

Research Letter

Reproduction numbers of SARS-CoV-2 Omicron subvariants

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Omicron is circulating globally as the dominant variant of SARS-CoV-2 and posing a substantial threat in 2022.¹ It is rapidly mutating into several descendent lineages and circulating recombinant forms.² The effective reproduction number (R_e) is a central concept in infectious disease epidemiology that refers to the average number of secondary infections generated by an infected case after considering the effects of population immunity and control measures. The relative reproduction number (relative R_e) describes the ratio between the reproduction numbers for two different variants, such as the relative R_e between Omicron subvariants and the Delta variant in this study. Accurate and timely estimation of the reproduction numbers is crucial for predicting disease development trends, evaluating the effectiveness of control measures and adjusting control measures promptly.

We identified 224 studies by searching PubMed, medRxiv and bioRxiv for articles that were published or pre-print from 1 January 2020 to 23 July 2022 (Supplementary Figure S1, Supplementary Methods). There were 153 studies removed during the process of title and abstract screening, leaving 71 studies for full-text assessment. Thirteen studies were eventually included in this review, providing 34 estimates of R_e or relative R_e . The reported Omicron substrains included BA.1, BA.2, BA.4, BA.5 and XG, where BA.1 and BA.2 were most studied (Supplementary Figures S2 and S3). These data involved 16 countries and mostly focused on Denmark, the United Kingdom, South Africa, the United States, South Korea and India (Supplementary Table S1).

Transmissibility comparisons were made between Omicron subvariants and the Delta variant, and the relative R_e estimates were summarized. Specifically, the pooled estimates of relative R_e for BA.1 and BA.2 were 2.08 (95% confidence interval, 95% CI:

1.57–2.58) and 3.31 (95% CI: 2.83–3.79), respectively (Figure 1, Supplementary Figures S4 and S5). For studies where BA.1 and BA.2 were collectively reported, the median estimates of the relative R_e ranged from 1.82 to 4.15. The other Omicron subvariants BA.4, BA.5, and XG were found to elicit 3.32 (95% credible interval, 95% CrI: 3.27–3.38), 3.39 (95% CrI: 3.30–3.49) and 2.67 (95% CrI: 2.62–2.73) times higher transmissibility than the Delta variant, respectively (Figure 1).³

When not compared with the Delta variant, the pooled R_e estimates of BA.1 and BA.2 were 3.22 (95% CI: 2.31–4.14) and 5.04 (95% CI: 4.33–5.75), respectively (Figure 1, Supplementary Figures S6 and S7). The median R_e estimates ranged from 2.79 to 6.32 when BA.1 and BA.2 were collectively reported. BA.4, BA.5 and XG had higher R_e estimates than the ancestral substrains, with median values of 5.11 (95% CrI: 4.56–5.66), 5.22 (95% CrI: 4.65–5.79) and 4.12 (95% CrI: 3.67–4.56), respectively (Figure 1).³

Meta-regression analyses were also performed for BA.1 and BA.2 to identify potential associations between the study regions and the estimated relative reproduction numbers. We found that the study region was associated with the reported relative ratio (Supplementary Figures S8 and S9) and the reproduction number (Supplementary Figures S10 and S11) of BA.1 and BA.2, by including the study region as a categorical variable.

The high transmission rate of Omicron has led to an epidemiological rebound in many countries, with the number of global BA.4 and BA.5 cases also rising and causing highly adverse impacts.⁴ Liu and Rocklöv found that the mean estimate of basic reproductive number of the Delta variant was 5.08, ranging from 3.2 to 8,⁵ and that of the Omicron variants, including BA.1 and BA.2, was 9.5 with a range from 5.5 to 24 (median: 10 and

