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Non-COVID-19 intensive care admissions during the pandemic: a multinational registry-based study FREE



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Abstract

Background The COVID-19 pandemic resulted in a large number of critical care admissions. While national reports have described the outcomes of patients with COVID-19, there is limited international data of the pandemic impact on non-COVID-19 patients requiring intensive care treatment.

Methods We conducted an international, retrospective cohort study using 2019 and 2020 data from 11 national clinical quality registries covering 15 countries. Non-COVID-19 admissions in 2020 were compared with all admissions in 2019, prepandemic. The primary outcome was intensive care unit (ICU) mortality. Secondary outcomes included in-hospital mortality and standardised mortality ratio (SMR). Analyses were stratified by the country income level(s) of each registry.

Findings Among 1 642 632 non-COVID-19 admissions, there was an increase in ICU mortality between 2019 (9.3%) and 2020 (10.4%), OR=1.15 (95% CI 1.14 to 1.17, $p < 0.001$). Increased mortality was observed in middle-income countries (OR 1.25 95% CI 1.23 to 1.26), while mortality decreased in high-

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income countries (OR=0.96 95% CI 0.94 to 0.98). Hospital mortality and SMR trends for each registry were consistent with the observed ICU mortality findings. The burden of COVID-19 was highly variable, with COVID-19 ICU patient-days per bed ranging from 0.4 to 81.6 between registries. This alone did not explain the observed non-COVID-19 mortality changes.

Interpretation Increased ICU mortality occurred among non-COVID-19 patients during the pandemic, driven by increased mortality in middle-income countries, while mortality decreased in high-income countries. The causes for this inequity are likely multi-factorial, but healthcare spending, policy pandemic responses, and ICU strain may play significant roles.

Data availability statement

Data may be obtained from a third party and are not publicly available. Requests for data will be subject to the requirements and policies of each CQR. Requests should be directed to the corresponding author.

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WHAT IS ALREADY KNOWN ON THIS TOPIC

- The COVID-19 pandemic has increased the global healthcare burden and has been associated with an excess death rate in many countries. Most studies are limited to patients with COVID-19 and single countries or regions. The few international comparisons are largely limited to high-income countries, while the burden of COVID-19 infections has disproportionately affected low-income and middle-income countries.

WHAT THIS STUDY ADDS

- To our knowledge, this is the first international comparison of critically ill non-COVID-19 patients throughout the pandemic. Overall mortality among non-COVID-19 patients increased, driven by increased mortality in middle-income countries (MICs), while mortality decreased in high-income countries. The burden of COVID-19 care may be associated with worse outcomes in these countries, but alone does not explain the differences in mortality. The increase in non-COVID-19 mortality is partly responsible for the excess death rate observed throughout the pandemic.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

- The pandemic has been associated with increased non-COVID-19 mortality and has disproportionately impacted ICU mortality in countries with lower income levels. Further research is required to examine the association between the pandemic and non-COVID-19 deaths, as well as causes of the observed inequity, and to find what can best be done to combat the challenges facing the delivery of intensive care in middle-income and low-income countries, especially as the pandemic continues.

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Introduction

The COVID-19 pandemic has had a broad healthcare impact, resulting in high intensive care unit (ICU) admission rates¹ and disruption to ICU service delivery.² Indirect effects have included decreases in cancer diagnosis rates,³ transplant surgeries⁴ and coronary artery percutaneous interventions.⁵ An excess death rate above the reported COVID-19 death rate has been observed, largely attributed to unreported COVID-19 cases.^{6 7}

Outcomes of patients requiring intensive care treatment due to severe COVID-19^{1 7–13} are dependent on patients' characteristics (eg, severity of illness, age and comorbidities) and organisational factors including ICU strain, surge capacity and geographical location within countries.^{1 9 14 15} Whether the COVID-19 pandemic changed the characteristics or outcomes of non-COVID-19 patients requiring intensive care treatment remains uncertain.

