

Rapid Communication

Shorter serial intervals and incubation periods in SARS-CoV-2 variants than the SARS-CoV-2 ancestral strain

Zhanwei Du, Ph.D.^{1,2,†}, Caifen Liu, M.Sc.^{1,2,†}, Lin Wang, Ph.D.³, Yuan Bai, Ph.D.^{1,2}, Eric H. Y. Lau, Ph.D.^{1,2}, Peng Wu, Ph.D.^{1,2}, and Benjamin J. Cowling, Ph.D.^{1,2,*}

¹WHO Collaborating Centre for Infectious Disease Epidemiology and Control, School of Public Health, Li Ka Shing Faculty of Medicine, The University of Hong Kong, 21 Sassoon Rd, Pok Fu Lam, Hong Kong Special Administrative Region, Hong Kong 999077, China, ²Laboratory of Data Discovery for Health Limited, Hong Kong Science Park, Hong Kong Special Administrative Region, 19 Science and Technology W Ave, Hong Kong 999077, China and ³Department of Genetics, University of Cambridge, Cambridge CB2 3EH, UK

*To whom correspondence should be addressed. Email: bcowling@hku.hk

†ZD and CL contributed equally to this manuscript.

Submitted 18 March 2022; Revised 7 April 2022; Editorial Decision 11 April 2022; Accepted 11 April 2022

Key words: COVID-19, SARS-CoV-2, variants of concern, serial interval, incubation period, systematic review, meta-analysis

Globally, five variants of concern (VOC) and two variants of interest (VOI) of SARS-CoV-2 have been identified by 1 January 2022,¹ with varying ability to escape from pre-existing immunity following prior infection or vaccination.² The ‘serial interval’ (SI) and ‘incubation period’ (IP) are two key epidemiological metrics, defined as the duration between symptom onset of successive cases in a transmission chain and the duration between exposure and symptom onset of a case, respectively, which can be used to characterize the COVID-19 transmission. Reliable estimates of these parameters are essential for determining the duration of the quarantine needed to minimize the transmission risk.³

We identified 46 studies by searching PubMed for articles published from 1 January 2020 to 10 March 2022, and additionally included four studies from our own reference list (Figure S1, Supplementary Methods). Of these, 17 studies were excluded through title and abstract screening, leaving 33 studies for full-text assessment. A total of 19 studies were finally included in this review, providing 29 and 29 estimates of SI and IP, respectively (Tables S1 and S2), and Delta and Omicron were the most studied (Tables S1 and S2). Estimates of SI were reported for Alpha, Delta and Omicron variants from South Korea, Singapore, Mainland China, the UK, the Netherlands, and Japan, and estimates of IP were for Alpha, Beta, Gamma, Delta, Omicron and L-Lineage strains from Mainland China, France, South Korea, the Netherlands, Japan and Norway.

The SI of the SARS-CoV-2 ancestral strain was 5.2 (95% CI: 4.9–5.5).⁴ The pooled estimate was derived to be 6.2 days before the epidemic peak (range: 5.1, 7.8) and 4.9 days after the epidemic peak (range: 1.9, 6.5) in mainland China.⁵ In contrast, the reported mean estimates of SI were shorter for the Alpha, Delta and Omicron variants, varying from 2.0 to 4.2 days in South Korea, Singapore, Mainland China, the UK, the Netherlands and Japan (Table S1, Figure 1). The pooled estimate of SI for the Delta and Omicron variants was 3.4 days (95% CI: 3.0, 3.7) and 3.1 days (95% CI: 2.9, 3.2), respectively (Figure S2). The pooled estimate of serial intervals was 3.1 (95% CI: 2.7–3.6) if out of an epidemic wave, 3.3 days (95% CI: 3.0, 3.6) before the transmission peak, and 3.6 (95% CI: 3.5–3.6) after the transmission peak (Figure S3). The IP of the ancestral strain was estimated to be 6.3 days (range: 1.8, 11.9) globally.⁶ The estimates of IP for SARS-CoV-2 variants ranged from 3.0 to 6.5 days (Table S2, Figure 1). Among them, the mean IP of Delta variant appeared to be shorter than the ancestral strain, with the pooled estimate of 4.8 days (95% CI: 3.9, 5.6), and the IP of Omicron variant appeared to be shorter than Delta, with the pooled estimate of 3.6 days (95% CI: 2.3, 4.9) (Figure S2). The pooled estimate of incubation periods was 5.2 (95% CI: 3.8–6.6) if not in an epidemic wave, 4.3 days (95% CI: 3.7–4.9) before the transmission peak, and 3.5 (95% CI: 1.3–5.7) after the transmission peak (Figure S4).

