

# Severity of COVID-19 pre- and During Omicron Period in Pediatric Patients: A Global Systematic Review

Deepa Malhotra<sup>1</sup>, Moe H. Kyaw<sup>1</sup>, Rodrigo Sini de Almeida<sup>2</sup>, Rajeev M. Nepal<sup>1</sup>, Pinelopi Nikolopoulou<sup>3</sup>, Stephen Wiblin<sup>4</sup>, Santiago MC Lopez<sup>1</sup>, Irini Zografaki<sup>3</sup>, Isabelle Whittle<sup>5</sup>, Sophie Pope<sup>5</sup>, Fiona Pearson<sup>5</sup>, Fraser Williams<sup>5</sup>, Daniel Curcio<sup>6</sup>

<sup>1</sup>Pfizer, USA, <sup>2</sup>Pfizer, Brazil, <sup>3</sup>Pfizer, Greece, <sup>4</sup>Pfizer, Australia, <sup>5</sup>Adelphi Values PROVE, Adelphi Mill, Bollington, Cheshire, SK10 5JB, UK, <sup>6</sup>Pfizer, Spain

## INTRODUCTION

- SARS-CoV-2 infections remain a significant health burden for patients worldwide, with evolving variants causing periodic surges and changes in disease severity.<sup>1-3</sup>
- The risk of COVID-19 hospitalization continues to be high among infants and is comparable to risk among older adults.<sup>4</sup>
- There is a need to understand the potential impact of SARS-CoV-2 variant evolution on COVID-19 severity among the pediatric population to inform future vaccination programs.

## AIM

- To understand COVID-19-related severity and medical outcomes in pediatric patients (aged ≤18 years) stratified by SARS-CoV-2 variant.

## METHODS

- The SLR was registered a-priori with PROSPERO (ID: CRD42024619193), conducted according to Cochrane gold standard methods and is reported following the PRISMA guidelines.
- EMBASE® and MEDLINE® databases were searched on November 26<sup>th</sup>, 2024, using the OVID platform.
- Database searches were supplemented by allied grey literature search of conference proceedings from ESCMID and IDWeek from January 1<sup>st</sup>, 2022 to December 31<sup>st</sup>, 2024.
- Two independent reviewers screened titles and abstracts, then full text publications of citations retrieved from the database searches against Population, Exposure, Comparisons, Outcomes (PECO) eligibility criteria.
- Eligible publications reported acute COVID-19 outcomes indicative of disease severity (e.g., hospital or ICU admission, mortality), by SARS-CoV-2 variant infection status in individuals aged ≤18 years.

## RESULTS

- A total of 2,482 records were identified with 46 unique studies reporting pediatric data were included (Table 1).
- Statistical comparison (unadjusted and adjusted estimates) between pre-Omicron and post-Omicron (most recent variant captured was XBB.1.5) variant periods were reported for each of hospitalization, ICU admission, and organ support by 6 studies, and for mortality by 4 studies.
- For all hospitalization, ICU admission, and mortality outcomes, either no statistically significant change or a statistically significant (as determined by study author testing) decrease in severity was reported when comparing post-Omicron emergence versus pre-Omicron (Figure 1).
- Findings were mixed for organ support outcomes. A statistically significant increase in non-invasive ventilation, oxygen therapy, and receipt of vasopressors during post-Omicron was reported in 2 studies. However, 6 organ support outcomes indicated a statistically significant decrease in severity during post-Omicron, and 6 found no statistical difference.
- Five studies (three reporting adjusted estimates) stratified outcomes by extent of comorbidity (e.g., number, specific conditions). Across all assessed periods, comorbidities were statistically significant predictors of worse outcomes among patients with COVID-19, with severity of outcomes increasing with number of comorbid conditions.

