Characterisation of the first 250 000 hospital admissions for COVID-19 in Brazil: a retrospective analysis of nationwide data

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Summary

Background Most low-income and middle-income countries (LMICs) have little or no data integrated into a national surveillance system to identify characteristics or outcomes of COVID-19 hospital admissions and the impact of the COVID-19 pandemic on their national health systems. We aimed to analyse characteristics of patients admitted to hospital with COVID-19 in Brazil, and to examine the impact of COVID-19 on health-care resources and in-hospital mortality.

Methods We did a retrospective analysis of all patients aged 20 years or older with quantitative RT-PCR (RT-qPCR)-confirmed COVID-19 who were admitted to hospital and registered in SIVEP-Gripe, a nationwide surveillance database in Brazil, between Feb 16 and Aug 15, 2020 (epidemiological weeks 8–33). We also examined the progression of the COVID-19 pandemic across three 4-week periods within this timeframe (epidemiological weeks 8–12, 19–22, and 27–30). The primary outcome was in-hospital mortality. We compared the regional burden of hospital admissions stratified by age, intensive care unit (ICU) admission, and respiratory support. We analysed data from the whole country and its five regions: North, Northeast, Central-West, Southeast, and South.

Findings Between Feb 16 and Aug 15, 2020, 254 288 patients with RT-qPCR-confirmed COVID-19 were admitted to hospital and registered in SIVEP-Gripe. The mean age of patients was 60 (SD 17) years, 119 657 (47%) of 254 288 were aged younger than 60 years, 143 521 (56%) of 254 243 were male, and 14 979 (16%) of 90 829 had no comorbidities. Case numbers increased across the three 4-week periods studied: by epidemiological weeks 19–22, cases were concentrated in the North, Northeast, and Southeast; by weeks 27–30, cases had spread to the Central-West and South regions. 232 036 (91%) of 254 288 patients had a defined hospital outcome when the data were exported; in-hospital mortality was 38% (87 515 of 232 036 patients) overall, 59% (47 002 of 79 687) among patients admitted to the ICU, and 80% (36 046 of 45 205) among those who were mechanically ventilated. The overall burden of ICU admissions per ICU beds was more pronounced in the North, Southeast, and Northeast, than in the Central-West and South. In the Northeast, 1545 (16%) of 9960 patients received invasive mechanical ventilation outside the ICU compared with 431 (8%) of 5388 in the South. In-hospital mortality among patients younger than 60 years was 31% (4204 of 13 468) in the Northeast versus 15% (1694 of 11 196) in the South.

Interpretation We observed a widespread distribution of COVID-19 across all regions in Brazil, resulting in a high overall disease burden. In-hospital mortality was high, even in patients younger than 60 years, and worsened by existing regional disparities within the health system. The COVID-19 pandemic highlights the need to improve access to high-quality care for critically ill patients admitted to hospital with COVID-19, particularly in LMICs.

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Introduction

Millions of COVID-19 cases have generated an unprecedented strain on health-care systems worldwide, including increased rates of hospital admissions and increased demand for intensive care unit (ICU) beds, advanced respiratory support, and trained health-care professionals. The impact of the COVID-19 pandemic on each country's health system has been different, depending on the balance between supply and demand, which is associated with the capacity to expand the health system and with pandemic preparedness.

Brazil is an upper-middle-income country with 210 million inhabitants in a large territorial area. There is substantial heterogeneity between its five macroregions (North, Northeast, Central-West, Southeast, and South), including socioeconomic heterogeneity, which is reflected in the quality of regional health services, including the availability of hospital beds and trained

Research in context

Evidence before this study

We searched PubMed for nationwide studies describing the burden of the COVID-19 pandemic on countries' health systems, the use of resources in terms of intensive care unit (ICU) admissions and respiratory support, and in-hospital mortality for patients admitted to hospital with COVID-19, with a focus on low-income and middle-income countries (LMICs). We searched for studies published in English, from database inception to Oct 18, 2020, using the following search terms: "SARS-CoV-2" OR "COVID-19" OR "COVID" AND "critical care" OR "intensive care" OR "ICU" OR "mechanical ventilation" OR "ventilation" AND "hospital mortality". The majority of studies we found were single-centre or regional studies; few were from LMICs, and we found no detailed assessments of health-system burden. We found four nationwide studies, one from Germany and three from LMICs (Mexico, Iran, and Brazil). The studies from Iran and Brazil reported on patients admitted to hospital from the beginning of the COVID-19 pandemic and did not focus on health-care resource use or health-system burden. The study from Mexico reported in-hospital mortality among mechanically ventilated patients. There is, therefore, a scarcity of data on the use of health-care resources and in-hospital mortality for patients with COVID-19 in LMICs.

Added value of this study

In this retrospective analysis of data from a large, nationwide surveillance database in Brazil, an upper-middle-income country, we observed high in-hospital mortality in a large cohort of patients with quantitive RT-PCR (RT-qPCR)-confirmed COVID-19, as well as a high proportion of ICU admissions and patients requiring respiratory support. In-hospital mortality was notably high among patients younger than 60 years, particularly those who received invasive mechanical ventilation. The health-system burden varied between the five regions of the country; hospital admission rates and in-hospital mortality were associated with the temporal increase in COVID-19 cases across the country and underlying regional differences in the supply of hospital and ICU beds.

Implications of all the available evidence

Although Brazil has a unified health system that aims to provide universal health coverage, differences in health-system capacity exist across its five macroregions. The temporal and regional spread of COVID-19 placed a substantial burden on the health system across the country and overwhelmed the system in the five regions, particularly the North and Northeast, which saw higher hospital admission rates and higher in-hospital mortality in the first months of the pandemic. The regional differences in in-hospital mortality observed in this study were consistent with regional inequities in access to high-quality health care before the pandemic, indicating that COVID-19 disproportionately affects not only the most vulnerable patients but also the most fragile health systems. Community-based non-pharmacological interventions are crucial to mitigate the rate of COVID-19 transmission and to reduce the overall burden of COVID-19 in the population. Additionally, the high in-hospital mortality observed in our study, even among patients younger than 60 years, highlights the need for improvements in the structure and organisation of the health system, with an increase in the resources available—including equipment, consumables, intensive care space, and trained health-care workers—to support the implementation of evidence-based practice and improved health outcomes for patients with severe or critical COVID-19.

health-care workers.[1–3] Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spread to Brazil via international flights, and COVID-19 cases were initially concentrated in the large metropolitan areas, spreading from state capitals to the towns.[4]

Recent economic and political crises have intensified structural problems in Brazil's unified health system (*Sistema Único de Saúde*)—the aim of which is to provide universal health coverage—including gaps in governance and organisation, chronic underfunding, and low clinical effectiveness.[2,5] The COVID-19 pandemic has challenged the country's health system, with more than 8·2 million cases and 206 000 deaths reported by Jan 14, 2021. The existing regional disparities in access to health services and health outcomes were probably intensified by the pandemic, disproportionately affecting the most vulnerable socioeconomic groups in the population.

For the **latest number of reported COVID-19 cases and deaths** see https://coronavirus.jhu.edu/map.html

Most low-income and middle-income countries (LMICs) have little or no data integrated into a national surveillance system to identify characteristics or outcomes of hospital admissions for COVID-19 and the impact of the pandemic on their national health systems. Brazil's unified health system and its informatics department (DATASUS) have a long tradition of acquiring and maintaining public records of health-related information for administrative and epidemiological purposes.[6] We used data from a nationwide surveillance system to describe patient characteristics, intensive care use, and respiratory support for the first 250 000 patients admitted to hospital with COVID-19 in Brazil. We also aimed to investigate the impact of COVID-19 on the use of health-care resources and in-hospital mortality across the five macroregions in Brazil.

