Non-COVID-19 intensive care admissions during the pandemic

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

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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 COVID-19 patients, 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 to all admissions in 2019, pre-pandemic. 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

Amongst 1,642,632 non-COVID-19 admissions, there was an increase in ICU mortality between 2019 (9.3%) and 2020 (10.4%), odds ratio (OR)=1.15 (95% CI 1.14–1.17, p<0.001). Increased mortality was observed in middle-income countries (OR 1.25 95% CI 1.23-1.26), while mortality decreased in high-income countries (OR=0.96 95% CI 0.94-0.98). 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 amongst 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.

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Key messages

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 COVID-19 patients, 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- 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 amongst 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 MICs and LICs, especially as the pandemic continues.

Introduction

The COVID-19 pandemic has had a broad healthcare impact, resulting in high intensive care unit (ICU) admission rates[1] and disruption to ICU service delivery.[2] Indirect effects have included decreases in cancer diagnosis rates,[3] transplant surgeries,[4] 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 (e.g. severity of illness, age and co-morbidities), and organizational 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.

The primary aim of this study was to describe the mortality for non-COVID-19 ICU patients during the pandemic, compared to the pre-pandemic 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, de-identified, 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 to 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 supplementary appendix. 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].

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.

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]

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 (e.g. APACHE-II, SOFA, SAPS3) for each

CQR. Further detail on expected in-hospital mortality can be found in the supplementary 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 to 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 standard deviations were used when appropriate. Odds ratios for dichotomous variables and mean differences for continuous variables were used to compare between years. Chi-square 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 supplementary appendix. Four countries represented (Bangladesh, India, Nepal, and Pakistan) were Lower-Middle Income Countries (LMICs), three (Brazil, Argentina, Malaysia) were Higher-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 Finland). Of the 889,623 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 supplementary appendix.

Non-COVID-19 ICU admissions and demographics

Compared with 2019, non-COVID-19 admissions in 2020 decreased by 9% from 859,854 to 782,778. 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 (Figures 1a and 1b respectively). Many registries (Australia, New Zealand, Scotland, Finland, Netherlands, Japan, Argentina) had decreases in non-COVID-19 admissions of a similar magnitude to the increase in COVID-19 admissions, while some registries (Brazil, CCA, 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).

The mean age of non-COVID-19 patients was similar between the two 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).

Non-COVID-19 ICU mortality

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 1.14–1.17, $p<0.001$). 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 1.03–1.05, $p<0.001$).

These findings differed greatly between regions (Supplementary Tables 1 and 2, Figure 2a). The odds ratio (OR) for ICU mortality for HICs was 0.96 (95% CI 0.94-0.98), compared to an OR of 1.25 (95% CI 1.23-1.26) for LMICs and HMICs ($p<0.001$ for between group differences) (Figure 3a).

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

<u>Secondary outcomes</u>

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 0.95-0.98), compared to 1.26 (95% CI 1.24-1.27) for HMICs ($p<0.001$). This was consistent in those patients that received mechanical ventilation, OR=0.96 (95% CI 0.94-0.98) for HICs, OR=1.10 (1.08-1.12) for HMICs ($p<0.001$). No data was 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 Standardised Mortality Ratio (SMR) (Figure 2d), a risk-adjusted measure that incorporates disease severity.

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 intensive care unit 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 high-income countries in 2020 for non-COVID-19 patients. Similar findings were observed amongst 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 middle-income country with available SMR data), and stable ratios or small decreases in high-income countries. 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 81.6 patient-days 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: 6,797, CCA average: 3,329)[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 mortality[24], however few countries have mandatory minimum nursing ratios in critical care, and the usual nurse to patient ratio varies greatly (e.g., 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 high income countries having 11.4 nurses per 1000 members of the population, compared to 2.7 for middle-income countries.[26]

A decrease in mortality for non-COVID-19 patients was observed in many registries in 2020 however this was seen exclusively in high income countries. 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 health care 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 2nd 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 (e.g. staff new to critical care, decreased staff-to-patient ratios), and increased difficulty in maintaining quality assurance 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%.

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 (e.g. Brazil, 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 making international comparisons throughout the COVID-19 pandemic, including differing country demographics (e.g. 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 underreporting 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" orders,[35] and increased mortality.[36] During the pandemic increased ICU strain has also been associated with increased likelihood of interhospital transfer for ICU care,[37] 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 the data described in this study.

The strengths of this study include use of international collaborative databases through the LOGIC-ICU initiative,[17] 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 (e.g. 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 (e.g., 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 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 been 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 (e.g. CCA, JIPAD) 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 Sharing

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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Contributors

DP, EL, and JS conceived the study and developed the study design. Data was collected and provided by DP, EL, JS, AB, DA, MBMN, SB, GB, SC, CC, DD, AF, AG, RoH, RaH, MH, SH, NI, BKTV, NL, MPAL, 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 involved in commenting on subsequent revisions.

Table 1: Non-COVID-19 ICU admissions in 2019 and 2020

	Global 2019	Global 2020	Effect size	95% CI	P value
ICU Admissions					
Total (n)	859854	782788			
Elective Surgical	27.1%	25.8%	OR = 0.92	0.91 – 0.92	p < 0.001
Emergency Surgical	9.4%	9.8%	OR = 1.03	1.02 – 1.04	p < 0.001
Medical	48.6%	48.8%	OR = 1.01	1.00 – 1.01	p = 0.053
No information	14.9%	15.4%	OR = 1.34	1.32 – 1.35	p < 0.001
Age					
Years (SD)	61.4 (19.4)	61.2 (19.1)	MD = -0.17	-0.11 – -0.23	p < 0.001
Sex					
Male	53.2%	54.6%	OR = 1.06	1.05 – 1.07	p < 0.001
Mechanical Ventilation (MV)	29.4%	30.7%	OR = 1.08	1.07 – 1.08	p < 0.001
Illness Severity					
APACHE II Score - mean (SD) *	16.1 (8.6)	16.1 (8.1)	MD = -0.01	-0.05 – 0.04	p = 0.79
SOFA Score - mean (SD) †	3.1 (3.3)	3.1 (3.4)	MD = 0.08	0.07 – 0.09	p < 0.001
SAPS 3 Score - mean (SD) ‡	43.9 (16.8)	44.0 (16.7)	MD = 0.05	-0.02 – 0.12	p = 0.15
Predicted Risk of Death - % (SD)	14.5 (19.9)	14.6 (20.0)	MD = 0.02	-0.04 – 0.08	p = 0.59
Length of Stay (mean)					
ICU - mean days (SD)	4.7 (11.4)	4.7 (9.1)	MD = -0.03	-0.06 – -0.01	p = 0.004
Hospital - mean days (SD)	14.9 (58.2)	14.0 (48.2)	MD = -0.69	-0.78 – -0.59	p < 0.001
ICU Mortality					

ICU - all % (n) [95% Confidence Interval]	9·27% (839066) [9·21 - 9·34%]	10·42% (758925) [10·35 – 10·48%]	OR = 1.15	1.14 – 1.17	p < 0.001
ICU - if received MV % (n) [95% Confidence Interval]	22·80% (249808) [22·63 – 22·96%]	23·91% (235584) [23·73 – 24·08%]	OR = 1.04	1.03 – 1.05	p < 0.001
Hospital Mortality					
Hospital – all % (n) [95% Confidence Interval]	13·01% (749283) [12·94 – 13·09%]	14·52% (677468) [14·44 – 14·61%]	OR = 1.15	1.14 – 1.16	p < 0.001
Hospital - if received MV % (n) [95% Confidence Interval]	32·16% (182985) [31·94 – 32·37%]	33·62% (176604) [33·40 – 33·84%]	OR = 1.05	1.03 – 1.06	p < 0.001

* Includes data from Aus, NZ, Argentina, Finland, CCA

† Includes data from Aus, NZ, Brazil, Finland, Japan, Netherlands

‡ Includes data from Brazil, Uruguay, Denmark

OR: Odds ratio; MD: Mean Difference.

