1 **Serial intervals observed in SARS-CoV-2 B.1.617.2 variant cases**
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12 **Main**
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14 The SARS-CoV-2 lineage B.1.617 was declared a Variant of Concern by the World Health
15 Organization given preliminary evidence suggesting faster spread relative to other circulating
16 variants.[1] However, the epidemiological factors contributing to this difference remain unclear. In
17 particular, an increase in observed growth rate of COVID-19 cases could be the result of a shorter
18 generation interval (i.e. delay from one infection to the next) or an increase in the effective
19 reproduction number, R, of an infected individual (i.e. the average number of secondary cases
20 generated by an infectious individual), or both.[2] Whereas a shorter generation interval would
21 increase the speed but not the number of individual-level transmissions, a larger value of R would
22 require both faster and wider coverage of outbreak control measures such as vaccination or
23 physical distancing to suppress transmission.
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25 In Singapore, whole genome sequencing is performed for respiratory samples from COVID-19
26 cases who tested positive by PCR with a cycle threshold of 30 and below. The B.1.617.2 variant
27 was first identified in local cases on Apr 27, 2021. Despite high levels of adherence to mask
28 wearing and physical distancing in the country,[3,4] clusters of B.1.617.2 were detected and some
29 clusters displayed rapid growth of infections.
30

31 We investigated possible drivers of B.1.617.2 growth by studying the serial intervals (i.e. onset-
32 to-onset delay) — a proxy for the generation interval — between pairs of a primary case and a
33 secondary case occurring among household members. Exposure histories were reviewed for all
34 household transmission pairs involving COVID-19 cases infected with the B.1.617.2 variant and
35 notified between Apr 27 to May 22, 2021. The B.1.617.2 variant was detected in 97% of the
36 sequenced samples from local COVID-19 cases identified in this period. Secondary cases with
37 potential exposure to (i) more than one primary case in the household or (ii) to other cases outside
38 the household were omitted from analysis. Households with secondary cases having different
39 symptom onset dates were also omitted from the analysis as we were unable to rule out multiple
40 generations of transmission.
41

42 For comparison, we identified household transmission pairs prior to the partial lockdown in
43 Singapore on Apr 7, 2020 and applied the same exclusion criteria. This time period precedes the
44 occurrence of the major global SARS-CoV-2 variants[5] and most closely matches the social activity

1 and workplace arrangements in Apr 2021[6] where working from home was not the default.
2 Preliminary analysis showed that the primary cases in this period had a wider range of time from
3 symptom onset to isolation as compared to the B.1.617.2 primary cases (Supplementary figure
4 1). As such, the following sampling procedure was performed to ensure that we match the number
5 of transmission pairs and the distribution of time from symptom onset to isolation of primary cases.
6 For a given time from symptom onset to isolation of a B.1.617.2 primary case, we randomly
7 sampled, with replacement, the serial intervals of primary cases in the earlier period with matching
8 time from onset to isolation . We then fitted a skewed normal distribution to the sample of serial
9 intervals to account for negative serial intervals arising from pre-symptomatic transmission. The
10 process was repeated 1000 times to obtain the mean and 95% confidence interval (CI) of the
11 sample mean, median, mode and the difference of these statistics between the B.1.617.2 cases
12 and those prior to the lockdown.
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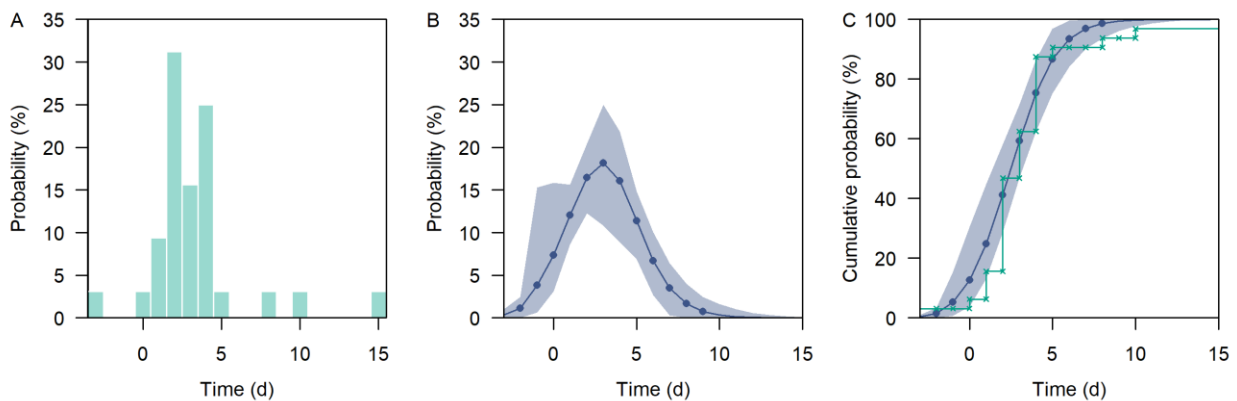
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16 Figure 1 Serial interval of household transmission pairs. (a) Probability mass function of serial
17 interval of B.1.617.2 cases (bar) , (b) probability density function of serial interval of cases
18 identified prior to the partial lockdown in Apr 7, 2020 with mean (dots) and 95% CI (shaded), (c)
19 empirical cumulative density function of (a) (green line) and estimated cumulative density function
20 of (b) with mean (blue dots) and 95% CI (blue shaded). Majority of the primary cases had known
21 exposure(s) outside the household and secondary cases do not have the same exposure as the
22 primary case thereby allowing us to identify the directionality of infection. Negative serial intervals,
23 which signifies pre-symptomatic transmission were also included in the analysis.
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25 There were 32 B.1.617.2 variant household transmission pairs and 63 household transmission
26 pairs identified before Apr 7, 2020. The median serial interval of the B.1.617.2 cases was three
27 days (Figure 1a) and three days (95% CI 2–4) in cases identified before Apr 7, 2020 after
28 matching the time from symptoms onset to isolation. (Figure 1b and c). The mode of the serial
29 interval was two days for B.1.617.2 cases and 2.7 days (95% CI -1–4) for cases prior to the
30 lockdown. The mean, median and mode of the serial interval distributions of B.1.617.2 cases and
31 the sampled cases prior to the lockdown was not found to be statistically different (Supplementary
32 Table 1).
33

Our early investigations of the recent B.1.617.2 cases, suggest no evidence to support a large difference (i.e. more than 1 day) in serial intervals among the samples studied which had an exclusion criteria applied to ensure consistency. In turn, this lends support to the hypothesis that the recent rapid growth is potentially driven by an increase in the average number of secondary cases generated by a case infected with the B.1.617.2 variant. Studies with proper control of confounding factors are thus crucial to tease out the key epidemiological factors that facilitate the increased transmissibility of the B.1.617.2 variant. These factors include, but are limited to, the viral load and shedding dynamics of B.1.617.2 cases, the exposure settings, and the vaccination status of infected persons. Without signs of lowered disease severity for B.1.617.2, contact tracing and testing around COVID-19 cases, along with vaccination and non-pharmaceutical interventions, continue to remain key SARS-CoV-2 outbreak control measures in the short term.

We declare no competing interest

Contributor statement
RP, AJK and VJL designed the analysis. RP and TZM contributed to the data collection. RP and AJK developed the model, performed the analysis and interpretation of the study findings. VJL and the CMMID COVID-19 working group members contributed to the interpretation of the study results. All authors contributed to writing the manuscript and approved the final version.

Code and data
The model code and de-identified data that underlie the results reported in this article is available online at https://github.com/rachaelpung/serial_interval_covid_b.1.617.2

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