Differential Patterns by Area-Level Social Determinants of Health in Coronavirus Disease 2019 (COVID-19)–Related Mortality and Non–COVID-19 Mortality: A Population-Based Study of 11.8 Million People in Ontario, Canada

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Background. Social determinants of health (SDOH) have been associated with coronavirus disease 2019 (COVID-19) outcomes. We examined patterns in COVID-19–related mortality by SDOH and compared these patterns to those for non–COVID-19 mortality.

Methods. Residents of Ontario, Canada, aged ≥20 years were followed from 1 March 2020 to 2 March 2021. COVID-19–related death was defined as death within 30 days following or 7 days prior to a positive COVID-19 test. Area-level SDOH from the 2016 census included median household income; proportion with diploma or higher educational attainment; proportion of essential workers, racially minoritized groups, recent immigrants, apartment buildings, and high-density housing; and average household size. We examined associations between SDOH and COVID-19–related mortality, and non–COVID-19 mortality using cause-specific hazard models.

Results. Of 11,810,255 individuals, we observed 3,880 COVID-19–related deaths and 88,107 non–COVID-19 deaths. After accounting for demographics, baseline health, and other area-level SDOH, the following were associated with increased hazards of COVID-19–related death (hazard ratio [95% confidence interval]: lower income (1.30 [1.04–1.62]), lower educational attainment (1.27 [1.07–1.52]), higher proportions essential workers (1.28 [1.05–1.57]), racially minoritized groups (1.42 [1.08–1.87]), apartment buildings (1.25 [1.07–1.46]), and large vs medium household size (1.30 [1.12–1.50]). Areas with higher proportion racially minoritized groups were associated with a lower hazard of non–COVID-19 mortality (0.88 [0.84–0.92]).

Conclusions. Area-level SDOH are associated with COVID-19–related mortality after accounting for demographic and clinical factors. COVID-19 has reversed patterns of lower non–COVID-19 mortality among racially minoritized groups. Pandemic responses should include strategies to address disproportionate risks and inequitable coverage of preventive interventions associated with SDOH.

Keywords. social determinants of health; COVID-19; mortality; inequality; race/ethnicity.

Increasing evidence has confirmed the central role of social determinants of health (SDOH) in shaping variations in coronavirus disease 2019 (COVID-19) disease burden and severity [1–6]. Across high-income countries, rates of COVID-19 diagnoses and deaths have been consistently correlated with socioeconomic status (SES) [5, 7] and disproportionately affecting racially minoritized groups [3, 8–10].

In the context of infectious disease, social and structural inequalities may shape differential health outcomes through differences in susceptibility, contact patterns and networks [11, 12] and reach/uptake of prevention interventions (eg, access to testing [12, 13], effective isolation and quarantine [14], ability to reduce nonhousehold contacts [15], access to vaccines [16], and quality of treatment [17, 18]).

To date, most studies have focused on SDOH such as SES as a composite index [5, 6, 13] and race/ethnicity as proxies for structural racism (biological differences [19], if any, are not the sole explanation for observed disparities by race/ethnicity).
Few studies have examined other SDOH such as educational attainment and occupation and housing conditions, and even fewer have examined several SDOH in conjunction [1, 2]. Moreover, studies on the relationship between SDOH and COVID-19 deaths were often conducted among diagnosed cases or hospitalized populations [7]. Although outcomes such as case fatality among diagnosed cases and mortality while hospitalized provided important information regarding disease severity by SDOH, these analyses are prone to collider biases [20]. For example, SDOH and severe COVID-19 outcomes both affect likelihoods of being diagnosed/hospitalized; restricting analyses among samples of diagnosed/hospitalized cases could distort the relationship between SDOH and COVID-19 outcomes [3, 5, 7].

In Canada, provisional Vital Statistics Deaths data have demonstrated higher age-standardized COVID-19–related mortality among urban residents (vs rural), lower-income areas, higher ethnocultural concentration areas, and residents of apartment buildings (vs detached homes) [21]. However, existing studies were not able to account for potential confounders such as comorbidities. Moreover, to date, no studies have estimated COVID-19–related mortality while at the same time accounting for mortality unrelated to COVID-19, which is a competing risk for COVID-19–related mortality [22]. Such an inquiry also provides opportunities to understand whether the same patterns of inequities drive both COVID-19 and non–COVID-19–related mortality.

