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CLINICAL INVESTIGATION

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Institutional, therapeutic, and individual factors associated with 30-day mortality after COVID-19 diagnosis in Canadian long-term care facilities

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Abstract

Background: Canadian long-term care facility (LTCF) residents experienced higher death rates compared to other countries during the first wave of the COVID-19 pandemic. This cohort study analyzes the individual, therapeutic, and institutional factors associated with death in LTCFs.

Methods: Institutional data for 17 LTCFs in Montreal, Canada were obtained from local administrative registries. Individual data for 1197 residents infected by SARS-CoV-2 between February 23 and July 11, 2020 were obtained through chart reviews. A multivariable modified Poisson regression model, which accounted for LTCF clustering, was used to identify resident and facility covariates associated with 30-day mortality after COVID-19 diagnosis.

Results: Severe shortage of licensed practical nurses (RR 2.60 95% CI 1.20–5.61) and medium-sized facilities compared to smaller-sized facilities (RR 2.73 95% CI 1.23–6.07) were associated with 30-day mortality. Later COVID-19 diagnosis (RR 0.98 95% CI 0.97–0.99 per additional day) was associated with survival. Individual risk factors for death included age (RR 1.33 95% CI 1.23–1.45 per additional 10 years), male sex (RR 1.46 95% CI 1.24–1.71), functional impairment (RR 1.08 95% CI 1.04–1.12 per unit increase of SMAF), as well as a diagnosis of congestive heart failure (RR 1.31 95% CI 1.04–1.66) and neurocognitive disorder (RR 1.31 95% CI 1.01–1.70). Among severe cases, anticoagulation was associated with survival (RR 0.70 95% CI 0.51–0.96).

Conclusions: This study identified practical nurse shortages and facility size as institutional risk factors for COVID-19 death. Anticoagulation was associated with survival among severe cases.

KEYWORDS

COVID-19, death, long-term care

INTRODUCTION

The COVID-19 pandemic has disproportionately affected the older adult population in long-term care facilities, especially in Canada, where death rates during the first wave were among the highest in the world.[1] Despite extensive literature on COVID-19 mortality risk factors in the hospital-based and general population, long-term care models incorporating both individual-level and institutional-level risk factors are lacking and much of the current evidence is of low certainty, with no clinical trials.[2,3] Furthermore, older adults are vastly underrepresented in COVID-19 drug therapy trials.[4]

At the individual level, older adults living in long-term care facilities (LTCFs) are especially vulnerable to COVID-19 complications because of the interaction between advanced age and multimorbidity.[5,6] Institutional and environmental factors specific to LTCFs also contribute to COVID-19 vulnerability, including: high occupancy density, shared living spaces, residents with cognitive and behavioral problems, lack of human and material resources, and outdated infrastructure.[7] These combined risk factors, as well as failure to adequately prepare LTCFs in the early days of the pandemic,[8] led to high case fatality ratios, estimated between 14% and 53%,[9–19] and swift disease progression (average time to death of 10 days).[10,20]

In Quebec, Canada's second-largest province (8.6 million inhabitants), the long-term care facility population accounted for 16% of all COVID-19 infections and nearly 70% of COVID-19 deaths, by the end of the first wave on July 11, 2020.[21] Of 453 LTCFs in the province, 178 had at least one case and the average case fatality ratio was 40%.[22] Given that COVID-19 mortality varied greatly from one facility to another, the objective of this study was to investigate known and novel explanatory factors at the resident and facility levels.

Key points

- Among a Canadian cohort of 1197 long-term care facility (LTCF) residents diagnosed with COVID-19 in the first wave of the pandemic, shortage of licensed practical nurses and facility size were associated with 30-day mortality.
- Administration of anticoagulation was associated with a lesser risk of death among severe cases.
- Individual risk factors for death included age, male sex, functional impairment, as well as a diagnosis of congestive heart failure or neurocognitive disorder.

Why does this paper matter?

Interventions and policies aiming to mitigate staff shortages and facility size, as well as the use of anticoagulation among severe cases, may help protect LTCF residents in the event of future COVID-19 outbreaks.

METHODS

Study population

Located at the epicenter of the country's COVID-19 epidemic, the Montreal Center-South district (MCS) was home to 2595 residents living in 17 publicly funded LTCFs (see Supplementary Text S2), of which 1197 contracted COVID-19 and 456 (37%) died from the illness during the first wave (defined by local public health authorities as February 23 to July 11, 2020[22]). Attack rates per facility ranged from 0.8% to 77.4%, while case fatality ratios per facility ranged from 0% to 52.1% (see Table S3).

At the beginning of the pandemic, each facility housed between 81 and 268 residents, whose profiles resembled the average LTCF population in Quebec: frail and cognitively impaired older adults, with an average age of around 80 and substantial functional impairment (see Table S2).

All COVID-19 cases, as identified through the MCS's clinical and administrative registries, were included in the analysis. Laboratory diagnosis was based on a positive nasopharyngeal polymerase chain reaction (PCR) test. For a minority of residents with an epidemiological diagnosis (i.e., compatible symptoms and close contact, without a positive laboratory result), the diagnosis was confirmed by the attending team in chart notes. A total of 1197 participants met the inclusion criteria for the analysis. There were no exclusion criteria.

Following a ministerial directive published on March 25, 2020 which requested that LTCFs in the province avoid transferring their residents to the hospital, most COVID-19 cases received in-facility care during the course of their illness.

Study design

Based on a retrospective cohort design, data collection began in January 2021 and ended in May 2021. Resident

paper charts were manually reviewed and data were abstracted by the first author and collaborators (see Supplementary Text S1). The research protocol was approved by the MCS's institutional review board and the Neurosciences and Aging ethics committee (approval number CER VN 20-21-28). Given that the study was based only on chart and registry reviews, with no interventions and no risk to subjects, participant consent was not required. All participants ($n = 1197$) were followed from the time of diagnosis until death or the end of the study, with no losses to follow-up.