Methods

Study design and participants

We did a retrospective analysis of all COVID-19 hospital admissions registered in the Influenza Epidemiological Surveillance Information System, SIVEP-Gripe (*Sistema de Informação de Vigilância Epidemiológica da Gripe*), a nationwide surveillance database used to monitor severe acute respiratory infections in Brazil.[7,8] Established by

Brazil's Ministry of Health in 2012, SIVEP-Gripe has been the primary source of information on COVID-19 hospital admissions and deaths in the country. COVID-19 notification is compulsory in Brazil and SIVEP-Gripe receives notifications of patients admitted to both public and private hospitals with COVID-19. For the period analysed in this study, patients admitted to hospital with COVID-19 were from 4407 (80%) of 5506 municipalities with a confirmed case in Brazil, comprising 96% of the population (appendix 2 p 4).

For each patient registered, information about the individual's demographics, self-reported symptoms, comorbidities, ICU admission and ventilatory support, and dates of symptom onset, hospital admission, ICU admission, and in-hospital outcome (death or discharge) are included. We accessed data in SIVEP-Gripe, which are already de-identified and publicly available (appendix 2 p 5). Following ethically agreed principles on open data, this analysis did not require ethical approval in Brazil.

Our period of analysis was from epidemiological week 8 (starting Feb 16, 2020) to epidemiological week 33 (until Aug 15, 2020). We included all consecutively registered patients with a positive quantitative RT-PCR (RT-qPCR) test result for SARS-CoV-2 who had been admitted to hospital and were aged 20 years or older. SARS-CoV-2 diagnostic tests followed national and international standards and were done in certified laboratories. We excluded patients with COVID-19 who were not admitted to hospital and who died in a non-hospital setting. Information on data management is summarised in appendix 2 (pp 6–8).

Other data sources

We obtained data on the total number of confirmed SARS-CoV-2 cases (those in hospital and those not in hospital) at the municipal level reported by each state's Health Department, which is collected by the brasil.io consortium, a group of volunteers who compile daily epidemiological bulletins. Brazilian population estimates for 2020 were retrieved from the Brazilian Institute of Geography and Statistics (*Instituto Brasileiro de Geografia e Estatística*; IBGE), and numbers of active hospital and ICU beds retrieved from the national registry of health facilities (*Cadastro Nacional de Estabelecimentos de Saúde*; CNES). A detailed description of the data sources is provided in appendix 2 (p 5).

Outcomes

The primary outcome was in-hospital mortality. We also evaluated the use of health-care resources (ICU admission and respiratory support, defined as none, non-invasive, or invasive).

Data analysis

The analysis was prespecified and defined before any reading of the data. The sample size was pragmatic and comprised all adult patients (aged ≥20 years) with COVID-19 admitted to hospital and registered in the database between epidemiological weeks 8 and 33.

We used medians and IQRs or means and SDs to summarise continuous variables, and calculated frequencies and proportions for categorical variables. We calculated age-adjusted and sex-adjusted rates for each macroregion by the direct method using the estimated Brazilian population for 2020 as a reference.

We examined the progression of the COVID-19 pandemic (total cases, hospital admissions, and in-hospital deaths) throughout the country by focusing on three different periods, each comprising four epidemiological weeks, to illustrate its spatial and temporal development: epidemiological weeks 8–12 (Feb 16 to March 21, 2020), epidemiological weeks 19–22 (May 3 to May 30, 2020), and epidemiological weeks 27–30 (June 28 to July 25, 2020). The first period comprised 5 weeks due to sparse data and the last period was censored until week 30 because of delayed entry of outcomes.

See Online for appendix 2

For more on the **brasil.io consortium** see https://brasil.io/dataset/covid19/caso_full/

For more on the **CNES** see http://cnes.datasus.gov.br/

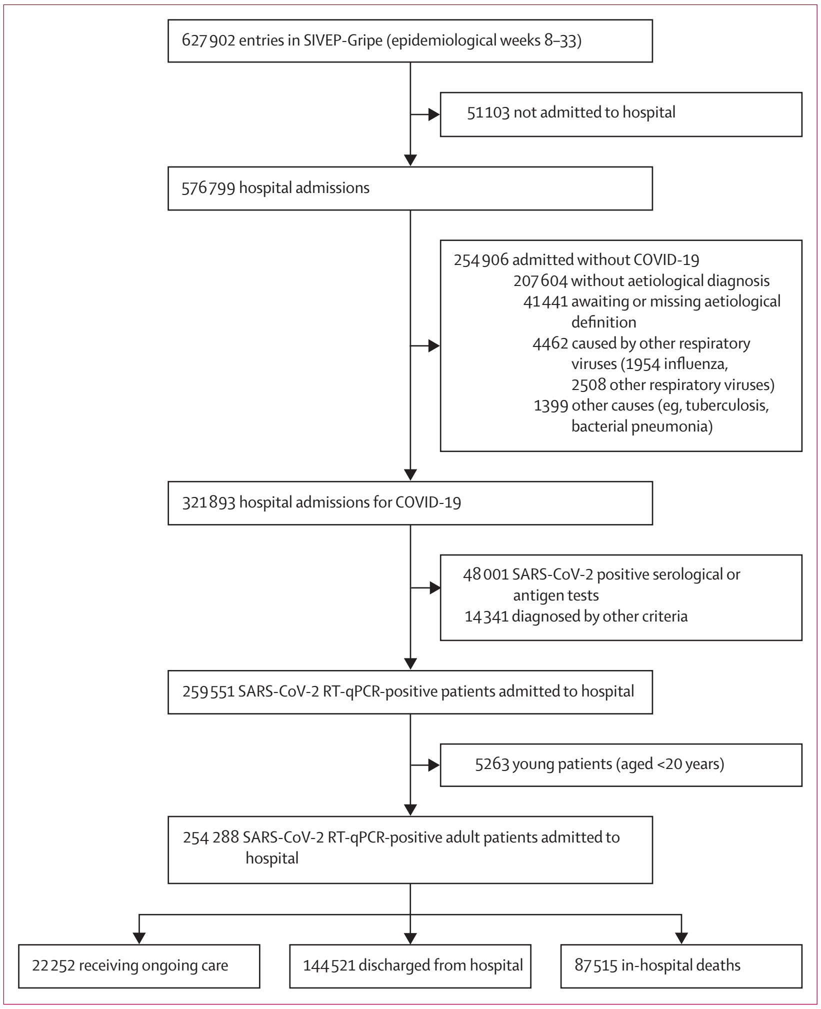

Figure 1: **Study profile**
SARS-CoV-2=severe acute respiratory syndrome coronavirus 2.