Using population-based data among 11.8 million adults in Ontario, Canada, we examined differential patterns in COVID-19–related mortality across a set of area-level SDOH including SES (median household income, proportion with diploma or higher educational attainment, proportion essential workers), ethnic diversity (proportion racially minoritized groups, proportion recent immigrants), and housing conditions (proportion apartment buildings, proportion high-density housing, average household size). We assessed whether patterns in COVID-19–related mortality by SDOH can be explained by demographics, baseline health, and other area-level SDOH. We also compared patterns by SDOH in COVID-19–related mortality vs those in non–COVID-19 mortality and in COVID-19 case fatality.

METHODS

Study Design and Residents
We conducted a population-based, retrospective, cohort study of community-dwelling adults in Ontario, Canada, a setting with universal healthcare [23]. Individuals aged ≥20 years residing in Ontario as of 1 March 2020 and having a valid health card were identified using Ontario’s Registered Persons Database (RPDB) and followed through 2 March 2021. We excluded residents in long-term care homes because they are not included in Canadian census data from which SDOH variables were determined [24, 25]. Data use was authorized under Section 45 of Ontario’s Personal Health Information Protection Act, which does not require ethics review.

Outcomes
Our primary outcome was COVID-19–related death, defined as death within 30 days following or 7 days prior to a positive COVID-19 test. Test result and date were determined based on records in the Ontario Laboratories Information System and the Public Health Case and Contact Management Solution (CCM). Date of death was determined using CCM and RPDB. We estimated that use of both CCM and RPDB capture 99.3% of COVID-19–related deaths (Supplementary Table 1). The secondary outcome was non–COVID-19 death, defined as death without any history of a positive COVID-19 test. COVID-19–related mortality and non–COVID-19 mortality were estimated using the full cohort as the denominator. COVID-19 case fatality was estimated using the subset of the cohort that was diagnosed with COVID-19 as the denominator.

We restricted our analyses to COVID-19–related deaths observed up to 2 March 2021 and cases diagnosed prior to 31 January 2021. Therefore, our analyses capture the first and second waves of regional pandemic representing the original strain of the virus (>95%) or the Alpha variant [26, 27].

Covariates
Based on available data and existing literature [4, 7, 8, 10, 12, 28], we developed a conceptual framework to select SDOH variables and potential confounders for the relationship between SDOH and outcomes, as hypothesized along the risk pathway of COVID-19–related mortality, including risk of infection, risk of testing if infected, and risk of death if diagnosed. Rationales of variable selection are detailed in Figure 1.

Our primary covariates included area-level SDOH, derived from the 2016 census at dissemination area (DA) level, the smallest geographic unit (representing 400–700 residents) for which census data are reported [24]. Area-level SDOH included factors that reflect SES (median household income, proportion with diploma or higher educational attainment, proportion essential workers), ethnic diversity (proportion racially minoritized groups, proportion recent immigrants), and housing conditions (proportion apartment buildings, proportion high-density housing, average household size). Proportion essential workers was defined as the proportion of working people in the DA who self-identify as working in sales, trades, manufacturing, or agriculture. Proportion racially minoritized groups was defined as the proportion of people who self-identify as non-White and non-Indigenous. Proportion apartment buildings was defined as the proportion of buildings that are apartments. For each SDOH variable, we ranked DAs at the city (for income) or provincial level (for other SDOH) and then
categorized them into quintiles. For example, a DA being in income quintile 1 means it is among the highest 20% of DAs in its city by median household income. Detailed definitions of these variables are shown in Table 1 footnotes.

All covariates other than SDOH were measured at the individual level, including age, sex (male vs female), other demographics (living in rural vs urban area, public health region), and baseline health (a set of comorbidity variables, Table 1; past 3-year hospital admission; past year outpatient physician visits).

All datasets were linked using unique encoded identifiers and analyzed at ICES.

Statistical Analyses
We examined and compared the demographics, baseline health, and SDOH of the full cohort, individuals who died related to COVID-19, and individuals who died without COVID-19 using descriptive statistics.