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The primary aim of this study was to describe the mortality for non-COVID-19 ICU patients during the pandemic, compared with the prepandemic period, using data from national clinical quality registries (CQRs). The hypothesis was that the pandemic resulted in increased mortality of non-COVID-19 ICU patients.

Methods

Design

This was an international, retrospective cohort study using routinely collected, deidentified, aggregated patient-level data from ICU CQRs over the 2019 and 2020 calendar years. As COVID-19 was first reported in China in December 2019 and the first cases outside China occurred in January 2020,¹⁶ all ICU admissions in the 2019 calendar year were considered non-COVID-19. These were compared with calendar year 2020, for which all contributing registries were considered to be affected by the COVID-19 pandemic regardless of the date of the first confirmed COVID-19 case in each CQR.

Setting

Eligible national CQRs were those that recorded data on patients admitted to adult ICUs in 2019 and 2020 and were able to identify the cohort of patients within the registry that were admitted with COVID-19. CQRs were identified through the 'Linking Of Global Intensive Care' initiative (LOGIC).¹⁷ Representatives from 15 additional national CQRs were contacted directly, of whom three agreed to participate. Further information on each of the participating registries can be found in the online supplemental appendix.

Supplemental material

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Variables

CQR data included characteristics of the CQRs (size, national coverage, available ICU beds, proportion of public and private hospitals) and aggregated patient data by patient group: COVID-19, non-COVID-19 and total for 2019 and 2020. [View PDF](#)

Population data, gross domestic product (GDP), country income category and healthcare expenditure were sourced from The World Bank.¹⁸ Country COVID-19 diagnoses rates were sourced from the Oxford COVID-19 Government Response Tracker.¹⁹ [PDF Help](#)

The primary outcome was ICU mortality, a metric available from all contributing CQRs. Secondary outcomes included ICU length of stay (LOS), mechanical ventilation, hospital mortality and standardised mortality ratio (SMR). Expected hospital mortality used for SMR was based on the illness severity score models (eg, APACHE-II, SOFA and SAPS3) for each CQR. Further detail on expected in-hospital mortality can be found in the online supplemental appendix.

Statistical analysis

CQRs provided only aggregate data; no individual patient data were analysed. The impact of the COVID-19 pandemic was assessed by temporal comparison of non-COVID-19 ICU admissions within each region in 2020 compared with 2019 and by comparison of patients admitted to ICUs between regions that were

differentially affected by the pandemic in 2020.

Descriptive analyses were provided on registry coverage, admission numbers, admission source, age, sex, mechanical ventilation, illness severity (based on local and international severity of illness scores), length of stay, ICU mortality and hospital mortality. SMRs were calculated as the ratio of the observed in-hospital mortality to the expected in-hospital mortality for each CQR.

The available registry-level data were aggregated into internationally representative statistics, using a fixed-effect model with inverse-variance weighting to account for differences between countries. The statistical analysis was performed using the Review Manager 5 (RevMan5) software.²⁰ Means with SD were used when appropriate. ORs for dichotomous variables and mean differences for continuous variables were used to compare between years. χ^2 tests of significance were used for categorical variables.

ICU admission numbers for each registry were indexed to population size and total COVID-19 cases in the community, extrapolating the available data based on the coverage of each registry within each country. Analysis of outcomes was stratified by country income level. Missing data were not imputed.

Results

There were 11 participating registries representing 15 countries in four continents. A comparison of the key features of the contributing registries can be found in the online supplemental appendix. Four countries represented (Bangladesh, India, Nepal and Pakistan) were lower-income and middle-income countries (LMICs), three (Brazil, Argentina and Malaysia) were higher income and middle-income countries (HMICs) and the remaining eight countries were high-income countries (HICs).