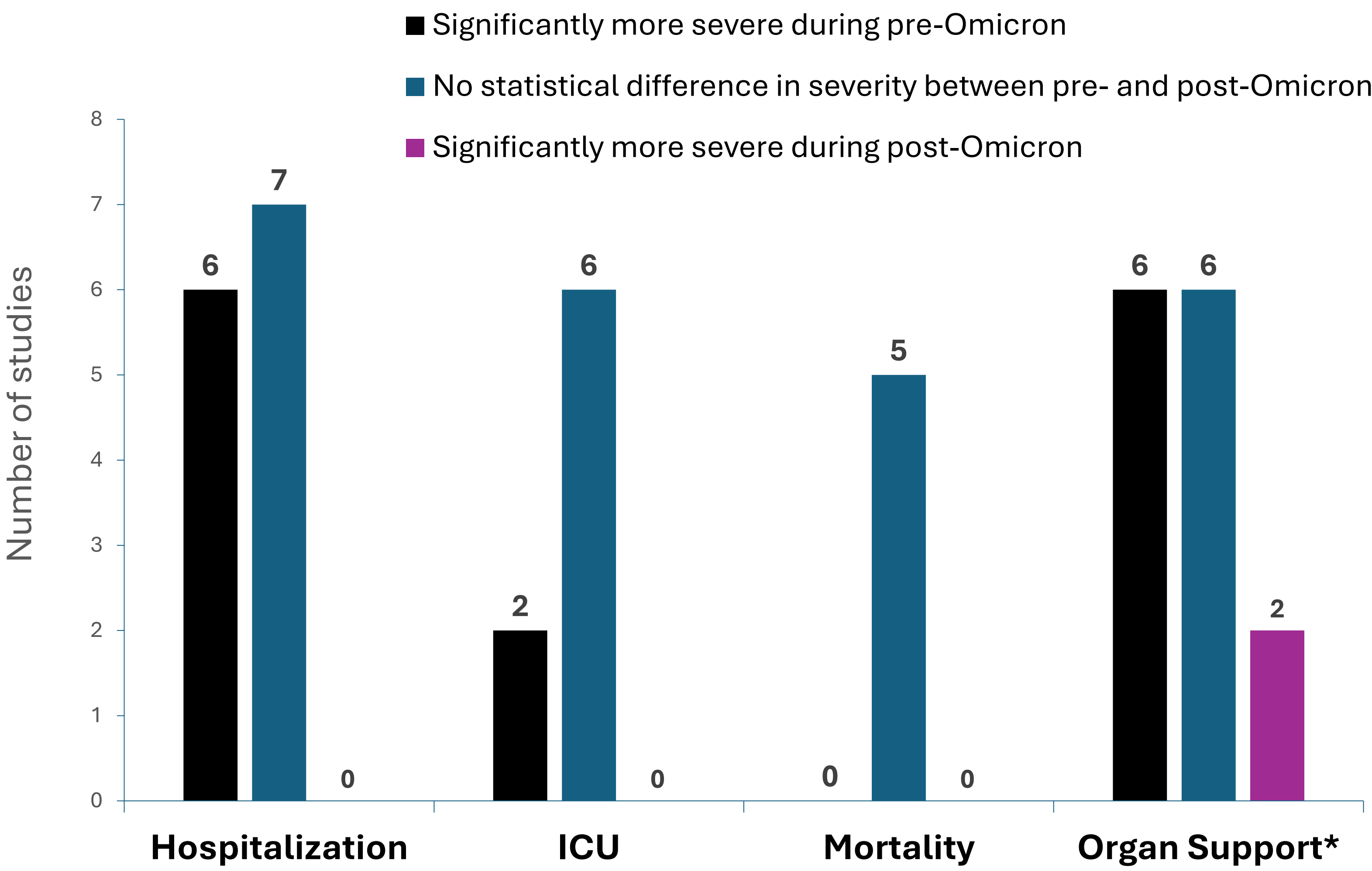
Table 1. Overview of study characteristics (N=46)