Figure 1a: Non-COVID-19 ICU Admissions per million members of the population

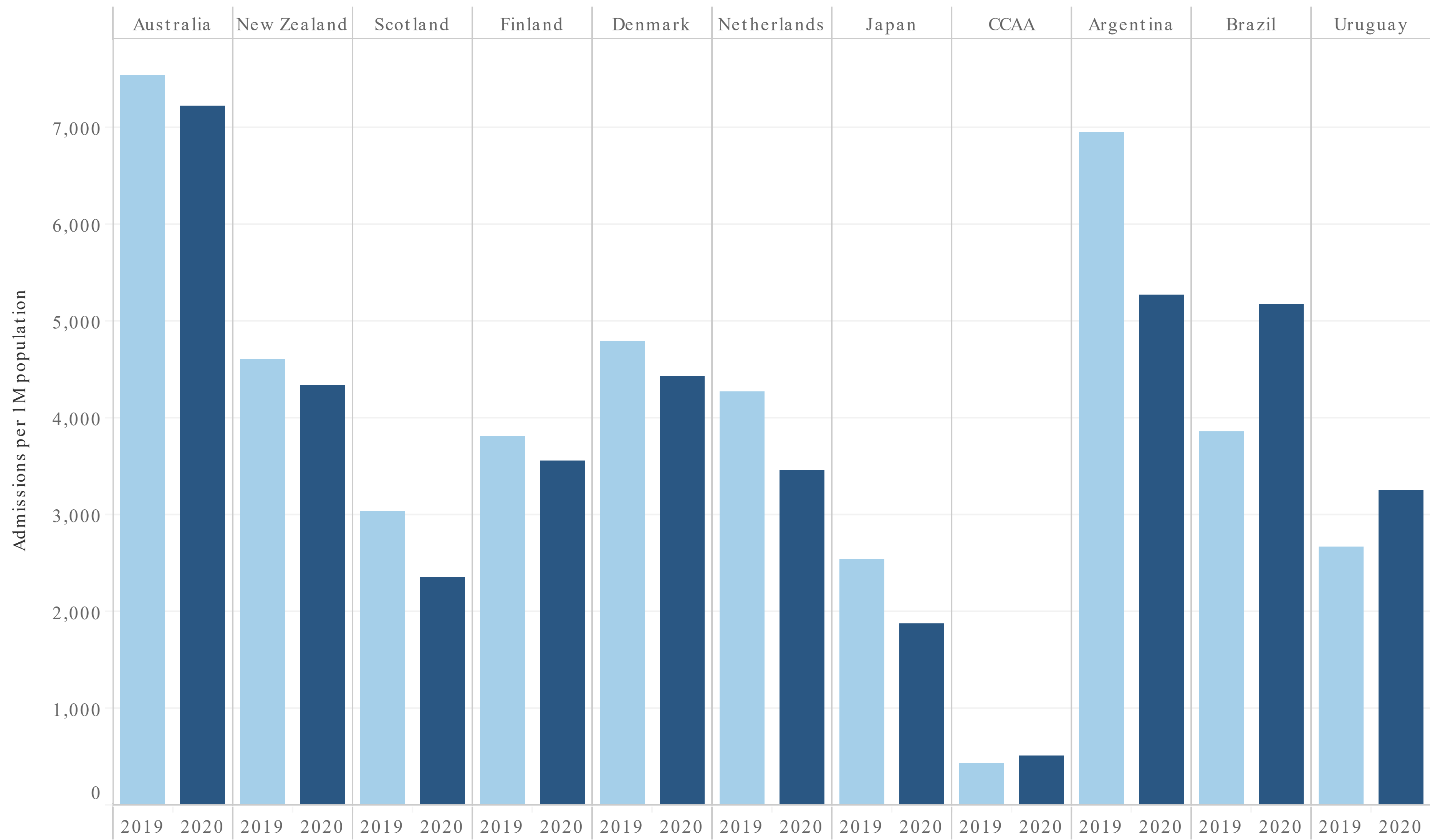


Figure 1c: Non-COVID-19 ICU Admissions per million members of the population, indexed to available beds