To examine the relationship between SDOH and COVID-19–related mortality, we used cause-specific hazard models [22, 34], where deaths without a positive COVID-19 test were treated as competing risk events (Supplementary Figure 1). We fitted unadjusted model and a set of adjusted models with a priori defined serial adjustment to assess the impact of different confounders. The models were fitted using the PHREG procedure of SAS [35]. Proportional hazard assumptions were assessed using scaled Schoenfeld residuals testing [36] (Supplementary Table 2).

To compare patterns by SDOH in non–COVID-19 mortality to those in COVID–19–related mortality, we repeated analyses using cause–specific hazard models to examine the relationship between SDOH and non–COVID–19 mortality, treating COVID–19 diagnosis as a competing risk.

To compare patterns by SDOH in COVID–19–related mortality with those in COVID–19 case fatality, we used multivariable logistic regression models to examine the associations between SDOH and COVID–19–related death among those who tested positive for COVID–19.

To quantify the absolute differences by area-level SDOH in COVID–19-related mortality, we used Fine and Gray
Table 1. Characteristics of Overall Community-Dwelling Adults in Ontario, Canada, and Those Who Died Related to Coronavirus Disease 2019 and Other Causes

| Characteristic                          | Number of Individuals Residing in Ontario as of 1 March 2020 | Number of COVID-19-related Deaths Between 1 March 2020 and 2 March 2021 | Number of Non-COVID-19 Deaths Between 1 March 2020 and 2 March 2021 |
|----------------------------------------|---------------------------------------------------------------|------------------------------------------------------------------------|---------------------------------------------------------------------|
| Total                                   | 11 810 255                                                    | 3880                                                                   | 88 107                                                              |
| Age (median, interquartile range), y<sup>1</sup> | 48 (34–62)                                                   | 81 (72–88)                                                            | 77 (65–86)                                                          |
| Age category, y<sup>2</sup>             |                                                               |                                                                        |                                                                     |
| 20–34                                   | 3 143 764 (26.6%)                                            | 23 (0.6%)                                                             | 2289 (2.6%)                                                        |
| 35–49                                   | 3 009 493 (25.5%)                                            | 84 (2.2%)                                                             | 4149 (4.7%)                                                        |
| 50–64                                   | 3 099 010 (26.2%)                                            | 399 (10.3%)                                                           | 14 334 (16.3%)                                                     |
| 65–74                                   | 1 487 522 (12.6%)                                            | 710 (18.3%)                                                           | 17 897 (20.3%)                                                     |
| 75–84                                   | 769 255 (6.5%)                                               | 1140 (29.4%)                                                          | 22 900 (26.0%)                                                     |
| 85+                                     | 301 211 (2.6%)                                               | 1524 (39.3%)                                                          | 26 538 (30.1%)                                                     |
| Male                                    | 5 777 603 (48.9%)                                            | 2249 (58.0%)                                                          | 48 501 (55.0%)                                                     |
| Residing in a rural area^d              | 1 192 569 (10.1%)                                            | 138 (3.6%)                                                            | 11 614 (13.2%)                                                     |
| Comorbidity^e                           |                                                               |                                                                        |                                                                     |
| Asthma                                  | 1 750 679 (14.8%)                                            | 752 (19.4%)                                                           | 14 671 (16.7%)                                                     |
| Chronic obstructive pulmonary disease   | 290 131 (2.5%)                                               | 643 (16.6%)                                                           | 17 064 (19.4%)                                                     |
| Hypertension                            | 3 085 359 (26.1%)                                            | 3205 (82.6%)                                                          | 63 356 (71.9%)                                                     |
| Diabetes                                | 1 471 040 (12.5%)                                            | 1847 (47.6%)                                                          | 32 328 (36.7%)                                                     |
| Congestive heart failure                | 264 194 (2.2%)                                               | 988 (25.5%)                                                           | 22 696 (25.8%)                                                     |
| Dementia or frailty score >15^f          | 164 018 (1.4%)                                               | 1215 (31.3%)                                                          | 18 742 (21.3%)                                                     |
| Cancer^g                                | 242 667 (2.1%)                                               | 235 (6.1%)                                                            | 15 663 (17.8%)                                                     |
| Chronic kidney disease^h                |                                                               |                                                                        |                                                                     |
| With no recent dialysis                 | 277 564 (2.4%)                                               | 937 (24.1%)                                                           | 16 286 (18.5%)                                                     |
| With recent fast 3 mol dialysis         | 11 131 (0.1%)                                                | 95 (0.4%)                                                             | 1723 (2.0%)                                                        |
| Immunocompromised                       | 89 318 (0.8%)                                                | 130 (0.4%)                                                            | 3997 (4.5%)                                                        |
| Advanced liver disease^i                | 86 612 (0.7%)                                                | 103 (0.2%)                                                            | 4337 (4.9%)                                                        |
| Cardiac ischemic disease^j              | 359 120 (3.0%)                                               | 707 (18.2%)                                                           | 15 166 (17.2%)                                                     |
| Ischemic stroke or transient ischemic attack^k | 112 634 (1.0%)                        | 370 (9.5%)                                                            | 6994 (7.9%)                                                        |
| Hospital admissions, past 3 y           |                                                               |                                                                        |                                                                     |
| 0                                       | 10 278 277 (87.0%)                                           | 1934 (49.8%)                                                          | 40 188 (45.6%)                                                     |
