International Journal of Infectious Diseases 121 (2022) 1–10

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Mortality trends and length of stays among hospitalized patients with COVID-19 in Ontario and Québec (Canada): a population-based cohort study of the first three epidemic waves☆

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A R T I C L E I N F O

Article history:
Received 23 December 2021
Revised 8 March 2022
Accepted 20 April 2022

Keywords:
COVID-19
hospitalization
mortality risk
length of stay in intensive care units

A B S T R A C T

Background: Epidemics of COVID-19 strained hospital resources. We describe temporal trends in mortality risk and length of stays in hospital and intensive care units (ICUs) among patients with COVID-19 hospitalized through the first three epidemic waves in Canada.
Methods: We used population-based provincial hospitalization data from the epicenters of Canada's epidemics (Ontario and Québec). Adjusted estimates were obtained using marginal standardization of logistic regression models, accounting for patient-level and hospital-level determinants.
Results: Using all hospitalizations from Ontario (N = 26,538) and Québec (N = 23,857), we found that unadjusted in-hospital mortality risks peaked at 31% in the first wave and was lowest at the end of the third wave at 6–7%. This general trend remained after adjustments. The odds of in-hospital mortality in the highest patient load quintile were 1.2-fold (95% CI: 1.0–1.4; Ontario) and 1.6-fold (95% CI: 1.3–1.9; Québec) that of the lowest quintile. Mean hospital and ICU length of stays decreased over time but ICU stays were consistently higher in Ontario than Québec.
Conclusions: In-hospital mortality risks and length of ICU stays declined over time despite changing patient demographics. Continuous population-based monitoring of patient outcomes in an evolving epidemic is necessary for health system preparedness and response.

Introduction

The COVID-19 pandemic has put immense pressure on health care systems. Canada's most populous provinces, Ontario and Québec, bore the brunt of the pandemic (Godin et al., 2021). These 2 provinces accounted for 70% of the country's total number of COVID-19 hospitalizations during the first 3 epidemic waves (INSPQ, 2021; PHO, 2021). The prolonged surges in hospital admissions led to rapid increases in hospital patient load, especially in

Abbreviations: CI, Confidence interval; ICU, Intensive care unit; LTCH, Long-term care home; PHU, Public health unit; VOC, Variant of concern.

☆ Please note that the order of authors has been changed since the first submission, the signed authorship agreement is attached as a supplementary material

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https://doi.org/10.1016/j.ijid.2022.04.048

intensive care units (ICUs), with associated cancellations of nonurgent care (Derfel, 2021; Favaro et al., 2021a, 2021b; Olivier, 2021).

In-hospital mortality provides a proxy measure of the severity of a pandemic and the quality and effectiveness of hospital care (Finelli et al., 2021). Worldwide, in-hospital mortality was highest in the first months of the pandemic but progressively declined afterward (Armstrong et al., 2020; Dennis et al., 2021). Reasons for this decline include changes in who became infected (eg, age and comorbidities) (Cummings et al., 2020; de Rosa et al., 2021), incremental improvements in clinical practice and treatment regimens (Horwitz et al., 2021), and refinement of critical care capacity (Bravata et al., 2021; Harris et al., 2018). However, the evolution of in-hospital mortality across its first three epidemic waves has yet to be systematically examined in Canada, and it remains unclear to what extent these different factors might explain changes in the risk of COVID-19 in-hospital mortality.

During the course of the pandemic, projections of future demands for hospital beds have helped decision-makers to manage and allocate limited healthcare resources (CDC, 2021; INESSS et al., 2020; ScienceTable, 2021). Predicting those demands requires estimates of the number of incoming patients and their length of stays (Rees et al., 2020). Understanding the drivers of in-hospital COVID-19 mortality is important to improve the accuracy of those projections. Additionally, the disproportionate needs for care in ICUs warrant a thorough investigation of temporal changes in length of ICU stays (Deschepper et al., 2021; Shryane et al., 2020). The latter is a key metric that provides information on likely healthcare burden (Rees et al., 2020).

In North America, most studies of in-hospital COVID-19 mortality were informed by the experiences of a single city (Mitra et al., 2020; Verma et al., 2021) or hospital (Mah et al., 2021; Yang et al., 2020) and the generalizability of these findings remains unclear. To address these knowledge gaps, we aim to (i) describe temporal trends in in-hospital COVID-19 mortality risk, (ii) understand drivers of changes in mortality risk, and (iii) estimate changes in length of hospital and ICU stays using data from the two largest provinces in Canada, where over 60% of the population reside.

Methods

Study design and setting

We conducted a retrospective population-based cohort study using provincial COVID-19 hospitalization databases from Ontario and Québec. Both provinces have a universal healthcare system and these databases capture all hospitalizations. Healthcare is under provincial jurisdiction and the magnitude of epidemic waves and clinical protocols for patients with COVID-19 differ across provinces.

Cohort eligibility criteria

Cohort entry occurs when individuals are admitted to an Ontario or Québec hospital with a COVID-19 diagnosis or the date of diagnosis if it occurs a week or more after admission (ie, presumed nosocomial infections) (Elkrief et al., 2020). We included all hospitalizations with a laboratory-confirmed COVID-19 diagnosis, admitted between March 1, 2020 and May 31, 2021 in Ontario and Québec. All observations were censored at discharge, death, or on August 15, 2021, whichever occurred first. Among the very few individuals that experienced reinfection, only hospitalizations related to the first laboratory-confirmed episode were included in Québec because reinfections are milder than primary infections (Qureshi et al., 2022). In Ontario, it is not possible to differentiate reinfection. Patients admitted or tested after discharge were excluded. Participants with missing date of discharge were excluded from the analyses of length of stays (Figure 1).