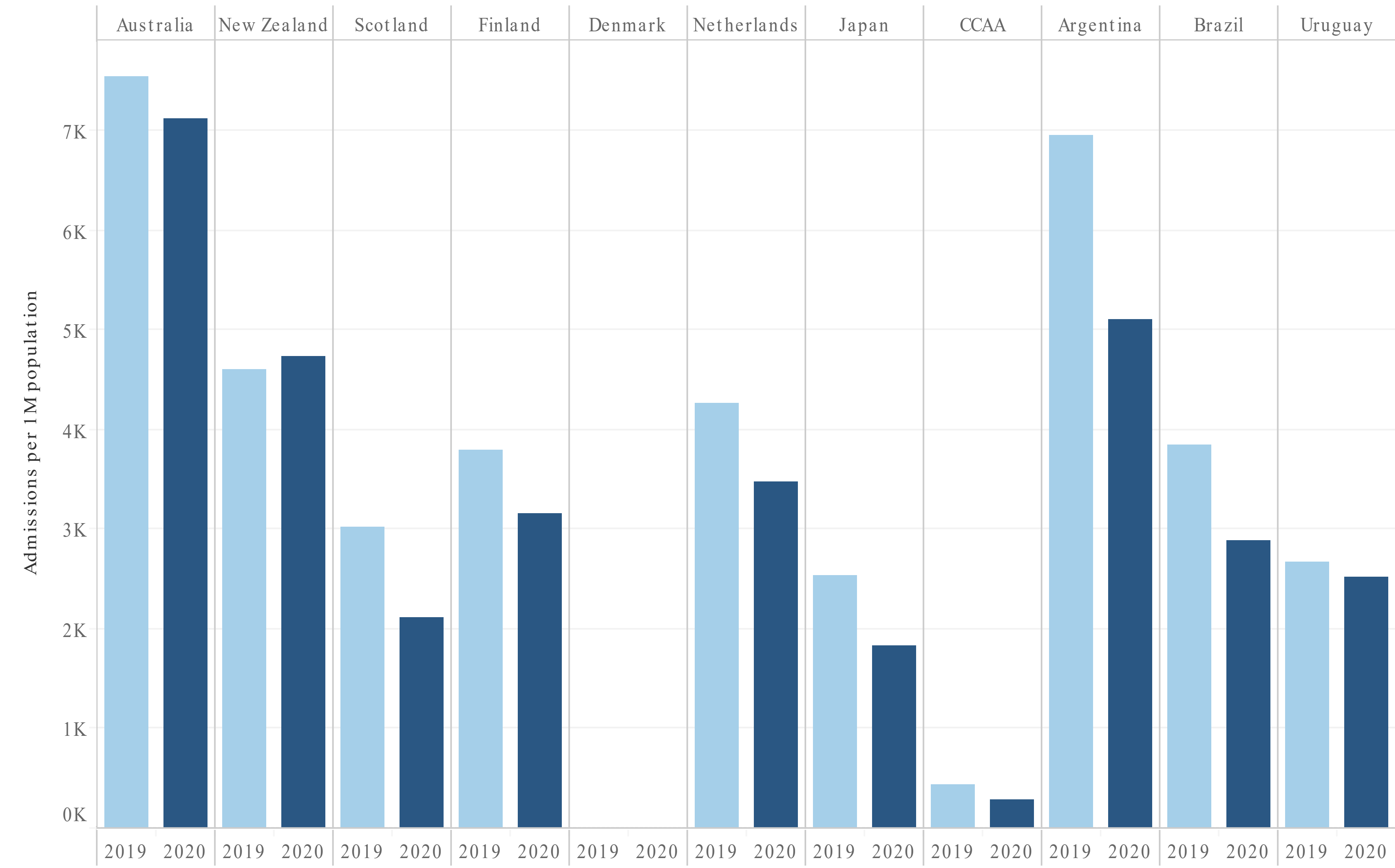


Figure 1b: COVID-19 ICU Admissions per 1M members of the population

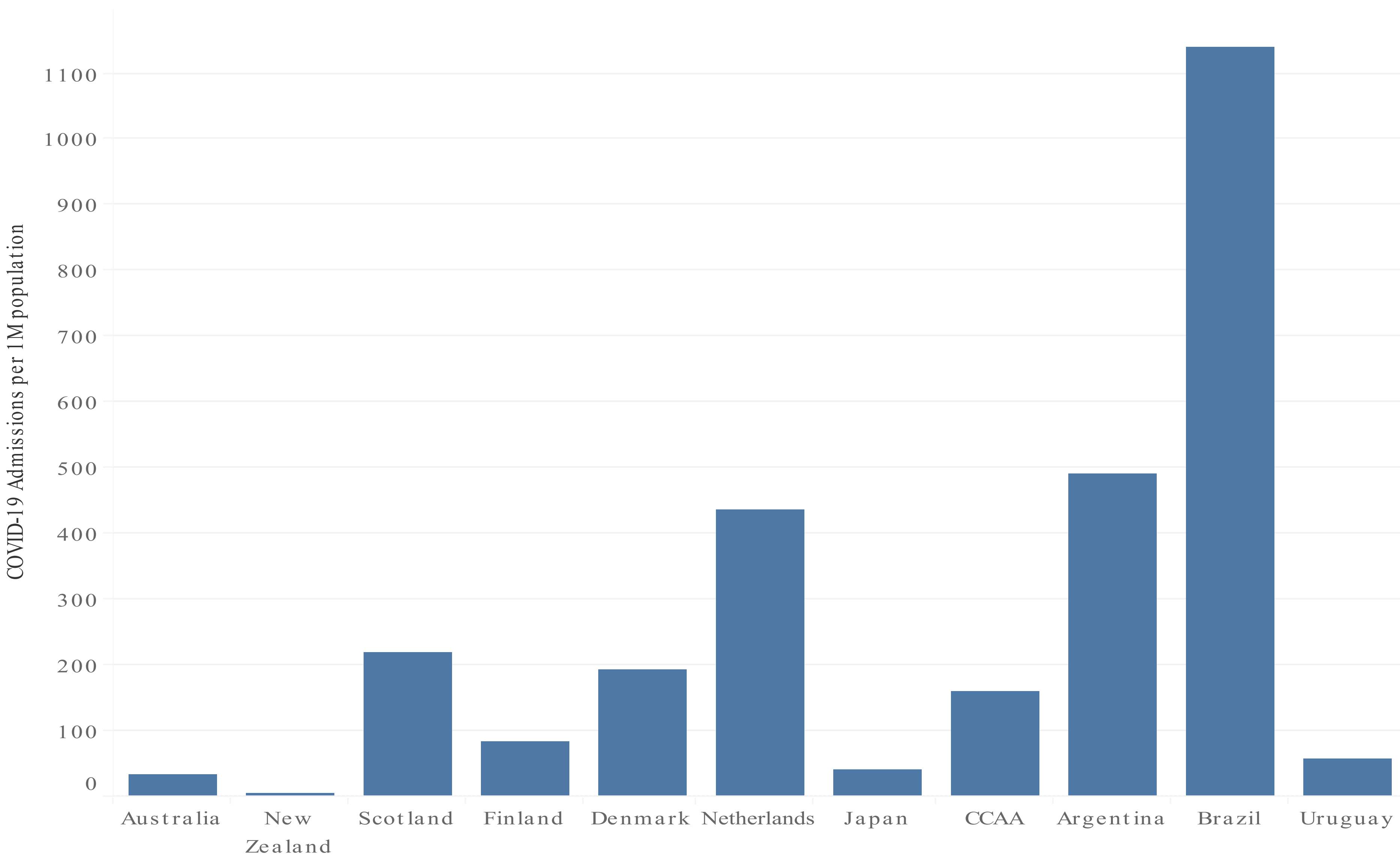


Figure 1d: Proportion of Non-COVID-19 patients receiving mechanical ventilation

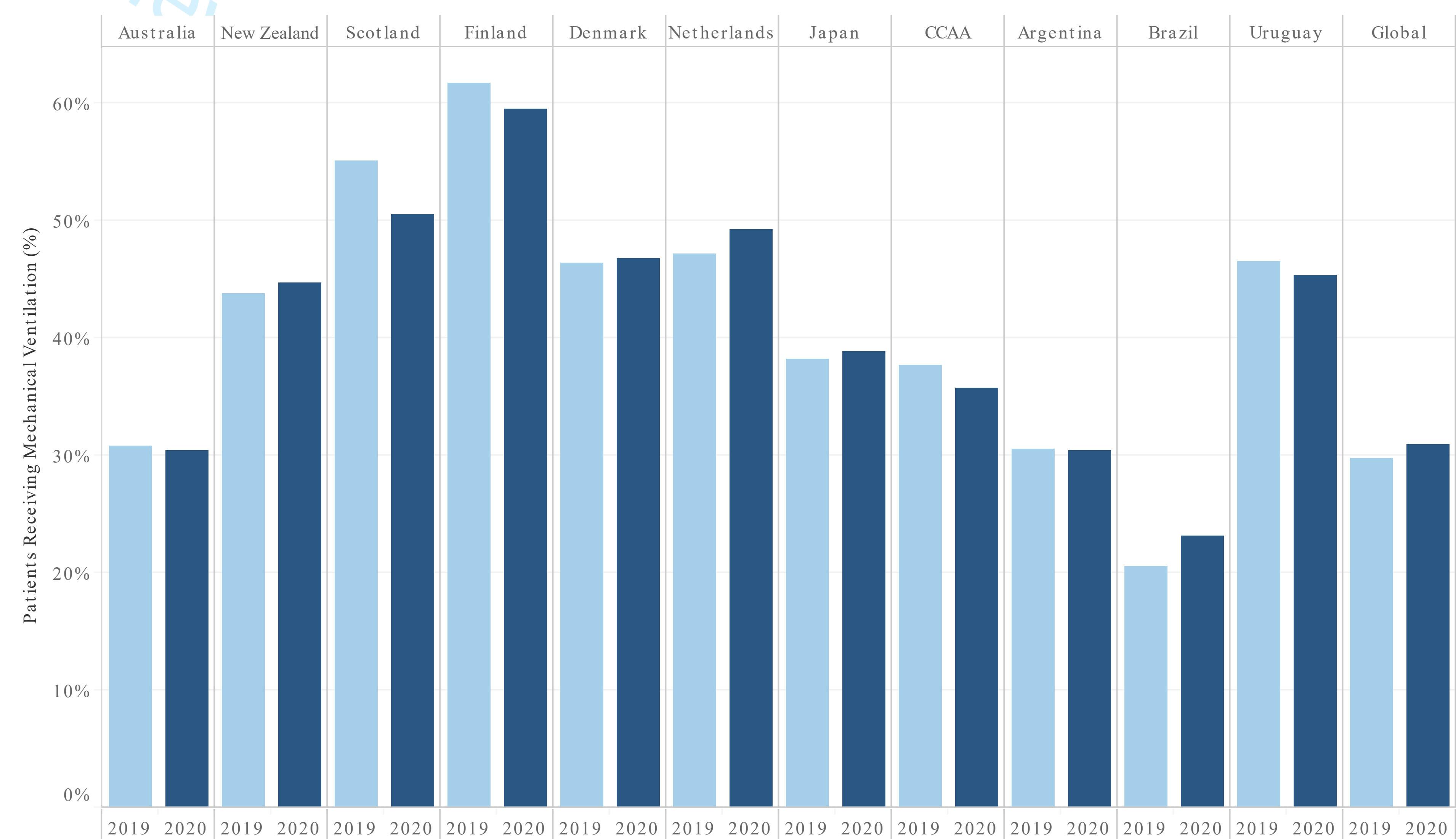