| 1                                       | 1 112 902 (9.4%)                                             | 856 (22.1%)                                                           | 20 623 (23.4%)                                                     |
| 2                                       | 265 192 (2.2%)                                               | 503 (13.0%)                                                           | 11 539 (13.1%)                                                     |
| 3 or more                               | 153 884 (1.3%)                                               | 587 (15.1%)                                                           | 15 757 (17.9%)                                                     |
| Outpatient physician visits, past y     |                                                               |                                                                        |                                                                     |
| 0–1                                     | 4 054 472 (34.3%)                                            | 313 (81.1%)                                                           | 10 673 (12.1%)                                                     |
| 2–4                                     | 3 111 063 (26.3%)                                            | 608 (15.7%)                                                           | 13 598 (15.4%)                                                     |
| 5–9                                     | 2 320 703 (19.6%)                                            | 882 (22.7%)                                                           | 16 897 (19.2%)                                                     |
| 9–14                                    | 1 429 068 (12.1%)                                            | 926 (26.9%)                                                           | 18 545 (21.0%)                                                     |
| 15 or more                              | 894 149 (7.6%)                                               | 1151 (29.7%)                                                          | 26 294 (32.2%)                                                     |
| Income quintile (1 = highest)^m,n        |                                                               |                                                                        |                                                                     |
| 1                                       | 2 361 451 (19.9%)                                            | 479 (12.3%)                                                           | 14 152 (16.1%)                                                     |
| 2                                       | 2 343 768 (19.8%)                                            | 552 (14.2%)                                                           | 14 613 (16.6%)                                                     |
| 3                                       | 2 364 279 (20.0%)                                            | 776 (20.0%)                                                           | 17 011 (19.3%)                                                     |
| 4                                       | 2 337 045 (19.8%)                                            | 933 (24.0%)                                                           | 19 418 (22.0%)                                                     |
| 5                                       | 2 301 617 (19.5%)                                            | 1120 (28.9%)                                                          | 22 469 (25.5%)                                                     |
| Missing                                 | 111 995 (0.9%)                                               | 20 (0.5%)                                                             | 444 (0.5%)                                                         |
| Educational attainment quintile (1 = highest)^o,p |                                           |                                                                        |                                                                     |
| 1                                       | 2 490 287 (21.1%)                                            | 638 (16.4%)                                                           | 14 904 (16.9%)                                                     |
| 2                                       | 2 513 154 (21.3%)                                            | 781 (20.1%)                                                           | 17 337 (19.7%)                                                     |
| 3                                       | 2 443 398 (20.7%)                                            | 729 (18.8%)                                                           | 17 755 (20.2%)                                                     |
| 4                                       | 2 260 406 (19.1%)                                            | 846 (21.8%)                                                           | 19 110 (21.7%)                                                     |
| 5                                       | 1 970 234 (16.7%)                                            | 852 (22.0%)                                                           | 18 328 (20.8%)                                                     |
| Missing                                 | 132 776 (1.1%)                                               | 34 (0.9%)                                                             | 673 (0.8%)                                                         |
| Proportion essential workers quintile (1 = lowest)^q,r,s |                                           |                                                                        |                                                                     |
| 1                                       | 2 533 697 (21.5%)                                            | 705 (18.2%)                                                           | 14 830 (16.8%)                                                     |
| 2                                       | 2 592 332 (21.9%)                                            | 780 (20.1%)                                                           | 17 367 (19.7%)                                                     |
| 3                                       | 2 315 922 (19.6%)                                            | 760 (19.6%)                                                           | 18 453 (20.9%)                                                     |
| 4                                       | 2 217 021 (18.9%)                                            | 794 (20.5%)                                                           | 18 163 (20.6%)                                                     |
| 5                                       | 2 018 450 (17.1%)                                            | 807 (20.8%)                                                           | 18 620 (21.1%)                                                     |
| Missing                                 | 132 633 (1.1%)                                               | 34 (0.9%)                                                             | 674 (0.8%)                                                         |
| Proportion racially minoritized groups quintile (1 = lowest)^t,u |                                           |                                                                        |                                                                     |
| 1                                       | 1 826 634 (15.5%)                                            | 260 (6.7%)                                                            | 18 046 (20.5%)                                                     |
| 2                                       | 1 964 891 (16.6%)                                            | 454 (11.7%)                                                           | 18 424 (20.9%)                                                     |
The household is deemed to be living in suitable accommodations (non–high-density housing) if its dwelling has enough bedrooms, as calculated using the National Occupancy Standard. Suitable accommodations refer to whether the dwelling has enough bedrooms for the size and composition of the household. A frequency of zeros permitted the creation of only 4 categories (the lower 2 quintiles combined); housing density/housing suitability refers to whether a private household is “living in suitable accommodations” according to the National Occupancy Standard, that is, whether the dwelling has enough bedrooms for the size and composition of the household. A household is deemed to be living in suitable accommodations (non-high-density housing) if its dwelling has enough bedrooms, as calculated using the National Occupancy Standard.