Data sources

Hospitalization data for Ontario was obtained from the Ontario's *Case and Contact Management* (CCM+), a provincial surveillance database for reporting diseases of public health significance. The approaches dealing with missing observations are summarized in Supplementary Text 1. Information on daily hospital capacity came from the bed census summary dataset. In Québec, data were obtained from the *Maintenance et exploitation des données pour l'étude de la clientèle hospitalière database* (MED-ÉCHO live). Daily hospital capacity data for each hospital were abstracted from the *Relevé quotidien du centre hospitalier*.

Outcome and variables

A total of three primary outcomes were studied. The first was all-cause in-hospital mortality, defined as a death occurring within 28 days of admission, which was in line with other studies (Churpek et al., 2021; Docherty et al., 2021; Group, 2021; UKHSA, 2022). Patients discharged or dying after 28 days were coded as alive at 28 days. The other outcomes were the length of hospital and ICU stays, defined as time from hospital and ICU admission, respectively, to discharge or death (inclusive of the latter; with no censoring).

We categorized patients on the basis of their admission date and corresponding epidemic wave: Wave 1 (before August 1, 2020), Wave 2 (August 1, 2020–March 20, 2021), and Wave 3 (after March 20, 2021). Hospitalizations with a first positive specimen for SARS-CoV-2 collected 7 days or more after admission, or whose living environment is the hospital, were classified as hospital-acquired infection. In such cases, the date of hospital admission for COVID-19 was replaced with the date of the first positive specimen to better reflect the time of infection. Patients who were admitted to the ICU the same day as their hospital admission were defined as direct ICU admission. Patients screened positive for a variant of concern (VOC), through mutations N501Y and E484K in Ontario and N501Y, del69/70, and E484K in Québec, were regarded as VOC-positive (mostly B.1.1.7, with some B.1.351 and P.1). Only those whose specimen was collected 14 days after their second dose were treated as vaccinated (only available in Québec by linking the provincial vaccine registry and MED-ÉCHO databases). Overall hospital load of patients with COVID-19 relative to hospital bed capacity (henceforth, hospital patient load) was calculated daily using the number of patients with COVID-19 currently hospitalized as the numerator and bed capacity (regular + ICU) as the denominator for each of the 88 hospitals in Québec and at the level of the 34 public health units in Ontario (due to data limitations). The distribution of all patient loads was categorized into quintiles from the lowest to highest independently for each province. The ICU patient load relative to the ICU bed capacity (henceforth, ICU patient load) was calculated on the basis of the same algorithm but using ICU bed capacity as the denominator. The gender of hospitalized patients (as a proxy for biological sex) was not available in Québec.

Statistical analyses

Unadjusted weekly mortality risk, stratified by age, wave, and quintiles of patient load were calculated as the proportion of patients admitted with COVID-19 that deceased within 28 days for each time period and group. Uncertainty was quantified using 95% Clopper-Pearson confidence intervals (CIs). Generalized linear models were used to fit smoothed curves of the weekly mortality risk

