Supplementary Information:

Quantifying the contribution of asymptomatic infection to the cumulative incidence

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This supplementary material provides details of the model structure and calculation of the proportion of the cumulative incidence attributable to asymptomatic transmission with relevant citations.

SI.1 Mathematical model

Let S be the proportion of susceptible individuals in the entire population, E the proportion of individuals who are infected but not yet infectious. We denote the proportion of asymptomatic and symptomatic infections in the population by A and I, respectively. We also denote the proportion of the population that is recovered and immune from infection by R. We omit the demographic factors, including birth and death.

We consider a standard SEAIRS epidemiological model [2] to describe the temporal evolution (dynamics) of each population group with the following differential equations:

$$S' = -c_I p_I IS - c_A p_A AS + R/\ell \tag{1a}$$
$$E' = +c_I p_I IS + c_A p_A AS - \sigma E \tag{1b}$$
$$A' = \alpha\sigma E - A/d_A \tag{1c}$$
$$I' = (1-\alpha)\sigma E - I/d_I \tag{1d}$$
$$R' = A/d_A + I/d_I - R/\ell \tag{1e}$$

Subscripts $\bullet_I$ and $\bullet_A$ relate to symptomatic and asymptomatic infections, respectively. The parameter c is the contact rate per capita per unit time; p is the probability of transmission given a contact is made (*i.e.*, the "intrinsic infectiousness"); $1/\sigma$ is the average duration of the latent period; α is the proportion of all cases that develop asymptomatic infection (herein, referred to as "asymptomatic fraction"); d is the average duration of infectiousness; and ℓ is the average duration of effective immunity. Note that ℓ can take an infinite

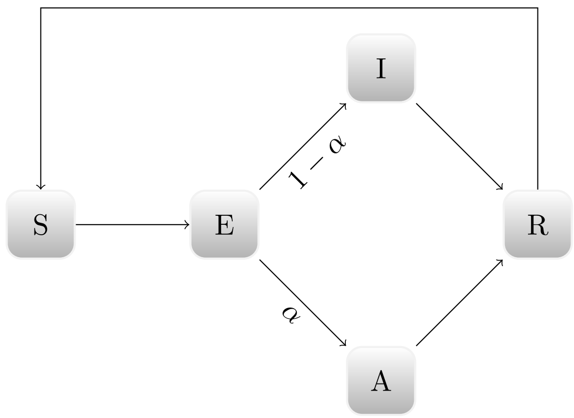

Figure S1: Schematic diagram of the SEAIRS model.

value, which in this case translates into a model of permanent immunity after infection. A schematic diagram for transitions between the model population groups is shown in Figure S1.

The incidence caused by symptomatic and asymptomatic cases is respectively $J_I = c_I p_I IS$ and $J_A = c_A p_A AS$. Hence, the proportion P of the cumulative incidence attributable to asymptomatic cases is

$$P = \frac{\displaystyle\int_0^\infty J_A(t)dt}{\displaystyle\int_0^\infty \Big(J_A(t) + J_I(t)\Big)dt} \tag{2}$$

We introduce the following ratios in order to measure the relative infectivity of the asymptomatic infection compared to the symptomatic infection:

$$\begin{aligned} r_c &= c_A/c_I \\ r_p &= p_A/p_I \\ r_d &= d_A/d_I \end{aligned}$$

We define the product of these three ratios, $r = r_c \times r_p \times r_d$ as the relative infectivity of the asymptomatic infection.

In order to determine P in the SEAIRS model, we define

$$K(t) = \frac{\displaystyle\int_0^t J_A(s)ds}{\displaystyle\int_0^t \Big(J_A(s) + J_I(s)\Big)ds} \tag{3}$$

Therefore, $P = \lim_{t\to\infty} K(t)$. Since the model approaches its equilibrium (which is no-zero for any $\ell > 0$), both numerator and denominator of $K(t)$ go to infinity as long as $0 < \alpha < 1$. Using the L'Hospital's rule, one can find the limit of K when $t \to \infty$ as

$$P = \lim_{t\to\infty} \frac{J_A(t)}{J_A(t) + J_I(t)} = \frac{c_{_A} p_{_A} A_\infty}{c_{_A} p_{_A} A_\infty + c_{_I} p_{_I} I_\infty}, \tag{4}$$

where A_∞ and I_∞ are the equilibrium states of the asymptomatic and symptomatic infections in the model. We now determine the equilibrium states of the SEAIRS model to express (4) in terms of the model parameters. From the SEAIRS model, we find that at the equilibrium (for a given initial condition), we have

$$\begin{aligned} A_\infty &= \alpha\sigma d_{_A} E_\infty \\ I_\infty &= (1-\alpha)\sigma d_{_I} E_\infty \end{aligned} \tag{5}$$

Using (5) in (4) and simplifying we have:

$$P = \frac{c_{_A} p_{_A} \alpha d_{_A}}{c_{_A} p_{_A} \alpha d_{_A} + c_{_I} p_{_I} (1-\alpha) d_{_I}} \tag{6}$$

Factoring $c_{_I} p_{_I} d_{_I}$ and using the definition of the relative infectivity r, we have the final expression for the proportion of the cumulative incidence attributable to asymptomatic cases:

$$P = \frac{\alpha r}{1 + \alpha(r-1)} \tag{7}$$

Note that P is independent of ℓ, so we can apply this argument for the limiting case of the SEAIRS model where $\ell \to \infty$, that is a SEAIR model, in which the immunity induced by infection is permanent. We also highlight that the relationship between P, α and r is independent from the basic reproductive number $\mathcal{R}_0$, defined as the number of secondary infections generated by a single infectious cases introduced into an entirely susceptible population [1]. Hence, equation (7) is applicable to a broad range of epidemics.

SI.2 Sources for asymptomatic fractions

Figure 1 in the main text shows the values of P as a function of the relative infectivity r and the asymptomatic fraction α. The shaded rectangles provide additional information on the plausible range of α for SARS [6, 8, 4], influenza [7, 5, 4], and Zika [3], representing possible contribution of asymptomatic infection to the cumulative incidence for a range of the relative infectivity.

SI.3 Computer code

All computer code to replicate this study and a user-friendly Excel spreadsheet performing the calculations presented here are available at:
`http://doi.org/10.1017/S0950268817000115`.

References

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