Figure 2a: Non-COVID-19 In-ICU Mortality

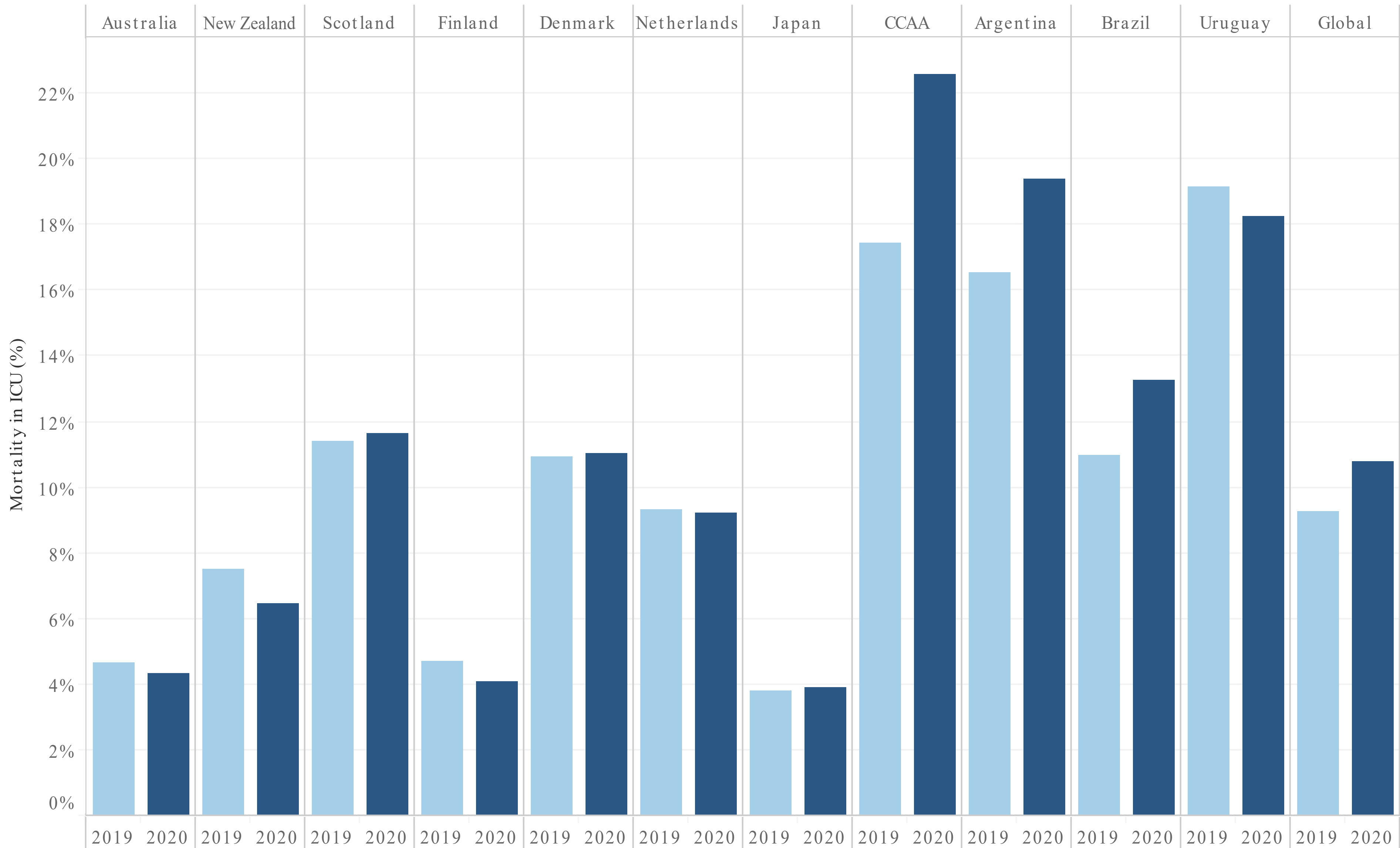


Figure 2c: Non-COVID-19 In-Hospital Mortality for patients that received mechanical ventilation

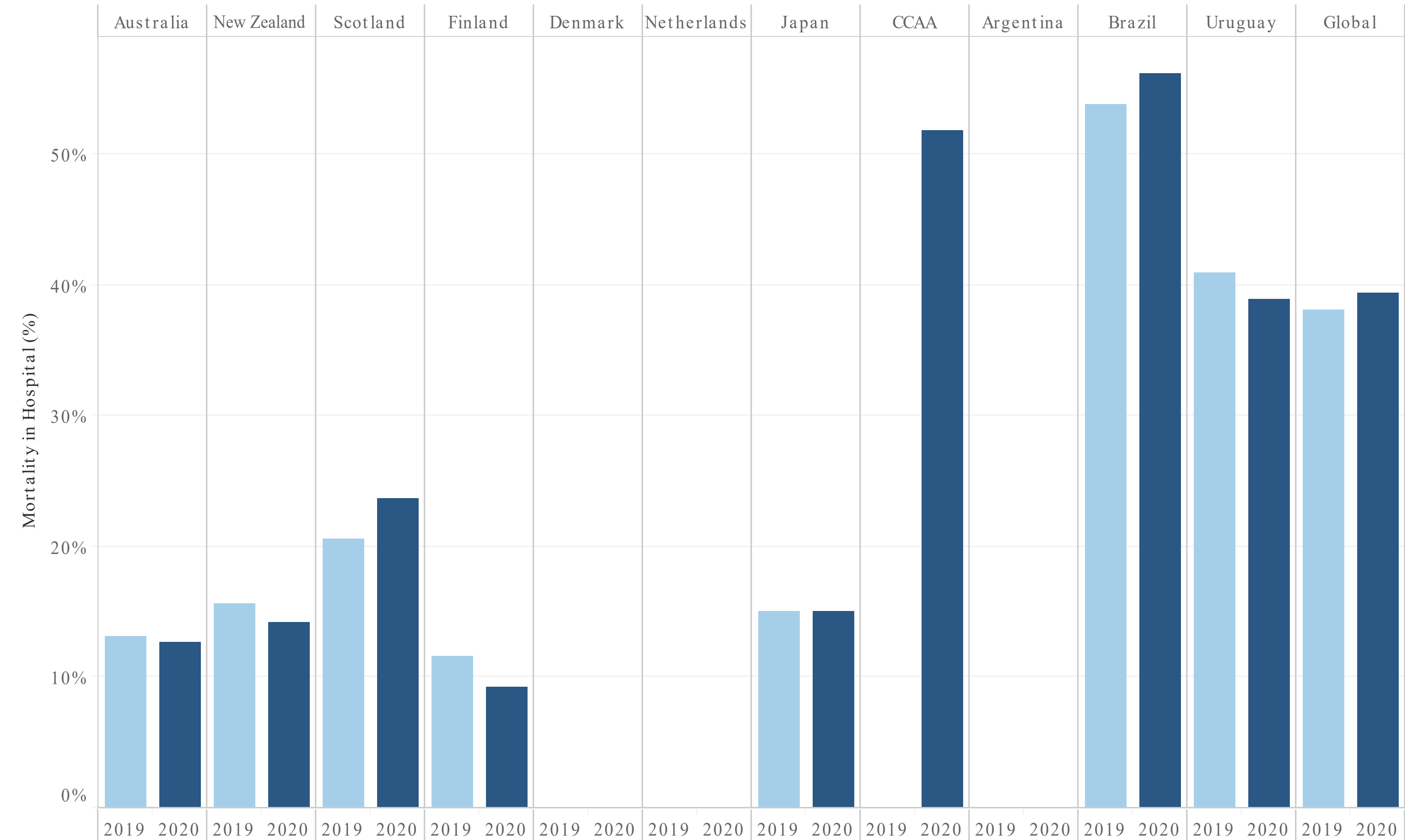


Figure 2b: Non-COVID-19 In-ICU Mortality for patients that received mechanical ventilation