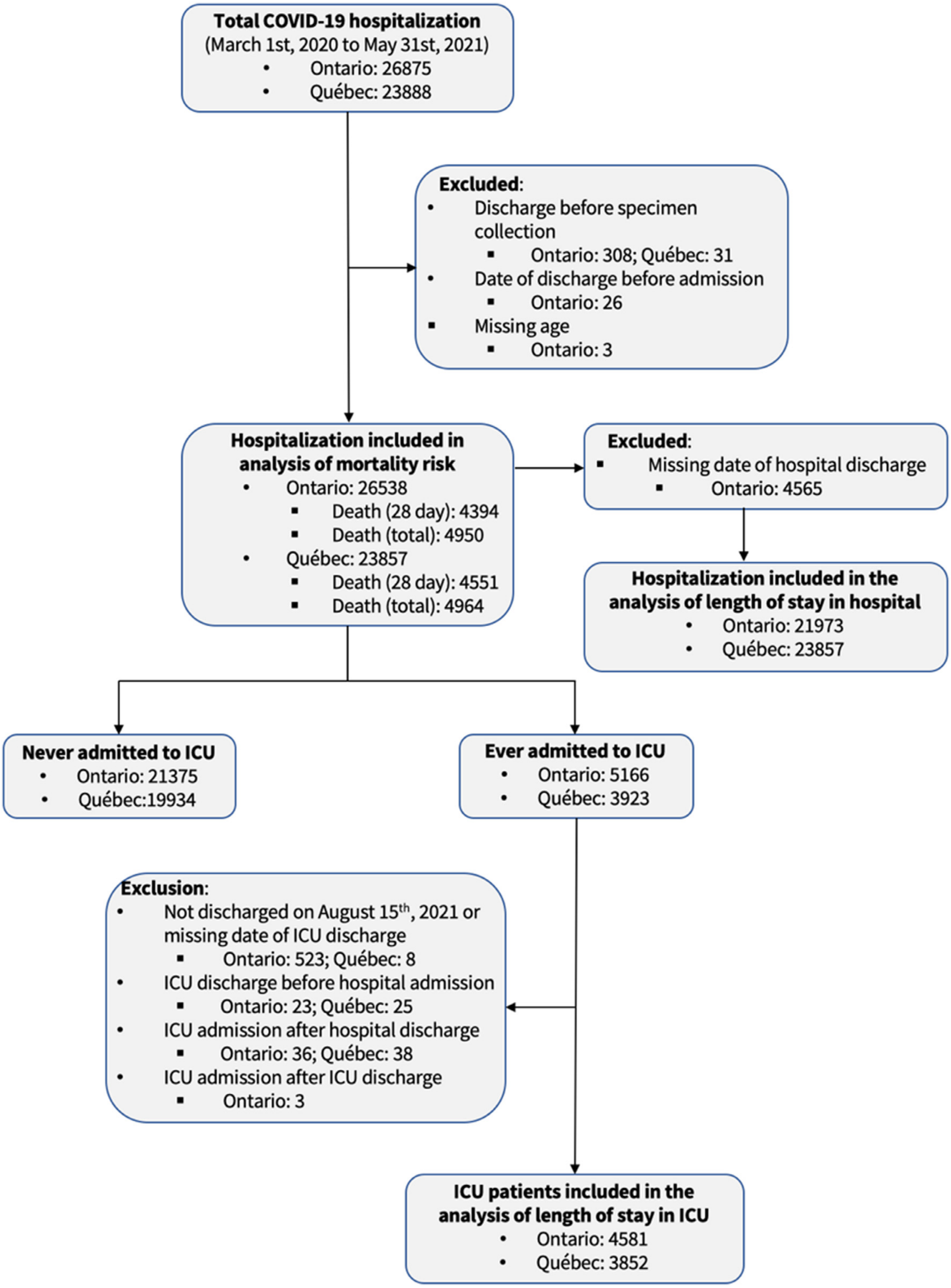

Figure 1. Flowchart of patients hospitalized with a laboratory-confirmed SARS-CoV-2 diagnosis included in the different analyses, by province (March 1, 2020–May 31, 2021).

(with cubic spline for the week of admission) and the mortality risk by age and wave. All analyses were performed for each province separately.

Adjusted estimates of mortality risk were obtained using logistic regression models with cubic splines for calendar time (3 knots). Additionally, the models adjusted for patient-level characteristics and hospital-level determinants. Patient-level variables included those associated with severe outcome: age (cubic spline with knots at 50, 70, and 80 years; chosen using the Akaike Information Criterion), gender (in Ontario), whether the patient was a resident of long-term care homes (LTCH), hospital-acquired infections status, direct ICU admission, VOC status, and vaccination status (in Québec) (Booth et al., 2021; Challen et al., 2021; Churpek et al., 2021; Lv et al., 2021). Hospital-level determinants comprise the COVID-19 hospital patient load (quintile ranking) at time of admission (Block et al., 2021) and facility-level fixed effects to control for measured/unmeasured time-invariant confounders. Because of lack of data disaggregation in Ontario, both patient load and region fixed effects were included at the public health unit level (PHU). Marginal standardization was used to obtain adjusted mortality risks over time, standardizing over all hospitalized patients. The 95% CI for overall adjusted mortality risks were generated using 1000 bootstrap replicates.

Finally, we examined change in hospital and ICU length of stays. Specifically, we calculated mean and standard deviation and used Kaplan-Meier stratified by age groups (0–49, 50–59, 60–69, 70–79, 80 years and older), by waves, and by hospital and ICU patient load quintiles. The significance of differences between survival curves was assessed using log-rank tests.

Ethics approval

Ethics approvals were obtained from the *Health Sciences Research Ethics Board* of University of Toronto (no. 39253) in Ontario and the *Institutional Review Board* of Faculty of Medicine and Health Sciences of McGill University in Québec (A06-M52-20B).

Results

There were 26,538 (Ontario) and 23,857 (Québec) COVID-19 hospitalizations during the study period. Among them, 4950 (Ontario) and 4964 (Québec) deceased. Most of the deaths occurred within 28 days of admissions: 4394 (89%) in Ontario and 4551 (92%) in Québec. Nearly one fifth of patients were admitted to the ICU during their hospital stay: 5166 (20%) in Ontario; 3923 (16%) in Québec. Hospital patient load ranged from 0%–47% in Ontario and 0%–51% in Québec (Table S1). The ICU patient load varied between 0%–83% in Ontario and between 0%–123% in Québec.

Hospitalization profiles varied over time: patients admitted during the third wave were younger than those admitted during the first two waves (Table 1). Patients with presumed hospital-acquired infections, those admitted directly to the ICU, those who were not fully vaccinated, and those infected with a VOC were more likely to die in the hospital. A decrease in the proportion of hospitalizations transferred from LTCH occurred after the first wave. These patients experienced higher mortality risk throughout the whole study period in Ontario. In Québec, however, LTCH patients were less likely to die in hospitals during the third wave, reflecting partly changes in directives between waves related to these transfers.

Time trends in crude mortality risk among hospitalized patients with COVID-19

The time trends in crude mortality risk were similar between provinces (Figure 2). In the first two months of the epidemic, the probability of in-hospital death peaked at 31% (95% CI: 27%–35%) in Ontario and 31% (95% CI: 28%–34%) in Québec, followed by a gradual decrease in mortality that lasted until the beginning of the second wave. Thereafter, the risk of in-hospital death gradually increased but plateaued at lower levels than in the first wave at 23% (95% CI: 20%–27%) in Ontario and 23% (95% CI: 19%–27%) in Québec. In both provinces, the risk declined from the middle of the second wave. Overall, the unadjusted mortality risk followed the number of new hospitalizations except for the third wave when mass vaccination was taking place.

There was a strong gradient in mortality risk with age in both provinces and generally, the absolute mortality risk decreased over time for all age groups (Figure 2). However, there may have been less of a difference among those aged 60–84 years between the second and third wave in Québec. Hospital patient load was also associated with mortality risk in the crude analyses in Québec: there was a monotonic increase in crude mortality risk with increasing quintiles of facility-level patient load (Figure S1). The trend in Ontario, where patient load was measured at the level of PHU, was stable through patient load quintiles.

Adjusted mortality risk over time

After adjusting for age, living environment, hospital-acquired infection status, direct ICU admission, VOC and vaccination status, and time-varying quintiles of hospital patient load, the estimated temporal trend in mortality risk was similar to the unadjusted ones in both provinces (Figure 3). Despite this, Québec exhibited a more pronounced decrease in the estimated mortality risk at the beginning of the epidemic: from 37.1% (95% CI: 27.7%–45.8%) to 15.2% (95% CI: 13.2%–17.4%). In Ontario, the estimated decline for the same period was from 24.7% (95% CI: 18.7%–31.6%) to 13.5% (95% CI: 11.3%–16.0%). The adjusted highest mortality risks during the second wave were comparable in Ontario (18.9%; 95% CI: 18.0%–19.8%) and in Québec (18.2%; 95% CI: 17.3%–19.0%) but the decline in the third wave was more pronounced in Ontario.