Measurements

Study variables were chosen based on a literature review[12,19,23–26] and the authors' clinical experiences. Outcome was all-cause mortality within 30 days of a COVID-19 diagnosis. Individual-level variables were manually abstracted from residents' paper charts (see Table S1) and included age, sex, SMAF (Functional Autonomy Measurement System,[27] a score from 1 to 14 proportional to a resident's functional impairment), goals of care A to D (from life-prolonging care A and B, to comfort care C and D),[28] medical conditions inspired by the modified Charlson Comorbidity Index,[29] date of COVID-19 diagnosis, and medical treatments (anticoagulation at prophylactic and therapeutic doses, corticosteroids, oxygen, and fluid therapies) which were administered prior or during COVID-19 episode. For variable coding, see Tables S4 and S5. Institutional-level variables were collected from MCS administrative registries and included the presence of a red zone (isolation area for COVID-19 cases) at the time of first outbreak, air changes per hour as measured a month after the first wave, average performance score on health ministry audits during the pandemic (which measured infection prevention and control practices as well as overall quality of care), proportion of shared rooms, and percentage of vacancies for healthcare aides (HCA), licensed practical nurses (LPN), and registered nurses (RN) according to human resources database from March 6, 2020. Data collection methods and full variable descriptions available in Supplementary Texts S1 and S3.

Statistical analysis

As the binary outcome of death was common, odds ratios would likely overstate the effect of some covariates,[30,31] so the initial multilevel logistic regression was changed a posteriori to a modified Poisson regression[32,33] to obtain incidence rate ratios. To account for the correlations in outcomes for individuals within the same facility, the variance was corrected using the cluster-robust variance (sandwich) estimator,[34] which is more appropriate for a small number of clusters (i.e., 17 facilities)[34] and is robust against model misspecification.[35,36]

As there were no missing data for institutional variables and complete data was available for 97.1% of the cohort's participants, with no significant pattern found in the individual missing data (missingness at random), a complete case analysis was performed. See Supplementary Text S5 and Figure S2.

To build the final regression model, we combined all basic variables (age, sex, SMAF, date of COVID-19 diagnosis) and all comorbidities – excluding instrument or ancestor variables (GOCs, hypertension, diabetes) which were not directly associated with mortality (see Figure S1)—in addition to the two treatment variables (anticoagulation and corticosteroids) that showed least signs of confounding by indication.[37] When adding facility factors to the model, because of collinearity issues between the three vacancies variables, we chose LPN (over RN and HCA) based on the Bayesian Information Criteria.[38] Details on model building are provided in the Supplementary Text S4.

We also conducted sensitivity analyses: a model which included goals of care (see Table S6) and two models which excluded hospital transfers during COVID-19 illness and epidemiological diagnoses (cases without a positive PCR test) (see Table S7). Full details of sensitivity analyses are provided in Supplementary Text S6.

All analyses were carried out using R statistical software, version 4.0.5, and package clubSandwich for cluster-robust variance estimation, considering two-sided $p < 0.05$ statistically significant.

RESULTS

Descriptive statistics for the cohort

This cohort of 1197 COVID-19 cases across 17 LTCFs included diverse residents (see Table 1), aged 19 to 107 (median 82), with a majority of women (58.6%), an average SMAF profile of 11 (out of 14), and predominantly goals of care B (30.2%) and C (52.2%). The most frequent comorbidity was neurocognitive disorder (73.1%), followed by hypertension (53.2%) and diabetes (28.0%). Half (50.5%) of the cohort was infected between March 24 and April 19, 2020 and the other half between April 20 and July 11, 2020. Only 32 cases (2.7%) were diagnosed epidemiologically, most of them at the time of death, and all other cases were laboratory confirmed. Sixty-three residents (5.3%) were transferred to the hospital over the course of their COVID-19 illness. Almost half

TABLE 1 Individual baseline characteristics of the cohort

	Deceased ($n = 451$)	Alive ($n = 746$)	Total ($n = 1197$)
Background information			
Age			
Mean (SD)	83.4 (10.6)	76.4 (14.3)	79.0 (13.4)
Median [Min, Max]	85 [51, 107]	78 [19, 106]	82 [19, 107]
Sex			
Female	245 (54.3%)	457 (61.3%)	702 (58.6%)
Goal of care[a]			
A	17 (3.8%)	87 (11.7%)	104 (8.7%)
B	110 (24.4%)	251 (33.6%)	361 (30.2%)
C	265 (58.8%)	360 (48.3%)	625 (52.2%)
D	59 (13.1%)	48 (6.4%)	107 (8.9%)
SMAF[b]			
Mean (SD)	11.4 (2.27)	10.7 (2.61)	11.0 (2.52)
Median [Min, Max]	12 [3, 14]	11 [1, 14]	11 [1, 14]
Missing	3 (0.7%)	0 (0%)	3 (0.3%)
Comorbidities			
Neurocognitive disorder	373 (82.7%)	502 (67.3%)	875 (73.1%)
Hypertension	251 (55.7%)	386 (51.7%)	637 (53.2%)
Diabetes mellitus	123 (27.3%)	212 (28.4%)	335 (28.0%)
Cerebrovascular disease	111 (24.6%)	151 (20.2%)	262 (21.9%)
Coronary heart disease	123 (27.3%)	135 (18.1%)	258 (21.6%)
Chronic pulmonary disease	98 (21.7%)	124 (16.6%)	222 (18.5%)
Kidney disease	87 (19.3%)	96 (12.9%)	183 (15.3%)
Congestive heart failure	71 (15.7%)	59 (7.9%)	130 (10.9%)
Any malignancy	43 (9.5%)	70 (9.4%)	113 (9.4%)
Liver disease	18 (4.0%)	38 (5.1%)	56 (4.7%)
Rheumatological disease	10 (21%)	14 (1.9%)	24 (2.0%)
HIV/AIDS	3 (0.7%)	5 (0.7%)	8 (0.7%)
Medical treatments			
Fluid therapy			
Yes	85 (18.8%)	68 (9.1%)	153 (12.8%)
No	350 (77.6%)	671 (89.9%)	1021 (85.3%)
Missing	16 (3.5%)	7 (0.9%)	23 (1.9%)
Oxygen therapy			
Yes	288 (63.9%)	95 (12.7%)	383 (32.0%)
No	157 (34.8%)	642 (86.1%)	799 (66.8%)
Missing	6 (1.3%)	9 (1.2%)	15 (1.3%)
Corticosteroids			
Yes	17 (3.8%)	24 (3.2%)	41 (3.4%)
No	416 (92.2%)	716 (96.0%)	1132 (94.6%)
Missing	18 (4.0%)	6 (0.8%)	24 (2.0%)