Data were provided for more than 1.7 million ICU admissions across 2082 ICUs. The mean age of patients admitted to the ICU was 61.3 years (SD 19.1), with substantial variation between registries (range 51.5 in the Collaboration for Research, Implementation and Training in Intensive Care in Asia (CCA) registry to 64.0 in Japan). Males accounted for 54.8% of patients (range 51.4% in Brazil to 63.8% in Japan). 89 623 patients admitted to an ICU in 2020, 106 835 (12.0%) were diagnosed with COVID-19. There was substantial inter-registry variation in absolute COVID-19 admissions and large variation in ICU admissions relative to the total community COVID-19 burden. Further detail can be found in the online supplemental appendix.

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Non-COVID-19 ICU admissions and demographics

Compared with 2019, non-COVID-19 admissions in 2020 decreased by 9% from 859 854 to 7 82 778. At the same time, beds included in the registries increased by 18.2% from 23 376 to 27 638. Indexed to available beds, non-COVID-19 admissions per available ICU bed decreased by 12.5% in 2020 (range 33.9% decrease in admissions in CCA to 3.1% increase in New Zealand).

The international trends in non-COVID-19 admissions per million population differed substantially from the trends for COVID-19 admissions (figure 1A,B respectively). Many registries (Australia, New Zealand, Scotland, Finland, Netherlands, Japan and Argentina) had decreases in non-COVID-19 admissions of a similar magnitude to the increase in COVID-19 admissions, while some registries (Brazil, CCA and

Uruguay) reported an increase in non-COVID-19 admissions in addition to COVID-19 admissions. However, when indexed to available beds, there was a decrease in non-COVID-19 admissions per million population in all registries except New Zealand (figure 1C).

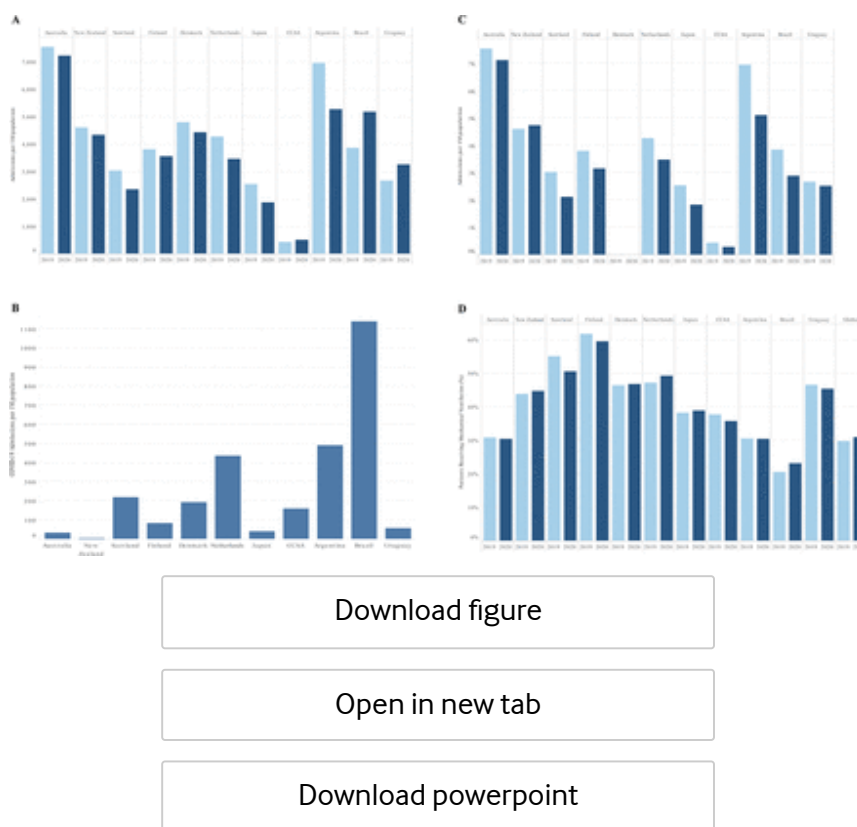


Figure 1

ICU admissions and characteristics. (A) Non-COVID-19 ICU admissions per million members of the population. (B) COVID-19 ICU admissions per million members of the population. (C) Non-COVID-19 ICU admissions per million members of the population, indexed to available beds. (D) Proportion of non-COVID-19 patients receiving mechanical ventilation. ICU, intensive care unit.