In the adjusted analyses, mortality risk was higher at the second and highest patient load quintile in Ontario, whereas it increased with the patient load in Québec. The adjusted odds of in-hospital mortality in the highest patient load quintile were 1.2-fold (95% CI: 1.0–1.4) and 1.6-fold (95% CI: 1.3–1.9) that of the lowest one in Ontario and Québec, respectively (Table S1). Additionally, the odds among patients that were male ($aOR_{Ontario}$: 1.4; 95% CI: 1.3–1.5), LTCH residents ($aOR_{Ontario}$=2.4, 95% CI: 2.1–2.7; $aOR_{Québec}$=1.7, 95% CI: 1.5–2.0), with presumed hospital-acquired infections ($aOR_{Ontario}$=1.5, 95% CI: 1.4–1.7; $aOR_{Québec}$=1.0, 95% CI: 1.0–1.2), directly admitted to the ICU ($aOR_{Ontario}$=3.7, 95% CI; 3.3–4.1; $aOR_{Québec}$=2.5, 95%CI: 2.1–3.1), or were infected with a VOC ($aOR_{Ontario}$=2.0, 95% CI: 1.7–2.3; $aOR_{Québec}$=1.3, 95% CI: 1.0–1.7) were higher in both provinces. In Québec, none of the fully vaccinated hospitalized patients with COVID-19 died.

Hospital and intensive care length of stays

Over the whole study period, the average length of ICU stays was longer in Ontario (17.2 days) compared to Québec (12.9 days; p-value <0.01). This trend was observed for all age groups (all p-values <0.01; Table S3). Length of stays in the ICU decreased steadily over time in Ontario from 19.4–15.6 days (all pairwise p-values <0.01; Figure 4). In Québec, average length of ICU stays were 13.5 days during the first wave and then stabilized at 12.6 days. Age was associated with length of stays in both province: hospitalized individuals aged 0–49 years and those aged 80 years and older spent less time in the ICU than others age groups (all pairwise p-values <0.01). The age-specific pattern was generally consistent across epidemic waves. Additionally, there was a trend of shorter length of stays in the ICU among hospitalized patients younger than 70 years of age with each wave in Ontario (p-value <0.01; Figure S2). No conclusive pattern was observed for the length of stays by ICU patient load (Figure S3). Patients who died and those who never used a ventilator spent less time in the ICU (p-value <0.01, except for the third wave; Figure S4–S5).

Overall length of hospital stays decreased over time from 17–19 days to 12 days (all pairwise p-values <0.01; Table S4). The between-province differences were smaller compared to length of ICU stays. Younger patients had shorter stays then those older than 60 years (p-value <0.01, Figure S6) and this pattern was consistent over time. In Québec, higher patient loads were associated with shorter length of hospital stays across time (p-value <0.01, except for third wave; Figure S7). The patterns by survival and ventilation status were similar as those for the ICU.

