Received: 24 March 2022 | Accepted: 6 July 2022

DOI: 10.1002/jhm.12946

ORIGINAL RESEARCH

Journal of Hospital Medicine | shm Society of Hospital Medicine

Variation in the risk of death due to COVID-19: An international multicenter cohort study of hospitalized adults

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Abstract

Background: There is wide variation in mortality among patients hospitalized with COVID-19. Whether this is related to patient or hospital factors is unknown.

Objective: To compare the risk of mortality for patients hospitalized with COVID-19 and to determine whether the majority of that variation was explained by differences in patient characteristics across sites.

Design, Setting, and Participants: An international multicenter cohort study of hospitalized adults with laboratory-confirmed COVID-19 enrolled from 10 hospitals in Ontario, Canada and 8 hospitals in Copenhagen, Denmark between January 1, 2020 and November 11, 2020.

Main Outcomes and Measures: Inpatient mortality. We used a multivariable multilevel regression model to compare the in-hospital mortality risk across hospitals and quantify the variation attributable to patient-level factors.

Results: There were 1364 adults hospitalized with COVID-19 in Ontario ($n = 1149$) and in Denmark ($n = 215$). In Ontario, the absolute risk of in-hospital mortality ranged from 12.0% to 39.8% across hospitals. Ninety-eight percent of the variation in mortality in Ontario was explained by differences in the characteristics of the patients. In Denmark, the absolute risk of inpatients ranged from 13.8% to 20.6%. One hundred percent of the variation in mortality in Denmark was explained by differences in the characteristics of the inpatients.

Conclusion: There was wide variation in inpatient COVID-19 mortality across hospitals, which was largely explained by patient-level factors, such as age and severity of presenting illness. However, hospital-level factors that could have affected care, including resource availability and capacity, were not taken into account. These findings highlight potential limitations in comparing crude mortality rates across hospitals for the purposes of reporting on the quality of care.

INTRODUCTION

The risk of dying from coronavirus disease 2019 (COVID-19) among those infected in high-income nations is less than 0.1%.[1] Among patients hospitalized with COVID-19, the risk is substantially higher, ranging from 1.4% to 28%.[2–8] Known patient-level characteristics associated with an increased risk of death include age, male sex, certain comorbid conditions, and disease severity.[2,3,5,9–14] However, most published studies are limited to single centers or multiple centers within the same health region.[15,16] Multicenter studies are predominantly from countries without a universal healthcare system and are consequently susceptible to selection bias.[6–8,17] Furthermore, the largest studies, including those in countries with universal healthcare, lack data on the severity of presenting illness (e.g., inflammatory markers, chest X-ray findings), which are important predictors of death.[5]

Estimation and reporting of COVID-19-related mortality risk are important for several reasons. Hospitals are under increasing scrutiny to report quality-of-care measures, and health system planners may track changes in mortality risk to inform future healthcare delivery and resource needs.[18] Patients and families may perceive the quality of clinical care at specific hospitals to be different if certain centers report a lower risk of dying.[19] Mortality risk and likely benefit from and overall success of critical care[20–22] are essential to inform care planning and overall goals of care discussions.

Reported COVID-19 mortality rates vary widely according to geographic region and hospital. However, if differences in relevant patient-level characteristics, such as age, sex, pre-existing conditions, and disease severity remain unaccounted for, crude mortality rates may be an inaccurate representation of the overall risk of death. The objective of this study was to determine whether mortality rates among patients hospitalized with COVID-10 varied across 18 hospitals in Ontario, Canada and Denmark, and to determine whether the majority of that variation was explained by variation in patient characteristics across those sites.

METHODS

Study setting and data source

We conducted an international multicentre cohort study at 10 hospitals in Ontario, Canada and 8 in Copenhagen, Denmark. Canada is a high-income nation with a culturally diverse population of approximately 38 million people. Ontario is Canada's most populous province with over 13 million adults and more than 1.3 million cases of SARS-CoV-2 infection to date. Residents of Ontario have public access to hospital care and physicians' services, and those aged ≥65 years are provided prescription drug insurance coverage. Denmark is a high-income nation with a culturally diverse population of approximately 5.8 million people and more than 3 million cases of SARS-CoV-2 infection. Residents of Denmark have universal access to healthcare.