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The mean age of non-COVID-19 patients was similar between the 2 years. The proportion of male patients increased slightly from 53.2% to 54.6% (range 52% in Brazil to 64% in Finland). All registries had a higher proportion of male patients in 2020 than 2019.

The proportion of non-COVID-19 patients receiving mechanical ventilation increased from 29.4% to 30.7%. Figure 1D shows rates of mechanical ventilation in non-COVID-19 patients by region and year. The overall increase in mechanical ventilation was primarily due to small increases in New Zealand, Denmark, the Netherlands and Brazil.

Overall admission illness severity scores and predicted risk of death (expected hospital mortality) among non-COVID-19 patients were similar in 2019 and 2020 (see table 1).

Table 1

Non-COVID-19 ICU admissions in 2019 and 2020

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Non-COVID-19 ICU mortality

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Overall, non-COVID-19 patients experienced an increase in all-cause ICU mortality from 9.3% in 2019 to 10.4% in 2020, OR 1.15 (95% CI 1.14 to 1.17, $p < 0.001$). This was consistent with a sensitivity analysis on those patients that received mechanical ventilation, with an increase in mortality from 22.8% to 23.9%, OR 1.04 (95% CI 1.03 to 1.05, $p < 0.001$).

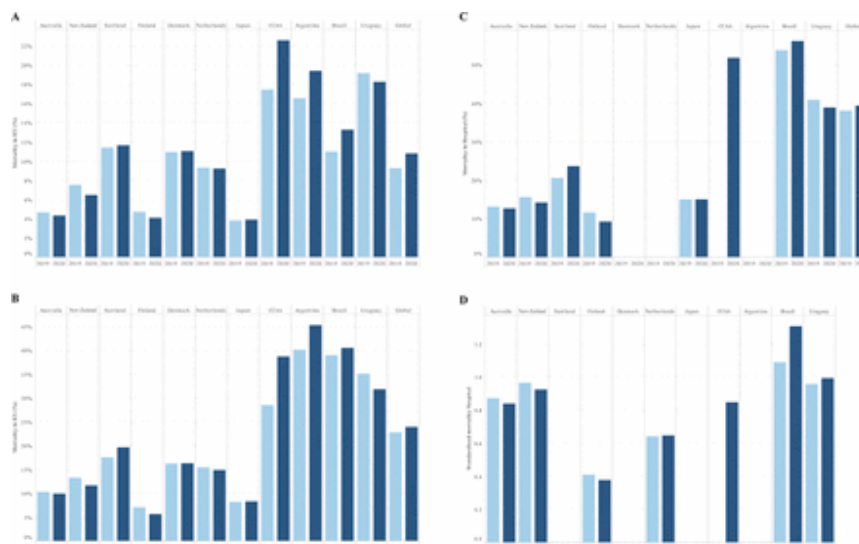
These findings differed greatly between regions (online supplemental tables 1 and 2, figure 2A). The OR for ICU mortality for HICs was 0.96 (95% CI 0.94 to 0.98), compared with an OR of 1.25 (95% CI 1.23 to 1.26) for LMICs and HMICs ($p < 0.001$ for between group differences) (figure 3A).

