Characterizing key attributes of COVID-19 transmission dynamics in China’s original outbreak: Model-based estimations

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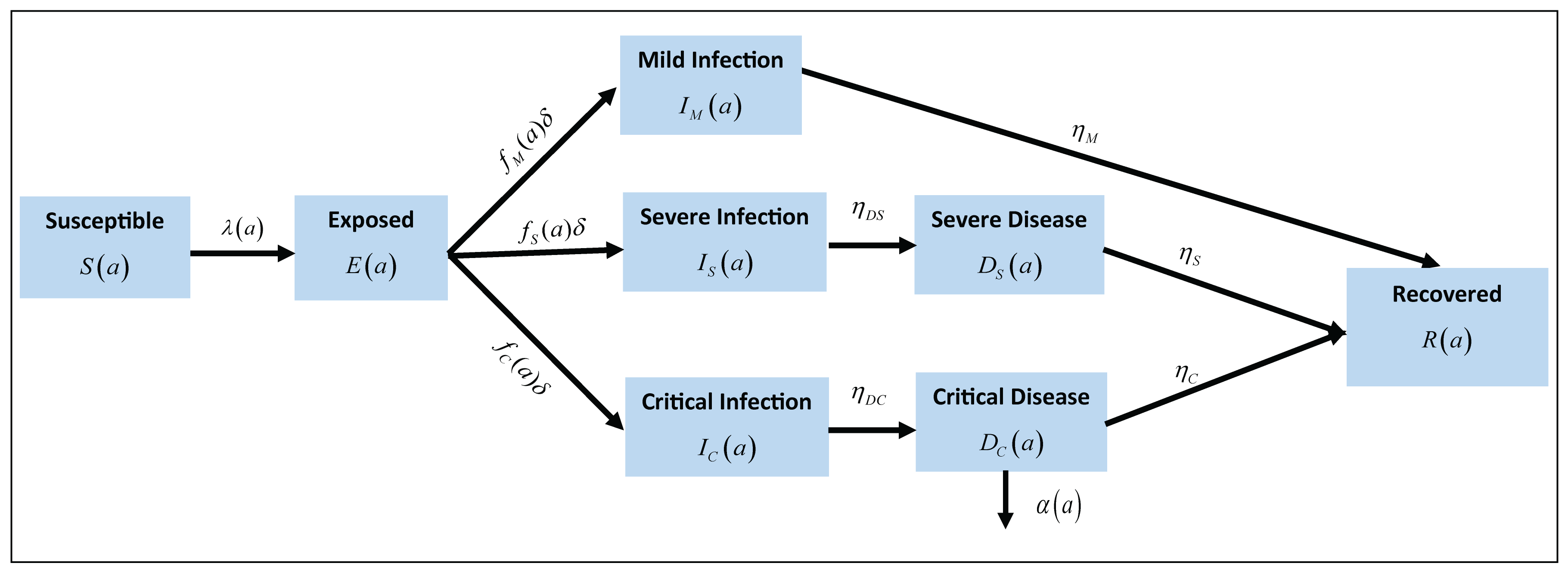
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**Section 1. Mathematical model**

We developed a deterministic compartmental mathematical model to describe the transmission dynamics and disease progression of the [severe acute respiratory syndrome coronavirus 2](https://en.wikipedia.org/wiki/Severe_acute_respiratory_syndrome_coronavirus_2) (SARS-CoV-2) in a population (S1 Fig). For simplicity, we will thereafter refer to this virus as COVID-19, given prevalent current use. This model stratifies the population into compartments according to age group (0-9, 10-19, 20-29,…, ≥80 years), and infection status (uninfected, infected), infection stage (mild, severe, critical), and disease stage (severe, critical).

**S1 Fig. Schematic diagram describing the basic structure of the COVID-19 model.**



*Model equations and description*

The model was expressed in terms of a system of coupled nonlinear differential equations for each age group. The index  denotes the different age cohorts  in the population, with each age group representing a ten-year age band apart from the last one (those ≥80 years of age). The population size and demographic structure were set by China’s demography as provided by the United Nations World Population Prospects database [[1](#_ENREF_1)]. However, the population size and distribution across age groups were fixed at 2020 levels, to disentangle the epidemiologic and demographic effects—a valid assumption given that the current time scale of the epidemic is only few months. All COVID-19 mortality was assumed to occur in individuals that are in the critical disease stage, as informed by the China outbreak data [[2](#_ENREF_2)].