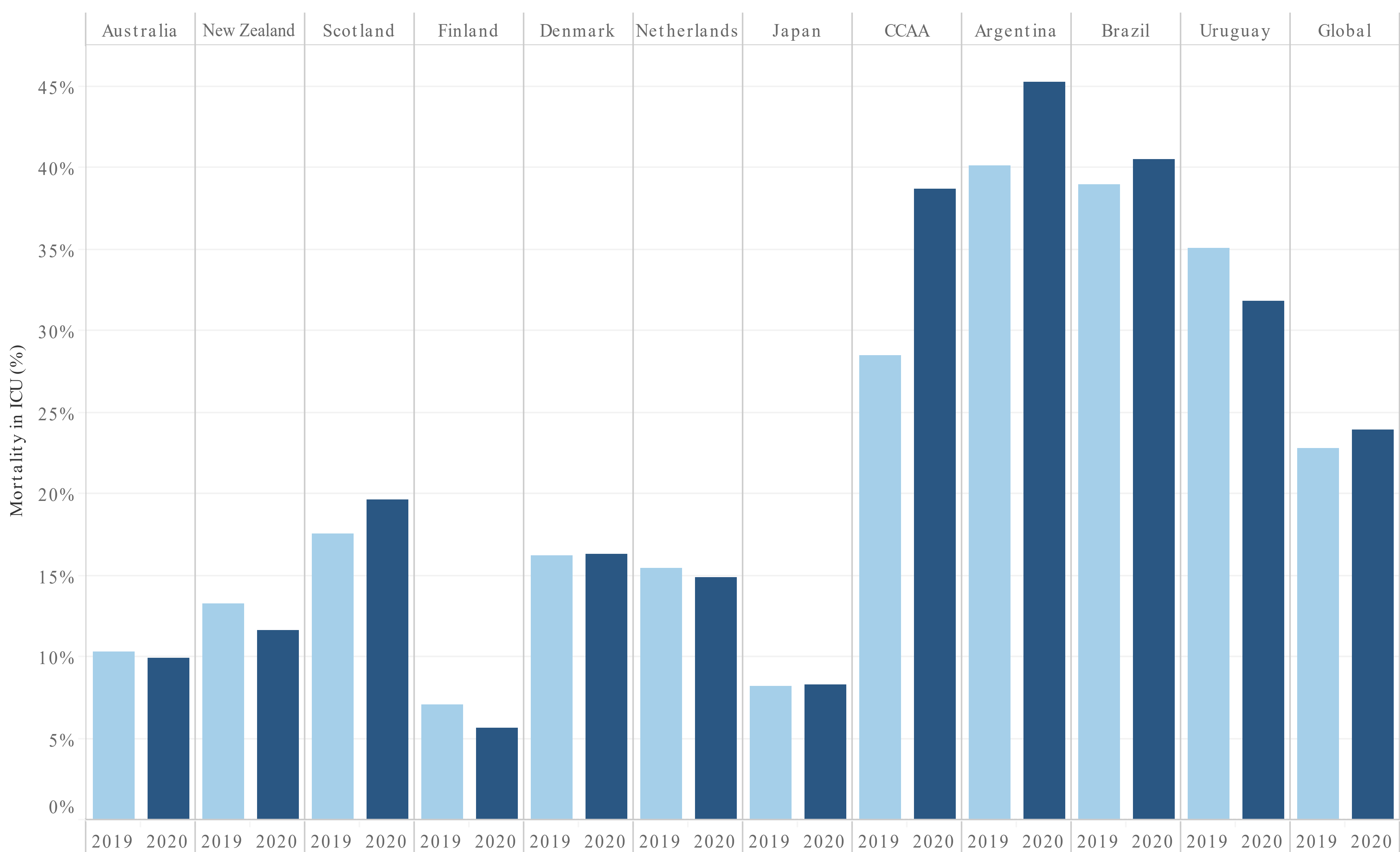


Figure 2d: Non-COVID-19 Standardised Mortality Ratio

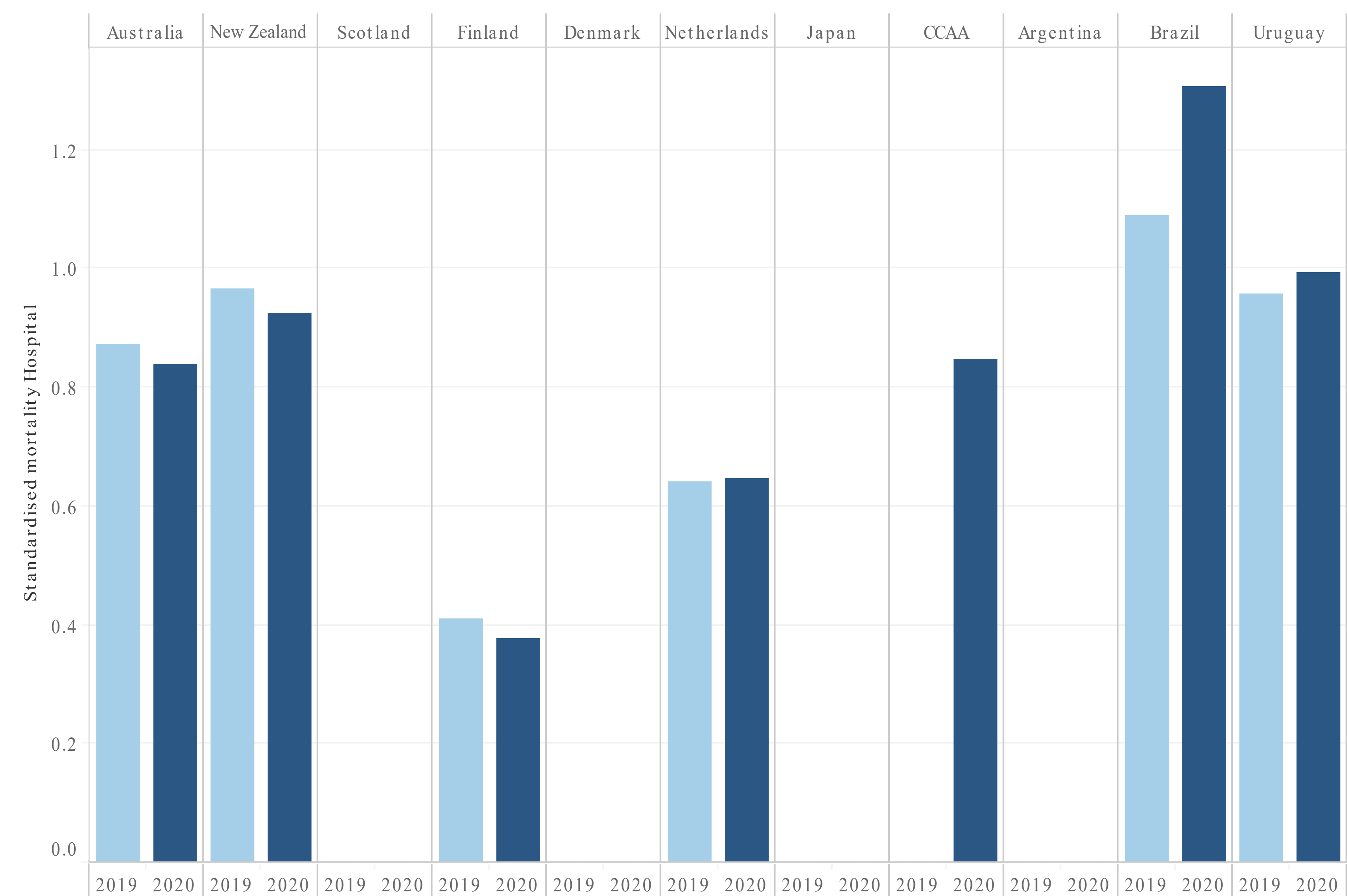


Figure 3a: Non-COVID-19 ICU Mortality, by Country Income Level

Study or Subgroup	2019 Events	2019 Total	2020 Events	2020 Total	Weight	Odds Ratio IV, Fixed, 95% CI
High Income Countries						
Australia	7937	171062	7156	165946	10.4%	0.93 [0.90, 0.96]
Denmark	3046	27837	2845	25840	3.8%	1.01 [0.95, 1.06]
Finland	942	19958	760	18627	1.2%	0.86 [0.78, 0.95]
Japan	1821	47921	1701	43615	2.5%	1.03 [0.96, 1.10]
Netherlands	6876	73959	5542	60359	8.1%	0.99 [0.95, 1.02]
New Zealand	1099	14642	910	14082	1.3%	0.85 [0.78, 0.93]
Scotland	1880	16491	1486	12777	2.1%	1.02 [0.95, 1.10]
Uruguay	705	3683	744	4080	0.9%	0.94 [0.84, 1.06]
Subtotal (95% CI)		**375553**		**345326**	**30.2%**	**0.96 [0.94, 0.98]**
Total events	24306		21144			
Test for overall effect: Z = 4.10 (P < 0.0001)						
LMICs + HMICs						
Argentina	4065	24580	2714	14003	3.9%	1.21 [1.15, 1.28]
Brazil	45847	418315	49734	375453	60.8%	1.24 [1.22, 1.26]
CCA	3600	20618	5454	24143	5.1%	1.38 [1.32, 1.45]
Subtotal (95% CI)		**463513**		**413599**	**69.8%**	**1.25 [1.23, 1.26]**
Total events	53512		57902			
Test for overall effect: Z = 34.42 (P < 0.00001)						
Total (95% CI)		**839066**		**758925**	**100.0%**	**1.15 [1.14, 1.17]**
Total events	77818		79046			
Test for overall effect: Z = 26.49 (P < 0.00001)						
Test for subgroup differences: Chi² = 499.85, df = 1 (P < 0.00001)						