Supplemental material

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[thorax-2022-219592supp002.pdf]



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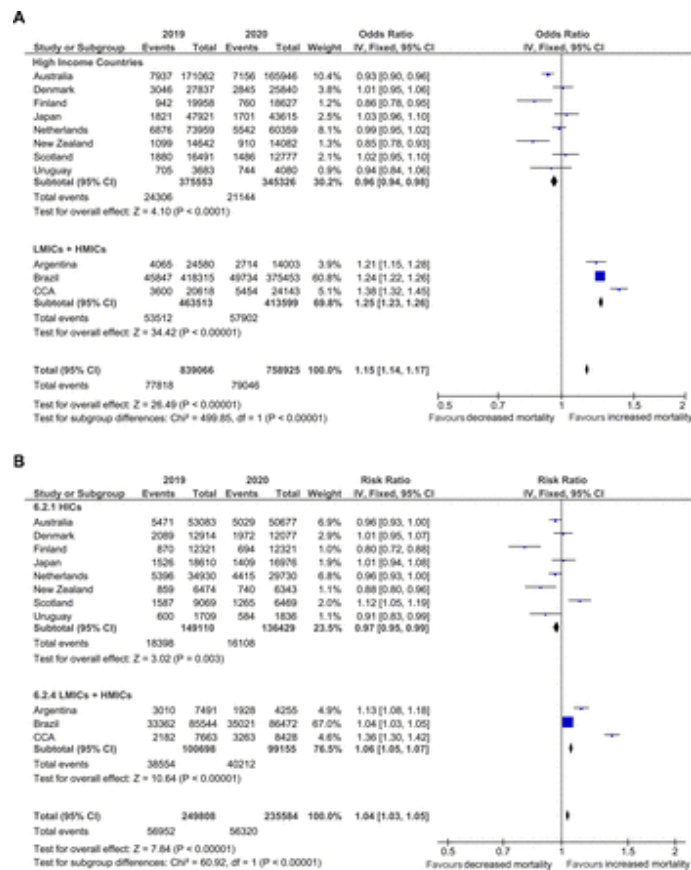
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Figure 2

Non-COVID-19 ICU outcomes. (A) Non-COVID-19 in-ICU mortality. (B) Non-COVID-19 in-ICU mortality for patients that received mechanical ventilation. (C) Non-COVID-19 in-hospital mortality for patients that received mechanical ventilation. (D) Non-COVID-19 standardised mortality ratio. ICU, intensive care unit.



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Figure 3

Non-COVID-19 ICU mortality, by country income level. (A) Non-COVID-19 ICU mortality, by country in COVID-19 ICU mortality if received mechanical ventilation, by country income level. ICU, intensive ca

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For patients that received mechanical ventilation, the trends were similar (figure 2B): HIC: OR 0.97 (95% CI 0.95 to 0.99) and LMIC and HMIC: OR 1.06 (95% CI 1.05 to 1.07) ($p < 0.001$ for between group differences) (figure 3B).

Secondary outcomes

There was a similar increase in overall in-hospital all-cause mortality for non-COVID-19 patients and for those patients that received mechanical ventilation. Similarly to in-ICU mortality, there were significant international differences in in-hospital mortality, shown in figure 2C. The OR for in-hospital mortality for HICs was 0.96 (95% CI 0.95 to 0.98), compared with 1.26 (95% CI 1.24 to 1.27) for HMICs ($p < 0.001$). This was consistent in those patients that received mechanical ventilation, OR=0.96 (95% CI 0.94 to 0.98) for HICs, OR=1.10 (1.08–1.12) for HMICs ($p < 0.001$). No data were available for LMICs.

In the six registries with complete data for hospital mortality and illness severity, the trends in observed ICU mortality are consistent with the SMR (figure 2D), a risk-adjusted measure that incorporates disease severity.

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Mean ICU length of stay for non-COVID-19 patients were similar (7.0 days in 2019 vs 7.2 days in 2020, while the mean hospital length of stay decreased from 14.9 days to 14.0 days ($p < 0.001$).

