Modeling asymptomatic transmission in COVID-19

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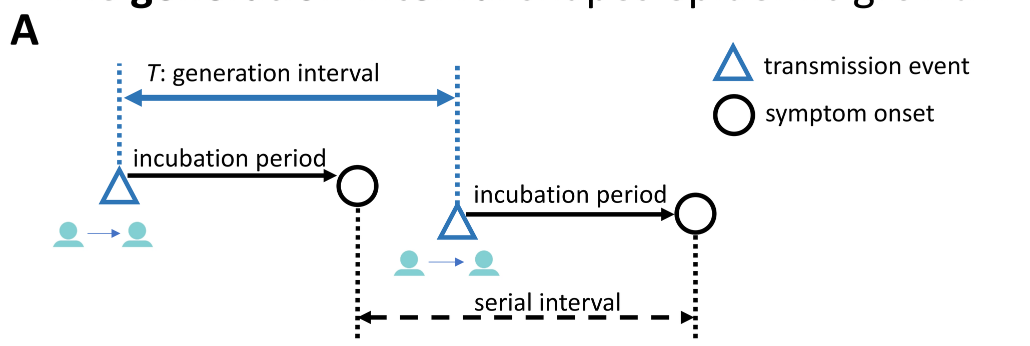
1. Overview

➤ The **generation interval** shapes epidemic growth



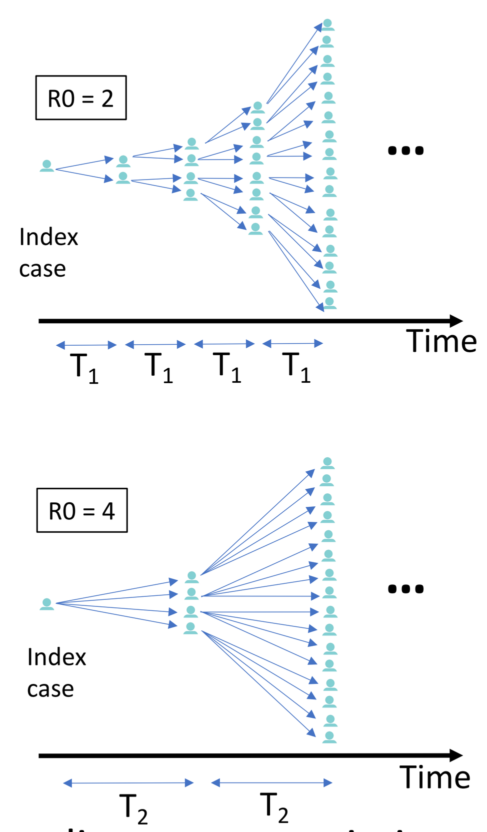


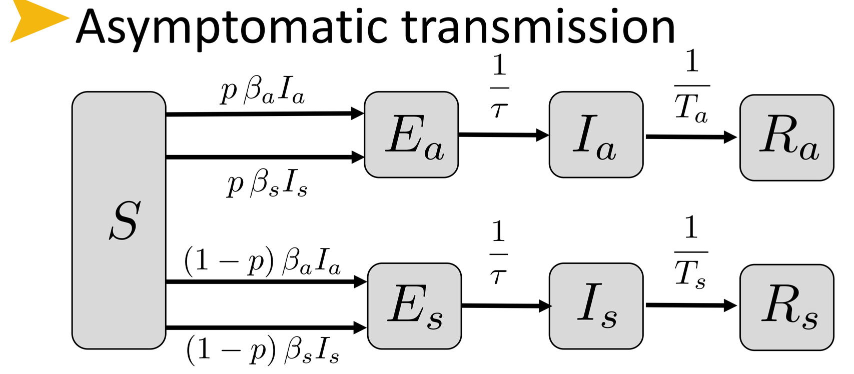
Figure 1. **(A)** The **generation interval (*T*)** is the time between when an individual is infected and when that individual infects another person. **(B)** *T* connects the reproduction number R_0 (an individual-level quantity measuring the "strength" of the epidemic) to the exponential growth rate *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]