TABLE 1 (Continued)

	Deceased ($n = 451$)	Alive ($n = 746$)	Total ($n = 1197$)
Anticoagulation			
Yes	76 (16.9%)	266 (35.7%)	342 (28.6%)
No	359 (79.6%)	477 (63.9%)	836 (69.8%)
Missing	16 (3.5%)	3 (0.4%)	19 (1.6%)
COVID-19 episode			
Date of diagnosis			
Mean (SD)	2020-04-17 (14.1)	2020-04-23 (15.2)	2020-04-21 (15.0)
Median [Minimum, Maximum]	2020-04-15 [2020-03-24, 2020-06-04]	2020-04-22 [2020-03-25, 2020-07-09]	2020-04-19 [2020-03-24, 2020-07-09]
Epidemiological case	30 (6.7%)	2 (0.3%)	32 (2.7%)
Hospital transfer	40 (8.9%)	23 (3.1%)	63 (5.3%)
Disease severity	451 (100%)	116 (15.5%)	567 (47.4%)

[a]Goal of care: A = Prolong life with all necessary care; B = Prolong life with some limitations to care; C = Ensure comfort as a priority over prolonging life; D = Ensure comfort without prolonging life.
[b]SMAF (Functional Autonomy Measurement System): 0 = no functional impairment (full autonomy), 14 = severe motor and cognitive impairment (full dependency for activities of daily living).

(47.4%) of all COVID-19 cases met the criteria for severe disease, as defined by the World Health Organization (oxygen saturation below 90%, respiratory rate above 30 breaths per minute, acute respiratory distress, or death).[39]

In terms of treatment, oxygen therapy was given in 32.0% of cases, anticoagulation in 28.6%, fluid therapy in 12.8%, and corticosteroids in 3.4% of cases. The anticoagulation variable is heterogeneous and could not be categorized by molecule (e.g., enoxaparin, warfarin, direct oral anticoagulants) or dose. While several residents were on antithrombotic medication for chronic medical conditions before their infection, others received thromboprophylaxis specifically for their COVID-19 episode. During the study period, oxygen was accessible in all LTCFs and was generally administered when saturation levels fell below 92% (or 90% for residents with chronic obstructive pulmonary disease), as per local protocols. On the other hand, the use of fluid therapy was not widespread in most LTCFs and varied from one ward to another (from never use to common use). Finally, physicians only began to prescribe corticosteroids for severe cases near the end of the first wave, when it was added as a therapeutic option in COVID-19 protocols, hence the small proportion in our cohort.

Overall, 477 individuals in the cohort died during the first wave. 451 deaths, of which 450 were attributed to COVID-19, occurred within 30 days of COVID-19 diagnosis. The average time to all-cause death was 11.3 days, with a range of 0 to 105 days.

As for institutional-level variables (see Table 2), the total number of beds ranged from 83 to 276. Seven facilities had only private rooms, while in the other ten facilities shared rooms made up 10.7% to 86.8% of all rooms. Around half of the facilities had a red zone (isolation area for COVID-19 cases) set up before their first outbreak. With 0.6 to 4 air changes per hour (ACH), ventilation parameters failed to meet recommended provincial standards (4 ACH in bedrooms, 3 ACH in hallways, and 10 ACH in bathrooms[40]) across all facilities. Staff shortages were widespread: the proportion of vacancies varied from 18.8% to 33.0% for HCA, 8.3% to 42.9% for LPN and 15.4% to 47.4% for RN. Health ministry audit scores varied from 1 (perfect score) to 2.07 (with 3 being the worst score).

Regression model for 30-day mortality

Results of the regression model are presented in Table 3. In this cohort of LTCF COVID-19 cases, when adjusting for individual and institutional factors, while accounting for clustering per facility, we found that the risk of dying 30 days after COVID-19 diagnosis for a resident living in an LTCF with 25% or more LPN vacancies was 2.60 times (95% CI 1.20–5.61) that of a resident in a facility with less than 15% vacancies. Compared to smaller-sized facilities, the risk of death for residents in medium-sized facilities increased by 2.73 times (95% CI 1.23–6.07). Furthermore, each subsequent day of diagnosis was associated with a 2% decrease in mortality (RR 0.98 95% CI 0.97–0.99).

On an individual level, each increase of 10 years in age raised the risk of death by 1.33 times (95% CI 1.23–1.45), while each additional point in the SMAF profile score increased the risk by 1.08 times (95% CI 1.04–1.12).