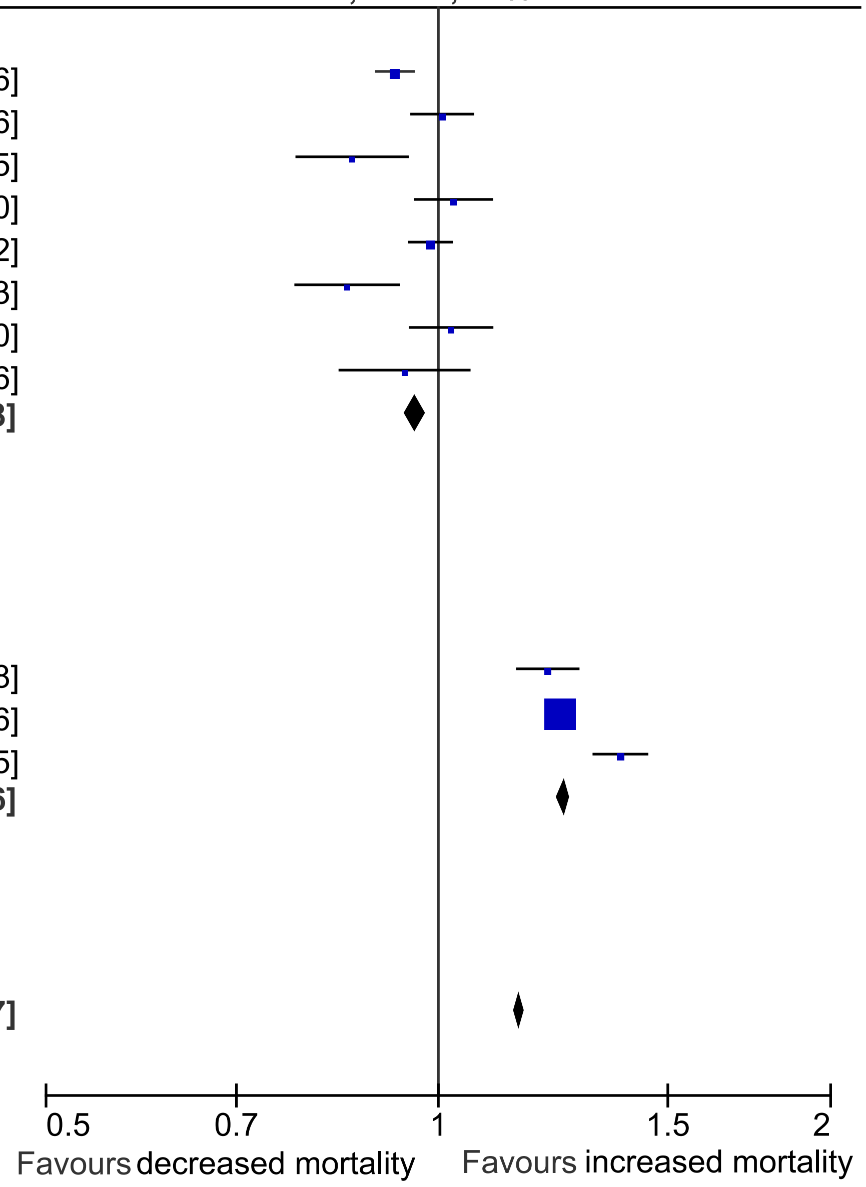
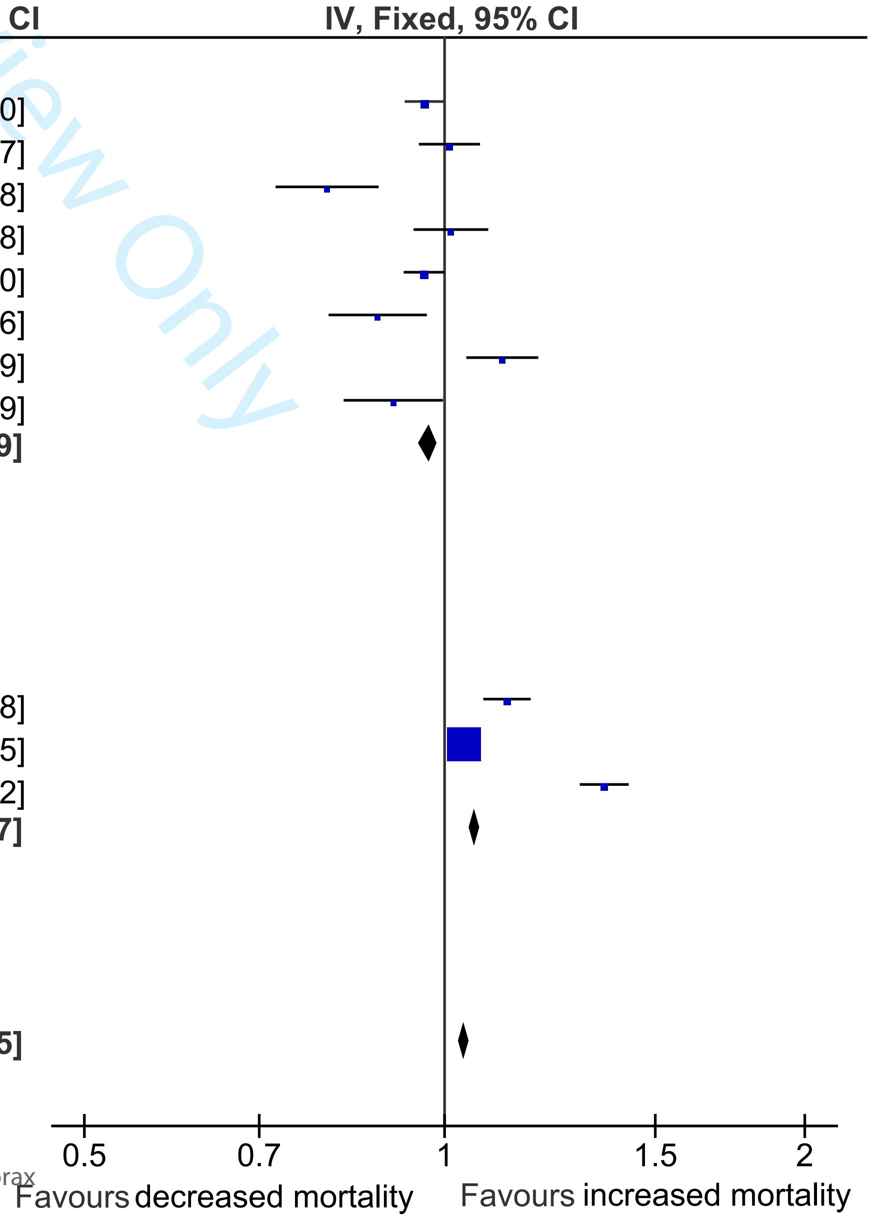


Figure 3b: Non-COVID-19 ICU Mortality if received mechanical ventilation, by Country Income Level

Study or Subgroup	2019 Events	2019 Total	2020 Events	2020 Total	Weight	Risk Ratio IV, Fixed, 95% CI
6.2.1 HICs						
Australia	5471	53083	5029	50677	6.9%	0.96 [0.93, 1.00]
Denmark	2089	12914	1972	12077	2.9%	1.01 [0.95, 1.07]
Finland	870	12321	694	12321	1.0%	0.80 [0.72, 0.88]
Japan	1526	18610	1409	16976	1.9%	1.01 [0.94, 1.08]
Netherlands	5396	34930	4415	29730	6.8%	0.96 [0.93, 1.00]
New Zealand	859	6474	740	6343	1.1%	0.88 [0.80, 0.96]
Scotland	1587	9069	1265	6469	2.0%	1.12 [1.05, 1.19]
Uruguay	600	1709	584	1836	1.1%	0.91 [0.83, 0.99]
Subtotal (95% CI)		**149110**		**136429**	**23.5%**	**0.97 [0.95, 0.99]**
Total events	18398		16108			
Test for overall effect: Z = 3.02 (P = 0.003)						
6.2.4 LMICs + HMICs						
Argentina	3010	7491	1928	4255	4.9%	1.13 [1.08, 1.18]
Brazil	33362	85544	35021	86472	67.0%	1.04 [1.03, 1.05]
CCA	2182	7663	3263	8428	4.6%	1.36 [1.30, 1.42]
Subtotal (95% CI)		**100698**		**99155**	**76.5%**	**1.06 [1.05, 1.07]**
Total events	38554		40212			
Test for overall effect: Z = 10.64 (P < 0.00001)						
Total (95% CI)		**249808**		**235584**	**100.0%**	**1.04 [1.03, 1.05]**
Total events	56952		56320			
Test for overall effect: Z = 7.84 (P < 0.00001)						
Test for subgroup differences: Chi² = 60.92, df = 1 (P < 0.00001)						



Supplementary Table 1: Characteristics of patients admitted to ICU in 2019 with Non-COVID-19 diagnoses