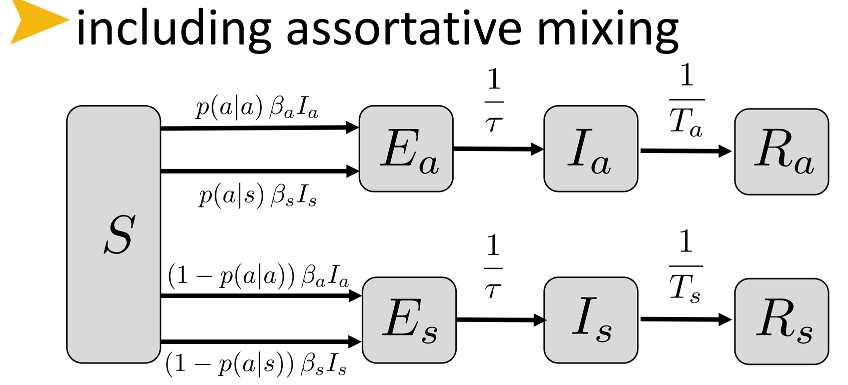
- Asymptomatic carriers may have similar potential to transmit [4], but are not aware → they do not isolate
- Symptomatic individuals isolate shortly after the onset of symptoms
- If asymptomatic carriers have longer generation intervals relative to symptomatic individuals, what is their impact on disease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

2. SEIR model: 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

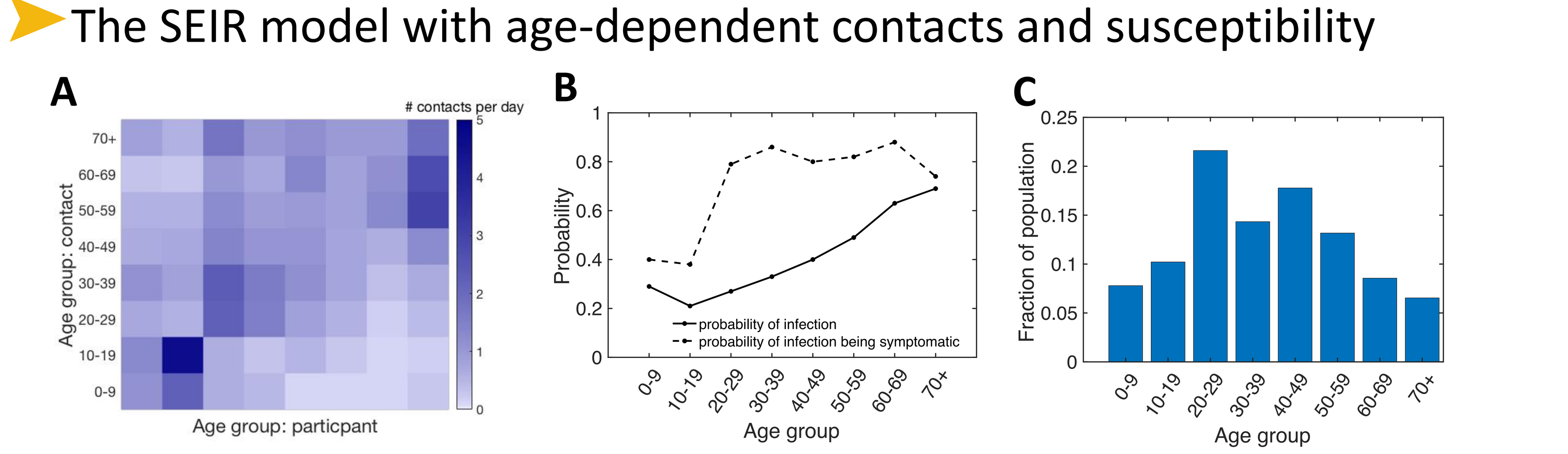


Figure 2. **Parametrization of the age-dependent SEIR model. (A)** contact matrix from Wuhan [5] by age, showing the average number of contacts one age group makes with another age group. **(B)** probability of being susceptible to infection by age (solid) and probability of having a symptomatic infection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