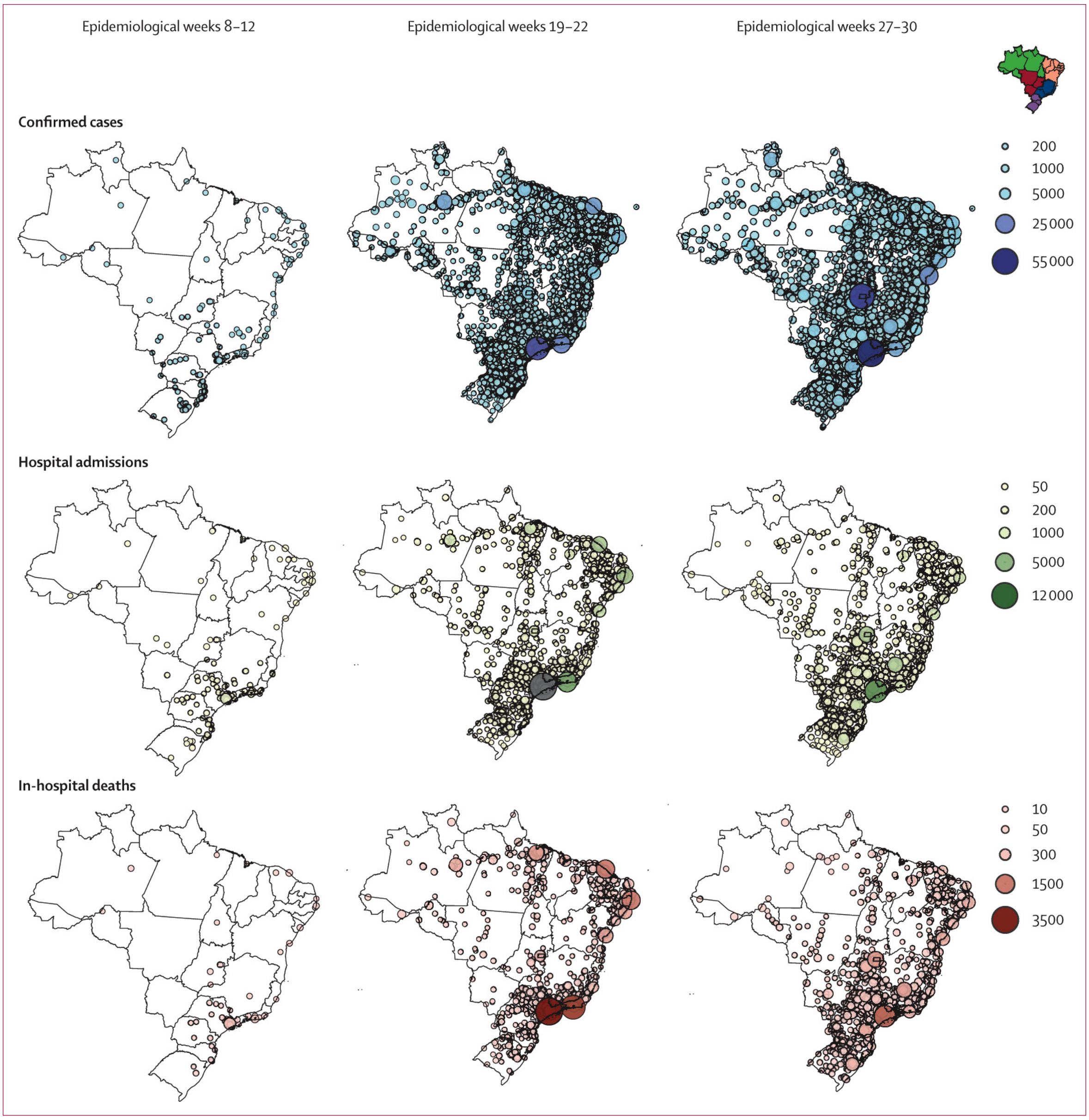

Figure 2: **Spatial and temporal spread of the COVID-19 pandemic across three 4-week periods in Brazil**
The maps show municipalities in which confirmed COVID-19 cases, hospital admissions, and in-hospital deaths were reported during three 4-week periods: epidemiological weeks 8–12 (Feb 16 to March 21, 2020), epidemiological weeks 19–22 (May 3 to May 30, 2020), and epidemiological weeks 27–30 (June 28 to July 25, 2020). Inset shows the five macroregions of Brazil: North (green), Northeast (light orange), Central-West (red), Southeast (blue), and South (purple).

We evaluated in-hospital mortality and the use of resources in the health system (ICU admission and respiratory support) for patients who had a hospital outcome. We compared the burden of hospital admissions (defined as the rate of hospital admissions per 100 000 population), in-hospital mortality, and the proportion of resource use between macroregions. We calculated in-hospital mortality by each macroregion for every 4-week period and estimated 95% CIs by the Agresti-Coull method. We also stratified the analysis by the following variables: age; sex; number of comorbidities (cardiovascular, renal, neurological, haematological, or hepatic comorbidities, diabetes, chronic respiratory disorder, obesity, or immunosuppression); level of education; self-reported race or skin colour (*Branco* [White], *Preto* [Black], *Pardo* [Brown], *Amarelo* [Asian], or *Indígena* [Indigenous]), hereafter referred to as self-reported race; ICU admission; and respiratory support. We also did a sensitivity analysis by including patients diagnosed by serological or antigen tests and clinical-epidemiological criteria, to account for potential selection bias towards severe COVID-19 cases because of the prioritisation of RT-qPCR tests.

	Brazil (n=254 288)	North (n=14 712)	Northeast (n=51 993)	Central-West (n=18 701)	Southeast (n=142 963)	South (n=25 919)
Age, years						
Mean (SD)	60 (17)	59 (17)	62 (18)	59 (17)	60 (17)	59 (17)
Median (IQR)	61 (47–73)	61 (46–73)	63 (49–76)	59 (46–71)	61 (47–73)	60 (47–72)
Age group, years						
20–39	34 170 (13%)	2285 (15%)	6672 (13%)	2798 (15%)	18 849 (13%)	3566 (14%)
40–49	37 618 (15%)	2187 (15%)	6566 (12%)	3115 (17%)	21 814 (15%)	3936 (15%)
50–59	47 869 (19%)	2510 (17%)	8742 (17%)	3725 (20%)	27 754 (20%)	5138 (20%)
60–69	52 800 (21%)	3033 (21%)	10 531 (20%)	3770 (20%)	29 817 (21%)	5649 (22%)
70–79	44 968 (18%)	2767 (19%)	10 275 (20%)	3067 (16%)	24 445 (17%)	4414 (17%)
≥80	36 863 (14%)	1930 (13%)	9207 (18%)	2226 (12%)	20 284 (14%)	3216 (12%)
Sex (n=254 243)						
Female	110 722 (44%)	5894 (40%)	22 987 (44%)	7971 (43%)	62 605 (44%)	11 265 (43%)
Male	143 521 (56%)	8816 (60%)	28983 (56%)	10 729 (57%)	80 340 (56%)	14 653 (57%)
Self-reported race* (n=181 499)						
White	89 374 (49%)	1340 (11%)	5515 (17%)	3322 (29%)	59 502 (58%)	19 695 (88%)
Black or Brown	88 773 (49%)	10 039 (86%)	26 579 (81%)	7622 (67%)	42 114 (41%)	2419 (11%)
Asian	2838 (2%)	209 (2%)	611 (2%)	265 (2%)	1606 (2%)	147 (1%)
Indigenous	514 (<1%)	121 (1%)	95 (<1%)	164 (2%)	87 (<1%)	47 (<1%)
Level of education (n=86 204)						
Illiterate	5399 (6%)	711 (10%)	1682 (14%)	280 (5%)	2250 (4%)	476 (4%)
Up to high school	38 417 (45%)	2964 (42%)	5203 (42%)	2133 (41%)	22 309 (45%)	5808 (50%)
High school	28 365 (33%)	2448 (34%)	3629 (29%)	1757 (34%)	17 040 (34%)	3491 (30%)
College or university	14 023 (16%)	981 (14%)	1835 (15%)	1006 (20%)	8311 (17%)	1890 (16%)
Number of comorbidities† (n=90 829)						
0	14 979 (16%)	788 (17%)	2794 (17%)	1654 (19%)	7803 (16%)	1940 (16%)
1–2	67 610 (74%)	3458 (77%)	12 088 (75%)	6199 (73%)	37 051 (75%)	8814 (73%)
≥3	8240 (10%)	271 (6%)	1221 (8%)	636 (8%)	4796 (9%)	1316 (11%)
Oxygen saturation <95%, (n=212 016)	147 596 (70%)	7 955 (67%)	27 410 (69%)	10 913 (64%)	85 739 (71%)	15 579 (67%)
Dyspnoea (n=226 724)	180 818 (80%)	11 379 (84%)	36 883 (83%)	13 709 (77%)	99 548 (79%)	19 299 (79%)
Respiratory distress (n=209 145)	143 977 (69%)	9802 (78%)	26 737 (70%)	11 286 (66%)	80 530 (68%)	15 622 (67%)
SARI criteria (n=211 032)	128 958 (61%)	9944 (77%)	26 177 (66%)	9362 (55%)	71 019 (60%)	12 456 (54%)
SARI without fever criteria (n=223 006)	171 574 (77%)	11 274 (85%)	33 684 (79%)	12 520 (72%)	96 488 (77%)	17 608 (73%)
Hospital admission in state capital (n=254 288)	138 235 (54%)	9018 (61%)	36 339 (70%)	13 195 (71%)	71 411 (50%)	8272 (32%)