The following set of equations was used to describe the epidemic dynamics in the first age group:

Population aged 0-9 years:

















For subsequent age groups, the following set of equations was used:

Populations aged 10+ years:

















The definitions of population variables and symbols used in the equations are listed in S1 Table.

**S1 Table. Definitions of population variables and symbols used in the model.**

|  |  |
| --- | --- |
| Symbol | Definition |
|  | Susceptible population |
|  | Latently infected population |
|  | Population with mild infection |
|  | Population with severe infection |
|  | Population with critical infection |
|  | Population with severe disease |
|  | Population with critical disease |
|  | Recovered population |
|  | Total population size |
|  | Number of age groups |
|  | Transition rate from one age group to the next age group |
|  | Susceptibility profile to the infection in each age group |
|  | Infectious contact rate |
|  | Duration of latent infection |
|  | Duration of mild infection infectiousness |
|  | Duration of severe infection infectiousness before isolation and/or hospitalization |
|  | Duration of severe disease following onset of severe disease |
|  | Duration of critical infection infectiousness before isolation and/or hospitalization |
|  | Duration of critical disease following onset of critical disease |
|  | Natural death rate |
|  | *Relative* case fatality rate in each age group |
|  | Disease mortality rate in each age group |
|  | Proportion of infections that will progress to be mild or asymptomatic infections |
|  | Proportion of infections that will progress to be severe infections |
|  | Proportion of infections that will progress to be critical infections |
|  | Age mixing matrix describing the mixing among the different age groups |
|  | Degree of assortativeness in the age group mixing |
|  | Basic reproduction number |
|  | Time delay between onset of actual infection and case notification |
|  | Time delay between actual death and reported death |

The force of infection (hazard rate of infection) experienced by each susceptible population  is given by

.

Here,  is the rate of infectious contacts parameterized to capture the effect of the public health interventions implemented in China through a Woods-Saxon function [[3-6](#_ENREF_3)]. This function is mathematically designed to describe and characterize transitions in terms of their scale or strength, smoothness or abruptness, thickness (duration), and the turning point [[3](#_ENREF_3), [4](#_ENREF_4)]:

,

where , , ,  are the fitting parameters used to describe the reduction in the rate of infectious contacts.

The mixing among the different age groups is dictated by the mixing matrix . This matrix provides the probability that an individual in the  age group will mix with an individual in the age group. The mixing matrix is given by



Here,  is the identity matrix.  measures the degree of assortativeness in the mixing. At the extreme , the mixing is fully proportional. Meanwhile, at the other extreme, , the mixing is fully assortative, that is individuals mix only with members in their own age group.

The disease mortality rate  was parametrized through an overall fitting factor multiplied by the observed crude age-stratified case fatality rate.

**Section 2.** **Parameter values**

The input parameters of the model were chosen based on current empirical data for COVID-19 natural history and epidemiology. The parameter values are listed in S2 Table.