3. Asymptomatic transmission

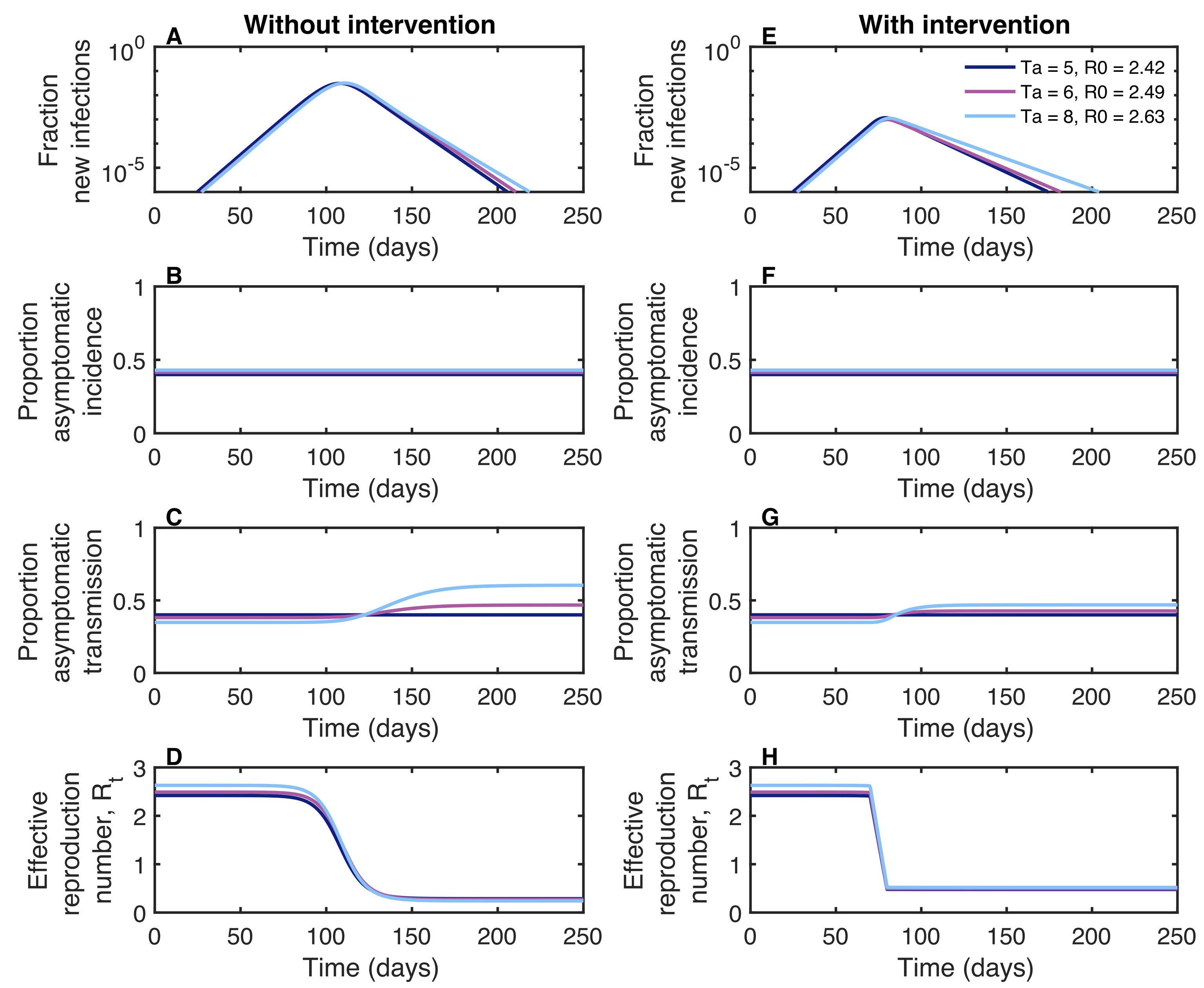


Figure 3. **Longer infectious periods of asymptomatic individuals affect the proportion of asymptomatic transmission. (A-D)** without intervention, the susceptible population is depleted. **(E-H)** changes observed in the proportion of asymptomatic transmission are lessened with intervention.