We used the electronic medical record at each hospital as the primary source of data. Manual data collection from the electronic medical record was performed at all sites by trained research

personnel. This study was approved by the institutional research ethics boards at each study site.

Study population

We included all adults 18 years or older at the time of hospital admission who were hospitalized with laboratory-confirmed COVID-19 between January 1, 2020 and November 11, 2020. We identified patients hospitalized with COVID-19 based on SARS-CoV-2 laboratory test results provided by infection control departments within each hospital. The sole exclusion criteria were: positive COVID-19 test >14 days prior to admission or age <18. In the analyses, we excluded patients who were transferred from an outside hospital because we did not have access to laboratory results or imaging findings from the sending hospital for the purposes of adjustment in our modeling. We intentionally included them in the study cohort to provide a more fulsome description of all patients across all study sites and because the provincial government instituted an Incident Management System during the pandemic whereby patients were routinely transferred between institutions to balance hospital capacity across the entire healthcare system.

Other variables

We collected data on variables known to be associated with inpatient mortality from COVID-19 based on prior literature.[2,3,5,9–14] Patient demographics included age, sex, English language proficiency, and place of residence before hospitalization (i.e., home, homeless, nursing, transfer from another hospital). Canada is a culturally and linguistically diverse, multicultural nation with a large immigrant population originating from a broad range of countries around the world. English is one of its two official languages spoken by approximately 56% of its citizens. In Denmark, Danish is the de facto national language and a large majority (86%) of Danes speak English as a second language. However, German is the second-most-spoken foreign language, with 47% reporting a conversational level of proficiency. Limited English proficiency has been previously shown to affect care outcomes, including during the COVID-19 pandemic.[23–29] Pre-existing comorbid conditions included those known to be associated with mortality from COVID-19 at the time the study was planned (e.g., diabetes, cardiovascular disease, pulmonary disease, smoking, and renal failure).[2,3,5,9–14] Diagnostic tests included laboratory markers associated with severity of illness (e.g., D-dimer, C-reactive protein [CRP], troponin)[5] and imaging results from chest X-ray. When multiple images were available, the first available during each admission was reviewed. Text mapping using natural language processing was used to classify findings in each report using the publicly available CHARTextract natural language processing tool.[30] We used "regular expression" NLP to classify the chest X-ray results as abnormal as this is one of the most commonly used approaches. We first identified common words and phrases that we expected to be highly associated with normal chest X-rays ("normal chest X-ray" and "clear") and others that would be highly associated with COVID pneumonia (e.g., "bi-basilar" and "opacification"). We then labeled a subset of the chest X-rays as being "normal" versus "abnormal" based on a review of the full chest X-ray report by two clinicians who have experience caring for patients hospitalized with COVID-19 (M. F. and K. Q.). We then provided the words and phrases to ChartExtract, a tool developed by our research team (https://lks-chart.github.io/CHARTextract-docs/) to identify how well these words discriminated between normal and abnormal chest X-rays and iteratively updated the included words and phrases. We also collected information on treatments such as the use of antibiotics and corticosteroids.

Patient follow-up

We followed each patient from the date of hospitalization for COVID-19 (the index date) until the first of either discharge from the hospital or inpatient death. As some hospitals have postacute care beds within their institution, we censored all outcomes at 30 days. Otherwise, patients who were not "discharged" from acute care when transferred to such beds would result in substantial differences in length of stay between sites and long-term risk of mortality.

Outcomes

The primary outcome was death in the hospital. We calculated the unadjusted mortality risk at each hospital as the number of COVID-19 patients who died within 30 days of the date of their admission to the hospital divided by the total number of patients hospitalized with COVID-19. We chose a 30-day outcome to align our results with multiple studies and clinical trials of hospitalized patients with COVID-19 that use a similar approach.[6,31,32] In the analyses, we excluded patients who were transferred from an outside hospital because we did not have access to laboratory results or imaging findings from the sending hospital. Adjustment variables included known risk factors, disease severity, and an indicator variable for each hospital. As secondary outcomes, we measured transfer to the intensive care unit (ICU) and the use of invasive ventilation.