Data are n (%) and represent the available data for each variable. SARI=severe acute respiratory infection. *Race was recorded as self-reported race or skin colour, classified as *Branco* (White), *Preto* (Black), *Pardo* (Brown), *Amarelo* (Asian), or *Indígena* (Indigenous). †The number of chronic comorbidities is the sum of the following comorbidities: cardiovascular, renal, neurological, haematological, or hepatic comorbidities, diabetes, chronic respiratory disorder, obesity, or immunosuppression.

Table 1: **Patient characteristics stratified by region**

The main analysis was based on complete case data, computing averages and proportions with the corresponding number of available data for each variable. However, SIVEP-Gripe contains a considerable amount of missing data for some variables, such as reported symptoms and comorbidities. In a post-hoc analysis, we evaluated the pattern of missing data and did a sensitivity analysis via multiple imputation by chained equations, generating 30 imputed datasets. A description of the multiple imputation is provided in appendix 2 (pp 9–15).

Brazil is divided into five macroregions: North, Northeast, Central-West, Southeast, and South. These macroregions have historical differences in health-system capacity and coverage. Thus, we did analyses for the whole country and for each macroregion.[9] All analyses were done in R, version 4.0.2. Multiple imputation was done in Stata 13.1. We followed STROBE guideline recommendations.

Role of the funding source

The funders had no role in any decision about the manuscript. All authors had full access to all the data in the study and OTR and LSLB verified the data, and all authors approved the final version of the manuscript for publication.

Results

Between Feb 16 and Aug 15, 2020, there were 3 278 692 confirmed cases of COVID-19, spread over 5506 (99%) of 5570 municipalities in Brazil. During this

	Brazil (n=232 036)	North (n=13 496)	Northeast (n=45 238)	Central-West (n=17 012)	Southeast (n=131 556)	South (n=24 734)
ICU admission and mortality						
ICU admission (n=205 493)	79 687 (39%)	3786 (32%)	14 867 (43%)	6682 (42%)	45 224 (38%)	9128 (38%)
ICU mortality*	23 780/43 582 (55%)	2037/2569 (79%)	4834/7357 (66%)	1753/3447 (51%)	11 058/22 472 (49%)	4098/7737 (53%)
Respiratory support (n=196 248)						
None	54 314 (28%)	3047 (28%)	8177 (25%)	4076 (27%)	32 756 (29%)	6258 (27%)
Yes, non-invasive	96 729 (49%)	4743 (43%)	14 485 (44%)	7561 (49%)	58 444 (51%)	11 496 (50%)
Yes, invasive	45 205 (23%)	3155 (29%)	10 322 (31%)	3667 (24%)	22 648 (20%)	5413 (23%)
Place of non-invasive respiratory support† (n=91 816)						
In ICU	27 236 (30%)	695 (15%)	3899 (29%)	2359 (32%)	16 930 (31%)	3353 (30%)
Outside ICU	64 580 (70%)	3889 (85%)	9675 (71%)	4904 (68%)	38 138 (69%)	7974 (70%)
Place of invasive respiratory support† (n=44 055)						
In ICU	38 079 (86%)	2577 (83%)	8415 (84%)	2970 (83%)	19 160 (87%)	4957 (92%)
Outside ICU	5976 (14%)	516 (17%)	1545 (16%)	629 (17%)	2855 (13%)	431 (8%)
Hospital mortality						
In-hospital mortality	87 515 (38%)	6727 (50%)	21 858 (48%)	5964 (35%)	45 269 (34%)	7697 (31%)
Median duration of stay, days (IQR)						
ICU (n=43 680)	7 (3–15)	6 (3–12)	7 (3–13)	7 (3–13)	7 (3–14)	9 (4–17)
Hospital (n=218 281)	8 (4–14)	7 (4–14)	8 (4–16)	8 (4–14)	8 (4–14)	8 (4–15)

Data are n (%) and represent the available data for each variable. ICU=intensive care unit. *ICU mortality was derived for patients with date of ICU discharge equal to the date of hospital death, so it was available for patients without missing values on both dates (n=43 582). †The sum of non-invasive and invasive respiratory support when stratified by place (in ICU and outside ICU) does not match the total respiratory support type because of missing values on the variable ICU admission.

Table 2: **Intensive care admission, need for respiratory support, ICU mortality, and in-hospital mortality among patients with a defined hospital outcome**

period, 576 799 hospital admissions were reported in the SIVEP-Gripe database (figure 1). Of these, 254 288 adult patients (aged ≥20 years) who were admitted to hospital had a positive RT-qPCR test result for SARS-CoV-2.

During epidemiological weeks 8–12, there were 1092 confirmed COVID-19 cases and 773 hospital admissions in the five macroregions. This increased to 413 458 confirmed cases and 58 034 hospital admissions during weeks 19–22, concentrated in the North, Northeast, and Southeast. During weeks 27–30, there were 1 092 353 confirmed COVID-19 cases and 59 748 hospital admissions, concentrated in the Northeast and Southeast, but expanding to the Central-West and South regions (figure 2). Crude and adjusted rates are summarised in appendix 2 (pp 16–17).

The mean age of patients was 60 (SD 17) years, and the Northeast had the highest proportion of patients aged 80 years or older (18% *vs* 12–14% in other regions). Black or Brown patients accounted for more than two-thirds of COVID-19 cases in the North, Northeast, and Central-West regions (table 1). Overall, 14 979 (16%) of 90 829 patients had no comorbidities and 67 610 (74%) of 90 829 had one to two comorbidities. Severe acute respiratory infection was present in 128 958 (61%) of 211 032 patients and was more frequent in the North than in other regions (table 1). Hypoxaemia (oxygen saturation <95%) was present in 147 596 (70%) of 212 016 patients overall and was similar across regions, while respiratory distress was more prevalent in the North and Northeast. Symptoms and comorbidities are described in appendix 2 (pp 18–20).

232 036 (91%) of 254 288 patients had a hospital outcome when the data were exported, whereas 22 252 were still in hospital. The median time from onset of symptoms to hospital admission was 6 (IQR 4–9) days in Brazil. 79 687 (39%) of 205 493 patients were admitted to the ICU, with a median time from onset of symptoms to ICU admission of 7 (IQR 4–10) days (table 2; appendix 2 p 21). 45 205 (23%) of 196 248 patients required invasive mechanical ventilation, and 5976 (14%) of 44 055 patients received invasive mechanical ventilation outside the ICU (table 2). In the Northeast, 1545 (16%) of 9960 patients received invasive mechanical ventilation outside the ICU, compared with 431 (8%) of 5388 in the South.