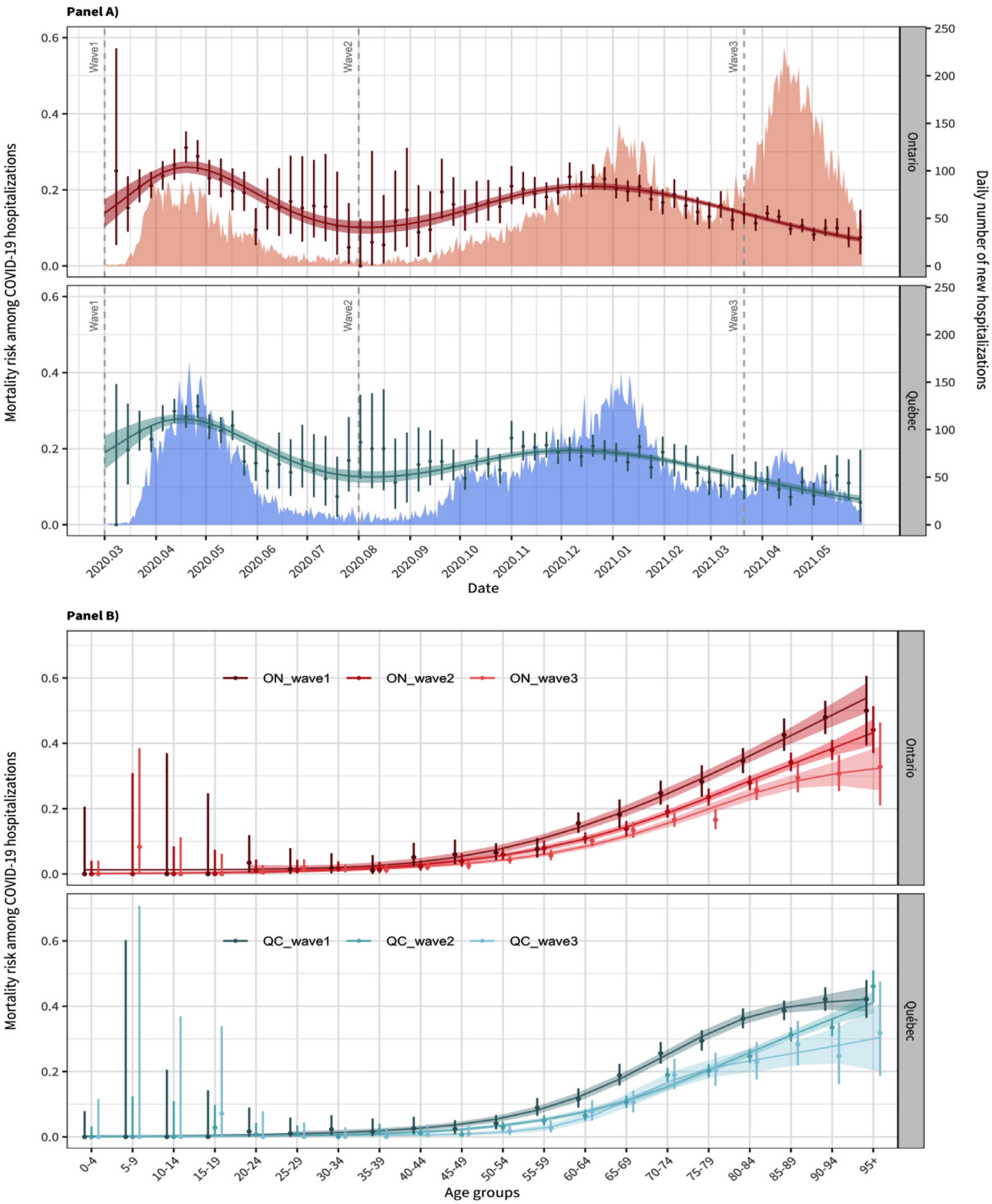

Figure 2. Panel A: Unadjusted weekly mortality risk among patients hospitalized with COVID-19 in Ontario and Québec. Point estimates are presented with 95% Clopper-Pearson confidence intervals. Mortality for the first week of March 2020 is not presented as only 5 and 1 patients were admitted in Ontario and Québec, respectively. Fitted mortality risk over time using binomial logistic regression models with cubic splines for week of admission are shown (curves) with associated confidence intervals (shaded areas around the curve). Daily numbers of new patients hospitalized with a COVID-19 diagnosis were presented as the shaded background. **Panel B**: Unadjusted mortality risk among patients hospitalized with COVID-19 by 5-year age groups, stratified by epidemic waves, with 95% Clopper-Pearson confidence intervals in Ontario and Québec. For each age group, mortality risks during Wave 1 (before August 1, 2020), Wave 2 (August 1, 2020 to March 20, 2021), and Wave 3 (March 21, 2021 to May 31, 2021) are shown separately in that order from left to right. There was no hospitalization aged 5–9 years in Ontario during Wave 1.

Table 1
Characteristics of patients hospitalized with a laboratory-confirmed SARS-CoV-2 diagnosis and proportion deceased in Ontario and Québec (March 2020 to May 2021).

	Ontario (N = 26,538)			Québec (N = 23,857)		
	Wave 1 (N = 4,751)	Wave 2 (N = 12,062)	Wave 3 (N = 9,725)	Wave 1 (N = 7,437)	Wave 2 (N = 13,240)	Wave 3 (N = 3,180)
Number of deaths						
	1,078	2,248	1,068	1,866	2,361	324
Overall mortality risk [95% confidence interval]						
	22.7% [21.5-23.9%]	18.6% [17.9-19.3%]	11.0% [10.4-11.6%]	25.1% [24.1-26.1%]	17.8% [17.2-18.5%]	10.2% [9.2-11.3%]
Age; mean (SD)						
At admission	67.8 (18.1)	68.3 (18.9)	59.9 (18.6)	71.5 (18.5)	69.9 (19.3)	60.8 (18.7)
At death	79.2 (12.5)	79.8 (11.8)	74.0 (13.2)	81.6 (10.7)	82.0 (10.5)	76.7 (11.2)
Sex; proportion (proportion deceased)						
Male	53.4% (23.0%)	54.2% (19.5%)	54.4% (11.8%)	Data not available		
Female	46.6% (22.3%)	45.5% (17.6%)	44.8% (9.9%)			
Other	0.1% (33.3%)	0.3% (20.5%)	0.8% (12.3%)			
Living in long-term care homes; proportion (proportion deceased)						
Yes	18.7% (41.6%)	8.5% (42.7%)	0.4% (30.8%)	11.3% (41.8%)	2.8% (33.2%)	1.3% (2.4%)
No	81.3% (18.3%)	91.5% (16.4%)	99.6% (10.9%)	88.7% (23.0%)	97.2% (17.4%)	98.7% (10.3%)
Presumed hospital-acquired infection; proportion (proportion deceased)						
Yes	10.8% (29.9%)	16.2% (24.4%)	6.4% (23.3%)	16.1% (31.2%)	13.4% (21.0%)	4.6% (20.7%)
No	89.2% (21.8%)	83.8% (17.5%)	93.6% (10.1%)	83.9% (23.9%)	86.6% (17.3%)	95.4% (9.7%)
Ever admitted to ICU; proportion (proportion deceased)						
Yes	21.5% (28.9%)	17.6% (30.3%)	20.7% (22.9%)	20.0% (24.6%)	19.6% (24.7%)	23.6% (18.2%)
No	78.5% (21.0%)	82.3% (16.1%)	79.3% (7.9%)	80.1% (25.2%)	80.4% (16.2%)	76.4% (7.7%)
Direct admission to ICU; proportion (proportion deceased)						
Yes	11.8% (31.6%)	8.2% (31.9%)	9.1% (22.7%)	3.1% (22.8%)	3.1% (24.2%)	4.4% (23.6%)
No	88.2% (21.5%)	91.8% (17.5%)	90.9% (9.8%)	96.9% (25.2%)	96.9% (17.6%)	95.6% (9.6%)
Fully vaccinated before positive test; proportion (proportion deceased)						
Yes	Data not available			Data not available		0.1% (0.0%)
No						99.9% (10.2%)
Infected with variants of concern; proportion (proportion deceased)						
Yes	Not applicable	4.7% (20.4%)	55.3% (14.2%)	Not applicable		39.8% (11.6%)
No		95.3% (18.6%)	44.7% (7.0%)			60.2% (9.3%)

ICU = intensive care unit.
[a]Only deaths occurred within 28 days of admission were included.
[b]Wave 1: March 1, 2020 to July 31, 2020); Wave 2: August 1, 2020 to March 20, 2021; Wave 3: March 21, 2021 to May 31, 2021.