Statistical analysis

We used descriptive statistics to characterize the study cohort and to report crude mortality risk. We modeled the primary outcome, death in hospital, on the linear probability scale using generalized linear models with log links. Due to convergence issues, we used Poisson regression rather than binomial regression to estimate relative risk. This approach was chosen over logistic regression because reporting of relative risk is much more intuitive and interpretable by readers and knowledge users than odds ratios. Further, logistic regression is intended for rare outcomes where the odds can approximate risk. In

our study, our outcome was relatively common, with an observed event rate typically exceeding 10%.

We built our statistical model in a stepwise fashion by treating hospitals as a fixed effect without accounting for patients clustered within institutions to examine these associations at the level of the patient. We then separately treated hospitals as a random effect to estimate the variation in the outcome explained by differences in patient characteristics and differences in the hospitals through the calculation of the variation partition coefficient (VPC). We estimated the VPC in this adjusted multilevel Poisson regression model using the method by Austin et al.,[33] which is defined as the proportion of the (unexplained) variation in the outcome that is due to between-cluster variation. We then measured the VPC values for an average person at low and high risk of death in the study cohort.[33] We computed the hospital-level risk-adjusted mortality rates in Ontario (as there was an insufficient number of sites to do the same in Denmark) following a similar approach used in a recent cohort study of 38,517 adults who were admitted with COVID-19 to 955 US hospitals to report the risk-standardized event rate (RSER) of 30-day in-hospital mortality.[6,34] Two important modifications had to be made: first, as we used Poisson regression rather than logistic regression, we had to use the exponential function as the inverse link function rather than the inverse of the logit function (the expit function). Second, as we used multiple imputation methods, we, therefore, had to pool model predictions and the resulting risk-standardized event rates.

The Danish Hospitals were collapsed into two regional sites because of how the Danish Health Care system is structured and the relatively small size of individual hospitals within each region that limited statistical comparison between Danish hospitals. Denmark is split into five administrative regions and each of these regions runs its hospitals independently. There is more interaction and collaboration between hospitals within the same region than interregionally. Further, the sociodemographics are similar within but differ between the two regions. One region consists of smaller cities and more rural geography while the other region is more urbanized.

Models were adjusted for age, sex, language proficiency, admission location, admission date, and the presence of comorbidities, including cardiovascular disease, diabetes, chronic obstructive pulmonary disease (COPD), asthma, CRP value, creatinine value, and chest X-ray findings. These covariates were chosen based on clinical experience caring for patients hospitalized with COVID-19 and factors associated with an increased risk of mortality based on the available literature.

In the Ontario data, we used multivariate imputation by chained equations via the mice package in R.[35] This is a form of "multiple imputation" that relies on an algorithm meant to "account for the process that created the missing data, preserve the relations in the data, and preserve the uncertainty about these relations"; this method has shown generally good performance across a variety of settings. We imputed missing covariate data for sex (0.1% missing), presence of diabetes (1.6% missing), presence of cardiovascular disease (1.5% missing), presence of asthma (1.4% missing), chest X-ray results (17.2% missing), CRP (47.3% missing), and creatinine (10.4% missing). We used the default settings of the mice algorithm and we imputed 10 data sets; model results are based on the pooled estimates across the separate imputed data sets. The mice package can be integrated with other R packages such as lme4, and pooled estimates from the glmer function were obtained. The mice algorithm is valid under the "missing at random" assumption, which states that the probability of missingness may depend on the observed data, including the outcome and the covariates. We did not investigate mice algorithms for data "missing not at random".