| Characteristic                                      | Number of Individuals Residing in Ontario as of 1 March 2020 | Number of COVID-19-related Deathsa Between 1 March 2020 and 2 March 2021 | Number of Non–COVID-19 Deathsb Between 1 March 2020 and 2 March 2021 |
|----------------------------------------------------|--------------------------------------------------------------|------------------------------------------------------------------------|---------------------------------------------------------------------|
| 3                                                  | 2,105,988 (17.8%)                                            | 666 (17.2%)                                                            | 17,568 (19.9%)                                                       |
| 4                                                  | 2,564,575 (21.7%)                                            | 964 (24.6%)                                                            | 16,729 (19.0%)                                                       |
| 5                                                  | 3,225,565 (27.3%)                                            | 1,502 (38.7%)                                                          | 16,672 (19.8%)                                                       |
| Missing                                            | 132,604 (1.1%)                                              | 34 (0.9%)                                                              | 668 (0.8%)                                                          |

Proportion recent immigrants (1 = lowest)

| 1                                                  | 5,963,039 (50.7%)                                            | 1,499 (38.6%)                                                          | 52,236 (59.4%)                                                      |
| 2                                                  | 2,412,998 (20.4%)                                            | 880 (22.7%)                                                            | 16,208 (18.4%)                                                      |
| 3                                                  | 3,236,805 (27.4%)                                            | 1,464 (37.7%)                                                          | 18,402 (20.9%)                                                      |
| Missing                                            | 178,913 (1.5%)                                              | 37 (1.0%)                                                              | 1,161 (1.3%)                                                       |

Proportion apartment buildings (1 = lowest)

| 1                                                  | 6,605,697 (55.9%)                                            | 1,613 (41.6%)                                                          | 42,666 (48.4%)                                                      |
| 2                                                  | 2,120,840 (18.0%)                                            | 687 (17.7%)                                                            | 18,576 (21.1%)                                                      |
| 3                                                  | 2,944,390 (24.9%)                                            | 1,545 (39.8%)                                                          | 26,093 (29.6%)                                                      |
| Missing                                            | 139,328 (1.2%)                                              | 35 (0.9%)                                                              | 772 (0.9%)                                                          |

