

# Differences in Case-Fatality-Rate of Emerging SARS-CoV-2 Variants

Jing Liu<sup>1</sup>, Haozhen Wei<sup>1</sup>, and Daihai He<sup>1</sup>

<sup>1</sup>The Hong Kong Polytechnic University

June 17, 2022

## Abstract

Variants of Severe-Acute-Respiratory-Syndrome Coronavirus-2 (SARS-CoV-2) has caused tremendous impact globally. It has been widely reported that the Omicron (B.1.1.529) variant is less deadly than the Delta (B.1.617.2) variant, presumably due to immunity from vaccination and previous infection. When measuring the severity of a variant, Case-Fatality-Rate (CFR) is often estimated. The purpose of this work is to calculate the change in CFR of different variants over time from a large number of countries/regions since the start of the pandemic in 2020.

Differences in Case-Fatality-Rate of Emerging SARS-CoV-2 Variants

Jing Liu<sup>1</sup>, Haozhen Wei<sup>1</sup>, Daihai He<sup>1,2,+</sup>

<sup>1</sup> Department of Applied Mathematics, Hong Kong Polytechnic University, Hong Kong, China

<sup>2</sup> Research Institute for Future Food, The Hong Kong Polytechnic University, Hong Kong, China

+ Corresponding author. Email: daihai.he@polyu.edu.hk (DH)

## Abstract

Variants of Severe-Acute-Respiratory-Syndrome Coronavirus-2 (SARS-CoV-2) has caused tremendous impact globally. It has been widely reported that the Omicron (B.1.1.529) variant is less deadly than the Delta (B.1.617.2) variant, presumably due to immunity from vaccination and previous infection. When measuring the severity of a variant, Case-Fatality-Rate (CFR) is often estimated. The purpose of this work is to calculate the change in CFR of different variants over time from a large number of countries/regions since the start of the pandemic in 2020.

**Keywords:** COVID-19, Omicron variant, Delta variant, CFR

## Background

The Coronavirus 2019 (COVID-19) pandemic, caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), hit the humankind tremendously with 528,996,258 reported cases and 6,287,786 reported deaths by June,2022(Coronaviridae Study Group of the International Committee on Taxonomy of Viruses, 2020; Worldometers, 2022). The rapid evaluation of the viruses led to variants with high transmissibility and high immune evasion ability and posed challenges for prevention and control (CDC, 2022). Among the new variants, the Delta variant (B.1.617.2) was first identified in December, 2020 (Yang&Jeffrey, 2021) and classified by the World Health Organization (WHO) as Variant of Concern (VOC) on June, 2021, updated as Variant Being Monitored (VBM) on April, 2022(CDC, 2022). The Omicron variant (B.1.1.529) was first detected in specimens collected on November, 2021, and classified as a Variant of Concern (VOC)(CDC,

2021). Several subvariants of Omicron variant has been reported so far. Previous studies on the case-fatality-ratio (CFR) of different variants were conducted in individual countries. Large-scale comparison across multiple countries is missing. The CFR is an important indicator of disease severity. Many factors may affect the estimates. Infection attack rate (proportion of population being infected) with previous variants, vaccination coverage, age structure of the population and the medical system preparedness may affect the CFR in different population/locations. In this work, we combine the reported cases and deaths and variant proportion over time in 50 locations to calculate the raw CFR for 7 variants (or subvariants), thus to get a large-scale picture of the changing pattern of the severity of SARS-CoV-2.

The Omicron variant spreads faster than the Delta variant due to the combined effects of increased transmissibility and immune evasion ability. In South Africa, the proportion of patients with Omicron infection presenting to emergency departments has fallen to half its previous level, and the proportion of Omicron patients presenting with acute respiratory conditions and requiring oxygen therapy and mechanical ventilation has fallen dramatically(Maslo et al., 2022).