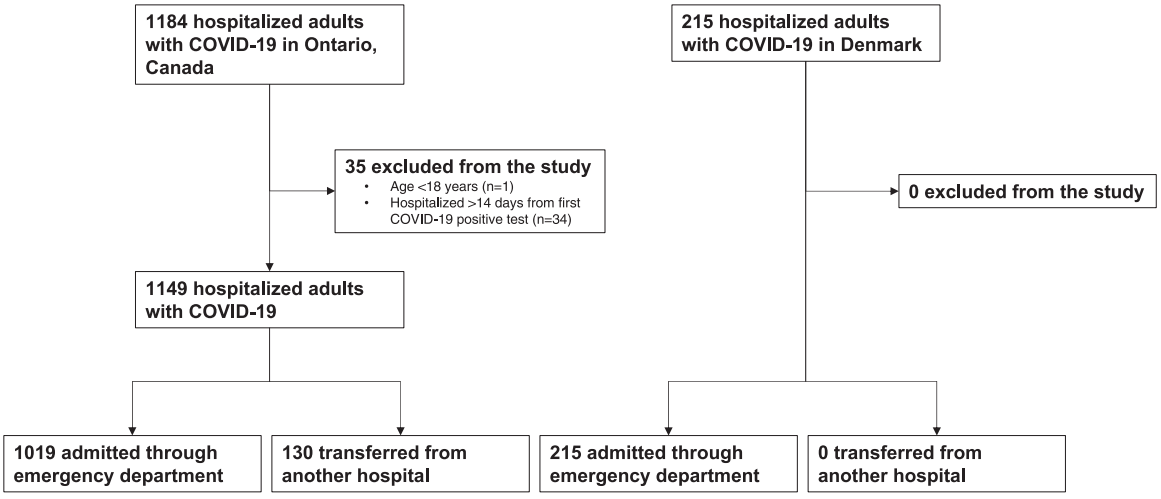

FIGURE 1 CONSORT diagram for the creation of the study sample. All adults hospitalized with laboratory-confirmed coronavirus disease 2019 (COVID-19) between January 1, 2020 and November 11, 2020 across 10 hospitals in Ontario, Canada and 8 hospitals in Copenhagen, Denmark were included in the study.

TABLE 1 Baseline characteristics of adults hospitalized with laboratory-confirmed COVID-19 between January 1, 2020 and November 11, 2020 across 10 hospitals in Ontario, Canada and 8 hospitals in Copenhagen, Denmark

	Ontario (*n* = 1149)	Denmark (*n* = 215)
Age, median (IQR)	67 (54–79)	69 (59–80)
Missing, *n* (%)	0 (0)	0 (0)
Age category, *n* (%)		
<50	228 (19.8)	22 (10.2)
50–59	174 (15.1)	37 (17.2)
60–69	225 (19.6)	52 (24.2)
70–79	236 (20.5)	51 (23.7)
80–89	199 (17.3)	44 (20.5)
90+	87 (7.6)	9 (4.2)
Female sex, *n* (%)	484 (42.2)	97 (45.1)
Missing, *n* (%)	1 (0.1)	0 (0)
Admitted from, *n* (%)		
Home	725 (63.1)	215 (100.0)
Nursing home	212 (18.5)	–
Homeless	82 (7.1)	–
External hospital	130 (11.3)	–
Limited English proficiency, *n* (%)	127 (11.6)	0 (0.0)
Current or former smoker	246 (24.6)	118 (54.9)
Missing, *n* (%)	0 (0)	0 (0)
Comorbidities, *n* (%)		
Hypertension	643 (57.0)	123 (57.2)
Diabetes	384 (34.0)	55 (25.8)
Cardiovascular disease	339 (30.0)	34 (15.8)
COPD/asthma	207 (18.3)	58 (27.0)
Chronic kidney disease	171 (15.1)	33 (15.4)
Missing	0 (0)	0 (0)
Diagnostic tests		
Creatinine (μmol/L), *n* (%)		
0–100	630 (54.8)	164 (76.3)
101–200	284 (24.7)	34 (15.8)
>200	116 (10.1)	17 (7.9)
Missing	119 (10.4)	0 (0.0)
CRP (mg/L), *n* (%)		
0–14.9	100 (8.7)	37 (17.3)
15–100	275 (23.9)	126 (58.9)
>100	230 (20.0)	51 (23.8)
Missing	544 (47.3)	1 (0.5)
D-dimer, *n* (%)		
<ULN	101 (8.8)	23 (10.7)
ULN-2*ULN	176 (15.3)	46 (21.4)
>2*ULN	343 (29.9)	105 (48.8)
Missing	529 (46.0)	41 (19.1)
Troponin, *n* (%)		
<ULN	455 (39.6)	89 (41.4)
ULN-2*ULN	157 (13.7)	37 (17.2)
>2*ULN	184 (16.0)	37 (17.2)
Missing	353 (30.7)	52 (24.2)
Chest X-ray performed, *n* (%)	951 (82.8)	212 (98.6)
COVID-19 pneumonia present on chest X-ray, *n* (%)	639 (55.6)	–[a]
Missing, *n* (%)	198 (17.2)	3 (1.4)

Abbreviations: COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; CRP, C-reactive protein; IQR, interquartile range; ULN, upper limit of normal.