Average household size quintile (1 = lowest)

| 1                                                  | 2,325,763 (19.7%)                                            | 1,028 (26.5%)                                                          | 25,171 (28.6%)                                                      |
| 2                                                  | 2,064,623 (17.5%)                                            | 571 (14.7%)                                                            | 19,138 (21.7%)                                                      |
| 3                                                  | 1,582,415 (13.4%)                                            | 405 (10.4%)                                                            | 12,471 (14.2%)                                                      |
| 4                                                  | 2,722,979 (23.1%)                                            | 861 (22.1%)                                                            | 17,020 (20.4%)                                                      |
| 5                                                  | 2,975,277 (25.2%)                                            | 960 (25.3%)                                                            | 12,625 (14.3%)                                                      |
| Missing                                            | 139,098 (1.2%)                                              | 35 (0.9%)                                                              | 772 (0.9%)                                                          |

Proportion high-density housing (1 = lowest)

| 1                                                  | 3,963,354 (33.7%)                                            | 1,018 (26.2%)                                                          | 31,975 (36.3%)                                                      |
| 2                                                  | 2,569,526 (21.7%)                                            | 675 (17.4%)                                                            | 20,016 (22.7%)                                                      |
| 3                                                  | 2,289,131 (19.4%)                                            | 722 (18.6%)                                                            | 15,862 (18.0%)                                                      |
| 4                                                  | 2,679,342 (22.7%)                                            | 1,370 (35.3%)                                                          | 17,732 (20.1%)                                                      |
| 5                                                  | 298,902 (2.5%)                                              | 95 (2.4%)                                                              | 2,252 (2.9%)                                                       |

Proportion with frailty (1 = lowest)

| 1                                                  | 1,598,960 (51.9%)                                            | 394 (12.7%)                                                            | 23,458 (26.1%)                                                      |
| 2                                                  | 1,298,026 (44.8%)                                            | 307 (10.0%)                                                            | 21,089 (23.2%)                                                      |
| 3                                                  | 698,382 (24.4%)                                             | 91 (2.9%)                                                              | 14,300 (16.0%)                                                      |
| 4                                                  | 298,902 (10.2%)                                             | 12 (0.4%)                                                              | 1,307 (1.5%)                                                       |
| 5                                                  | 48,198 (1.7%)                                              | 6 (0.2%)                                                               | 582 (0.7%)                                                         |

Number of COVID-19-related Deathsa Between 1 March 2020 and 2 March 2021

The look-back window for comorbidities was since 1991, unless otherwise specified.

Abbreviation: COVID-19, coronavirus disease 2019.

aDeath within 30 days following or 7 days prior to a laboratory-confirmed positive COVID-19 test.

bDeath without a laboratory-confirmed positive COVID-19 test. We did not include those who died more than 7 days prior or 30 days after a positive COVID-19 test in our definition of non–COVID-19 death, as we aimed to determine patterns of mortality by area-level social determinants of health without COVID-19 in our secondary outcome, limiting the assessment of the potential longer-term impact of COVID-19 on the outcome.

cAge as of 1 March 2020.

dWe defined rural as being located outside the commuting zone of a city with a population >10,000 [32].

The look-back window for comorbidities was since 1991, unless otherwise specified.

fFrailty score >15 in the last 5 years.

gTreatment in last 6 months or diagnosis in last year.

hDiagnosis in the last 5 years.

iImmunocompromised defined as diagnosed with human immunodeficiency virus (regardless of CD4 count) between 1991 and present, or had an organ or bone marrow transplant, or had another immunodeficient condition in the last 20 years.

jAdvanced liver disease defined as diagnosis of cirrhosis or decompensated cirrhosis.

kDiagnosis in last 5 years or had a procedure in last 20 years.

lInpatient diagnosis in the last 20 years.

mArea-level variables at the level of the census dissemination area.

nIncome quintile has variable cutoff values in each city or census area in order to take cost of living into account. A census dissemination area being in quintile 1 means it is among the highest 20% of dissemination areas in its city by median household income.

oFirst quintile represents areas with 0%–4.1% of people aged 25–64 years without a diploma; second quintile, 4.1%–7.5%; third quintile, 7.5%–11.4%; fourth quintile, 11.4%–17.1%; and fifth quintile, 17.1%–94.3%.