Discussion

This study of aggregated data from over 1.7 million ICU admissions (including 1.64 million non-COVID-19 ICU admissions) from 15 countries found an increase in all-cause mortality of patients with non-COVID-19 diagnoses admitted to an ICU in 2020 compared with 2019. Importantly, the overall increase in mortality was driven by an increase in mortality in middle-income countries (MICs; comprised of LMICs and HMICs), while mortality actually decreased in HICs in 2020 for non-COVID-19 patients. Similar findings were observed among patients that received mechanical ventilation. This is despite similar age, sex, illness severity, and mechanical ventilation rates between years.

The SMRs followed the trends of crude mortality, with a large increase in Brazil (the only MIC with available SMR data), and stable ratios or small decreases in HICs. As SMR is calculated using an illness severity score and its derived predicted risk of death, this suggests that mortality changes were not the result of changes in illness severity in 2020, and other factors contributed.

The causes of these findings are likely multifactorial, including ICU bed availability, healthcare practice and policy factors. Our data suggest an association between the COVID-19 ICU admission burden and non-COVID-19 outcomes. On average, HICs had a lower burden of COVID-19 than MICs (1.71 vs 4.01 admissions per bed, 21.62 vs 37.02 patient-days in ICU per bed). Brazil and the registry containing Bangladesh, India, Malaysia, Nepal and Pakistan (CCA), who both experienced increases in mortality for non-COVID-19 patients, both had high rates of COVID-19 admissions per available ICU bed (4.2 and 5.7, respectively) and a high burden of care for COVID-19 patients as measured by patient-days in ICU per bed (51.5 and 31.4, respectively). This is compared with Australia and New Zealand, which both had falls in mortality for non-COVID-19 patients and a lower burden of COVID-19, with 0.3 and 0.05 COVID-19 admissions per ICU bed, and only 2.5 and 0.4 patient-days in ICU per bed, respectively. Comparatively, the Netherlands also had a high burden of COVID-19, with 6.6 admissions per bed and [View PDF](#) in ICU per bed but had stable mortality for non-COVID-19 patients.

Although such comparisons are limited by confounders such as country demographics and pandemic public health measures, it is plausible that greater healthcare system resourcing in the Netherlands compared with Brazil, Bangladesh, India, Malaysia, Nepal and Pakistan provided pandemic capacity that influenced outcomes. This is supported by the large differences in GDP per capita (US\$; Netherlands: 52 397, Brazil: 6797, CCA average: 3329)²¹ and healthcare expenditure as a proportion of GDP between the countries (Netherlands: 9.97%, Brazil: 9.51%, CCA average: 3.74%).²² In addition to differences in funding, many MICs face additional challenges in providing critical care including inequitable regional distribution of ICUs, a high proportion of private ICU beds with a low proportion of the population with access to private healthcare, and lower staff-to-patient ratios.²³

Intrinsic differences in the design of critical care systems between countries likely also have an impact on ICU outcomes, including nurse-to-patient ratios in critical care units, thresholds for admission to ICU and demographics of the broader community in each country. For example, an increase in the number of ICU patients per ICU nurse has been previously shown to be associated with increased mortality²⁴; however few countries have mandatory minimum nursing ratios in critical care, and the usual nurse-to-

patient ratio varies greatly (eg, 1:1 for ventilated patients in Australia and New Zealand to 1:5 in Brazil).²⁵ While nurse-to-patient ratios have an independent association with ICU mortality, which may have impacted the observed changes in mortality in our study, ratios are also likely to be influenced by country income level, with HICs having 11.4 nurses per 1000 members of the population, compared with 2.7 for MICs.²⁶

A decrease in mortality for non-COVID-19 patients was observed in many registries in 2020; however, this was seen exclusively in HICs. It is plausible that these health systems were relatively under resourced prior to the pandemic and that the positive mortality impact was a result of increased resourcing and healthcare expenditure in 2020 that outweighed the increased strain on intensive care. Comparatively, in MICs and low-income countries, the additional ICU strain may have stretched systems unable to cope with the increased critical care demands of the pandemic. However, further research is required to investigate this hypothesis.