[a]Text mapping using natural language processing was not available for the Danish data set.

Because different hospitals used different assays for troponin and D-dimer, we expressed the reported values relative to the upper limit of normal for each assay (e.g., >2 times the upper limit of normal). We transformed CRP and creatinine into categorical variables to align with cutoffs identified in prior studies.[36] Analyses were performed using R software (version 3.6.2): the glmer function in the lme4 package was used for the multilevel model; the VPC was determined using code from a published method[33] and multiple imputations were performed using the mice package.

RESULTS

We identified a total of 1364 patients hospitalized with COVID-19 (Ontario $n = 1149$, range for each individual hospital 57–212; Denmark $n = 215$, range from individual hospitals 34–181) (Figure 1). The baseline characteristics of hospitalized patients in Ontario were similar to those in Denmark with some notable differences. A higher proportion of adults in Denmark were older adults aged ≥60 years, were admitted from home, were current or former smokers, had COPD/asthma, and had more severe diseases indicated by CRP levels that were greater than two times the upper limit of normal. A lower proportion of adults in Denmark had limited English proficiency, diabetes, and cardiovascular disease (Table 1).

The baseline characteristics of those transferred from an external hospital were generally similar to the study sample with some exceptions (Supporting Information: Table 1). Transferred patients had a higher mean age, and a higher proportion was male; a lower proportion resided in a nursing home, had limited English proficiency, hypertension, heart failure, CKD, was current or former smokers, and had an abnormal chest X-ray.

There was wide variability across Ontario hospitals in mean patient age, proportion from a nursing home, proportion who were homeless, and the severity of presenting illness. There was also wide variability across hospitals in comorbid conditions, such as diabetes and cardiovascular disease across the included sites in Ontario. The unadjusted risk of in-hospital death across all hospitals ranged from 12.0% to 39.8%; the overall hospital mortality risk was 21.2%. After excluding patients who were transferred from another hospital, the unadjusted risk of 30-day mortality at each site ranged from 8.7% to 40.6%, and the overall mortality risk was 21.7%. An average of 23.6% were transferred to the ICU (range 13.1%–35.1%) and an average of 22.9% received invasive ventilation (range 7.3%–41%)(Figure 2). In the multivariable Poisson regression model, the variables with the strongest association with mortality were related to patient age or markers of illness severity (Table 2). Ninety-eight percent of the variation in mortality in Ontario was explained by differences in the characteristics of the average patient (VPC 2.0%; range 0.02%–2.0%). The adjusted RSER did not demonstrate significant variation across hospitals in Ontario (Supporting Information: Figure 2).

In Denmark, there was considerably less variability across patient-level factors (Supporting Information: Figure 1). The unadjusted risk of in-hospital death across the regional sites ranged from 13.8% to 20.6% and the overall median mortality risk was 14.9% (Supporting Information: Figure 1). No patients were transferred from another hospital. An average of 14.0% of patients were transferred to the ICU (range 12.1%–14.4%) and 12.1% received invasive ventilation (range 11.6%–14.7%; Supporting Information: Figure 1). In the multivariable Poisson regression model, the strongest predictors of mortality were patient age or markers of illness severity. One hundred percent of the variation in mortality in Denmark was explained by differences in the characteristics of the average patient (VPC 0%) (Table 2).