4. Asymptomatic transmission & assortative mixing

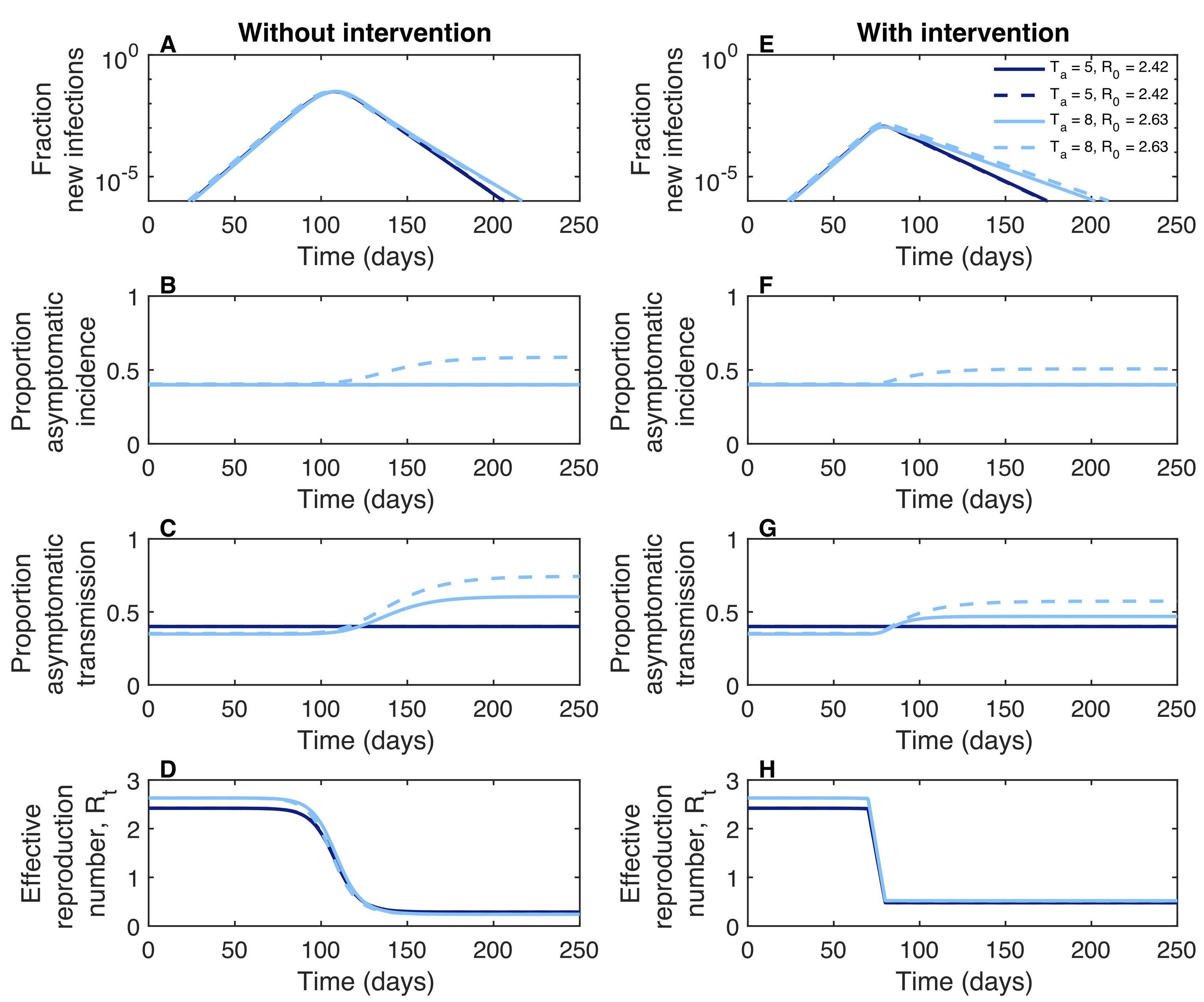


Figure 4. **Addition of assortative mixing to longer time-scales of asymptomatic transmission increases the proportion of asymptomatic incidence. (A-D)** no intervention; **(E-H)** with intervention, increases in the proportion of asymptomatic incidence (as well as transmission) are lessened.