Comparing our data to the Oxford COVID-19 Government Response Tracker (OxCGRT) shows little correlation between government responses and non-COVID-19 ICU mortality in 2020. OxCGRT reports a health and containment index based on 14 indicators of government response including 'lockdown' style measures and healthcare investment, with a maximum index of 100 (the most stringent). Countries with high health and containment indices did not have improved non-COVID-19 ICU mortality in 2020 in this study. For example, Argentina had the highest average daily index in 2020 (63) and had an increase in ICU mortality (OR=1.13). Comparatively, Finland had the second lowest index (36), while Australia had a high index (52) and both countries had decreases in ICU mortality (OR=0.8 and OR=0.96, respectively). However, more stringent government responses during the pandemic have previously been associated with decreased COVID-19 mortality,²⁷ and it is possible that without stringent responses, non-COVID-19 mortality would have been higher.

Another factor that may have influenced non-COVID-19 ICU mortality is the creation of additional ICU beds, through the subsequent requirement for altered staffing arrangements (eg, staff new to critical care, decreased staff-to-patient ratios), and increased difficulty in maintaining quality initiatives, as shown prior to the pandemic.²⁸ Brazil had a large increase in ICU bed capacity in 2020 with an increase of 21.2%, while the CCA and Argentinian ICUs had more modest increases of 1.8% and 4.4%, respectively. Finland, Scotland and Uruguay also had increases of 12%–21%, while Australia, Japan and the Netherlands had stable bed capacity. New Zealand, which had the lowest COVID-19 load, had a decrease in ICU bed capacity of 6.7%. [View PDF](#)

Total admissions per available bed fell in 2020, likely due in part to longer lengths of stay of COVID-19 patients increasing bed occupancy. Total patient-days per ICU bed are a better measure of ICU bed strain, and this increased in registries with a high burden of COVID-19 (eg, Brazil and the Netherlands) despite large decreases in non-COVID-19 patient-days per bed.

The existing literature on the impact of the COVID-19 pandemic on international ICU outcomes is relatively limited. While many studies have been published on the characteristics and ICU outcomes of patients with COVID-19 within individual countries^{10–13} these have been small and often single-centre studies. Relatively few studies have made international comparisons among these patients,⁸ and reported mortality rates are highly variable. A number of studies have highlighted the difficulties in

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making international comparisons throughout the COVID-19 pandemic, including differing country demographics (eg, age structure), COVID-19 testing practices and case definitions, definitions of COVID-19 deaths, access to healthcare, available ICU resources and ICU admission and management practices.^{29 30} While one Argentinian study showed that the management of non-COVID-19 ICU patients had changed during the pandemic without altering outcomes,³¹ and one Brazilian study demonstrated an increase in in-hospital mortality for non-COVID-19 patients in 2020,³² to our knowledge, this is the first international study comparing the outcomes of non-COVID-19 patients admitted to ICU during the COVID-19 pandemic. While the same difficulties of comparing outcomes exist as for COVID-19 patients, their impact is minimised in this study by comparing the change in mortality within each registry between 2019 and 2020.

A growing number of studies have been published on the observed excess death rate during the COVID-19 pandemic.^{6 7 33 34} The excess death rate observed in many countries has been attributed to COVID-19 infections, with under-reporting and misidentifying COVID-cases used to explain the gap between COVID-19 related deaths and the excess death rate. However, this study suggests that the global excess death rate may also be partly due to a deterioration in health outcomes for non-COVID-19 patients. Furthermore, a number of studies on excess deaths have identified a decrease in overall country mortality during the pandemic, including in Australia, Denmark, Japan, New Zealand and Uruguay,^{6 7} in keeping with the findings in this study. These studies have attributed the decrease in deaths in these countries to a decrease in non-COVID-19 infectious mortality and fewer road traffic accidents due to lockdowns.