Discussion

Using population-based provincial surveillance databases containing records of all hospitalized patients with COVID-19 in the two largest Canadian provinces, this study found important variations in mortality risk. Part of the observed decline over the three epidemic waves could be explained by changes in patient characteristics. Specifically, we found that the demographic profile of those acquiring infection (eg, age, LTCH residents), hospital-acquired infections, VOC, and higher patient loads were associated with higher mortality risk. During periods of highest patient load, the adjusted in-hospital mortality increased in both provinces. The length of ICU stay was consistently longer in Ontario than Québec. Patients aged 0–49 years and those 80 years and older were discharged from the ICU more rapidly.

The observed substantial decrease in mortality risk during the first wave in both provinces is consistent with results from studies in the United Kingdom and the United States that adopted the same definition of in-hospital death (Anesi et al., 2021; Docherty et al., 2021; Jones et al., 2021). Furthermore, given the discrepant epidemiological curves between Ontario and Québec, the similarity in the adjusted temporal trends in mortality risk also provides evidence that factors beyond patient profiles could have played a role. Reasons behind the persistent reduction in mortality could include adoption of new therapeutics and treatments. For example, dexamethasone and anti-IL-6 receptor monoclonal antibodies, which have been shown to reduce mortality among severely ill patients in the RECOVERY trial (Group, 2021), became part of treatment guidelines in early summer of 2020. Other potential factors include the cumulative experiences of hospital teams and the availability of updated evidence-based COVID-19 protocols (Asch et al., 2021; Coppock et al., 2021; Jones et al., 2021). The availability of the first doses of COVID-19 vaccines in the third wave may also have contributed to the continuous decreasing mortality risk during that period (Scobie et al., 2021).

Overall, our analyses suggest that part of in-hospital mortality risk reductions could be sustained if hospital capacity is maintained and hospital-acquired infections are prevented. These findings are aligned with those from studies conducted worldwide (Bravata et al., 2021; Elkrief et al., 2020; French et al., 2021; Gray et al., 2021; Ponsford et al., 2021). Limited critical care resources and rapidly increasing staff-to-patient ratio could have influenced patient outcomes during periods of high transmission (Docherty et al., 2021; Sprivulis et al., 2006). Additionally, nosocomial infections could exacerbate mortality risk because this population has vulnerable health conditions and comorbidities (Ponsford et al., 2021; Richterman et al., 2020).

Concomitant with reductions in mortality risks, decreases in the length of ICU stays have been observed in multiple settings during the first wave (Roth et al., 2021; Shryane et al., 2020). Our results suggest a continuous decline in ICU stay throughout the study period. Despite the similar temporal patterns between provinces, we observed that the length of ICU stay in Ontario was consistently longer than it in Québec, and the proportion of patients admitted to the ICU was higher in Ontario as well. Interprovincial differences in clinical practices, such as criteria for ICU admission and discharge, could explain part of these differences; other reasons include the changing demographic profiles of COVID-19 admissions. For example, patients aged 0–49 years and those 80 years and older spent less time in the ICU than the others. Potentially because younger patients ($\leq$50 years) improve more rapidly (Voinsky et al., 2020) and those in the oldest age group experience higher mortality in the ICU (ICNARC, 2020; Oliveira et al., 2021). These findings are consistent with the observed shorter