	Australasia		Europe				Asia		South America		
	Australia	**New Zealand**	**Scotland**	**Finland**	**Denmark**	**Netherlands**	**Japan**	**CCA**	**Argentina**	**Brazil**	**Uruguay**
ICUs in registry	168	18	24	26	40	81	57	58	78	1469	21
ICU beds in registry	2286	268	252	268	··	1150	666	746	808	16757	175
Admissions											
Total (n)	179735	15342	16494	19945	27837	73959	48495	20684	24580	428906	3877
Per Million Population (n)	7538	4599	3024	3802	4788	4264	2534	435	6949	3855	2667
Per available ICU bed	78·62	57·25	65.45	74·42	··	64·31	72·82	27·73	30·42	25·60	22·15
Age											
Years (SD)	62·5 (17·9)	57·4 (19·6)	··	57·1 (21·2)	60.6 (21.3)	62·8 (15·9)	63·5 (21·3)	50·7 (21·6)	··	61·5 (19·7)	59 (19·2)
Sex											
Male	56%	60%	··	64%	60%	61%	61%	56%	··	50%	59%
Mechanical Ventilation (MV)	31%	44%	55%	62%	46%	47%	38%	38%	31%	21%	47%
Illness Severity											
APACHE II Score - mean (SD)	15·0 (7·3)	16·0 (7·8)	··	18·3 (8·3)	··	··	··	20·9 (7·9)	18.1 (14.8)	··	··
SOFA Score - mean (SD)	3·7 (2·8)	4·2 (2·9)	··	6·1 (3·4)	··	5·9 (3·9)	4·9 (3·6)	··	··	1·9 (2·8)	··
SAPS 3 Score - mean (SD)	··	··	··	··	58.5 (19.7)	··	··	··	··	42·9 (16·1)	50·3 (18·7)
Predicted Risk of Death - % (SD)	8·3 (15·8)	10·7 (18·4)	··	20·4 (23·3)	··	20·0 (20·0)	··	32·1 (23·8)	17·2 (22·1)	14·9 (19·9)	24·5 (25·9)
Length of Stay (mean)											
ICU - mean days (SD)	3.0 (5·1)	2·9 (6·1)	4.1 (6.6)	3·2 (5·3)	3.2 (24.8)	3·1 (6·9)	4·5 (6·8)	3·9 (6·6)	6·9 (16·6)	5·8 (13·0)	7.0 (20·7)
ICU – median days (IQR)	1.7 (2.2)	1.4 (2.0)	2 (2.1)	1.6 (2.4)	1.2 (2.7)	1.1 (2.0)	2.0 (3.0)	2.0 (3.0)	3.0 (4.3)	3.0 (5.0)	3.0 (6.0)
Hospital - mean days (SD)	15·2 (80·2)	14·5 (88·6)	16.2 (23.7)	12·6 (15·9)	··	13·5 (110·8)	35·4 (51·5)	··	··	12·8 (27·0)	16·3 (31·6)
Hospital – median days (IQR)	7.9 (10.8)	8.1 (11.5)	9.0 (14.0)	8.0 (10.0)	··	8.0 (9.0)	21 (26)	··	··	7.0 (9.0)	8.0 (15)
In-ICU Mortality											
Non-COVID-19 – All % (n)	4·6% (7937)	7·5% (1099)	11.4% (1880)	4·7% (942)	10.9% (3046)	9·3% (6876)	3·8% (1821)	17·5% (3600)	16·5% (4065)	11% (45847)	19·1% (705)
Non-COVID-19 – If received MV % (n)	10·3% (5471)	13·3% (859)	17.5% (1587)	7·1% (870)	16.2% (2089)	15·4% (5396)	8·2% (1526)	28·5% (2182)	40·2% (3010)	39·0% (33362)	35·1% (600)
In-Hospital Mortality											
Non-COVID-19 – all % (n)	7·2% (12360)	10·3% (1507)	14.4% (2381)	8·3% (1664)	··	12·8% (9484)	8·6% (4158)	··	··	16·2% (65096)	23·5% (841)
Non-COVID-19 – if received MV % (n)	13·1% (6938)	15·7% (1014)	20.6% (1871)	11·6% (1424)	··	··	15·0% (2857)	··	··	53·8% (44050)	40·9% (685)

·· indicates data not available
*The CCA registry includes ICUs from Bangladesh, India, Malaysia, Nepal, and Pakistan
OR: Odds ratio; MD: Mean Difference; IQR: Inter-quartile Range

Supplementary Table 2: Characteristics of patients admitted to ICU in 2020 with Non-COVID-19 diagnoses

	Australasia		Europe				Asia		South America		
	Australia	**New Zealand**	**Scotland**	**Finland**	**Denmark**	**Netherlands**	**Japan**	**CCA**	**Argentina**	**Brazil**	**Uruguay**
ICUs in registry	173	18	23	26	41	81	70	102	58	1469	21
ICU beds in registry	2346	250	280	302	··	1150	830	1336	627	20304	213
Admissions											
Total (n)	174302	14759	12797	18638	25839	60359	43773	24494	14003	389353	4471
Per Million Population (n)	7219	4333	2346	3547	4431.01	3461	1868	508	5273	5179	3248
Per available ICU bed	74·30	59·04	45.70	61·72	··	52·49	52·74	18·33	22·33	19·18	20·99
Age											
Years (SD)	62·1 (17·9)	58·3 (18·7)	··	56·7 (21·1)	61 (20.7)	62·6 (15·9)	64·5 (20·4)	50·1 (20·4)	··	61·3 (19·4)	58·8 (19·7)
Sex											
Male	56%	61%	··	64%	60%	62%	61%	58%	··	52%	60%
Mechanical Ventilation (MV)	30%	45%	51%	60%	47%	49%	39%	36%	30%	23%	45%
Illness Severity											
APACHE II Score - mean (SD)	15·0 (7·2)	15·7 (7·5)	··	18·0 (8·3)	··	··	··	22·6 (8·4)	16.6 (11.7)	··	··
SOFA Score - mean (SD)	3·7 (2·8)	4·2 (2·9)	··	6·0 (3·4)	··	6·1 (3·9)	5·0 (3·7)	··	··	2·0 (3·0)	··
SAPS 3 Score - mean (SD)	··	··	··	··	57.5 (21.5)	··	··	··	··	43·0 (15·9)	49·6 (18·5)
Predicted Risk of Death - % (SD)	8·1 (15·7)	9·6 (17·2)	··	19·5 (22·8)	··	20·0 (20·0)	··	35·5 (24·8)	18·6 (21·2)	15·0 (19·9)	23·6 (25·1)
Length of Stay (mean)											
ICU - mean days (SD)	2·9 (4·7)	2·9 (5·8)	3.9 (6.3)	3·0 (4·8)	3.4 (6.7)	3·0 (7·0)	4·4 (6·0)	4·0 (7·5)	7·7 (13·0)	6·0 (11·1)	6·6 (13·7)
ICU – median days (IQR)	1.7 (2.2)	1.6 (2.0)	2 (3.2)	1.5 (2.2)	1.2 (2.5)	1.0 (1.8)	2.0 (3.0)	2.0 (3.0)	3.0 (5.0)	3.0 (5.0)	3.0 (6.0)
Hospital - mean days (SD)	13·9 (85)	14·7 (106·9)	15.7 (20.9)	11·9 (16·5)	··	12·8 (16·6)	32·7 (42·5)	12·9 (12·4)	··	12·2 (21·0)	13·6 (19·5)
Hospital – median days (IQR)	7.8 (10.5)	8.1 (11.3)	9.0 (14)	8.0 (10)	··	7.9 (9.0)	21 (24)	8.0 (16)	··	7.0 (9.0)	7.0 (13)
In-ICU Mortality											
Non-COVID-19 – all % (n)	4·3% (7156)	6·5% (910)	11.6% (1486)	4·1% (760)	11% (2845)	9·2% (5542)	3·9% (1701)	22·6% (5454)	19·4% (2714)	13·2% (49734)	18·2% (744)
Non-COVID-19 – if received MV % (n)	9·9% (5029)	11·7% (740)	19.6% (1265)	5·6% (694)	16.3% (1972)	14·9% (4415)	8·3% (1409)	38·7% (3263)	45·3% (1928)	40·5% (35021)	31·8% (584)
In-Hospital Mortality											
Non-COVID-19 – all % (n)	6·8% (11208)	8·9% (1248)	15.6% (2000)	7·3% (1366)	··	12·9% (7791)	8·5% (3699)	30·1% (7271)	··	19·6% (70197)	23·4% (880)
Non-COVID-19 – if received MV % (n)	12·6% (6378)	14·2% (900)	23.7% (1530)	9·2% (1132)	··	··	15% (2567)	51·8% (4366)	··	56·2% (46201)	38·9% (662)

·· indicates data not available

*The CCA registry includes ICUs from Bangladesh, India, Malaysia, Nepal, and Pakistan

OR: Odds ratio; MD: Mean Difference; IQR: Inter-quartile Range

Supplementary Appendix

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Information on participating registries

Data from Argentina was provided by the Argentine Society of Intensive Care/Sociedad Argentina de Terapia Intensiva (SATI) from the national registry, SATI-Q. Further information can be found at https://www.satiq.net.ar/

Data from Australia and New Zealand was provided by the Australian and New Zealand Intensive Care Society (ANZICS) Centre for Outcome and Resource Evaluation, which runs the bi-national CQR. Further information can be found at https://www.anzics.com.au/anzics-registries/

Data from Brazil was provided by the Brazilian Society of Intensive Care (AMIB) and Epimed Solutions which run the national registry UTIs Brasileiras. Further information can be found at http://www.utisbrasileiras.com.br/

Data from Denmark was provided by the national Danish Intensive Care Database (DID). Further information can be found at https://pubmed.ncbi.nlm.nih.gov/27822095/

Data from Finland was provided by the Finnish Intensive Care Consortium (FICC), which run the national database – BM-ICU (maintained by TietoEvry).

