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Research Letter

Serial interval distribution of SARS-CoV-2 infection in Brazil

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The novel severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2) emerged in China in December 2019[1] and was declared a pandemic by the World Health Organization on 11 March 2020. Current assessments of SARS-CoV-2 transmission dynamics rely on accurate estimates of key epidemiological parameters, including the serial interval, which can be defined as the time between symptom onset of the source and the onset of symptoms of the recipient.[2] Moreover, serial interval estimations can help disentangling the duration of pre-symptomatic transmission upon infection. When the serial interval is greater than the incubation period, an epidemic is characterized by symptomatic transmission. However, existence of pre-symptomatic transmission can be inferred when the serial interval is shorter than the incubation period.

We estimate the serial interval of SARS-CoV-2 from 65 infector–infectee pairs from Brazil. Data were provided by the Brazilian Ministry of Health following ethical approval (CONEP protocol number 30127020.0.0000.0068). All confirmed cases of SARS-CoV-2 infection notified on the REDCap system

between 25 February and 19 March were analysed. We received data on infector and infectee pairs by the Brazilian Ministry of Health, and we measured the serial intervals by computing the difference between the dates of symptom onset of each pair.

The median serial interval in our data was estimated at 3 (standard deviation = 3.29) days. We identified four (6.15% of 65) negative serial intervals (symptom onset in the infectee preceded the infector) and seven (10.77% of 65) zero-valued serial intervals (symptom onset on the same day for the infector–infectee pair). It is common to censor observed serial intervals to include only positive values; however there is no strong theoretical justification for this. As such, we fit a serial interval probability distribution that allows for negative values by modelling the serial interval as: Serial Interval $= \lfloor t_{\text{inf},1} + \Delta t_{\text{lat},1} + \Delta t_{\text{lat},2} + \Delta t_{\text{int},2} \rfloor - \lfloor t_{\text{inf},1} + \Delta t_{\text{lat},1} + \Delta t_{\text{int},1} \rfloor$, where $\lfloor \cdot \rfloor$ is the floor operator, $t_{\text{inf},1}$ is a random variable uniformly distributed in the interval $[0, 1]$, $(\Delta t_{\text{lat},1}, \Delta t_{\text{lat},2})$ are independent and identically distributed (i.i.d.) chi-squared random
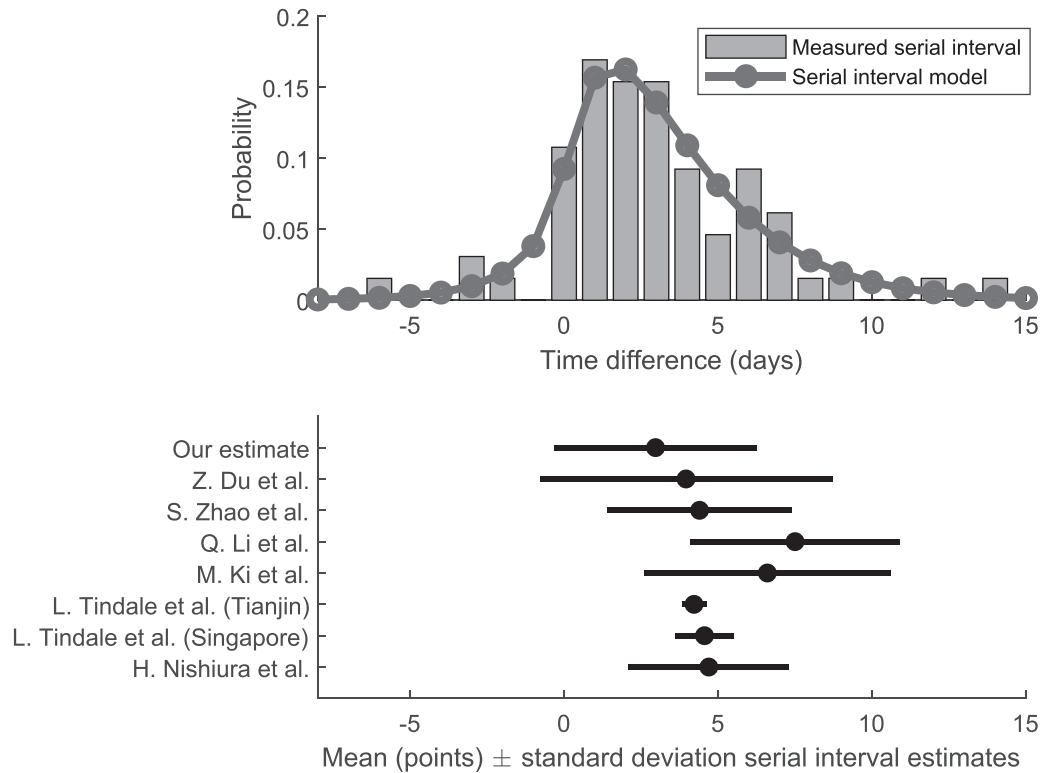
Figure 1. Serial interval estimation from Brazilian SARS-CoV-2 confirmed cases compared with the modelled distribution. Lower panel shows the mean ± standard deviation serial interval estimates from the current literature.

