Time between infections versus time between symptom onset in COVID-19: implications for estimating the reproduction number

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Background: The effective reproduction number $R_e(t)$ is the average number of new infections directly generated from each existing infection under the conditions at time t. $R_e(t)$ can be calculated from the number of daily infections and the time between subsequent infections—the infection-infection distribution, G(t). The infection-infection distribution G(t) is often approximated by the symptom-symptom distribution S(t), because the time of infection can be difficult to determine. However, if the time between infection and symptom onset—the infection-symptom distribution H(t)—varies substantially, then the infectee can develop symptoms before the infector and S(t) can be negative, such as in the case of COVID-19. In this case, it may be improper to approximate G(t) with S(t).

Methods: Given parametric equations for the symptom-symptom distribution S(t) and the infection-symptom distribution H(t), we develop a method to recover the infection-infection distribution G(t) using approximate deconvolution. We then compare estimates of $R_e(t)$ for the Greater Toronto Area using G(t) to those using S(t); two definitions of S(t) are considered, which do and do not allow negative values, respectively.

Results: We estimated the time between COVID-19 infections G(t) to be Gamma-distributed with mean 4.08 and standard deviation 3.19 days. The negative-permitting distribution S(t) had equal mean but larger variance than G(t), resulting in underestimation of $R_e(t)$ relative to G(t), whereas the non-negative S(t) had similar variance but larger mean, resulting in overestimation of $R_e(t)$.

Discussion: Approximation of the infection-infection distribution G(t) with the symptom-symptom distribution S(t) may result in biased estimates of the effective reproduction number R(t). The infection-infection distribution G(t) can also be understood as the distribution of infectiousness; thus accurately distinguishing G(t) from S(t) may also have implications for isolation interventions. Future work should explore possible correlation between S(t), H(t), and G(t) and estimation of confidence intervals for distribution parameters.

Open Science: The daily GTA case data used are not public. All other analysis code and data are available at: https://github.com/mishra-lab/covid-r