In United States, the number of deaths in the Omicron wave (analyzed from December 15, 2021 to March 15, 2022) was very similar to that seen in the Delta wave (analyzed from July 15, 2021 to November 15, 2021). However, the number of confirmed cumulative cases during this period was twofold higher with Delta. The CFR of Omicron variant is about half that of Delta variant in the both US and South Africa (Sigal et al., 2022).

### CFR of variants across 51 locations

Here we extend the comparison to all previous VOCs in 51 counties/regions. We use reported death divided by reported cases in 30-day sliding window with a two-week shift between reported death and reported cases.

$$\text{Case Fatality Ratio (CFR in\%)} = \frac{\text{Number of deaths from disease in the past 30 days}}{\text{Number of confirmed cases of disease in the past 15 to 45 days}} \times 100\%$$

Based on the biweekly variant proportion data(Hodcroft, 2021; Hannah Ritchie et al., 2020), we determine the dominant time interval for each variant in each location when the proportion of a variant is above 50% among all samples processed. Namely the raw CFR in a time interval when the proportion of variant is above 50% is assigned as the CFR for the variant in that location. We calculated the mean CFR values for each variant in its dominant time interval in each location. Figure 1 summarized the mean CFR for each variant across 51 locations.

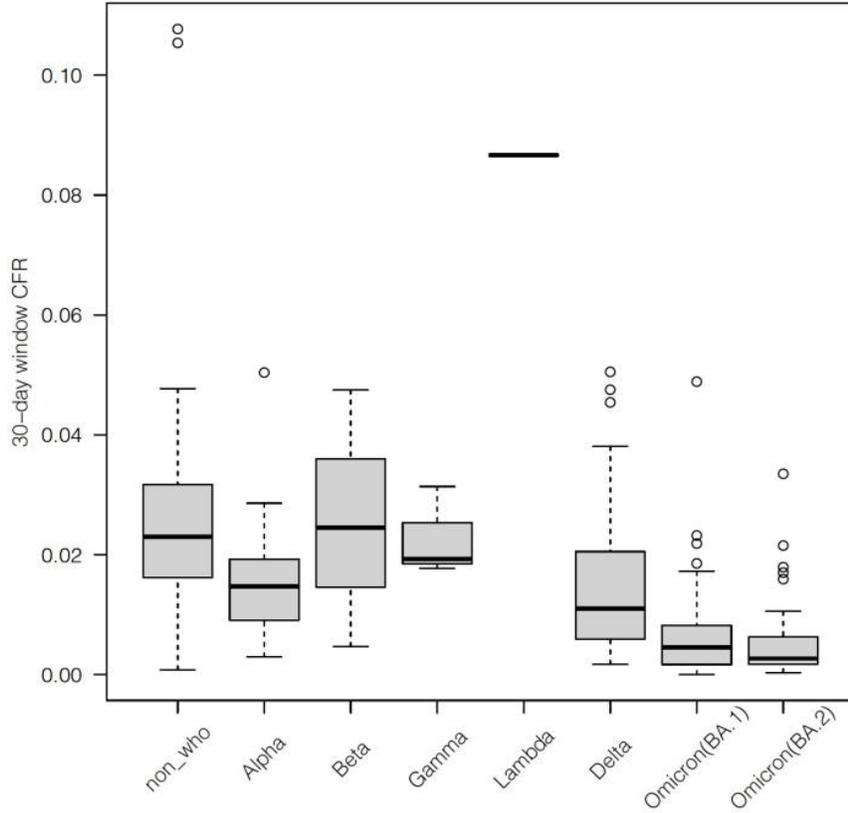


Figure 1. The summary of the mean case-fatality ratio (CFR) during its dominant time interval in 51 locations for eight variants or subvariants.

### Age stratified CFR

In South Africa, the CFR during Omicron variant dominant time interval (November 21, 2021, to January 22, 2022) was substantially lower than that during Delta variant dominant time interval (May 9 to September 18, 2021), for 20+ age groups (see Table 1)(Jassat et al, 2022). This could be due to implementation of vaccination among adults and infection induced immunity across all ages.