5. Changes in the average age of infection

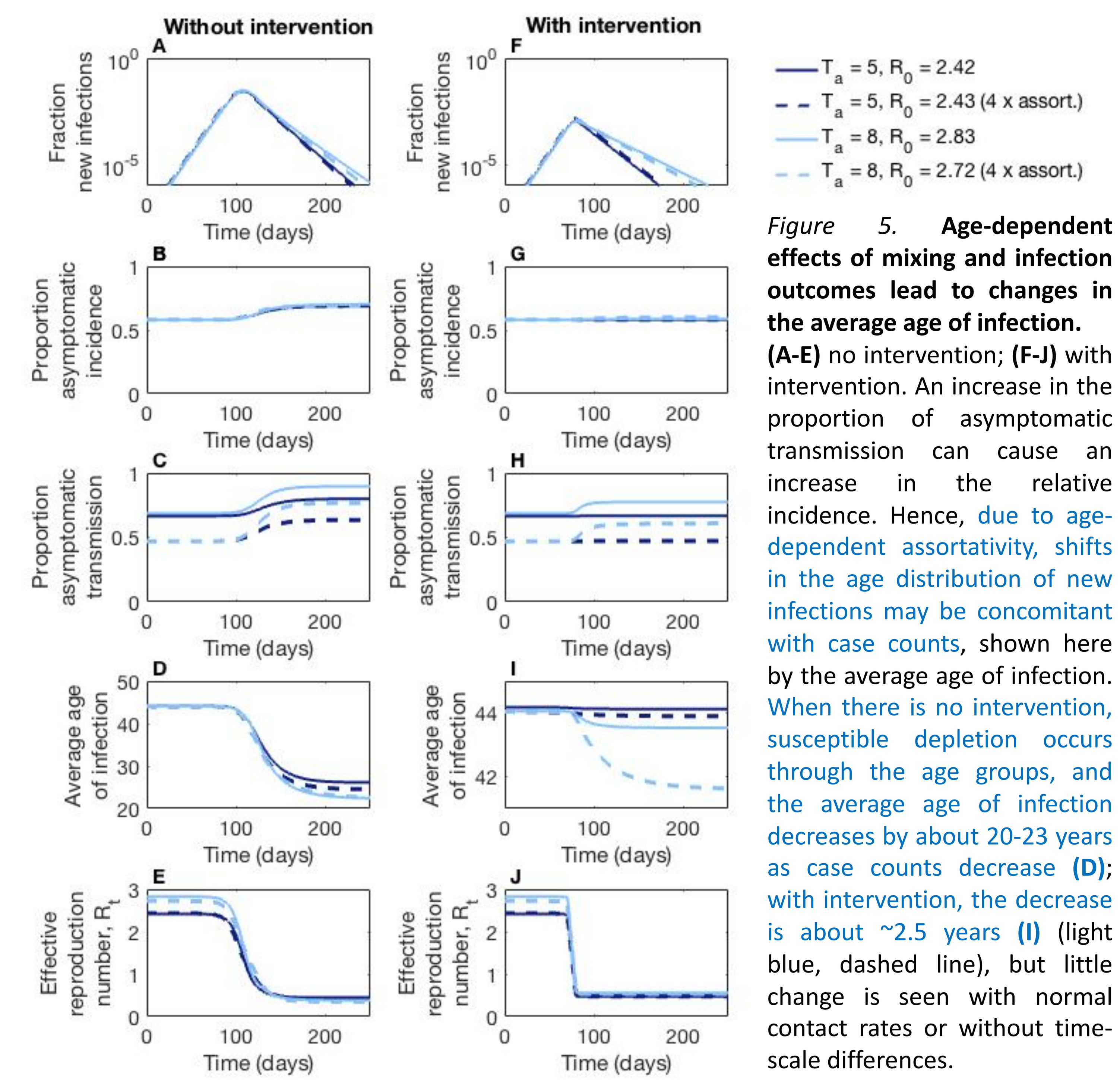


Figure 5. **Age-dependent effects of mixing and infection outcomes lead to changes in the average age of infection. (A-E)** no intervention; **(F-J)** with intervention. An increase in the proportion of asymptomatic transmission can cause an increase in the relative incidence. Hence, due to age-dependent assortativity, shifts in the age distribution of new infections may be concomitant with case counts, shown here by the average age of infection. When there is no intervention, susceptible depletion occurs through the age groups, and the average age of infection decreases by about 20-23 years as case counts decrease **(D)**; with intervention, the decrease is about ~2.5 years **(I)** (light blue, dashed line), but little change is seen with normal contact rates or without time-scale differences.

6. Conclusions

Consequences of asymptomatic individuals transmitting for longer periods (relative to symptomatic individuals):

- the fraction of new cases attributed to asymptomatic transmission can decrease when total case counts are increasing and increase when total case counts are decreasing (**Fig. 3C,G**).
- Due to assortative mixing, the fraction of new cases that are asymptomatic may also increase when total case counts decrease (**Fig. 4B,F**).

➤ With age-dependent contacts and susceptibility estimates, longer infectious periods of asymptomatic carriers may explain shifts in the age distribution of infection:

- case counts increase then the average age of those infected should go up, whereas as case counts decrease then the average age of those infected should go down (**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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