variables of mean 3.03 days and $(\Delta t_{int,1}, \Delta t_{int,2})$ are i.i.d. chi-squared random variables of mean 0.95 days. See the supplementary material for theoretical motivation, methods and sensitivity analysis.

Figure 1 shows the comparison between the observed and modelled serial intervals as well as the means ± standard deviations for a number of serial interval probability distributions presented in the literature.[3–8] Our proposed model for the serial interval probability distribution approximates well the serial intervals measured from data.

We provide two additional analyses of the data in the supplementary material: (i) Du *et al.*[3] took an alternative approach fitting a normal distribution to 468 publicly reported serial intervals in which 12% had negative values. For this reason, we fit a normal distribution to the observed serial intervals and compare it to the distribution presented in Du *et al.*,[3] obtaining a lower mean and variance, (ii.) we censor the data to include only positive values, obtaining a distribution of mean 3.83 days that is best fit by a lognormal distribution.

The mean serial interval in Brazil of 2.97 days is the shortest reported to our knowledge, but we emphasize that the serial interval is not usually concentrated around the mean due to its high standard deviation (3.29 days) and non-symmetry. Furthermore, our serial interval estimate is shorter than the reported incubation period, implying that the infectious period for SARS-CoV-2 begins before symptom onset. This is in line with recent observations of a large proportion of undocumented infections, complicating containment of the virus.[10] The short

mean observed, and the relatively high probability of zero or negative serial intervals reinforces previous results from Ganyani *et al.*,[9] which estimate a large proportion of pre-symptomatic transmission for Singapore and Tianjin. Together, our findings imply that even with screening measures for travellers in airports, cruises or bus stations, the risk of transmission might remain relatively high.

Our report presents the first serial interval estimates for SARS-CoV-2 from Latin America. Our estimates are based on national case notification data, and this is a strength compared with datasets compiled from media reports. However, there are at least two important sources of bias. Firstly, there is a tendency for secondary cases to recall more recent contacts—recency or recall bias—resulting in a shorter estimate of the serial interval. Similarly, contact tracing is likely to be most effective for recent contacts. Secondly, self-isolation following symptom onset will remove longer serial intervals that would have occurred due to transmission during the symptomatic phase. This second point highlights the role of contextual factors such as isolation practices, population density, location of transmission, proportion of the population infected, in determining the serial interval. In addition, the number of serial intervals observed (65) is fairly small, resulting in a relatively large uncertainty in some of the estimated parameters (e.g. the confidence interval for the probability of negative serial intervals is [1.72%, 15.29%]).

In conclusion, we estimate a mean serial interval of COVID-19 at 2.97 days for Brazil. This estimate is shorter than published

incubation periods, implying pre-symptomatic undocumented transmission. Our estimate includes a substantial proportion of negative serial intervals that implies a substantial proportion of secondary transmission prior to the onset of symptoms.

Supplementary Data

Supplementary data are available at *JTM* online.

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Authors' Contribution

C.A.P.J., L.B. and V.H.N. did the main analysis. C.A.P.J., L.B., D.S.C., O.G.P., E.C.S. and N.R.F. wrote the first draft; V.B.P., W.K.O., J.H.R.C., E.C.S., F.G., D.S.C. helped with data collection and ethics protocol. A.D., C.A.D., N.R.F. and E.C.S. helped with the refinement of the analyses and interpretation of the results.

Conflict of interest

None declared.

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