pFirst quintile represents areas with 0%–32.5% of working people in the area who self-identified as working in an essential job, including sales, trades, manufacturing, and agriculture; second quintile, 32.5%–42.3%; third quintile, 42.3%–49.8%; fourth quintile, 50.0%–57.5%; and fifth quintile, 57.5%–114.3%.

qFirst quintile represents areas with 0%–2.2% of people in the area who self-identified as racially minoritized groups; second quintile, 2.2%–7.5%; third quintile, 7.5%–18.7%; fourth quintile, 18.7%–43.5%; and fifth quintile, 43.5%–100%.

rFirst quintile represents areas with 0%–2.1% of people in the area being recent immigrants who came to Canada within the last 5 years; second quintile, 2.1%–4.7%; and third quintile, 4.7%–41.2%. The high frequency of zeros permitted the creation of only 3 categories (ie, the lower 3 quintiles combined and the fourth and fifth quintiles).

sFirst quintile represents areas with 0%–7.3% of buildings in the area are apartment buildings; second quintile, 7.4%–37.7%; and third quintile, 37.7%–100%. The high frequency of zeros permitted the creation of only 3 categories (ie, the lower 3 quintiles combined and the fourth and fifth quintiles).

tFirst quintile represents areas with 0%–2.1 people/dwelling; second quintile, 2.2–2.4; third quintile, 2.5–2.6; fourth quintile, 2.7–3; and fifth quintile, 3.1–5.7.

uFirst quintile represents areas with 0%–2.6% of households are considered high-density housing; second quintile, 2.7%–6.2%; third quintile, 5.3%–8.7%; fourth quintile, >8.7%. The high frequency of zeros permitted the creation of only 4 categories (the lower 2 quintiles combined); “housing density/housing suitability” refers to whether a private household is “living in suitable accommodations” according to the National Occupancy Standard, that is, whether the dwelling has enough bedrooms for the size and composition of the household. A household is deemed to be living in suitable accommodations (non-high-density housing) if its dwelling has enough bedrooms, as calculated using the National Occupancy Standard.
subdistribution hazard models [22, 37]. Based on the fitted models adjusted for individual-level demographics and baseline health, we estimated the adjusted marginal cumulative incidence functions [38] and calculated the difference in the 1-year cumulative probability of COVID-19–related death between the most (SDOH level with the worst outcome; eg, lowest income quintile) and the least (SDOH level with the best outcome; eg, highest income quintile) at-risk group for each SDOH variable.

All analyses were conducted using SAS 9.4 [35]. R 4.1.2 was used to generate figures [39]. The confidence intervals (CIs) were derived from a robust sandwich covariance matrix to account for clustering by DA [40].

RESULTS

Of 11 810 255 community-dwelling adults (median age, 48 years) included, 206 671 (1.75%) tested positive for COVID-19, 3880 (0.03%) died related to COVID-19, and 88 107 (0.75%) died without a COVID-19 diagnosis. Individuals with missing data (N = 111 955, 0.9%) on area-level SDOH were excluded from the multivariable regression analyses (Supplementary Figure 2).

Deaths related to COVID-19 were disproportionately concentrated among older adults, males, and individuals living in urban areas (Table 1). COVID-19–related deaths were also disproportionately concentrated among individuals living with a comorbidity and those with more prior healthcare use (Table 1). Compared with the full cohort, COVID-19–related deaths were overrepresented in areas with less social advantage (eg, 28.9% vs 19.5% lived in the lowest-income areas) and in areas with a higher proportion of racially minoritized groups (38.7% vs 27.3%) and recent immigrants (37.7% vs 27.4%; Table 1).

Area-level SDOH and COVID-19–related Mortality

In the unadjusted models, areas with lower SES, higher ethnic diversity, higher proportion of apartment buildings and high-density housing, and lowest or highest household size (vs medium) were associated with increased hazard of COVID-19–related death (Figure 2A, Supplementary Table 3). We observed a dose–response relationship between all area-level SDOH variables and COVID-19–related mortality, except for household size (medium household size was associated with the lowest COVID-19–related mortality and was treated as the reference group; Figure 2).