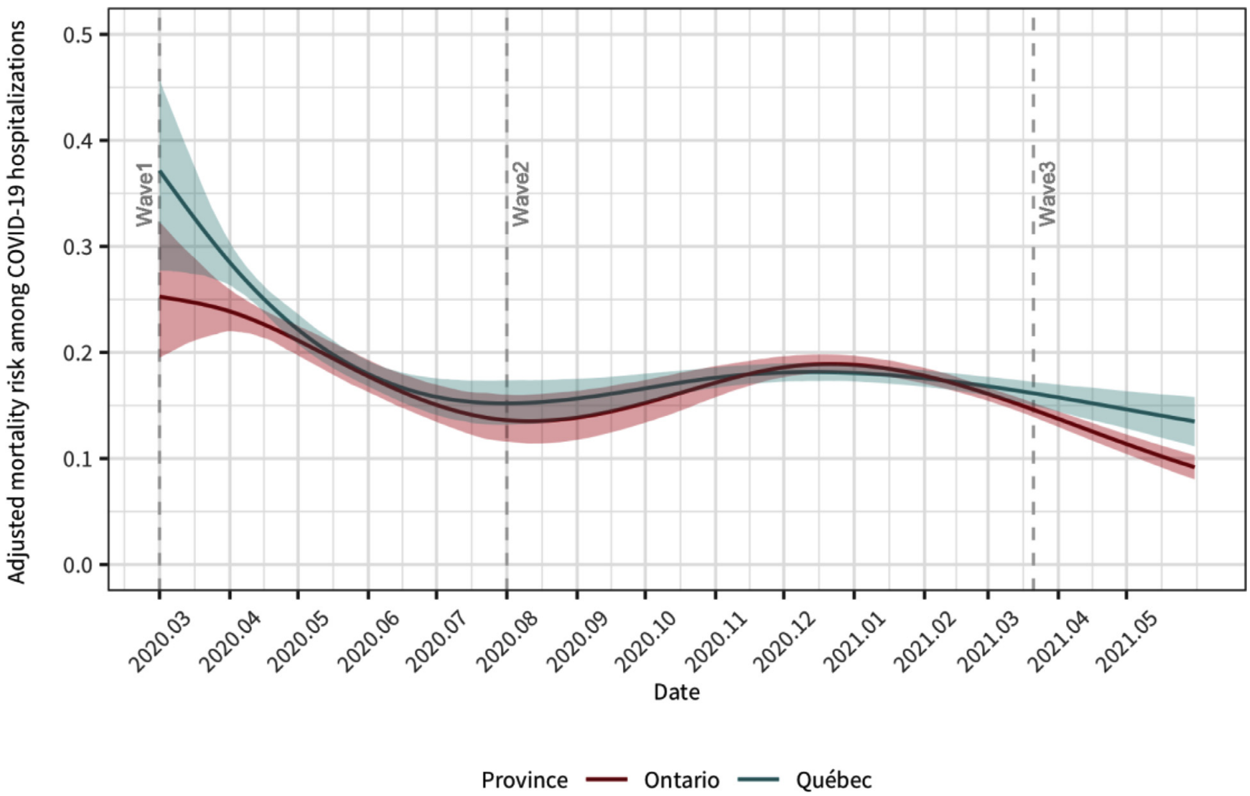

Figure 3. Adjusted mortality risk among patient hospitalized with COVID-19 and 95% bootstrapped confidence intervals in Ontario (in red) and Québec (in blue) since March 1, 2020. The models were adjusted for quintile of hospital patient load at time of admission, age (cubic spline with 3 knots at 50, 70, and 80 years), sex (in Ontario), whether the patient was from long-term care home, had a hospital-acquired infection, direct admission to the intensive care unit, infection with a variant of concern, full vaccination status (in Québec), and either facility-level fixed effects (in Québec) or public health unit-level fixed effects (in Ontario). The absolute adjusted mortality risks were obtained by marginalizing over each province patient's characteristics, which respective distributions differ slightly.

ICU stay among those who died and those who never used a ventilator.

Tracking the evolution of patient outcomes can help improve hospital services, supply chain management, human resources planning, and prioritize future research (Bateson and McPeake, 2022). Additionally, the average length of ICU stays is a critical metric required to project census ICU beds, which has been a limiting factor of healthcare systems in several settings (Lapidus et al., 2020). Timely availability of high-quality surveillance data should be prioritized. Despite differences in the proportion of patients admitted to the ICU and their length of stay, the in-hospital mortality risks were relatively consistent between Ontario and Québec. Improving our understanding of the ICU demand may contribute to optimize patient outcomes, help planning for sufficient hospital capacity, and adapt to potential increases in patient flows (Bravata et al., 2021; Rossman et al., 2021).

Our study should be interpreted considering certain limitations. First, we were unable to control for sex (Zha et al., 2021), ethnicity (Price-Haywood et al., 2020; Xia et al., 2022), and comorbidities(Garibaldi et al., 2021)—factors that could be associated with COVID-19 mortality. Although we were able to control for some of the main predictors of COVID-19 mortality (eg, age, hospital-acquired infections, LTCH residents), we cannot rule out residual confounding. Additionally, we considered all patients with a laboratory-confirmed SARS-CoV-2 diagnosis; although, it might not be the principal reason for the hospitalization. Second, the administrative and surveillance databases used do not provide detailed information on treatments received by patients. This limitation hampered our ability to examine how evolving standards of care and specific treatments affected mortality outcomes. Third, we defined our mortality outcome as patients who died within 28 days after admission, which may slightly underestimate mortality risk. However, this definition captures close to 90% of the total in-hospital deaths and our results are robust to expanding the death definition to within 56 days of admission. Additionally, it has the merit of measuring the immediate impact of COVID-19 on deaths more accurately (Heneghan and Oke, 2020). Fourth, the CCM+ data from Ontario did not allow the addition of facility-level variables and vaccine status. We addressed this by using PHU-level variables to (partially) control for interhospital variations. Further, the lack of vaccine status should not affect the results based on the small number of fully vaccinated patients ($<$0.01%) and the similar timeline of vaccination program implemented during the study period. Finally, missing dates of discharge in Ontario were assumed to be missing completely at random. The potential for bias is low, however, as these errors in data entry and transmission are likely independent of hospitalization—as shown in our examination of the characteristics of hospitalizations with observed and missing dates of discharge.

Strengths of this study includes its representativeness: all hospitalizations in these two provinces are included. This study also adds considerably to the timeline—spanning over three epidemic waves—of COVID-19 inpatient mortality risks and length of ICU stays. We controlled for some of the key confounders and results were relatively consistent across provinces operating under different health jurisdictions.

In conclusion, this study demonstrates temporal variability in mortality risk among hospitalized patients that could not be explained by changes in demographic profiles of patients with COVID-19 across epidemic waves. Findings highlight the importance of strategies to buffer against surges in hospital capacity and limiting nosocomial outbreaks to reduce in-hospital mortal-