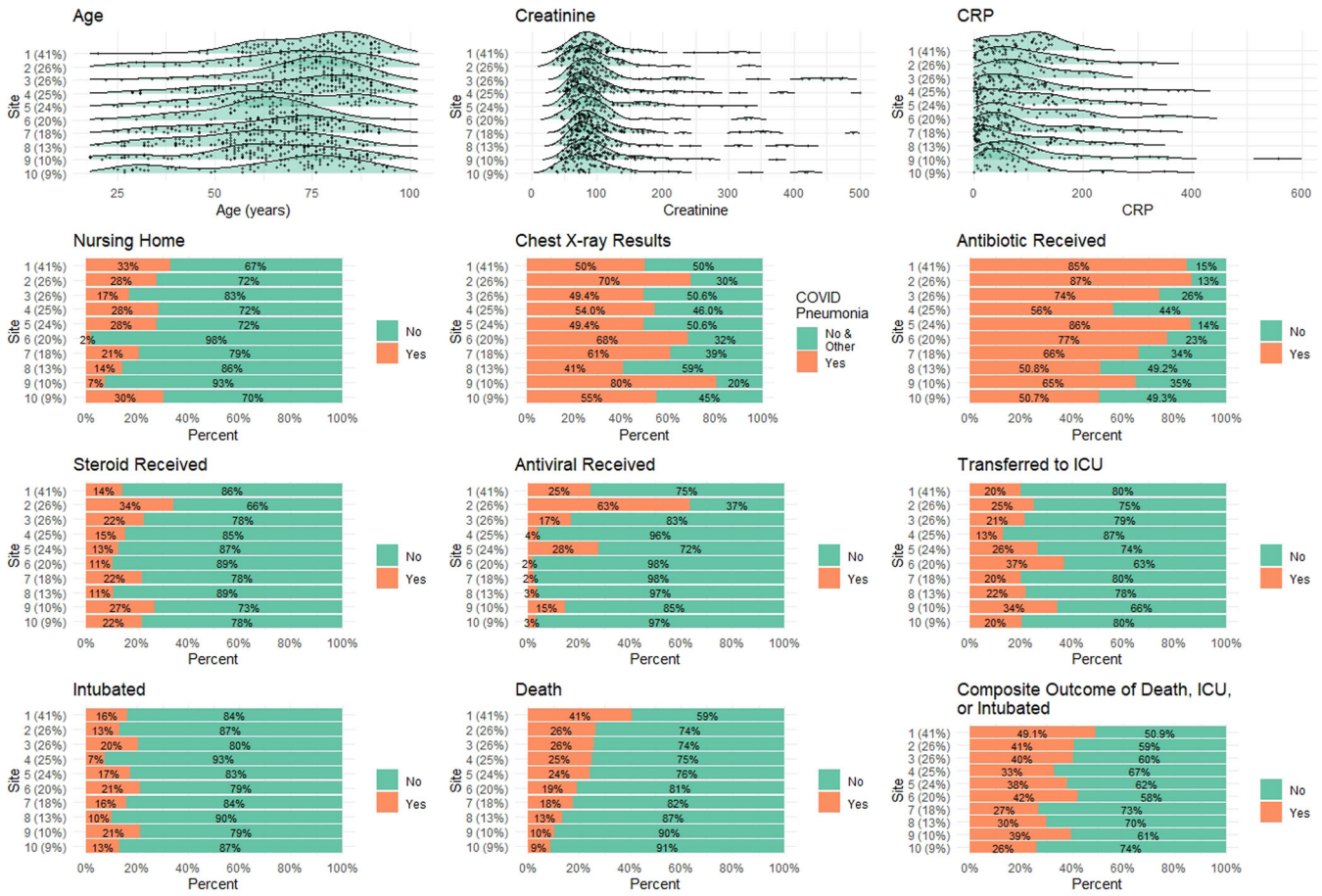

FIGURE 2 Plots of key patient factors and outcomes demonstrating variation across study sites among adults hospitalized with laboratory-confirmed coronavirus disease 2019 (COVID-19) between January 1, 2020 and November 11, 2020 across 10 hospitals in Ontario, Canada. All outcomes were censored at 30 days.

TABLE 2 Results of the multivariable Poisson regression models among adults hospitalized with laboratory-confirmed COVID-19 between January 1, 2020 and November 11, 2020 across 10 hospitals in Ontario, Canada (*N* = 1019) and 8 hospitals in Copenhagen, Denmark (*N* = 215)