The overall in-hospital mortality was 38% (87 515 of 232 036 patients), increasing steeply with age (3780 [12%] of 30 603 patients aged 20–39 years; 6162 [18%] of 33 968 patients aged 40–49 years; 11 818 [27%] of 43 376 patients aged 50–59 years; 20 317 [42%] of 48 270 patients aged 60–69 years; 22 651 [55%] of 41 434 patients aged 70–79 years; and 22 787 [66%] of 34 385 patients aged ≥80 years); in-hospital mortality was slightly higher for male patients than for female patients (figure 3; appendix 2 pp 22–23). The overall in-hospital mortality for patients without comorbidities was 32% (4494 of 13 836 patients; figure 3; appendix 2 p 24). The overall proportion of in-hospital deaths was higher among patients who were illiterate (3146 [63%] of 4993), Black or Brown (34 345 [43%] of 80 392), or Indigenous (202 [42%] of 477; figure 3; appendix 2 p 24). Overall, in-hospital mortality was higher in patients admitted to the ICU (47 002 [59%] of 79 687) than in those admitted to the ward (29 361 [29%] of 125 806). It was also higher in patients who received invasive mechanical ventilation (36 046 [80%] of 45 205) than in those who did not (36 942 [24%] of 151 043). In-hospital mortality for patients aged 20–39 years who required mechanical ventilation was 57% (1858 of 3278 patients) and for those aged 60 years and older it was 87% (25 879 of 29 853; figure 3; appendix 2 p 25). In-hospital mortality was higher among patients who presented with hypoxaemia (60 583 [45%] of 135 620 patients), respiratory distress (56730 [43%] of 132 188), or dyspnoea (68 083 [41%] of 165 977; appendix 2 p 26) than in patients without these clinical features. ICU mortality (23 780 [55%] of 43 582 patients) followed the same pattern as in-hospital mortality across regions, with the highest rates observed in the North and Northeast (table 2).

The general characteristics of each macroregion are shown in table 3. There were notable disparities in the number of hospital and ICU beds between macroregions and between state capitals and towns. The rate of hospital admissions for COVID-19 was 153 per 100 000 inhabitants in Brazil, when considering patients with a defined hospital outcome (appendix 2 p 27). Over time, hospital admission rates differed between regions. The crude in-hospital mortality was higher during weeks with high rates of hospital admissions, particularly in the North, Central-West, and South (figure 4). Over the entire period, there were noticeable regional differences in hospital admission rates, particularly when stratified by age (figure 5). The North had the highest incidence of COVID-19 hospital admissions among patients aged 70 years and older, followed by the Southeast, Central-West, Northeast, and South regions. The North also had the highest incidence of patients aged 70 years and older requiring invasive mechanical ventilation, followed by the Central-West, Southeast, Northeast, and South regions (figure 5; appendix 2 pp 27–28). When considering ICU admissions per ICU bed, the North had the highest rate of admissions (2246 per 1000 ICU beds), followed by the Southeast (2217 per 1000 ICU beds), Northeast (2073 per 1000 ICU beds), Central-West (2001 per 1000 ICU beds), and South (1793 per 1000 ICU beds; appendix 2 p 29). Overall, 54% of patients were admitted to hospital in the state capitals, but this proportion was lower for the South (32%) and higher for the North (61%), Northeast (70%), and Central-West (71%) regions (table 1).

In-hospital mortality was higher overall in the North and Northeast (table 2) and when stratified by age (figure 5; appendix 2 p 28). Among patients aged 20–39 years, in-hospital mortality was 20% (393 of 1976) in the North, 19% (1083 of 5587) in the Northeast, 10% (1736 of 17 170) in the Southeast, and 8% (284 of 3372) in the South. In-hospital mortality among patients younger than 60 years was 31% (4204 of 13 468) in the Northeast versus 15% (1694 of 11 196) in the South. Regional differences in mortality were greater for patients younger than 60 years who were admitted to the ICU or mechanically ventilated (figure 5; appendix 2 p 28). For instance, in-hospital mortality for mechanically ventilated patients younger than 60 years was 77% (2559 of 3317) in the Northeast compared with 55% (1054 of 1929) in the South.

The pattern of hospital resource use differed between regions (appendix 2 pp 30–31). Overall, there was an age-related increase in the proportion of patients admitted to the ICU and requiring invasive mechanical ventilation. However, in the North and Northeast there was a plateau in the proportion of patients aged 60 years and older admitted to the ICU and requiring invasive mechanical ventilation. Additionally, the proportion of patients who

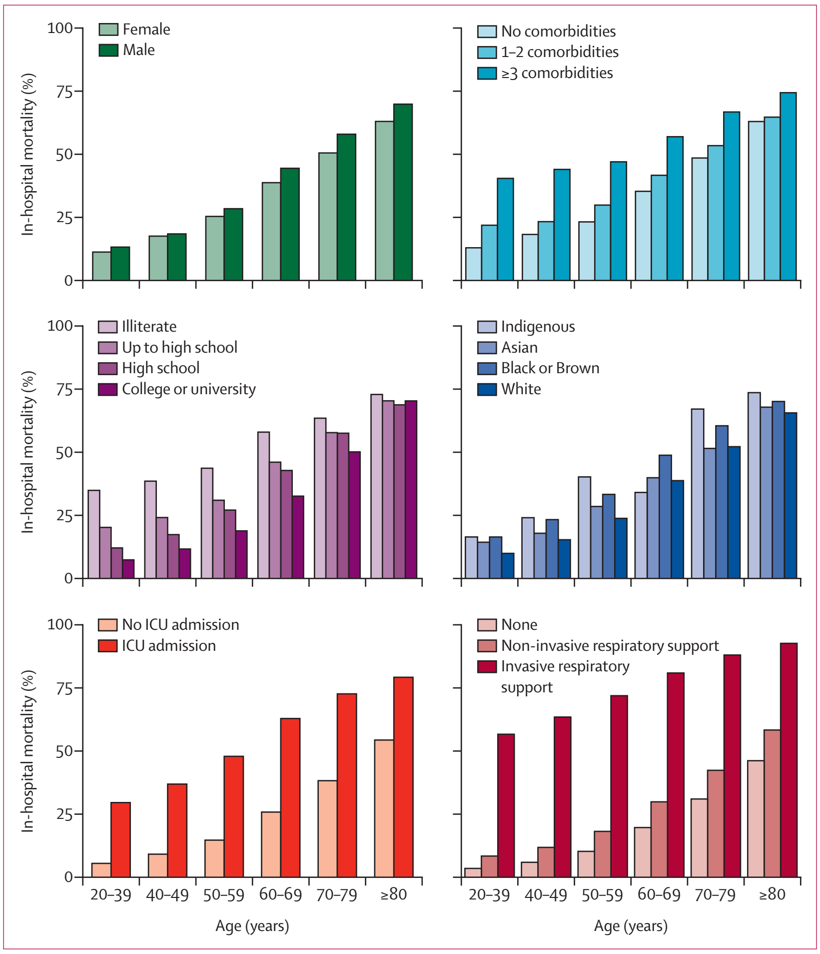

Figure 3: **In-hospital mortality stratified by age, sex, comorbidities, level of education, self-reported race, ICU admission, and invasive mechanical ventilation for patients with COVID-19 admitted to hospital in Brazil**
Data are from patients with a defined hospital outcome; proportions of patients were calculated on the basis of complete case data for sex, comorbidities, level of education, self-reported race, ICU admission, and invasive ventilation variables. Data on race were collected as self-reported race or skin colour, classified as *Branco* (White), *Preto* (Black), *Pardo* (Brown), *Amarelo* (Asian), or *Indígena* (Indigenous). ICU=intensive care unit.

