

### **Overview**

EuCARE project study reveals information on hospital mortality in Wild-type, Alpha, Delta and Omicron SARS-CoV-2 waves and concludes that younger age, combined with immunization and previous infections, reduces mortality.

## About the Study

The multinational study "In-hospital mortality during the wild-type, alpha, delta, and omicron SARS-CoV-2 waves: a multinational cohort study in the EuCARE project", led by the EuCARE partner from Karolinska Institutet (KI) involving partners from several different EuCARE centers concluded that in-hospital mortality at 28 days has decreased throughout the SARS-CoV-2 pandemic, particularly since the appearance of the Omicron variant. The study considered the different waves of viral variants, including Wild-type, Alpha, Delta and Omicron variants.

The study, published in the renowned scientific journal Lancet Regional Health- Europe, identified age as an important modifier for the association between viral variant and mortality risk, and evidence suggesting that the observed decrease in in-hospital mortality reflects a combined effect of vaccine immunity and previous infections. This study is an important contribution to the existing literature, since studies investigating trends of age-stratified in-hospital mortality from multiple countries and settings are scarce.

# **Research Approach**

Same inclusion criteria for patients hospitalised with COVID-19 across multiple countries, primarily in Europe, but also outside of Europe, while most other original research articles have been confined to one center, one region, or one country. This favors external validity by investigating the overall effects of SARS-CoV-2 variants across a wide range of countries and continents. The study uses data from the hospitalized cohort part of the EuCARE project,

which included 38,585 adults hospitalised with SARS-CoV-2 Wild-type, Alpha, Delta, or Omicron infection across 10 centers in 9 countries: Germany, Italy, Kenya, Lithuania, Mexico, Poland, Portugal, Sweden, and United Kingdom.

# **Key Messages**

#### **Declining Mortality Across Variants**

The study finds a clear decline in in-hospital mortality over the course of the pandemic, particularly after the emergence of the Omicron variant. Variants, such as Alpha, Delta and Omicron BA.1 sub-lineage, had a higher mortality risk, compared to Omicron BA.2 and BA.5 sub-lineages. This trend is especially pronounced among vaccinated individuals and those who have had prior infections, suggesting a protective effect of immunity.

#### Age as a Modifier of Mortality Risk

Age emerged as a crucial factor in modifying the association between viral variants and mortality risk. Older and frailer individuals were at higher risk, regardless of the viral variant, emphasising the need for interventions targeting these populations.

#### Impact of Vaccination and Previous Infections

The study underscores that the observed decline in mortality reflects the combined protective effect of vaccine-induced immunity and immunity acquired through prior infections. When analysing only unvaccinated patients, there was no differences in mortality between the earlier and later variants, indicating that vaccination has been key in reducing the severity of outcomes.

#### **Multinational and Age-Stratified Analysis**

By using data from a diverse range of countries, including low- and middle-income nations, the study provides a comprehensive view of the global impact of SARS-CoV-2 variants on hospital mortality. This age-stratified analysis of in-hospital mortality across different global settings is one of the first, filling an important gap in existing research.

# **Policy Implications**

#### **Targeted Vaccination Campaigns for Vulnerable Groups**

The study reinforces the critical need for continued vaccination efforts, particularly for older adults and those with underlying health conditions. Special attention should be paid to ensuring equitable access to vaccines across all regions, especially in countries with lower vaccination rates.

#### Strengthening Public Health Surveillance

The evolving nature of SARS-CoV-2 variants and their differential impacts on mortality highlights the importance of robust public health surveillance systems. Policymakers should

invest in infrastructure to track variant prevalence, vaccine coverage, and hospital outcomes in real-time. This will help adjust response strategies quickly in the face of emerging variants and changing epidemiological trends.

#### **Comprehensive Prevention Measures**

In addition to vaccination, continued emphasis on other preventive measures—such as maskwearing, physical distancing, and improving ventilation in high-risk settings—should be part of comprehensive public health strategies. These measures remain important, particularly in healthcare settings and in regions with high transmission rates or lower vaccination coverage.

#### **Global Cooperation and Data Sharing**

The study's multinational approach demonstrates the value of international collaboration in understanding the global impact of the pandemic. Governments and international organizations should continue to support initiatives that promote data sharing and collaborative research, particularly across diverse regions. This will be crucial for monitoring future pandemics and other emerging infectious diseases.

#### Long-term Care and Support for the Elderly and Frail

The study findings related to older adults remaining at higher risk underscores the need for sustained efforts to protect these populations. This includes not only vaccination but also targeted healthcare interventions and support systems for long-term care. Policymakers should ensure that resources are allocated to improve the quality of care for elderly and frail individuals, both in hospitals and community settings.

## Recommendations

- Increase vaccination rates among high-risk populations, particularly the elderly and those with comorbidities.
- Invest in global surveillance and data sharing to monitor evolving SARS-CoV-2 variants and their impacts.
- Implement comprehensive public health measures, including vaccination, mask-wearing, and improved ventilation, especially in healthcare settings.
- Continue supporting vulnerable populations with long-term care and healthcare interventions tailored to their needs.

# About the EuCARE Project

The EuCARE Project is an initiative funded by the European Union with the aim of better understanding various aspects of the COVID-19 pandemic, including in-hospital mortality, long COVID and the impact of containment measures. With a multinational and collaborative approach, EuCARE is making significant contributions to advancing knowledge about the disease and its ramifications.

### Resources

Manuscript



EuCARE website