	Unadjusted		Adjusted	
	Ontario	Denmark	Ontario	Denmark
Covariate	RR (95% CI)	RR (95% CI)	RR (95% CI)	RR (95% CI)
Age group, ref = <60				
60–69	3.31 (1.78, 6.17)	3.01 (0.61, 14.90)	2.68 (1.39, 5.15)	1.97 (0.40, 9.81)
70–79	4.65 (2.61, 8.30)	5.31 (1.20, 23.53)	3.44 (1.83, 6.48)	4.08 (0.95, 17.57)
80–89	7.41 (4.26, 12.9)	7.05 (1.64, 30.37)	5.40 (2.90, 10.0)	3.37 (0.67, 16.93)
90+	11.9 (6.85, 20.8)	8.05 (1.51, 42.88)	7.84 (4.06, 15.1)	6.19 (1.16, 32.98)
Male sex	1.09 (0.84, 1.41)	1.92 (0.92, 3.99)	1.09 (0.85, 1.41)	1.28 (0.55, 2.97)
Limited English proficiency,[a] ref= no	1.26 (0.88, 1.80)	–	0.80 (0.56, 1.16)	–
Admission location, ref = home				
Nursing home	2.26 (1.75, 2.91)	–	1.22 (0.93, 1.59)	–
Admitted after April 25, 2020	0.70 (0.53, 0.92)	1.81 (0.94, 3.51)	0.91 (0.68, 1.23)	1.56 (0.82, 2.96)
Cardiovascular disease present	2.08 (1.61, 2.69)	3.08 (1.61, 5.89)	1.18 (0.91, 1.53)	1.86 (0.98, 3.52)
Diabetes present	1.69 (1.30, 2.19)	1.23 (0.60, 2.53)	1.18 (0.92, 1.52)	0.69 (0.35, 1.38)
COPD or asthma present	0.97 (0.69, 1.36)	0.54 (0.22, 1.35)	0.86 (0.62, 1.19)	0.65 (0.25, 1.69)
CRP group, ref = 0–15				
15–100	1.85 (0.95, 3.59)	4.40 (0.60, 32.58)	1.47 (0.78, 2.76)	3.46 (0.44, 27.49)
>100	3.07 (1.60, 5.88)	11.47 (1.58, 83.54)	1.99 (1.02, 3.86)	8.85 (1.07, 73.41)
Creatinine group, ref = 0–100				
101–200	2.33 (1.74, 3.12)	3.54 (1.78, 7.03)	1.58 (1.17, 2.12)	2.21 (0.93, 5.27)
>200	2.90 (2.06, 4.08)	2.57 (0.96, 6.89)	1.96 (1.35, 2.84)	1.09 (0.43, 2.81)
Chest X-ray findings, ref = normal				
COVID pneumonia	2.47 (1.51, 4.07)	N/A	1.94 (1.18, 3.17)	N/A
Other	2.62 (1.47, 4.67)	N/A	1.66 (0.94, 2.91)	N/A
Site	Ref	ref = site 1	Ref = 7	ref = site 1
10	0.34 (0.12, 0.94)		0.35 (0.13, 0.94)	
9	0.51 (0.27, 0.99)	0.94 (0.39, 2.29)	0.60 (0.32, 1.13)	0.77 (0.32, 1.82)
8	0.78 (0.44, 1.41)		1.00 (0.60, 1.67)	
5	1.01 (0.56, 1.82)		1.02 (0.59, 1.77)	
6	1.13 (0.60, 2.16)		1.23 (0.63, 2.43)	
2	1.16 (0.65, 2.08)		0.96 (0.54, 1.70)	
3	1.32 (0.78, 2.25)		1.07 (0.62, 1.86)	
4	1.33 (0.82, 2.15)		1.00 (0.64, 1.58)	
1	2.22 (1.43, 3.44)		1.56 (1.00, 2.46)	

Note: Patients who were transferred from external hospitals were excluded from the analysis. All outcomes were censored at 30 days. There were no deaths among hospitalized patients aged <50 years in Denmark.

Abbreviations: CI, confidence interval; COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; CRP, C-reactive protein, N/A, not available; RR, regression ratio.

[a]Limited English proficiency was imputed for one hospital that did not collect this data (*n* = 57 patients).

DISCUSSION

In this international multicentre cohort study of 1364 hospitalized patients with COVID-19, there was wide variation in the risk of in-hospital death across hospitals. However, the large majority of this variation was explained by patient-level factors, and not the care provided within the hospitals themselves. These findings suggest that the observed variation in mortality across hospitals was mostly explained by underlying differences in the patients admitted to each hospital, with differences in the quality or processes of care within a hospital likely playing a much smaller role.