	Brazil	North	Northeast	Central-West	Southeast	South
Population*						
Projected population	211 755 692	18 672 591	57 374 243	16 504 303	89 012 240	30 192 315
Projected adult population	151 778 729	12 049 813	39 882 347	11 678 574	65 803 414	22 364 581
Area, km²	8 510 296	3 850 510	1 552 167	1 606 317	924 565	576 737
Population per km²	24·9	4·8	37·0	10·3	96·3	52·4
Age and sex distribution						
Mean age, years (SD)	34·5 (21)	29·8 (20)	33·1 (21)	33·3 (21)	36·0 (22)	36·2 (22)
Mean age of adult population, years (SD)†	44·3 (17)	40·9 (15)	43·3 (17)	43·2 (16)	45·3 (17)	45·6 (17)
Age groups, years						
<20	59 976 963 (28·3%)	6 622 778 (35·5%)	17 491 896 (30·5%)	4 825 729 (29·2%)	23 208 826 (26·1%)	7 827 734 (25·9%)
20–39	68 451 093 (32·3%)	6 448 447 (34·5%)	19 048 242 (33·2%)	5 484 644 (33·2%)	28 059 711 (31·5%)	9 410 049 (31·2%)
40–49	29 255 478 (13·8%)	2 357 103 (12·6%)	7 654 000 (13·3%)	2 386 731 (14·5%)	12 717 264 (14·3%)	4 140 380 (13·7%)
50–59	23 875 081 (11·3%)	1 600 270 (8·6%)	5 930 317 (10·3%)	1 825 822 (11·1%)	10 724 660 (12·0%)	3 794 012 (12·6%)
60–69	16 732 972 (7·9%)	974 828 (5·2%)	3 893 805 (6·8%)	1 155 857 (7·0%)	7 919 342 (9·0%)	2 789 140 (9·2%)
70–79	9 023 052 (4·3%)	470 277 (2·5%)	2 245 607 (4·0%)	575 162 (3·5%)	4 225 114 (4·7%)	1 506 892 (5·0%)
≥80	4 441 053 (2·1%)	198 888 (1·1%)	1 110 376 (1·9%)	250 358 (1·5%)	2 157 323 (2·4%)	724 108 (2·4%)
Sex						
Female (%)	51%	50%	52%	51%	51%	51%
Administrative divisions						
Number of states	27	7	9	4	4	3
Municipalities	5570	450	1794	467	1668	1191
Hospital bed supply						
Adult beds in February (per 100 000 population)						
Hospital beds	235	197	220	254	239	259
ICU beds	25	14	18	29	31	23
Proportion of adult beds in state capitals (%)						
Hospital beds	37%	47%	41%	52%	36%	20%
ICU beds	51%	72%	62%	73%	47%	29%

ICU=intensive care unit. *Projection for 2020. Source: Brazilian Institute of Geography and Statistics (data sources summarised in appendix 2, p 5). †Patients aged ≥20 years.

Table 3: **Demographic, administrative, and health-system regional characteristics of Brazil**

were admitted to the ICU and mechanically ventilated was similar across age groups in the North, but the proportion of patients admitted to the ICU was higher than those receiving invasive mechanical ventilation in the other regions (appendix 2 pp 30–31).

When considering patients admitted to hospital with COVID-19 defined by clinical and laboratory diagnosis, there were 314 615 patients in total, and the majority of the additional patients (n=60 327) were from the North (n=12 790; a relative increase of 87%) and Northeast (n=19 499; a relative increase of 37%). Overall, the characteristics of these patients were similar to those of patients with COVID-19 confirmed by RT-qPCR (appendix 2 p 32). When analysing patients with a defined hospital outcome (284 747), in-hospital mortality in patients with COVID-19 confirmed by clinical, RT-qPCR, and serological and antigens tests was similar to that in patients with COVID-19 confirmed by RT-qPCR (38% [108 566 of 284 747] *vs* 38% [87 515 of 232 036]; appendix 2 p 33), although it was lower in the North (11 099 [44%] of 25 061 *vs* 6727 [50%] of 13 496). Overall, when stratified by age, number of comorbidities, level of education, self-reported race, ICU admission, invasive mechanical ventilation, and region, the pattern of in-hospital mortality in patients with COVID-19 confirmed by clinical, RT-qPCR, and serological and antigen tests was similar to that in patients with RT-qPCR-confirmed COVID-19 (appendix 2 pp 34–43). The health-system burden in the North compared with other regions was more pronounced in the sensitivity analysis than in the main analysis (appendix 2 p 38).

Overall, the analysis of multiple imputed data showed similar results to the complete case data and we observed only two differences. The proportion of patients with three or more comorbidities increased from 9% in the complete case to 26% in the multiple imputed data (appendix 2 p 15). This change reflected the observed in-hospital mortality when stratified by number of comorbidities, particularly for young patients (eg, 40% in the complete case *vs* 19% in the multiple imputed data for patients with three or more comorbidities; appendix 2 pp 44–45). The other difference was in mechanically ventilated patients aged 20–39 years in the Northeast; in-hospital mortality in this age group for the complete case data was 70%, but the figure decreased to 65% in the imputed analysis (appendix 2 p 46).

Discussion

In this study, we retrospectively analysed data from patients admitted to hospital with COVID-19 during the first 5 months of the pandemic in Brazil, using a nationwide database covering each macroregion. We analysed more than 250 000 patients with COVID-19, with a mean age of 60 years. Of these, 16% had no comorbidities and 72% received some respiratory support (invasive or non-invasive). We observed high in-hospital mortality, even among young patients, and substantial regional differences in terms of resources available and observed outcomes.

The overall in-hospital mortality was 38%, which is similar to that of other national cohorts (appendix 2 p 47). However, if we consider that the analysed population was, on average, 10 years younger (47% of patients aged <60 years) than that analysed in large European series,[10–12] the in-hospital mortality in Brazil is noticeably higher. At the beginning of the pandemic, it was initially thought that LMICs might be less affected as they have younger populations than high-income countries.[13] However, we observed high mortality even in young patients across all regions in Brazil (20% in patients <60 years; appendix 2 p 22). In a nationwide study of 23 367 patients with COVID-19 who were admitted to hospital and had a defined hospital outcome in Iran, the cumulative risk of death in 30 days was 24% overall and 42% for those aged 65 years or older.[14] In a nationwide study in Germany,[12] 17% of patients (1727 of 10 021) received non-invasive or invasive mechanical ventilation, and in-hospital mortality was 22% (2229 of 10 021) overall and 5% (135 of 2896) for patients younger than 60 years. In a study in Mexico, in-hospital mortality was 74% (8861 of 12 018) among mechanically ventilated patients.[15] Comparisons with other cohorts are challenging because of the scarcity of nationwide data and the lack of international standard criteria for assessing disease severity, the need for hospital admission, and case definitions. Although different criteria for hospital admissions and other patient characteristics (eg, comorbidities) could explain some of the observed differences in hospital admissions, respiratory support, and mortality between countries, the mismatch between demand and supply leading to a collapse of the health-care system could partly explain the high in-hospital mortality in Brazil.[16–18]