TABLE 2 Institutional baseline characteristics for the 17 LTCFs

LTCF ID	Beds (occupancy)	Shared rooms (%)	Red zone[a] (Y/N)	ACH[b]	HCA vacancy (%)	LPN vacancy (%)	RN vacancy (%)	Audit score[c] (SD)	Deaths (case fatality ratio)
1	116 (99.1%)	0 (0%)	N	2.5	21/88 (24%)	5/26 (19%)	3/15 (20%)	1.33 (0.47)	11 (22.9%)
2	83 (97.6%)	20 (24%)	N	1.9	18/71 (25%)	3/15 (20%)	4/11 (36%)	1.33 (0.47)	5 (19.2%)
3	184 (94.6%)	52 (28%)	N	2.1	36/139 (26%)	3/36 (8%)	6/25 (24%)	1.08 (0.27)	13 (38.2%)
4	96 (97.9%)	0 (0%)	Y	0.8	16/71 (23%)	6/15 (40%)	4/12 (33%)	1.55 (0.63)	23 (39.0%)
5	168 (94.0%)	18 (11%)	Y	2.3	19/101 (19%)	5/36 (14%)	5/18 (28%)	1.20 (0.40)	2 (33.3%)
6	128 (100%)	64 (50%)	Y	2.1	31/106 (29%)	5/23 (22%)	3/17 (18%)	1.00 (0)	0 (0%)
7	276 (97.1%)	56 (20%)	Y	2.3	69/230 (30%)	9/57 (16%)	13/39 (33%)	1.65 (0.48)	69 (47.3%)
8	193 (98.4%)	98 (51%)	Y	2	61/185 (33%)	5/54 (9%)	7/29 (24%)	1.69 (0.81)	14 (17.3%)
9	158 (98.1%)	78 (49%)	Y	1.5	44/160 (28%)	5/39 (13%)	12/31 (39%)	1.38 (0.62)	22 (25.3%)
10	174 (98.9%)	54 (31.0%)	Y	1.4	41/148 (28%)	6/33 (18%)	9/27 (33%)	1.00 (0)	4 (50%)
11	220 (99.5%)	0 (0%)	N	1.2	38/184 (21%)	15/47 (32%)	12/32 (38%)	1.27 (0.45)	40 (34.2%)
12	168 (94.6%)	0 (0%)	N	1	34/122 (28%)	4/31 (13%)	4/26 (15%)	1.67 (0.62)	41 (33.3%)
13	100 (96%)	0 (0%)	Y	2	17/75 (23%)	9/21 (43%)	2/10 (20%)	1.36 (0.48)	35 (49.3%)
14	144 (98.6%)	0 (0%)	N	2	33/127 (26%)	7/27 (26%)	9/19 (47%)	2.07 (0.93)	30 (41.7%)
15	185 (93.5%)	0 (0%)	N	0.6	44/157 (28%)	7/34 (21%)	10/26 (38%)	2.06 (0.92)	74 (50.0%)
16	152 (98.0%)	132 (87%)	N	3.5	39/133 (29%)	7/44 (16%)	7/26 (27%)	1.73 (0.68)	35 (36.5%)
17	125 (97.6%)	20 (16%)	N	4	22/93 (24%)	3/20 (15%)	5/20 (25%)	1.45 (0.49)	38 (52.1%)
Mean (SD)	157.1 (47.1)	21.6 (24.5%)		1.9 (0.97)	25.8% (3.6)	20.3% (9.6)	29.4% (8.6)	1.46 (0.31)	26.8 (21.2)

[a]Red zone (isolation area for COVID-19 cases): Y = yes, a red zone was available at the time the first COVID-19 case was declared in the facility; N = no.
[b]Ventilation: ACH = air changes per hour (average per facility).
[c]Audit score (from 1 to 3, given by Ministry of Health inspectors, based on the assessment of IPC practices and general quality of care): 1 = adequate; 2 = requires monitoring; 3 = alarming.

TABLE 3 Modified Poisson regression model with individual and institutional covariates

	Unadjusted RR (95% CI)	Adjusted RR (95% CI)
Age (per 10-year increase)	1.03 (1.02–1.03)	1.33 (1.23–1.45)
Sex		
Female	*Reference*	*Reference*
Male	1.19 (1.03–1.38)	1.46 (1.24–1.71)
SMAF[a]	1.09 (1.05–1.12)	1.08 (1.04–1.12)
Date of diagnosis (per day increase)	0.98 (0.97–0.99)	0.98 (0.97–0.99)
Congestive heart failure	1.53 (1.23–1.91)	1.31 (1.04–1.66)
Neurocognitive disorder	1.76 (1.37–2.27)	1.31 (1.01–1.70)
Coronary heart disease	1.36 (1.12–1.66)	1.12 (0.92–1.36)
Chronic pulmonary disease	1.22 (0.99–1.50)	1.15 (0.91–1.45)
Kidney disease	1.32 (1.02–1.72)	1.00 (0.82–1.23)
Cerebrovascular disease	1.17 (0.98–1.38)	1.08 (0.89–1.30)
Liver disease	0.85 (0.48–1.48)	1.15 (0.65–2.03)
HIV or AIDS	1.00 (0.33–2.97)	1.25 (0.48–3.29)
Rheumatologic disease	1.11 (0.66–1.85)	1.17 (0.58–2.35)
Any malignancy	1.01 (0.73–1.40)	0.96 (0.73–1.27)
Anticoagulation	0.52 (0.31–0.86)	0.65 (0.42–1.02)
Corticosteroids	1.13 (0.78–1.63)	1.28 (0.96–1.70)
LPN vacancies[b]		
<15%	*Reference*	*Reference*
15%–25%	1.28 (0.79–2.06)	1.46 (0.97–2.22)
25% or more	1.22 (0.76–1.96)	2.60 (1.20–5.61)
Beds (tertiles)		
≤152	*Reference*	*Reference*
158 to 185	0.98 (0.63–1.52)	2.73 (1.23–6.07)
193 to 276	0.91 (0.47–1.76)	1.22 (0.61–2.44)
Air changes per hour	1.03 (0.79–1.33)	1.51 (0.93–2.47)
Presence of red zone	0.95 (0.61–1.50)	1.24 (0.89–1.72)
Audit performance	1.33 (0.75–2.35)	1.39 (0.58–3.33)
Shared rooms		
None	*Reference*	*Reference*
<30%	1.15 (0.83–1.60)	1.21 (0.56–2.61)
30% or more	0.70 (0.38–1.29)	0.80 (0.45–1.41)

[a]SMAF (Functional Autonomy Measurement System): 0 = no functional impairment (full autonomy), 14 = severe motor and cognitive impairment (full dependency for activities of daily living).
[b]Percentage of unfilled vacancies among licensed practical nurses (LPN).