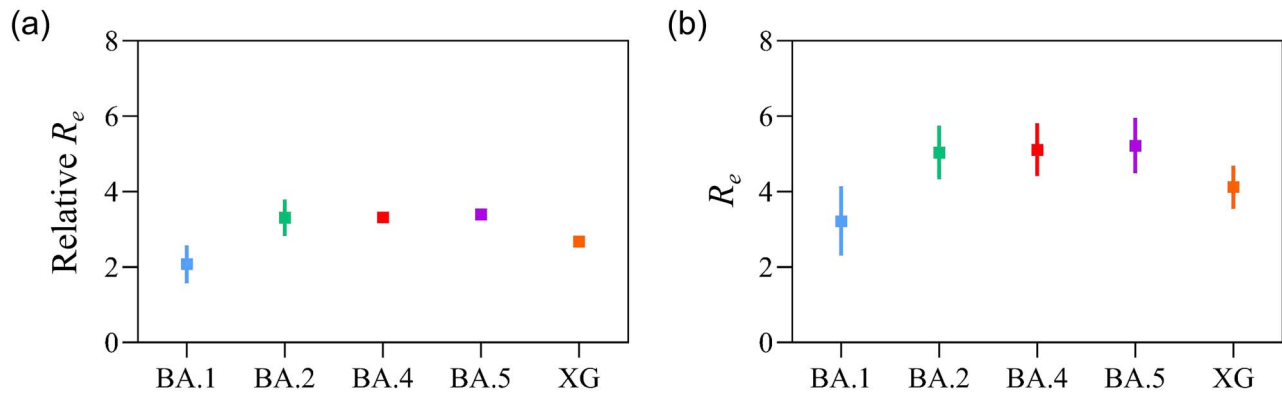


Figure 1. Reproduction number estimates for the Omicron subvariants. (a) Estimates of effective reproduction numbers for each Omicron subvariant (e.g. BA.1, BA.2, BA.4, BA.5 and XG). (b) Estimates of relative effective reproduction numbers to the Delta variant for each Omicron subvariant. The estimates of BA.1 and BA.2 were pooled values, whereas those of BA.4, BA.5 and XG were directly retrieved from Kimura *et al.*³. The dots and error bars show the estimated mean and 95% confidence interval, respectively

interquartile range, IQR: 7.25–11.88).⁶ We identified that the Omicron subvariants had higher transmission potential than that of the Delta variant, in which BA.5 has the highest reproduction number, followed by BA.4, BA.2, XG and BA.1. Liu and Rocklöv also stated an average R_e value of 3.4 with a range from 0.88 to 9.4 (median: 2.8 and IQR: 2.03–3.85) for Omicron during outbreaks of BA.1 and BA.2,⁶ than which the R_e estimates of Omicron subvariants are generally higher in our analyses.

BA.4 and BA.5 lineages are replacing other Omicron subvariants and have been the dominant lineages.^{4,7} The government needs to take stricter public health measures and vaccinations before the outbreak is past the point of being contained. BA.4 and BA.5 have greatly increased neutralization resistance,⁸ and substantially escape neutralizing antibodies induced by infection and vaccination,⁹ thereby further compromising the efficacy of vaccines. There is a clear need for governments to accelerate the development of more efficient COVID-19 vaccines (e.g. universal coronavirus vaccines¹⁰).

However, estimates of reproduction numbers may vary widely due to various factors that were not included in this review, such as time and locations of studies, exposure patterns, vaccine promotion and distribution, and travel restrictions. In addition, we only studied the relative reproduction numbers to assess the transmission ability of Omicron and its subvariants and did not include studies of transmission advantage using other metrics. Besides, this review could be biased, given that our study contains some preprints that have not been certified by peer review.

In conclusion, multiple estimates of the effective reproduction numbers have been reported for the Omicron subvariant, and the study regions are considered to be associated with the relative reproduction numbers. COVID-19 is still posing serious threats, and it is necessary to strengthen public health measures while expanding vaccine coverage.

Supplementary data

Supplementary data are available at *JTM* online.

Data availability

All data are collected from open source with detailed descriptions in the Methods section.

Author Contributions

S.W., F.Z. and Z.W. conceived the study, designed statistical and modelling methods, conducted analyses, interpreted results, and wrote and revised the manuscript; C.G., Z.D. and Z.W. interpreted results and revised the manuscript.

Code availability

Code used for data analysis is freely available upon request.

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Competing interests

Not applicable.

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