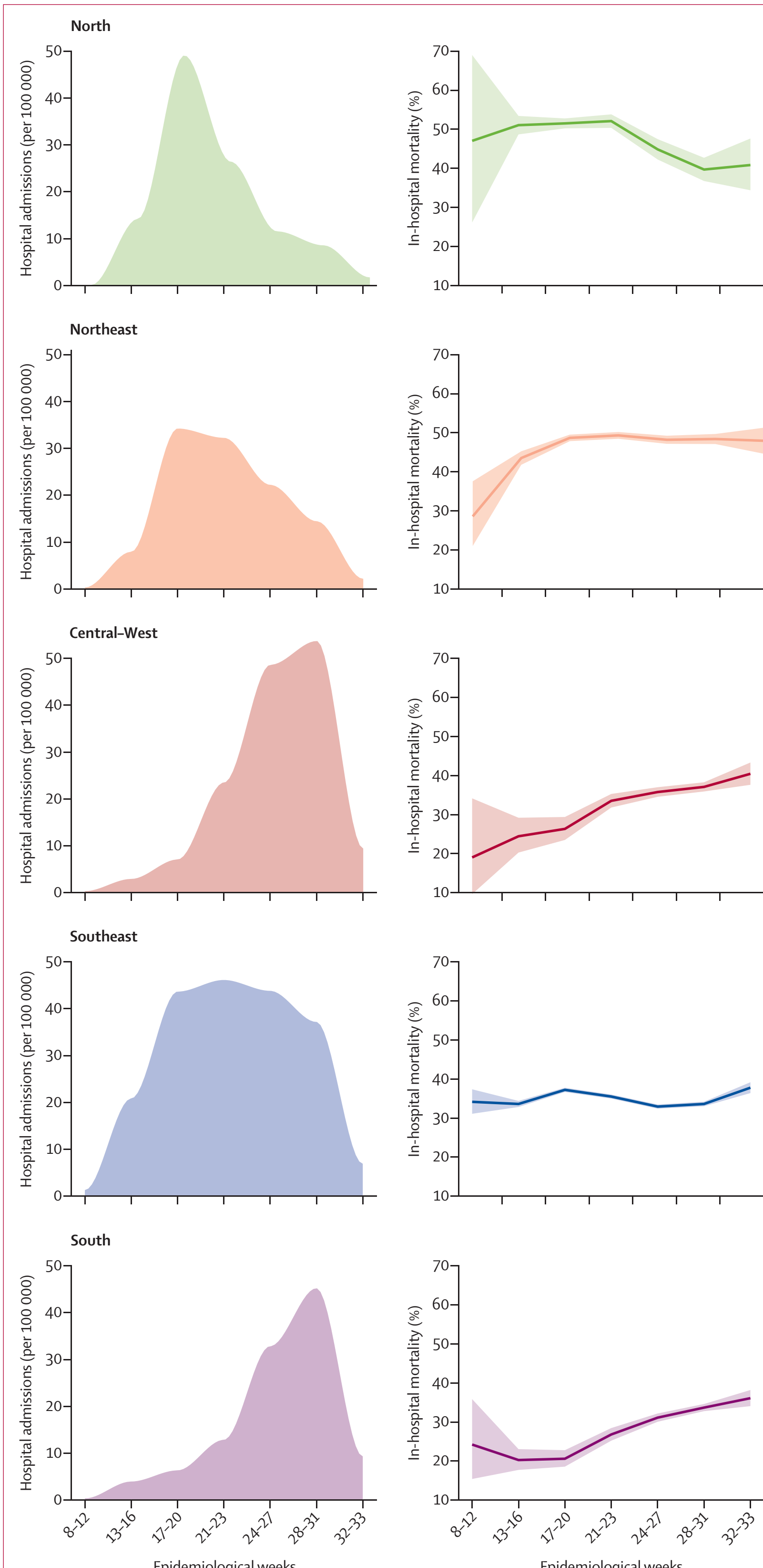

***Figure 4:* Temporal increase in COVID-19 hospital admission rates per 100 000 adult population and crude in-hospital mortality in the five macroregions of Brazil**

The x-axis denotes the epidemiological week when symptom onset occurred. Shaded areas on the right panel correspond to the upper and lower 95% CIs for in-hospital mortality, estimated by the Agresti-Coull method.

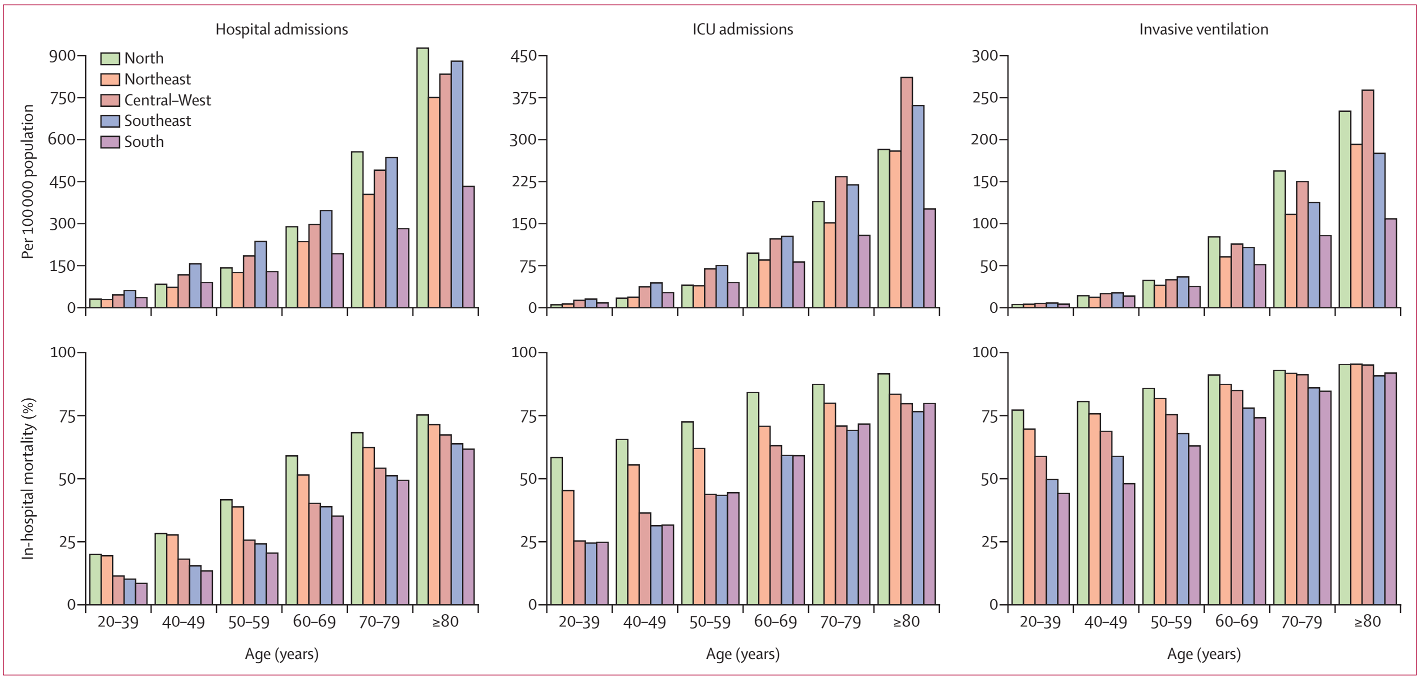

Figure 5: **Health-system burden and in-hospital mortality stratified by age in patients with COVID-19 admitted to hospital in the five macroregions of Brazil**
Burden is defined as the rate of hospital admissions per 100 000 population of each region (top row), and in-hospital mortality as the proportion of patients who died in hospital (bottom row). Data are from patients with a defined hospital outcome and proportions were calculated on the basis of complete case data for ICU admissions and patients receiving invasive mechanical ventilation. ICU=intensive care unit.