Men were 1.46 times (95% CI 1.24–1.71) more likely to die than women and residents with congestive heart failure or neurocognitive disorder had a significantly increased risk of death (RR 1.31 95% CI 1.04–1.66 and RR 1.31 95% CI 1.10–1.70). Results were comparable in the sensitivity analyses (see Supplementary Text S6).

Among the subgroup of severe cases ($n = 567$), when adjusting for individual risk factors, the use of anticoagulation decreased the risk of dying by 30% (RR 0.70 95% CI 0.51–0.96), while no significant associations were found for the other medical treatments (Table 4).

DISCUSSION

This study suggests that the risk of dying within 30 days of a COVID-19 diagnosis was influenced not only by LTCF residents' individual characteristics but also by facility-wide risk factors such as shortage of nurses and number of beds, as well as the use of anticoagulation among severe cases (Figure 1).

At a time when Quebec LTCFs were compelled to deliver acute and intensive care to avoid hospital overflow, lower staff ratios may have contributed to COVID-19 mortality.[41] Besides administering medication, LPN in Quebec follow essential clinical parameters, including vital signs, symptoms, and nutritional status.[42] They have increased direct contact with residents compared to RN while possessing enhanced clinical skills compared to HCA. Therefore, LPN shortage could increase the risk of COVID-19 death through the delayed detection of clinical deterioration, as well as less contact and care. However, data on staff vacancies were imprecise (i.e., did not include short-term leaves) and collinearity between the three vacancies variables did not allow them to be jointly assessed in the final model.

Facility size has been identified as a risk factor for COVID-19 deaths in many previous studies,[43–45] likely due to high occupancy density, which may lead to increased exposure to the virus and less personalized care.[45] However, while medium-sized facilities were associated with death compared to smaller facilities in our study, we did not find a statistically significant association between larger facilities or shared rooms, possibly because of lack of power. In line with previous literature, the quality of care measure in our study (i.e., audit performance) was not a significant predictor of death, suggesting that mortality in LTCFs was not driven by low-scoring facilities. Surprisingly, the presence of a red zone (COVID-19 isolation area) was not protective against death, which may be explained by the deleterious impacts of transferring residents outside their wards and

TABLE 4 Medical treatments and association with 30-day COVID-19 mortality

	Relative risks and 95% confidence intervals		
	Unadjusted model (all cases $n = 1197$)	**Unadjusted model (severe cases $n = 567$)**	**Adjusted model[a] (severe cases $n = 567$)**
Anticoagulation	0.52 (0.31–0.86)	0.66 (0.50–0.88)	0.70 (0.51–0.96)
Corticosteroids	1.13 (0.78–1.63)	0.82 (0.63–1.06)	0.95 (0.72–1.26)
Oxygen therapy	3.83 (2.78–5.26)	0.90 (0.83–0.97)	0.96 (0.88–1.04)
Fluid therapy	1.62 (1.29–2.03)	0.88 (0.76–1.01)	1.00 (0.86–1.16)

[a]Adjusted for age, sex, SMAF (functional impairment), date of COVID-19 diagnosis, congestive heart failure, neurocognitive disorder, coronary heart disease, chronic pulmonary disease, kidney disease, cerebrovascular disease, liver disease, HIV/AIDS, rheumatological disease, any malignancy.

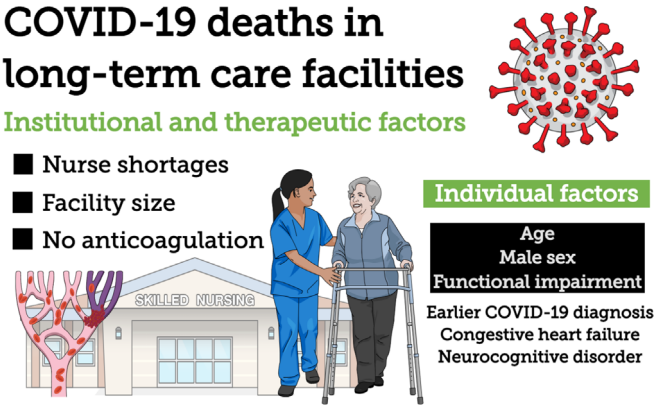

FIGURE 1 Factors associated with 30-day mortality after COVID-19 diagnosis

into temporary spaces, as well as the prolonged isolation periods which were common in the first wave. In turn, the association between death and air changes per hour was not significant in our study, but the imprecision of the measure and small inter-facility variations may have prevented the detection of meaningful differences.

Use of anticoagulation was previously associated with a reduction in mortality in LTCF settings[10,46–48] likely because of its protection against thromboembolic complications. In our full cohort model, the association was borderline significant, but this was likely a case of confounding by indication[37]: during the first wave, thromboprophylaxis was administered only to more severe cases, as per local clinical protocols. A subgroup analysis with severe cases ($n = 567$) showed a significant benefit for anticoagulation. However, the anticoagulation variable is limited by its heterogeneity, as it could not be categorized by molecule (e.g., enoxaparin, warfarin, direct oral anticoagulants) or dose. Furthermore, the same confounding by indication explains why oxygen and fluid therapies were associated with higher mortality when analyzing the full cohort but did not alter survival among severe cases. Dexamethasone, which seemed to increase the survival of hospitalized residents under oxygen,[49] was not associated with survival benefits in our study.