| Characteristic                          | Pubs, N (%) |
|---|-------------|
| Study design                            |             |
| Case-control study                      | 8 (17)      |
| Prospective cohort study                | 5 (11)      |
| Retrospective cohort study              | 33 (72)     |
| WHO region                              |             |
| African Region                          | 2 (4)       |
| Americas                                | 24 (52)     |
| Eastern Mediterranean                   | 1 (2)       |
| European                                | 12 (26)     |
| Western Pacific                         | 7 (15)      |
| Exposure (variant)*                     |             |
| Pre-Omicron                             | 23 (50)     |
| Omicron                                 | 29 (63)     |
| Dominant variant definition             |             |
| Defined by study author/external source | 38 (83)     |
| Variant sequenced                       | 8 (17)      |
| Outcomes reported*                      |             |
| Hospitalization                         | 38 (83)     |
| ICU                                     | 30 (65)     |
| Mortality                               | 28 (61)     |
| Organ support†                          | 28 (61)     |

ICU: intensive care unit; WHO: World Health Organization.  
\*Included studies may have reported multiple variants or outcomes, therefore, total counts and proportions can exceed the number of studies (n=46) and cumulative percentage may exceed 100%. †Forms of organ support included types of invasive and non-invasive ventilation and oxygen therapy, receipt of vasopressors.

## RESULTS (cont.)

Figure 1. Comparative direction of effect between pre- and post-Omicron periods across healthcare outcomes indicative of COVID-19 severity (assessed through association testing)



ICU: intensive care unit.  
Each bar represents an individual outcome reported in each study, therefore studies may be represented more than once for each outcome category)  
\*Forms of organ support included types of invasive and non-invasive ventilation and oxygen therapy, receipt of vasopressors.

## CONCLUSIONS

### Key Findings...

most (24/40) outcomes indicated no **statistically significant difference** in the proportions of hospitalization, ICU admission, mortality, receipt of organ support, or in hospital and ICU length of stay between SARS-CoV-2 variant predominance **during pre- vs post-Omicron**

Of the 14 studies reporting a statistically significant change in hospitalization, ICU admission, and mortality outcomes, all indicated a decrease in severity following Omicron emergence

### Implications...

these findings underscore the continued importance of pediatric COVID-19 vaccination, as a key strategy to reduce severe outcomes among children in the post-Omicron era

### Further research...

should assess trends in acute pediatric COVID-19 disease severity in contemporary lineages (e.g., LP.8.1, NB.1.8.1, and XFG) and whether these similarly occur in chronic COVID-19 conditions (i.e., Long COVID)

References  
1. Chen B, Farzan M, Choe H. SARS-CoV-2 spike protein: structure, viral entry and variants. Nat Rev Microbiol. Jul 2025;23(7):455-468. doi:10.1038/s41579-025-01185-8  
2. Arabi M, Al-Najjar Y, Mhaimeed N, et al. Severity of the Omicron SARS-CoV-2 variant compared with the previous lineages: A systematic review. J Cell Mol Med. Jun 2023;27(11):1443-1464. doi:10.1111/jcmm.17747  
3. Relan P, Motaze NV, Kothari K, et al. Severity and outcomes of Omicron variant of SARS-CoV-2 compared to Delta variant and severity of Omicron sublineages: a systematic review and meta-analysis. BMJ Glob Health. Jul 2023;8(7):doi:10.1136/bmjgh-2023-012328  
4. Centers for Disease Control and Prevention. COVID-19—Associated Hospitalizations and Maternal Vaccination Among Infants Aged <6 Months — COVID-NET, 12 States, October 2022–April 2024. Updated 26th September 2024. Accessed October 2025, <https://www.cdc.gov/mmwr/volumes/73/wr/mm7338a1.htm>

Disclosures  
This study was sponsored by Pfizer Inc. Pfizer employees may hold stock or stock options.  
Employees of Adelphi Values PROVE received funding from Pfizer Inc. to conduct this study.  
For more information, please contact: Deepa Malhotra  
66 Hudson Blvd E, New York, NY 10001, USA.  
deepa.malhotra@pfizer.com