Estimates of the IP often suggest the characteristics of the viruses, and may also be associated with the host factors whereas

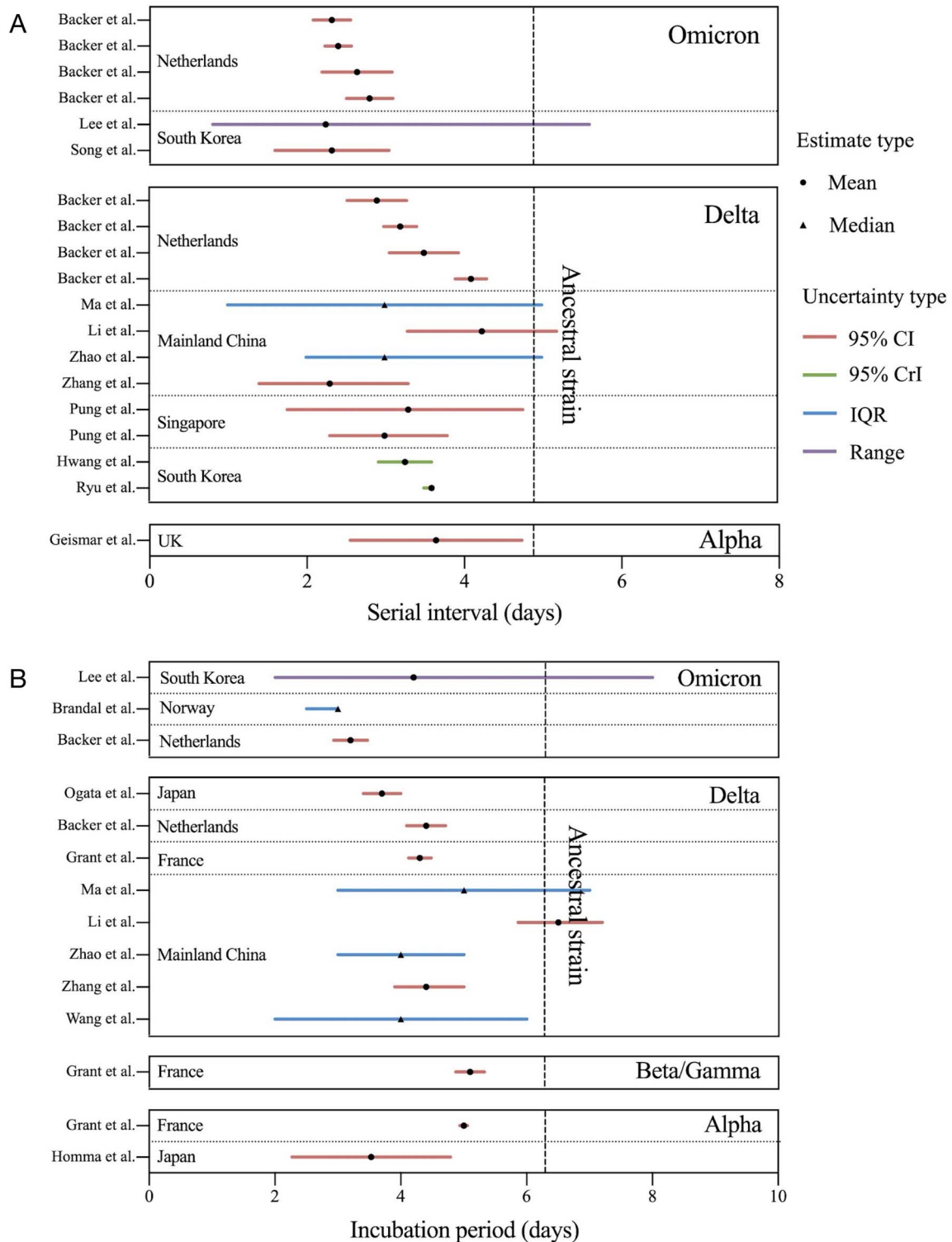


Figure 1. Estimation of serial intervals and incubation periods of SARS-CoV-2 variants. The SARS-CoV-2 variants, including Alpha, Delta and Omicron reported in 11 studies, respectively, presented by variant and country. The horizontal segments indicate CI (in red), CrI (in green), IQR (in blue) and range (in purple). Points represent the estimates reported as mean and triangles as median. The horizontal dotted line denotes the pooled estimate of the ancestral strain which was 4.9 days for SI after the epidemic peak in mainland China.⁵ (B) The vertical dotted line denotes the pooled estimate of the ancestral strain which was 6.3 days (range: 1.8, 11.9) globally for IP.⁶

SI estimates can change in response to public health interventions and population behavioural patterns. The changes in SI and IP before and after transmission peaks may not only measure

the effectiveness of infection control interventions but may also indicate rising population immunity from vaccines and natural infection. However, some factors potentially impacted estimates

of SI and IP such as the study location, the study period, mass testing, travel restriction, human behaviour, and effectiveness of other mitigation strategies, which were not included to adjust the pool estimates in this study because of data availability. Besides, we limit our search to published articles in PubMed only, while many other useful and important publications may appear in other databases (e.g. Embase and Web of Science).

In conclusion, multiple estimates of the SI and IP have been reported for the SARS-CoV-2 ancestral strain and five variants. In-time and reliable estimation of the two epidemiological metrics through an epidemic is critical for the assessment on the impact of mitigation efforts and the potential need to adjust for control measures including entry restrictions, duration of quarantine, tests to be conducted during quarantine and other social measures.

Supplementary data

Supplementary data are available at *JTM* online.

Acknowledgements