**S2 Table. Model assumptions in terms of parameter values.**

|  |  |  |  |
| --- | --- | --- | --- |
| **Parameter** | **Symbol** | **Value** | **Justification** |
| Duration of latent infection |  | 3.69 days | Based on existing estimate [[7](#_ENREF_7)] and based on a median incubation period of 5.1 days [[8](#_ENREF_8)] adjusted by observed viral load among infected persons [[9](#_ENREF_9)] and reported transmission before onset of symptoms [[10](#_ENREF_10)] |
| Duration of infectiousness | ;; | 3.48 days | Based on existing estimate [[7](#_ENREF_7)] and based on observed time to recovery among persons with mild infection [[7](#_ENREF_7), [11](#_ENREF_11)] and observed viral load in infected persons [[9](#_ENREF_9), [10](#_ENREF_10)] |
| Duration of severe disease following onset of severe disease |  | 28 days | Observed duration from onset of severe disease to recovery [[11](#_ENREF_11)] |
| Duration of hospitalization for critical infection |  | 28 days | Observed duration from onset of critical disease to recovery [[11](#_ENREF_11)] |
| Life expectancy in China |  | 77.47 years | United Nations World Population Prospects database [[1](#_ENREF_1)] |
| Crude case fatality rate in each age group |  |  | Observed crude case fatality rate based on China data as of February 11, 2020 [[2](#_ENREF_2), [12](#_ENREF_12)] |
| Age 0-9 years |  | 0% |  |
| Age 10-39 years |  | 0.2% |  |
| Age 40-49 years |  | 0.4% |  |
| Age 50-59 years |  | 1.3% |  |
| Age 60-69 years |  | 3.6% |  |
| Age 70-79 years |  | 8.0% |  |
| Age 80+ years |  | 21.9% |  |
| Proportion of infections that will progress to be mild or asymptomatic infections |  |  | Observed proportion of infections that eventually develop mild or asymptomatic in China [[11](#_ENREF_11), [13](#_ENREF_13), [14](#_ENREF_14)] |
| Age 0-9 years |  | 88.9% |  |
| Age 10-49 years |  | 88.0% |  |
| Age 50-59 years |  | 82.5% |  |
| Age 60+ years |  | 71.2% |  |
| Proportion of infections that will progress to be severe infections |  |  | Observed proportion of infections that eventually develop severe disease in China [[11](#_ENREF_11), [13](#_ENREF_13), [14](#_ENREF_14)] |
| Age 0-9 years |  | 11.1% |  |
| Age 10-49 years |  | 9.9% |  |
| Age 50-59 years |  | 10.3% |  |
| Age 60+ years |  | 7.8% |  |
| Proportion of infections that will progress to be critical infections |  |  | Observed proportion of infections that eventually develop critical disease in China [[11](#_ENREF_11), [13](#_ENREF_13), [14](#_ENREF_14)] |
| Age 0-9 years |  | 0.0% |  |
| Age 10-49 years |  | 2.2% |  |
| Age 50-59 years |  | 7.2% |  |
| Age 60+ years |  | 20.9% |  |

**Adjustment for the outlying values for the number of cases and deaths reported on February 13, 2020**

There was a change in coronavirus case definition in China on February 13, 2020, to include, in addition to the laboratory-confirmed cases, those who are clinically-diagnosed [[15](#_ENREF_15), [16](#_ENREF_16)]. This led to a very sharp one-day increase in the reported numbers of infections and deaths, respectively [[17](#_ENREF_17)]. These “outlying observations” included the “excess” cases not accounted for in previous days.

To correct for this data artifact, we distributed the number of cases reported on February 13, 2020 over a time duration including this date and previous dates. This was done through the condition:



Here,  is the increment added to the reported number of cases in each -day starting with February 13 and moving backward,  is the adjusted number of cases in February 13,  and  are fitting parameters, and  calculated using the above constraint. Model fitting (and uncertainty analysis) yielded the following estimates:  = 1,187 (95% uncertainty interval (UI): 970-1,453) and  = 25 (95% UI: 22-29) days.

Similarly, we distributed the number of deaths reported on February 13, 2020 over a time duration including this date and previous dates. This was done through the condition:



Here,  is the increment added to the reported number of cases in each -day starting with February 13 and moving backward,  is the adjusted number of cases in February 13,  and  are fitting parameters, and  calculated using the above constraint. Model fitting (and uncertainty analysis) yielded the following estimates:  = 109 (95% UI: 104-114) and  = 16 (95% UI: 13-20) days.