Our results suggest that a later diagnosis was strongly associated with survival. The lack of tests at the beginning of the pandemic likely led to a substantial number of undetected (usually milder) cases. More timely testing later on, and therefore earlier detection and isolation of positive cases, may also have decreased exposure to viral loads for all residents. In addition to the phenomenon known as "depletion-of-susceptibles,"[50] beneficial changes in practices (e.g., shorter isolation periods, improved COVID-specific resident care, better staffing), could have further contributed to improved survival over time.

Age and male sex are consistently associated with mortality in all segments of the population including in LTCF.[25,48,51] Functional impairment[19] also increased the risk of death in our study, possibly due to prolonged close contact with staff (and therefore exposure to higher viral loads), related clinical syndromes (e.g., delirium, deconditioning, dysphagia), as well as impaired ability to communicate or fulfill basic needs.[52] While previous literature associated several medical conditions with COVID-19 death in LTCFs,[25,48,53] our study adjusted for multiple confounders and identified two significant diagnoses collected from resident charts: congestive heart failure and neurocognitive disorder. The heart's weakened ability to resist the stress of COVID-19 infection and higher rates of cardiac complications, as well as the presence of at-risk behaviors (e.g., intrusive wandering, no mask-wearing) leading to exposure to higher viral loads, respectively, could have contributed to the death.

The main strengths of this study are the large cohort size with a high number of events (deaths), as well as detailed individual and institutional-level data for exposures, confounders, and outcome ascertainment. No losses to follow-up and rare missing data decreased the likelihood of selection bias. Institutional factors such as the presence of COVID-19 isolation area and air changes per hour had not been previously studied, and the impact

of medical treatments in long-term care settings (anticoagulation, corticosteroids, fluid, and oxygen therapies) were not well known. Furthermore, the baseline cohort characteristics and the final results were in line with previous LTCF literature on COVID-19.

However, reproducibility of the chart abstraction process was not measured. The charts of deceased versus alive residents were assigned to different reviewers, none of whom were blinded to the outcome, which could have led to information bias and inter-reviewer differences.

Furthermore, the observational nature of the study limits causal inference and the small number of LTCFs limited the power of the institutional-level analysis. The data being from the first wave, there was imprecision (e.g., underdetection of mild and asymptomatic cases due to deficient testing capacities) and the findings may be less generalizable to subsequent waves. While some unmeasured institutional variables (such as shared bathrooms) and individual variables (such as race) were not controlled for, most known risk factors were included and major residual confounding is unlikely. Finally, while it is unlikely that vaccination alters the positive associations found in this study, it is possible that the balance of risk factors has changed in the current post-vaccine era.

Overall, the results of this study help fill research gaps in long-term care settings. Anticoagulation could be an essential therapeutic modality for severe cases, but clinical trials are required for LTCF populations. Finding solutions to staff shortages, especially for LPN, appears to be a crucial step to prevent COVID-19 mortality, and may also improve the overall quality of care. Smaller facilities on a more human scale, such as the Green House Project in the United States[54] and Dementia Villages in the Netherlands,[55] would have the double advantage of decreasing occupancy density and enhancing staff ratios, among other benefits. As the threat of new variants and future pandemics looms ahead, the potential avenues identified in this study may contribute to better protect the vulnerable LTCF population in the short and long term.

AUTHOR CONTRIBUTIONS

Xi Sophie Zhang, Kate Zinszer, and Katia Charland contributed equally to the concept and design of the study, with CQ and QDN in supporting roles. Xi Sophie Zhang was responsible for the acquisition of data along with the collaborators listed below. Xi Sophie Zhang performed the initial analysis, under the supervision of Kate Zinszer and Katia Charland, and was supported by all other authors for data interpretation. Xi Sophie Zhang drafted the initial manuscript, under the supervision of Kate Zinszer, and all authors revised the content. All authors contributed equally to the final approval of the version to be published.

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CONFLICT OF INTEREST

The authors have no conflicts and have completed the ICMJE uniform disclosure form at http://www.icmje.org/disclosure-of-interest/.

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REFERENCES

1. Sepulveda ER, Stall NM, Sinha SK. A comparison of COVID-19 mortality rates among long-term care residents in 12 OECD countries. *J Am Med Dir Assoc*. 2020;21(11):1572-1574. doi:10.1016/j.jamda.2020.08.039
2. Stratil JM, Biallas RL, Burns J, et al. Non-pharmacological measures implemented in the setting of long-term care facilities to prevent SARS-CoV-2 infections and their consequences: a rapid review. *Cochrane Database Syst Rev*. 2021;9(9):CD015085. doi:10.1002/14651858.CD015085.pub2
3. Dykgraaf SH, Matenge S, Desborough J, et al. Protecting nursing homes and long-term care facilities from COVID-19: a rapid review of international evidence. *J Am Med Dir Assoc*. 2021;22(10):1969-1988. doi:10.1016/j.jamda.2021.07.027
4. Prendki V, Tau N, Avni T, et al. A systematic review assessing the under-representation of elderly adults in COVID-19 trials. *BMC Geriatr*. 2020;20(1):538. doi:10.1186/s12877-020-01954-5
5. Su Z, McDonnell D, Li Y. Why is COVID-19 more deadly to nursing home residents? *QJM*. 2021;114:543-547. doi:10.1093/qjmed/hcaa343