The use of mortality as a measure for reporting hospital performance is commonplace and is often linked at a policy level to fiscal reimbursement.[37] However, our study demonstrates the potential fallibility of mortality as a performance metric without proper adjustment for patient-level differences in the populations served by each hospital. For example, age was found to be the strongest risk factor for death due to COVID-19, which aligns with prior research.[14,15] While rates of ICU admission and invasive ventilation tended to vary by hospital, as has been previously reported[38,39] (which may reflect differences in a culture of practice within an institution[40]), we found that the variation in the risk of death was minimally explained by differences between hospitals and their care practices such as the use of critical care. The overall differences in the use of these resources between Ontario and Denmark may also be related to the fact that Denmark has approximately half the number of ICU beds per capita as Canada, yet a similar ventilator capacity, which may alter thresholds for admission to the ICU and the use of invasive ventilation.[41–43]

Our study is novel because it compares mortality risk due to COVID-19 within large healthcare systems across multiple centers locally, provincially, and internationally. We also included detailed clinical data on the severity of illness of patients at hospital admission, which are shown to be among the strongest predictors of mortality.[5] Given our sole exclusion criteria of test date and patient age, our study sample is also representative of the local population of patients admitted to the hospital for COVID-19. Most prior studies of patients with COVID-19 are limited to single centers or multiple centers within the same health region with a high risk of selection bias.[15,16] Previously, several large cohort studies reported wide variation across centers in unadjusted patient outcomes, such as mortality, readmission, and intubation among patients with a wide range of conditions. In these studies, the observed variation was largely explained by institution-level factors.[38,39,44,45] More recent work examining mortality in hospitalized patients with COVID-19 again demonstrated substantial variation between studies.[2,3,5,9–14] However, when accounting for both important patient and hospital-specific factors in our study, the overall risk of mortality due to COVID-19 was more strongly associated with patient-level factors. Taken together, differences in mortality and patient outcomes in COVID-19 are likely to be largely explained by patient differences, rather than institution-specific differences, such as in care processes.

LIMITATIONS

Our study has limitations. First, we adjusted for both a comprehensive set of patient-level factors known to be associated with mortality in hospitalized patients with COVID-19 and clustered them by site, but the possibility of residual confounding remains. We did not collect the level of oxygenation support at all sites, comorbid cancer, immunocompromise, or obesity, as these were either not known factors early in the pandemic at the time of study creation or were not readily available in the electronic patient chart. Additionally, we were unable to measure individual hospital capacity or the availability of critical care resources at any given time period during the pandemic, which may impact hospital-level care and outcomes.[46,47] The inclusion of these variables in future studies could further increase the relative impact found at a patient level, as opposed to hospital-level data. Second, we studied a relatively early period within the pandemic. Important advances in therapeutics and vaccines have subsequently emerged, and therefore, we may slightly overestimate the overall risk of death.[31] However, we did not observe any important effect of distinct time periods before and after the widespread adoption of these therapeutics, such as dexamethasone, in our analytic models that were associated with mortality risk. Patients who were discharged from the hospital or still alive at the end of the study period may have subsequently died, leading to an underestimation in the risk of death among our cohort. Still, our cohort's 20.2% overall mortality is in line with prior published findings in hospitalized patients with COVID-19 during the early phases of the pandemic.[2–5] Third, we studied patients in two high-income nations, and the generalizability of our findings to middle- and low-income nations is unknown. Fourth, we lacked individual-level data on race, ethnicity, income, and other important socioeconomic factors. These factors are associated with both hospitalization and inpatient mortality,[4,8] and future studies will be needed to understand the effects of these factors on COVID-19 mortality. Fifth, we did not examine variation in outcomes using time-to-event analysis. We intentionally focused on early inpatient outcomes rather than longer-term outcomes because patients with acute COVID generally deteriorate rapidly and many patient and system-level factors may contribute to long-term risk of mortality.

CONCLUSION

There was wide variation in inpatient COVID-19 mortality across hospitals that was largely explained by patient-level factors, such as age and severity of presenting illness. However, hospital-level factors that could have affected care, including resource availability and capacity, were not taken into account. These findings highlight potential limitations in comparing crude mortality rates across hospitals for the purposes of reporting on the quality of care.

ACKNOWLEDGMENT

This study was funded by the Department of Medicine at the University of Toronto.

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CONFLICT OF INTEREST

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Quinn KL, Abdel-Qadir H, Barrett K, et al. Variation in the risk of death due to COVID-19: An international multicenter cohort study of hospitalized adults. *J Hosp Med*. 2022;1-10. doi:10.1002/jhm.12946