We acknowledge the financial support from AIR@InnoHK administered by Innovation and Technology Commission and the Collaborative Research Fund (Project No. C7123-20G) of the Research Grants Council of the Hong Kong SAR Government, Seed Fund for Basic Research for New Staff of the University of Hong Kong (grant no. 202009185062), National Natural Science Foundation of China (grant no. 72104208), and Health and Medical Research Fund, Food and Health Bureau, Government of the Hong Kong Special Administrative Region (grant no. 21200632).

Authors' contributions

Z.W.D., C.L. and B.J.C. conceived the study, designed statistical and modelling methods, conducted analyses, interpreted results,

wrote and revised the manuscript; L.W., Y.B., E.H.Y.L. and P.W. interpreted results and revised the manuscript.

Conflict of interests

BJC consults for AstraZeneca, Fosun Pharma, GlaxoSmithKline, Moderna, Pfizer, Roche and Sanofi Pasteur. BJC is supported by the AIR@InnoHK program of the Innovation and Technology Commission of the Hong Kong SAR Government. The authors report no other potential conflicts of interest.

Data availability

All data are collected from open source with detailed description in Supplementary Method.

Code availability

Code used for data analysis is freely available upon request.

References

1. World Health Organization. *Tracking SARS-CoV-2 variants*. 2022. Available at: <https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/> (23 April 2022, date last accessed).
2. World Health Organization. *Novel Coronavirus (2019-nCoV) situation reports*. 2022. Available at: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports> (23 April 2022, date last accessed).
3. Li Q, Guan X, Wu P *et al*. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N Engl J Med* 2020; 382:1199–207.
4. Alene M, Yismaw L, Assemie MA, Ketema DB, Gietaneh W, Birhan TY. Serial interval and incubation period of COVID-19: a systematic review and meta-analysis. *BMC Infect Dis* 2021; 21:257.
5. Ali ST, Yeung A, Shan S *et al*. Serial intervals and case isolation delays for COVID-19: a systematic review and meta-analysis. *Clin Infect Dis* 2021 Available at: <http://dx.doi.org/10.1093/cid/ciab491>.
6. Xin H, Wong JY, Murphy C *et al*. The incubation period distribution of coronavirus disease 2019 (COVID-19): a systematic review and meta-analysis. *Clin Infect Dis* 2021 Available at: <http://dx.doi.org/10.1093/cid/ciab501>.