6. Lau-Ng R, Caruso LB, Perls TT. COVID-19 deaths in long-term care facilities: a critical piece of the pandemic puzzle. *J Am Geriatr Soc*. 2020;68(9):1895-1898. doi:10.1111/jgs.16669
7. Andrew M, Searle SD, McElhaney JE, et al. COVID-19, frailty and long-term care: implications for policy and practice. *J Infect Dev Ctries*. 2020;14(5):428-432. doi:10.3855/jidc.13003
8. Faghanipour S, Monteverde S, Peter E. COVID-19-related deaths in long-term care: the moral failure to care and prepare. *Nurs Ethics*. 2020;27(5):1171-1173. doi:10.1177/0969733020939667
9. Agostinis P, Vianello V, Dereani E, et al. Response to a massive SARS-CoV-2 infection in a nursing home transformed into a caring center. *Aging Clin Exp Res*. 2021;33:443-450. doi:10.1007/s40520-020-01784-w
10. Atalla E, Zhang R, Shehadeh F, et al. Clinical presentation, course, and risk factors associated with mortality in a severe outbreak of COVID-19 in Rhode Island, USA, April-June 2020. *Pathogens*. 2020;10(1):8. doi:10.3390/pathogens10010008
11. Bernabeu-Wittel M, Ternero-Vega JE, Díaz-Jiménez P, et al. Death risk stratification in elderly patients with covid-19. A comparative cohort study in nursing homes outbreaks. *Arch Gerontol Geriatr*. 2020;91:104240. doi:10.1016/j.archger.2020.104240
12. Bielza R, Sanz J, Zambrana F, et al. Clinical characteristics, frailty, and mortality of residents with COVID-19 in nursing homes of a region of Madrid. *J Am Med Dir Assoc*. 2021;22(2):245-252. doi:10.1016/j.jamda.2020.12.003
13. Brouns SH, Brüggemann R, Linkens A, et al. Mortality and the use of antithrombotic therapies among nursing home residents with COVID-19. *J Am Geriatr Soc*. 2020;68(8):1647-1652. doi:10.1111/jgs.16664
14. Blain H, Rolland Y, Benetos A, et al. Atypical clinical presentation of COVID-19 infection in residents of a long-term care facility. *Eur Geriatr Med*. 2020;11:1085-1088. doi:10.1007/s41999-020-00352-9
15. Fejt V, Krátká Z, Zelená H, Fürst T. Age is not a disease: evolution of protective antibodies against SARS-CoV-2 in seniors from the Břevnice nursing home. *Cas Lek Cesk*. 2020;159(7-8):303-311.
16. Kittang BR, von Hofacker S, Solheim SP, Krüger K, Løland KK, Jansen K. Outbreak of COVID-19 at three nursing homes in Bergen. *Tidsskr Nor Laegeforen*. 2020;140(11). doi:10.4045/tidsskr.20.0405
17. McMichael TM, Currie DW, Clark S, et al. Epidemiology of Covid-19 in a long-term care facility in King County, Washington. *N Engl J Med*. 2020;382(21):2005-2011. doi:10.1056/NEJMoa2005412
18. Huemer F, Rinnerthaler G, Jörg B, et al. Results of a hospitalization policy of asymptomatic and pre-symptomatic COVID-19-positive long-term care facility residents in the province of Salzburg-a report from the AGMT COVID-19 Registry. *Geroscience*. 2021;43:1877-1897. doi:10.1007/s11357-021-00352-y
19. Lee DS, Ma S, Chu A, et al. Predictors of mortality among long-term care residents with SARS-CoV-2 infection. *J Am Geriatr Soc*. 2021;69:3377-3388. doi:10.1111/jgs.17425
20. Janus SIM, Schepel AAM, Zuidema SU, de Haas EC. How typical is the spectrum of COVID-19 in nursing home residents? *J Am Med Dir Assoc*. 2020;22:511-513.e3. doi:10.1016/j.jamda.2020.12.028
21. INSPQ. Données COVID-19 au Québec. Updated May 10, 2020. Accessed May 10, 2020. https://www.inspq.qc.ca/covid-19/donnees
22. Fortin E, De Serres G, Gilca R, Deceuninck G, Brousseau N. *Portrait de la maladie à coronavirus 2019 (COVID-19) chez les résidents des centres d'hébergement et de soins de longue durée (CHSLD) du Québec*. February 12, 2020. https://www.inspq.qc.ca/sites/default/files/publications/3088-portrait-chsld-covid19.pdf
23. De Vito A, Fiore V, Princic E, et al. Predictors of infection, symptoms development, and mortality in people with SARS-CoV-2 living in retirement nursing homes. *PLoS One*. 2021;16(3):e0248009. doi:10.1371/journal.pone.0248009
24. Patel MC, Chaisson LH, Borgetti S, et al. Asymptomatic SARS-CoV-2 infection and COVID-19 mortality during an outbreak investigation in a skilled nursing facility. *Clin Infect Dis*. 2020;71:2920-2926. doi:10.1093/cid/ciaa763
25. Panagiotou OA, Kosar CM, White EM, et al. Risk factors associated with all-cause 30-day mortality in nursing home residents with COVID-19. *JAMA Intern Med*. 2021;181:439-448. doi:10.1001/jamainternmed.2020.7968
26. Ballin M, Bergman J, Kivipelto M, Nordström A, Nordström P. Excess mortality after COVID-19 in Swedish long-term care facilities. *J Am Med Dir Assoc*. 2021;22(8):1574-1580. doi:10.1016/j.jamda.2021.06.010
27. Raîche M. Les profils Iso-SMAF. Accessed April 13, 2021. https://www.expertise-sante.com/outils-cliniques/outils-rsipa/profils-iso-smaf/
28. Institut national d'excellence en santé et en services sociaux (INESSS). Les niveaux de soins: normes et standards de qualité. Written by Michel Rossignol and Lucy Boothroyd. Quebec, QC: INESSS; 47p.
29. Quan H, Li B, Couris CM, et al. Updating and validating the Charlson Comorbidity Index and score for risk adjustment in hospital discharge abstracts using data from 6 countries. *Am J Epidemiol*. 2021;173(6):676-682. doi:10.1093/aje/kwq433
30. Zou G. A modified Poisson regression approach to prospective studies with binary data. *Am J Epidemiol*. 2004;159(7):702-706. doi:10.1093/aje/kwh090
31. Gallis JA, Turner EL. Relative measures of association for binary outcomes: challenges and recommendations for the Global Health Researcher. *Ann Glob Health*. 2019;85(1):137. doi:10.5334/aogh.2581
32. Zou GY, Donner A. Extension of the modified Poisson regression model to prospective studies with correlated binary data. *Stat Methods Med Res*. 2013;22(6):661-670. doi:10.1177/0962280211427759
33. Chen W, Qian L, Shi J, Franklin M. Comparing performance between log-binomial and robust Poisson regression models for estimating risk ratios under model misspecification. *BMC Med Res Methodol*. 2018;18(1):63. doi:10.1186/s12874-018-0519-5
34. Pustejovsky JE, Tipton E. Small-sample methods for cluster-robust variance estimation and hypothesis testing in fixed effects models. *J Bus Econ Stat*. 2017;36:672-683. doi:10.1080/07350015.2016.1247004
35. Bell RM, McCaffrey DF. Bias reduction in standard errors for linear regression with multi-stage samples. *Surv Methodol*. 2002;28(2):169-181.
36. Imbens GW, Kolesár M. Robust standard errors in small samples: some practical advice. *Rev Econ Stat*. 2022;98(4):701-712. doi:10.1162/REST_a_00552

