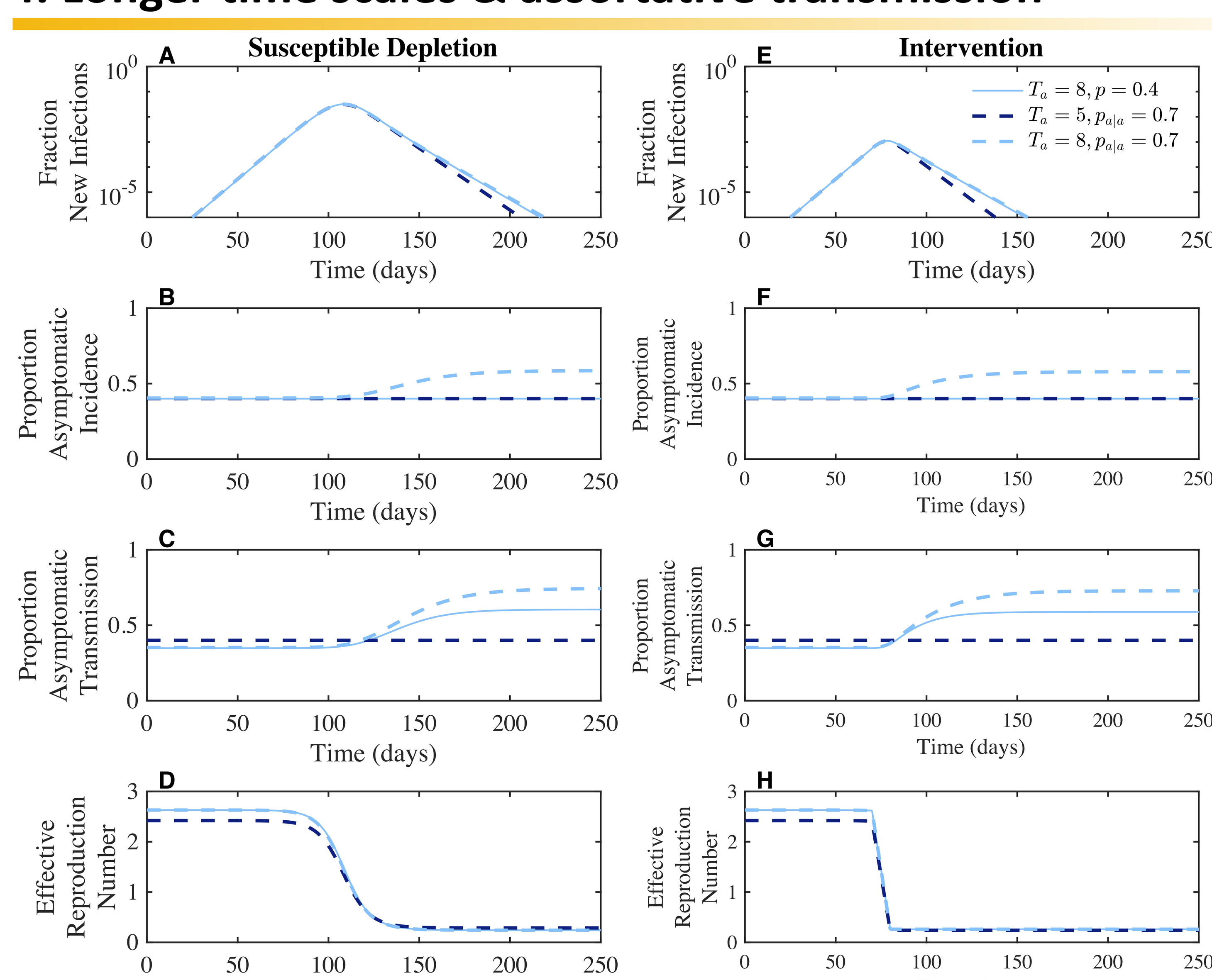


Figure 4. **Longer generation intervals coupled with assortative transmission increase the proportion asymptomatic transmission and incidence.** Setting the symptomatic infectious period to T_s = 5 days, the dashed lines correspond to increasing assortative transmission such that the exponential growth rate and initial proportion of asymptomatic incidence match across simulations. The asymptomatic infectious period is T_a = 5 days (dark blue) and T_a = 8 days (light blue). For comparison, solid light blue curve is when T_a = 8 without assortative transmission (same as in Figure 3). **(A-D)** With susceptible depletion. **(E-H)** Changes are comparable with intervention when the reproduction number is reduced to similar levels as with susceptible depletion.