**Section 3.** **The basic reproduction number *R0***

Using the second generation matrix method described by Heffernan *et al.* [[18](#_ENREF_18)], the basic reproduction number was derived to be:

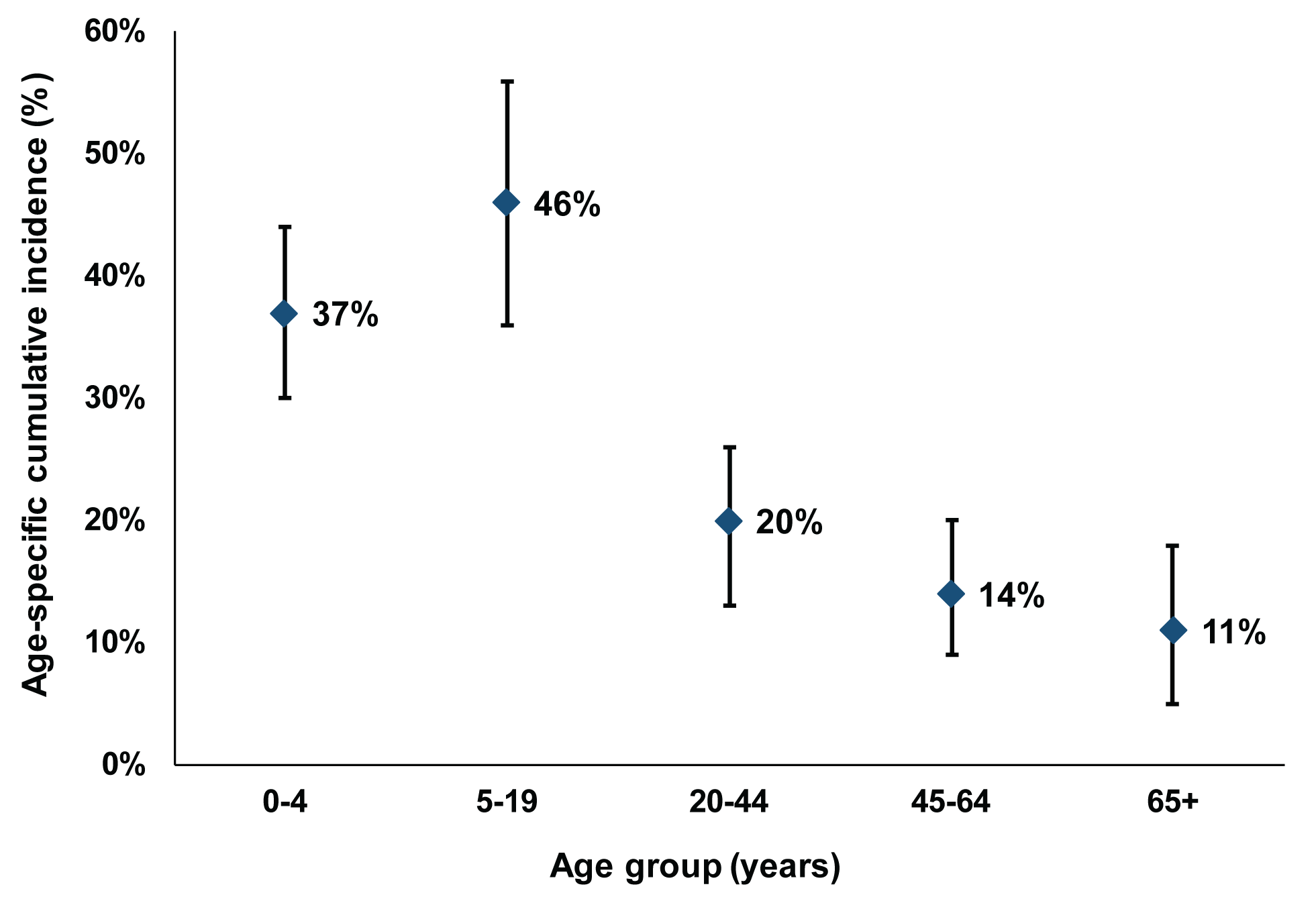
,

where  is the proportion of the population in each age group.

**S2 Fig.** **Uncertainty analysis estimating the range of uncertainty around key model predictions. Results of 500 uncertainty runs showing (A) the time-dependent crude case fatality rate in the total population defined as the cumulative number of deaths out of the cumulative number of diagnosed infections, (B) the age-dependence of the relative susceptibility to the infection, (C) the time-dependent basic reproduction number, and (D) the time-dependent rate of infectious contacts.**

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**S3 Fig.** **Age-specific cumulative incidence of the 2009 influenza A (H1N1) pandemic (H1N1pdm) virus [**[**19**](#_ENREF_19)**].**



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