**Table 1.** The summary of case-fatality ratio (CFR) of Delta variant and Omicron variant among different age groups in South Africa.

CFR	Delta	Omicron	Relative difference
All ages	2.60%	0.78%	70%
Age <5 years	0.57%	0.48%	15.8%
Age 5–19 years	0.06%	0.09%	-50%
Age 20–39 years	0.45%	0.24%	46.7%
Age 40–59 years	2.54%	0.64%	74.4%
Age [?]60 years	11.71%	2.38%	79.7%

In Table 1, the relative difference is defined as  $(1 - \frac{CFR_{omicron}}{CFR_{delta}})\%$ . For all ages, the CFR of Delta variant is

more than three-fold of the CFR of Omicron for overall age group and 40+ ages groups. The 5-19 age group has the lowest CFR for both variants.

Italy has a high proportion of elderly people (>65 age accounting 23% of the population) in 2019, which could have led to a higher CFR compared to other countries. Among 70-79 age group, the CFR is about 12.8% in Italy and 8.0% in China; among 80+ age group, the CFR is about 20.2% in Italy and 14.8% in China, in early 2020(Onder et al., 2020). 86% of patients in the Washington ICU have underlying chronic conditions such as kidney disease and heart failure(Arentz et al., 2020). Population age structure and prevalence of comorbidity influence CFR.

### Impact of Vaccination

Zhao et al showed that, in the United Kingdom during May and June 2021, Delta variant had a smaller CFR than pre-variant and the CFR of pre-Delta variant dropped substantially while the vaccine coverage increased and the drop of the CFR of Delta variant is less evident (probably due to short study period)(Zhao et al., 2021). In the United States, Johnson et al compared the CFR among unvaccinated and fully vaccinated individuals in 25 US jurisdictions and the vaccine efficacy substantially dropped over time (see Table 2) (Johnson et al., 2021).

**Table 2.** The summary of case-fatality ratio (CFR) of Delta variant and Omicron variant in unvaccinated people and fully vaccinated people in United States.

Time	CFR among Unvaccinated	CFR among Fully vaccinated	Vaccine Efficacy in reduction
Pre-Delta (2021, 4-5)	1.05%	0.10%	90.5%
Delta emergence (2021, 6)	1.37%	0.24%	82.5%
Delta predominance (2021, 7-11)	1.22%	0.32%	73.8%
Omicron emergence (2021, 12)	0.11%	0.03%	72.7%

The vaccine efficacy (VE) is defined as  $(1 - \frac{CFR_{vaccinated}}{CFR_{unvaccinated}})\%$ . The VE drop substantially over time, due to a combined effect of natural waning of immune protection and immune evasion of Delta and Omicron variant.

### Limitation

The work utilized bi-weekly variant sequencing data and reported deaths and cases. The under reporting of COVID-19 deaths and cases will impact the estimate of CFR. The CFR is an overestimate of the true infection-fatality-rate. If the reporting is consistent, the CFR across variants should be a fair comparison.

### Conclusion

In this work, we compared the CFR for seven variants across 51 locations. We showed that the CFR dropped over time, presumably due to vaccine-induced immune and infection induced immune. The drop from Delta variant to Omicron variant is substantial and the difference between subvariants of Omicron is not evident.

### Ethics approval and consent to participate

The data used in this study were collected originally via the public domains, and thus neither ethical approval nor individual consent was applicable.

### Availability of materials

Data are publicly available online.

### Consent for publication

Not applicable.

## Funding

We were supported by the Collaborative Research Fund (Grant Number HKU C7123-20G) of the Research Grants Council (RGC) of Hong Kong, China.

## Acknowledgments

None.

## Disclaimer

The funding agencies had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; or decision to submit the manuscript for publication.

## Conflict of interests

All authors have no conflict of interest.

## Author's contributions

DH and JL conceived the study, carried out the analysis and drafted the manuscript. All authors discussed the results, and revised the manuscript, and approved it for publishing.

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