5. A decrease in the average age of infection

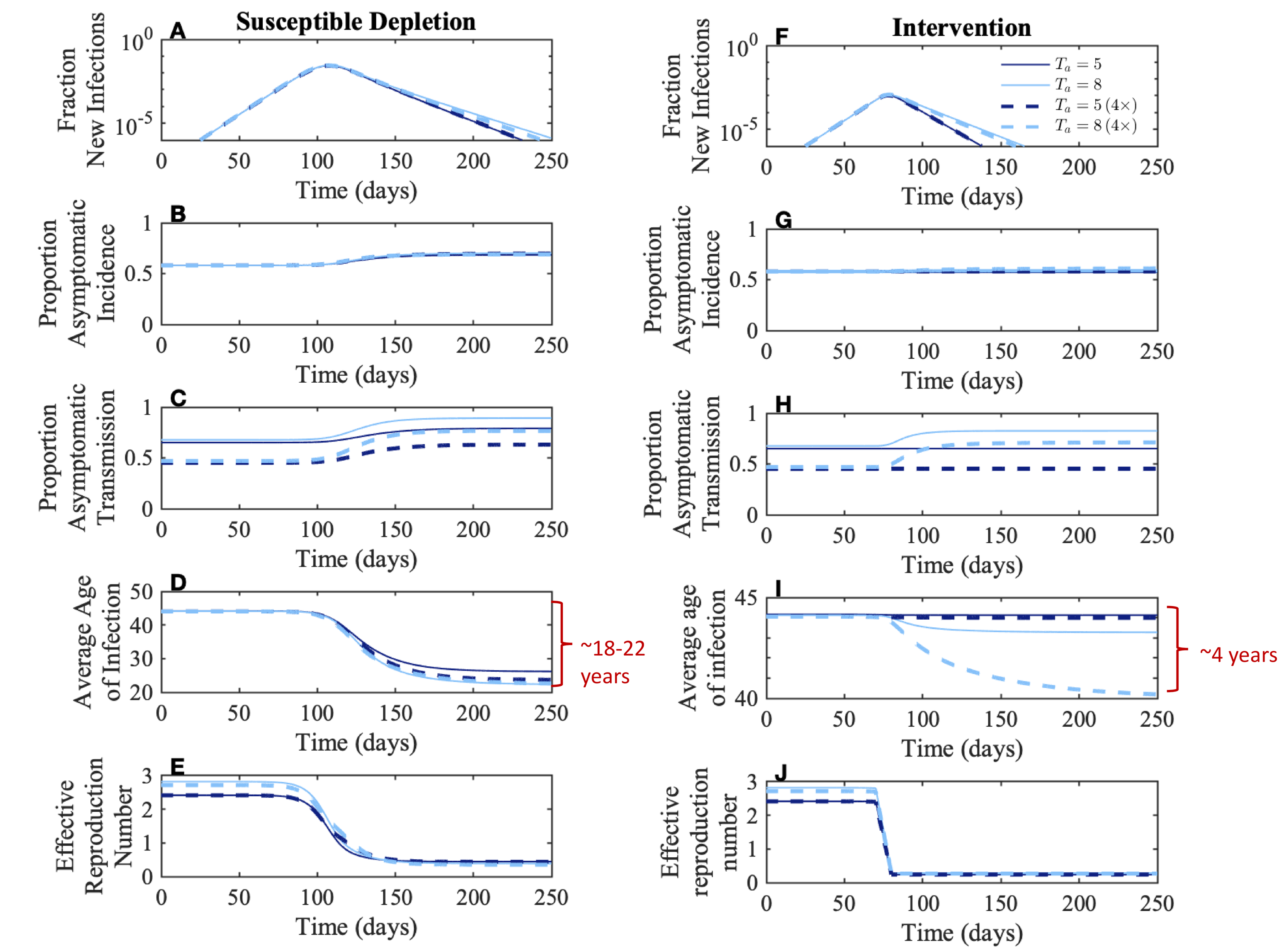


Figure 5. **Longer generation intervals of asymptomatic infections coupled with age-dependent assortative mixing and disease factors can decrease the average age of infection.** Solid lines indicate baseline contact rates. Dashed lines indicate 4 times (4x) the assortative mixing by age from baseline contacts. We compare when asymptomatic and symptomatic infectious periods equal ($T_a = T_s$ = 5 days) and when the asymptomatic infectious period is longer (T_a = 8 days vs. T_s = 5 days).

6. Conclusions

Consequences of longer periods of transmission for asymptomatic individuals relative to symptomatic individuals:

- The proportion of new infections from asymptomatic transmission can increase when total infections decrease (**Fig. 3C,G**).
- Including assortative transmission may also increase the proportion of new asymptomatic infections (**Fig. 4B,F**).

➤ Coupling longer time scales with age-dependent contacts and susceptibility estimates shifts the age distribution of infection toward younger age groups:

- When total new infections decrease the average age of those infected should go down due to the increase in the proportion of asymptomatic infections (which tend to occur in younger individuals)
- Such changes in age may explain the decrease in the median age of infection over summer 2020 in the US (**Fig. 5 D,I**; see data from CDC, Fig. 1 of [7]).

➤ Overall, these results show the importance of the relative contribution of asymptomatic transmission toward overall disease dynamics in COVID-19.

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