Several factors might have contributed to the differences observed in mortality and resource use among the regions of Brazil during the pandemic. These include the existing regional heterogeneity of the health system, followed by the temporal spread of the epidemic, and disparities in adherence to best practices for clinical management of severely ill patients. Despite the high absolute number of hospitals and ICU beds in the country compared with some western European countries,[19,20] the heterogeneous regional distribution of these resources is a considerable barrier to equitable access to health care. The North and Northeast regions have the lowest number of hospital beds per person in Brazil. The difference is even more pronounced when analysing ICU beds: the Southeast had approximately two times more ICU beds per person than the North at the beginning of the pandemic in Brazil. Additionally, ICU beds are concentrated in state capitals and coastal regions,[21,22] generating an additional barrier to access to health services, especially after COVID-19 spread to inland areas. The regional differences were also reflected in the proportion of patients admitted to hospital in state capitals, which was noticeably lower in the South and Southeast regions, possibly reflecting better availability of health services to meet the demand across these regions.

The rapid rise in COVID-19 cases affected the Southeast, North, and Northeast regions early (figure 4; appendix 2 p 16), and the last two of these regions have the most fragile health systems in Brazil. A cross-sectional study of the prevalence of SARS-CoV-2 antibodies in Brazil[23] identified a rapid initial escalation of SARS-CoV-2 seroprevalence in the North and Northeast regions of the country; seroprevalence was higher among those of Indigenous ancestry and those with low socioeconomic status compared with other groups. Although the North and Northeast are characterised by younger populations (aged <60 years), in-hospital mortality was even higher in these regions than in other regions, with an increased number of patients requiring ICU admission and invasive ventilation. For mechanically ventilated patients younger than 60 years, mortality was 77% (2559 of 3317) in the Northeast compared with 55% (1054 of 1929) in the South. The high proportion of mechanically ventilated patients in the ICU, the number of patients ventilated outside the ICU, and the potential limitations of advanced respiratory support and ICU admission for patients aged 60 years and older reflect the strain on the health system observed in these regions.

Other studies that evaluated severely ill patients admitted to ICUs in Brazil before the COVID-19 pandemic have also shown high in-hospital mortality. In a large national survey that analysed patients who received invasive or non-invasive mechanical ventilation for at least 24 h, the in-hospital mortality was 42%. In-hospital mortality was 52% for patients with acute respiratory distress syndrome,[22] which is present in a considerable proportion of patients admitted to hospital with COVID-19.[24] A nationwide study of patients admitted to

ICUs in Brazil with sepsis (the lung being the main source of infection in 61%) found that in-hospital mortality was 56% and that there was an association between low availability of hospital resources and in-hospital mortality.[21] In a study of patients with severe community-acquired pneumonia admitted to ICUs of public hospitals in Brazil, in-hospital mortality was 66·7%.[25] These data indicate high mortality rates in critically ill patients in Brazil before the onset of the COVID-19 pandemic, especially among patients who were ventilated. The increased burden on the health system in low-resource regions during the pandemic is likely to have exacerbated this situation.

Outcomes of critically ill patients—such as those admitted to hospital with COVID-19—are determined by factors other than resources and devices. Organisational factors and implementation of the best practices available result not only in better outcomes, such as mortality, but also in improved ICU efficiency. Previous analyses of ICUs in Brazil have shown that there is considerable room for improvement in adherence to best practices, such as target sedation levels, low-tidal-volume ventilation,[26,27] and active surveillance of nosocomial infections.[28,29] These practices are all associated with better patient outcomes. The findings of this study highlight the heterogeneity of care delivered to severely ill patients in a middle-income country. The high-quality care provided in some hospitals contrasts sharply with that provided in most facilities, which is frequently of lower quality.

In LMICs, health systems are commonly stretched in terms of resources and staff, and early containment of a pandemic has tremendous advantages, leading to lower numbers of cases and hospital admissions, which, in turn, allows time for expansion of bed numbers, staff training, and resources.[30] However, in response to the COVID-19 pandemic, much attention was dedicated to available resources such as ICU beds and ventilators, and little to training of health professionals in the best evidence to support clinical practice or the early identification of severe cases or clinical management of ventilated patients. The presence of universal health coverage is a fundamental strategy to ensure that everyone has access to testing or treatment without financial hardship. However, a coordinated national response, increasing the health system's resilience to prevent its collapse in the face of a surge of patients, and clear communication of best practices are essential to reduce preventable deaths in LMICs.

This study had limitations. First, although the notification of COVID-19 hospital admissions is compulsory in Brazil, we cannot guarantee 100% coverage of all patients with COVID-19 who were admitted to hospital. However, the total population of the municipalities with at least one patient admitted to hospital that were included in this analysis comprises more than 96% of the population of Brazil. We would expect that more severe cases were notified during the initial phase of the pandemic, leading to overestimates of in-hospital mortality. Nonetheless, SIVEP-Gripe is the official national database and is used to count all hospital admissions and deaths related to COVID-19; therefore, we did not expect any significant reporting bias. Second, there are regional differences in access to resources such as RT-qPCR tests. Particularly in the North and Northeast, a greater number of patients with COVID-19 were diagnosed by serological or antigen tests and clinical-epidemiological criteria. In our sensitivity analysis, we observed a higher number of patients in hospital with COVID-19 in these regions and lower in-hospital mortality in the North. Third, changes and improvements in clinical practice probably occurred in relation to COVID-19 over time, but assessment of temporal changes affecting in-hospital mortality was beyond the scope of this study. Fourth, this study was a descriptive analysis stratified by age and region and did not aim to answer causal questions about several potential confounding factors and the dynamics of the pandemic. Therefore, we did not adjust for some patient characteristics (eg, malnutrition), treatment (eg, antiviral drugs), health-system characteristics (eg, public *vs* private sector hospitals, expansion of ICU beds, and so on), or regional characteristics (eg, inequities and economic development). Finally, 9% of patients were still in hospital at the time the data were exported for analysis, but we have no indication that the outcome of these patients would change the main findings of the current analysis.

In conclusion, in this analysis of a large nationwide database of confirmed COVID-19 hospital admissions in the first 5 months of the pandemic, we describe the dynamics of the rise in COVID-19 cases across five macroregions in Brazil, and the clinical and demographic characteristics of patients admitted to hospital, and we provide evidence of the impact of regional inequities on outcomes, and the collapse of the more fragile regional health systems during the pandemic. In-hospital mortality was high, even in younger age groups, particularly among patients who were mechanically ventilated.

Contributors
OTR, LSLB, SH, FB, and FAB participated in the design and concept of the study. OTR, LSLB, and JGMG analysed the data. OTR, LSLB, JGMG, JFM, and FAB wrote the first version of the manuscript. OTR, FB, SH, and FAB supervised the study. All authors had full access to all data in the study, participated in data interpretation, revised the manuscript, and approved the final version of the manuscript for publication. OTR and LSLB verified the underlying data.

Declaration of interests
We declare no competing interests.

Data sharing
All de-identified data, including individual participant data, are publicly available. The data sources are described in the manuscript and in appendix 2 (p 5). The raw data, dictionary, and code used for the analysis are available in a GitHub repository.

For the **GitHub repository** see https://github.com/oranzani/Ranzani_Bastos_etal_LRM_COVID19Brazil

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