Data from Japan was provided by the Japanese Society of Intensive Care Medicine (JSICM) from the national database JIPAD (Japanese Intensive care PAtient Database). Further information can be found at https://www.jipad.org/en

Data from the Netherlands was National Intensive Care Evaluation (NICE) foundation, which runs the national NICE registry. Further information can be found at http://www.stichting-nice.nl/

Data from Scotland was provided by the Scottish Intensive Care Society (SICS) Audit Group which runs the national CQR – SICSAG. Further information can be found at https://www.sicsag.scot.nhs.uk/

Data from Uruguay was provided by the Uruguayan Society of Intensive Care Medicine/ Sociedad Uruguaya de Medicina Intensiva (SUMI) and Epimed Solutions which run the national registry UCIs Uruguayas. Further information can be found at http://www.ucisuruguayas.com.uy

Data from Bangladesh, India, Malaysia, Nepal and Pakistan was provided by the Collaboration for Research, Implementation and Training in Intensive Care in Asia network through the CRIT CARE ASIA (CCA) registry. https://www.tropmedres.ac/units/moru-bangkok/malaria/critical-illness

Information on Expected In-Hospital Mortality

Each CQR uses its own local calibration of their chosen illness severity model to calculate the predicted in hospital mortality. Each CQR uses the predicted mortality for benchmarking ICUs with their relevant region, and the illness severity models are periodically re-calibrated to ensure ongoing validity. An example of the methodology can be found here:

Moralez, G. M., Rabello, L. S. C. F., Lisboa, T. C., Lima, M. D. F. A., Hatum, R. M., De Marco, F. V. C., Alves, A., Pinto, J. E. D. S. S., de Araújo, H. B. N., Ramos, G. V., Silva, A. R., Fernandes, G. C., Faria, G. B. A., Mendes, C. L., Ramos Filho, R. Á., de Souza, V. P., do Brasil, P. E. A. A., Bozza, F. A., Salluh, J. I. F., Soares, M., … ORCHESTRA Study Investigators (2017). External validation of SAPS 3 and MPM0-III scores in 48,816 patients from 72 Brazilian ICUs. Annals of intensive care, 7(1), 53. https://doi.org/10.1186/s13613-017-0276-3

Some CQRs have developed their own models of predicted in-hospital mortality (e.g. ANZROD in Australia and New Zealand, JROD in Japan). These models were created and are maintained for the purpose of comparing outcomes between ICUs within each CQR. An example of the methodology used in creating these models can be found here:

Endo, H., Uchino, S., Hashimoto, S. et al. Development and validation of the predictive risk of death model for adult patients admitted to intensive care units in Japan: an approach to improve the accuracy of healthcare quality measures. j intensive care 9, 18 (2021). https://doi.org/10.1186/s40560-021-00533-z

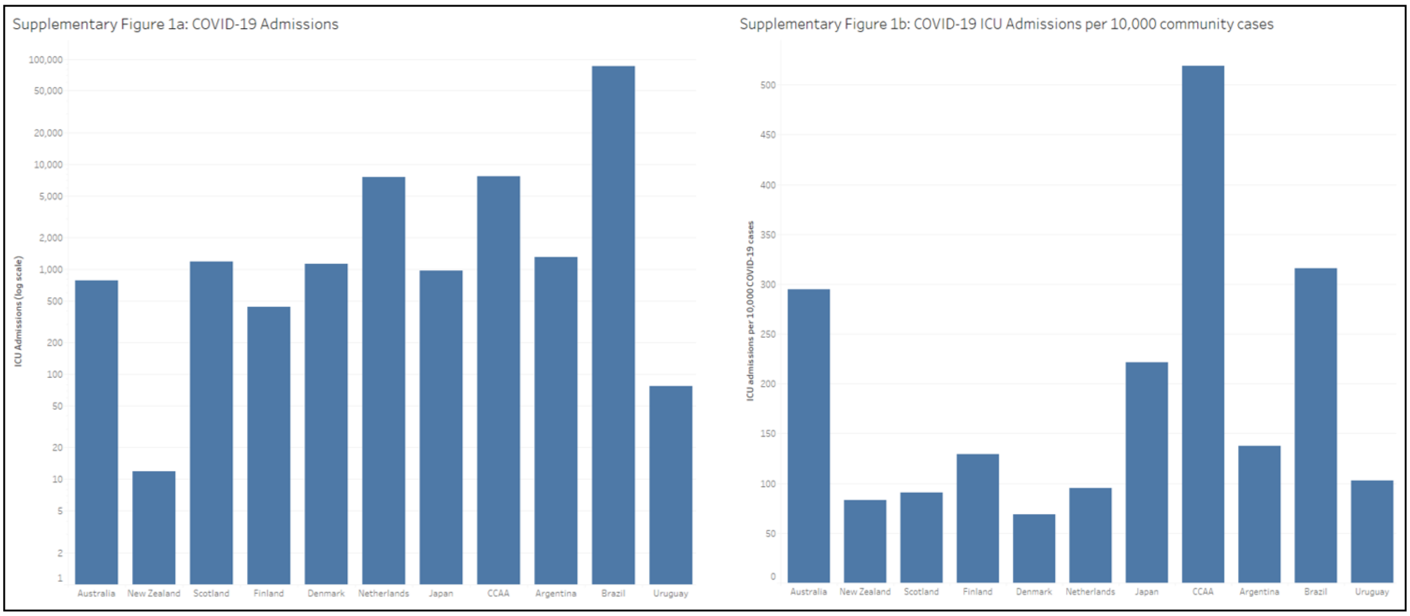
The expected (or predicted) in hospital mortality calculated used either of the above models then provides an estimate of the risk of death during hospital admission. By comparing the expected in-hospital mortality rate with the observed mortality rate, it can be calculated whether there were more or fewer deaths than expected – i.e. the standardised mortality ratio (SMR). SMR = number of observed deaths / number of expected deaths. When the SMR <1 fewer deaths than expected occurred, and when the SMR >1 more deaths than expected occurred. As the expected mortality rate is calculated from models that incorporate illness severity, when more deaths than expected occur, it is likely that factors other than illness severity have influence the observed mortality rate.

Table 1: Characteristics of participating ICU registries

Country / Region	Data source (registry name)	Population	ICUs in registry (n) 2019	ICUs in registry (n) 2020	ICU beds in registry (n) 2019	ICU beds in registry (n) 2020	2020 Coverage (% total ICUs)	Public ICUs (%)	Individual records (n)	Illness severity model (s): APACHE II	APACHE III	SOFA	SAPS 2	SAPS 3	Local Model	Model for Expected In-Hospital Mortality
Asia*	CCA*	1827·1M	58	102	746	1336	1·34%†	61%	52830	x						APACHE II
Argentina	SATI-Q	45·4M	78	58	808	627	5·85%‡	45%	40104	x						APACHE II
Australia	ANZICS	25·7M	168	173	2286	2346	94·0%	81%	361400	x	x	x			x	ANZROD - local model
Brazil	UTIs Brasileiras	212·6M	1469	1469	16757	20304	35·4%	62%	888223			x		x		SAPS 3
Denmark	DID	5·8M	40	41	··	··	100%	100%	54804					x		SAPS 3
Finland	FICC	5·5M	26	26	268	302	95·0%	100%	35363	x		x	x		x	SAPS 2
Japan	JIPAD	125·8M	57	70	666	830	18·6%	70%	93239	x	x	x		x	x	JROD – local model
Netherlands	NICE Registry	17·4M	81	81	1150	1150	100%	100%	141883		x	x				APACHE III
New Zealand	ANZICS	5·1M	18	18	268	250	67·0%	94%	29055	x	x	x			x	ANZROD - local model
Scotland	SICSAG	5·5M	24	23	252	280	100%	100%	29497	x						APACHE II
Uruguay	UCIs Uruguayas	3·5M	21	21	175	213	39·6%	19%	8156					x		SAPS 3

·· indicates data not available
*The CCA registry includes ICUs from Bangladesh, India, Malaysia, Nepal, and Pakistan
† CCA coverage is based on % of national bed coverage as opposed to % of ICUs coverage. Coverage calculated from previously published data from Bangladesh[1], India[2], Malaysia[3], Nepal[4], and Pakistan[5]
‡ Calculated from data published by the Ministry of Health, Argentina[6]

Supplementary Figure 1: COVID-19 ICU admissions in 2020



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