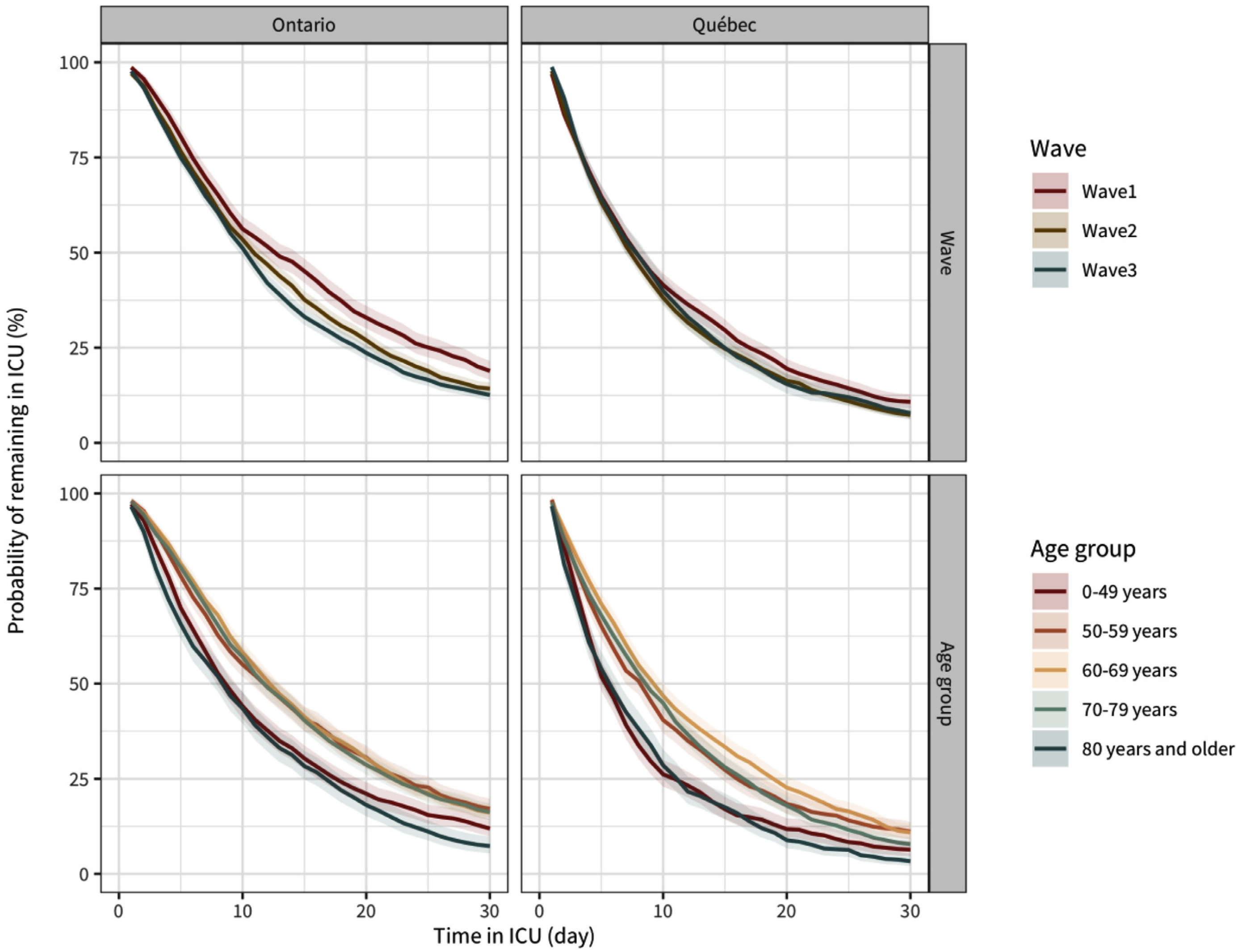

Figure 4. Kaplan-Meier curves for length of stays in intensive care units (ICU) among patients hospitalized with COVID-19, stratified by age group and by wave, in Ontario (top row) and Québec (bottom row). Waves are defined as followed: first wave 1 (before June 30, 2020), second wave (August 23, 2020 to March 20, 2021), and third wave (March 21, 2021 to May 31, 2021).

ity risk. As the epidemic continues, there remains a potential for future surges from emergence of new variants especially if associated with increased virulence, the potential for waning protection against severity from vaccines, and the potential for reduction in hospitalization with the scale-up of outpatient therapeutics. Hence, continued monitoring of the evolution of patient outcomes and re-evaluation of the length of ICU stay will be essential to adapt and inform hospital capacity planning to improve patient outcomes.

Authors' contribution

YX, SM, DB, and MMG conceived and designed the study. YX conducted the statistical analysis, conducted the literature search, and drafted the manuscript. HM supported data curation and cleaning for Ontario. HM, DB, MB, BS, AC, AV, IG, NK, SM, and MMG interpreted results, drafted and edited the manuscript, and critically reviewed it for intellectual content. All authors approved the final version of the manuscript.

Acknowledgments

This work was supported by McGill's Interdisciplinary Initiative for Infection and Immunity (Mi4) (to MM-G) and a grant from the Canadian Institutes of Health Research (to SM). YX is supported by a doctoral award from the Fonds de recherche du Québec – Santé (FRQS). BS research program is funded by a Canada Research Chair (Tier 2) in Economics of Infectious Diseases; MM-G research program is funded by a Canada Research Chair (Tier 2) in Population Health Modeling; NK is supported by a career award from the Fonds de Recherche Québec – Santé (FRQ-S; Junior 1); and SM research program is funded by a Canada Research Chair (Tier 2) in Mathematical Modeling and Program Science. The Ontario datasets were made available by the Ontario Ministry of Health. All Québec datasets came from Québec Health Insurance databases (Régie de l'assurance maladie du Québec, RAMQ) and databases from the Québec Ministry of Health and Social Services (Ministère de la Santé et des Services sociaux, MSSS). The access to these databases is made possible through a tripartite agreement between the MSSS, the RAMQ, and the Institut national d'excellence en santé et en services sociaux.

Declaration of interest

MM-G reports an investigator-sponsored research grant from Gilead Sciences Inc., and contractual arrangements from the Institut national de santé publique du Québec (INSPQ), the Institut d'excellence en santé et services sociaux (INESSS), the World Health Organization, and the Joint United Nations Programme on

HIV/AIDS (UNAIDS), all outside of the submitted work. NK reports research funding from Gilead Sciences; advisory fees from Gilead Sciences, ViiV Healthcare, Merck, and Abbvie; and speaker fees from Gilead Sciences and Merck, all outside of the submitted work.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijid.2022.04.048.

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