37. The European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP). Guide on Methodological Standards in Pharmacoepidemiology (Revision 4). EMA/95098/2010. Available at http://www.encepp.eu/standards_and_guidances.
38. Shmueli G. To explain or to predict? *Stat Sci*. 2010;25(3):289-310. doi:10.1214/10-STS330
39. Rochwerg B, Siemieniuk RA, Agoritsas T, et al. A living WHO guideline on drugs for covid-19. *BMJ*. 2020;370:m3379. doi:10.1136/bmj.m3379
40. CSA Group. *CSA Z317.2:19 Special requirements for heating, ventilation, and air-conditioning (HVAC) systems in health care facilities*. 2019. Standards on the design, construction, and maintenance of health care facilities and systems. https://www.csagroup.org/store/product/
41. Li Y, Temkin-Greener H, Shan G, Cai X. COVID-19 infections and deaths among Connecticut nursing home residents: facility correlates. *J Am Geriatr Soc*. 2020;68:1899-1906. doi:10.1111/jgs.16689
42. Ordre des infirmières et infirmiers auxiliaires du Québec. *L'exercice de l'infirmière auxiliaire en centre d'hébergement de soins de longue durée (CHSLD)*. 2020. *OIIAQ - Développement de la profession*. https://www.oiiaq.org/files/content/Profession/Developpement-de-la-profession/IA-EN-CHSLD/OIIAQ_2020_Lexercice-lIA_CHSLD_V3.pdf
43. Brown KA, Jones A, Daneman N, et al. Association between nursing home crowding and COVID-19 infection and mortality in Ontario, Canada. *JAMA Intern Med*. 2020;181:229-236. doi:10.1001/jamainternmed.2020.6466
44. Unruh MA, Yun H, Zhang Y, Braun RT, Jung HY. Nursing home characteristics associated with COVID-19 deaths in Connecticut, New Jersey, and New York. *J Am Med Dir Assoc*. 2020;21(7):1001-1003. doi:10.1016/j.jamda.2020.06.019
45. Morciano M, Stokes J, Kontopantelis E, Hall I, Turner AJ. Excess mortality for care home residents during the first 23 weeks of the COVID-19 pandemic in England: a national cohort study. *BMC Med*. 2021;19(1):71. doi:10.1186/s12916-021-01945-2
46. Tarteret P, Strazzulla A, Rouyer M, et al. Clinical features and medical care factors associated with mortality in French nursing homes during the COVID-19 outbreak. *Int J Infect Dis*. 2021;104:125-131. doi:10.1016/j.ijid.2020.12.004
47. Couderc AL, Correard F, Hamidou Z, et al. Factors associated with COVID-19 hospitalizations and deaths in French nursing homes. *J Am Med Dir Assoc*. 2021;22(8):1581-1587.e3. doi:10.1016/j.jamda.2021.06.023
48. España PP, Bilbao A, García-Gutiérrez S, et al. Predictors of mortality of COVID-19 in the general population and nursing homes. *Intern Emerg Med*. 2021;16:1487-1496. doi:10.1007/s11739-020-02594-8
49. RECOVERY Collaborative Group, Horby P, Lim WS, et al. Dexamethasone in hospitalized patients with Covid-19. *N Engl J Med*. 2021;384(8):693-697. doi:10.1056/NEJMoa2021436
50. Fireman B, Gruber S, Zhang Z, et al. Consequences of depletion of susceptibles for hazard ratio estimators based on propensity scores. *Epidemiology*. 2020;31(6):806-814. doi:10.1097/EDE.0000000000001246
51. Cangiano B, Fatti LM, Danesi L, et al. Mortality in an Italian nursing home during COVID-19 pandemic: correlation with gender, age, ADL, vitamin D supplementation, and limitations of the diagnostic tests. *Aging (Albany NY)*. 2020;12(24):24522-24534. doi:10.18632/aging.202307
52. Zhang XM, Jiao J, Cao J, et al. Frailty as a predictor of mortality among patients with COVID-19: a systematic review and meta-analysis. *BMC Geriatr*. 2021;21(1):186. doi:10.1186/s12877-021-02138-5
53. Abadía Otero J, Briongos Figuero LS, Gabella Mattín M, et al. The nutritional status of the elderly patient infected with COVID-19: the forgotten risk factor? *Curr Med Res Opin*. 2021;37:549-554. doi:10.1080/03007995.2021.1882414
54. Power GA, Carson J. The promise of transformed long-term care homes: evidence from the pandemic. *Healthc Manage Forum*. 2021;35:25-28. doi:10.1177/08404704211037794
55. Werner RM, Hoffman AK, Coe NB. Long-term care policy after Covid-19 — Solving the nursing home crisis. *N Engl J Med*. 2020;383:903-905. doi:10.1056/NEJMp2014811

SUPPORTING INFORMATION

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

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Figure S2. (A) Histogram and patterns of missing data per variable. (B) Missing data matrix.

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