A number of studies published prior to and during the COVID-19 pandemic have established associations between ICU strain and altered patient outcomes, including less adherence to evidence-based practices,²⁸ shorter times to initiating 'do not resuscitate' orders³⁵ and increased mortality.³⁶ During the pandemic, increased ICU strain has also been associated with increased likelihood of interhospital transfer for ICU care³⁷ and with increased mortality for both COVID-19 patients and non-COVID-19 patients.³⁸ Previously described associations between strain and mortality are consistent with those described in this study.

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The strengths of this study include use of international collaborative databases through the LOGIC-ICU initiative¹⁷ to facilitate the comparison of critical care outcomes between countries and the conduct of international critical care research. The study included over 1.7 million admissions from 15 countries, with each registry containing data from a large group of participating hospitals.

Limitations of the study include the use of aggregate data from each of the databases, limiting more detailed analysis. Data collection for each of the registries is not internationally standardised (eg, different models of illness severity), and some registries were unable to provide complete data for this study. In some registries, the reported number of ICU beds in 2020 did not include additional surge beds. The aggregated registry data precluded reporting combined medians for non-normally distributed variables (eg, ICU length of stay); however, reporting mean LOS provides a more accurate measure of resource utilisation. Additionally, the annualised data provided necessitated the assumption that all patients admitted in 2020 were influenced by the pandemic, which may introduce bias, and precluded further analysis of the timing of COVID-19 outbreaks within countries, which may have had a significant

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impact on ICU strain. We were unable to access previous years of data to further examine the year-to-year variation in ICU mortality in these registries and cannot compare the observed change in mortality to a historical control.

The classification of COVID-19 cases required confirmed laboratory testing in all registries except the CCA registry, which included confirmed laboratory testing cases as well as clinically suspected COVID-19 cases. It is possible that some patients with COVID-19 may be inadvertently misclassified as non-COVID-19. Although this group is likely to be small, the impact of misclassification cannot be definitively determined. Cause of death was not reported, precluding further analysis. Finally, the relatively small national coverage of some registries (eg, CCA, Japan) may limit the generalisability of the findings within some countries and may introduce bias due to differences between participating and non-participating ICUs.

In summary, this study has demonstrated a global increase in non-COVID-19 ICU mortality during the pandemic. The impact on mortality has been highly variable between countries, with some countries experiencing large increases in mortality, and others experiencing a decrease in mortality. Many factors likely contribute to the direction and magnitude of the impact of the pandemic on mortality for non-COVID-19 patients; however country income level seems to have a strong influence. Further research conducted through international collaborative databases is vital to understanding and preventing further excess deaths.

Data availability statement

Data may be obtained from a third party and are not publicly available. Requests for data will be subject to the requirements and policies of each CQR. Requests should be directed to the corresponding author.

Ethics statements

Patient consent for publication

Not applicable.

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Ethics approval

The project received approval as a low-risk project from the Human Research Ethics Committee of Alfred Health, Melbourne, Australia (HREC 131/21) and from the ethics committee of the Instituto D'or de Pesquisa e Ensino, Rio de Janeiro, Brazil (Number: 44181021.3.0000.5249).














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

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Data supplement 3

Footnotes

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Collaborators: The Linking of Global Intensive Care collaboration was integral in connecting participating registries to collaborate on this study.

Contributors: DP, EL and JS conceived the study and developed the study design. Data were collected and provided by DP, EL, JS, AB, DA, MBMN, SB, GB, SC, CFC, DAD, ALF, AG, RoH, RaH, MH, SH, NI, BKTV, NIL, MdPAL, HO, DP, MR and MS. JM and DP accessed and verified the data. JM analysed the data, with assistance from DP and MB. JM, DP, EL and JS wrote the initial draft, and all authors were commenting on subsequent revisions. JM is responsible for the overall content as the

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