Adjustment for individual-level demographics either attenuated or amplified the associations between COVID-19–related mortality and area-level SES (Figure 2A–2C). Further adjustment for baseline health slightly reduced the associations between COVID-19–related mortality and SES (Figure 2C, 2D). After further adjustment for other area-level SDOH, SES...
remained an independent determinant of COVID-19–related mortality, although the magnitude of association was greatly reduced (Figure 2D, 2E). Fully adjusted hazard ratios (aHRs; 95% CIs) were 1.30 (1.04–1.62) for lowest vs highest income, 1.27 (1.07–1.52) for lowest vs highest proportion with diploma or higher educational attainment, and 1.28 (1.05–1.57) for highest vs lowest proportion essential workers (Figure 2E, Supplementary Table 3).

Adjustment for age and sex increased the magnitude of associations between area-level ethnic diversity and COVID-19–related mortality (Figure 2A, 2B). Additional adjustment for other individual-level demographics largely reduced the magnitude of associations (Figure 2B, 2C). Further adjustment for baseline health had a minimal influence on the associations (Figure 2C, 2D). Additional adjustment of other area-level SDOH reduced the magnitude of associations between COVID-19–related mortality and proportion racially minoritized groups and nullified the association between COVID-19–related mortality and proportion recent immigrants (Figure 2D, 2E). The fully aHR (95% CI) was 1.42 (1.08–1.87) for highest vs lowest proportion racially minoritized groups (Figure 2E, Supplementary Table 3).

After adjustment for individual-level demographics, baseline health, and other area-level SDOH, proportion apartment buildings was independently associated with increased hazard of COVID-19–related death (aHR, 1.25; 95% CI, 1.07–1.46), while proportion high-density housing was not (Figure 2E, Supplementary Table 3). The nonmonotonic relationship between COVID-19–related mortality and area-level household size persisted after full adjustment. The fully aHR (95% CI) was 1.30 (1.12–1.50) for highest vs medium area-level household size (Figure 2E, Supplementary Table 3).

Area-level SDOH and Non–COVID-19 Mortality and COVID-19 Case Fatality

In contrast to the pattern with COVID-19–related mortality, areas with higher proportion racially minoritized groups (highest vs lowest: aHR, 0.88; 95% CI, .84–.92) and large household size (highest vs medium: aHR, 0.85; 95% CI, .83–.88) were independently associated with decreased hazard of non–COVID-19 death (Figure 3A, 3B; Supplementary Table 4). Only lower area-level income was independently associated
with increased COVID-19 case fatality (Figure 3C, Supplementary Table 4).

**Adjusted Cumulative Probability of COVID-19–related Death**

After accounting for individual-level demographics and baseline health, the estimated absolute difference in the cumulative probability of COVID-19–related death over a 1-year period ranged from 0.006% to 0.020%, comparing the most and least at-risk SDOH group (Figure 4).

**DISCUSSION**

In a population-based cohort of 11.8 million adults in Ontario, Canada, we found that areas characterized by lower SES, greater ethnic diversity, more apartment buildings, and large vs medium household size were associated with increased hazards of COVID-19–related mortality, after accounting for individual-level demographics, baseline health, and other area-level SDOH. In contrast, areas with higher proportion racially minoritized groups and larger household size were associated with reduced hazard of non–COVID-19 mortality. With the exception of income, the area-level SDOH examined in this study were not independently associated with COVID-19 case fatality.

Our findings mirror those from studies in other countries, including the United Kingdom [4], Switzerland [5], Chile [13], and the United States [6], that have shown that areas with lower SES, measured by a composite index, were associated with increased risk and mortality of COVID-19. In contrast, areas with higher proportion racially minoritized groups and larger household size were associated with reduced hazard of non–COVID-19 mortality. With the exception of income, the area-level SDOH examined in this study were not independently associated with COVID-19 case fatality.

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to remote work had limited ability to shelter in place during periods of broad-scale restrictions on mobility and were less likely to receive benefits such as paid sick leave [41, 42], leading to heightened exposure risk and barriers to effective quarantine or isolation [12, 14]. The relationship between area-level income and case fatality might reflect delayed diagnosis or access to and quality of clinical care for persons living in lower-income neighborhoods [17, 43, 44]. Emerging evidence suggests that in-hospital mortality with COVID-19 was amplified during periods of higher patient load. Such inpatient surges were most likely to occur in hospitals serving lower-income areas experiencing the highest rates of cases [17, 43–45].

Our finding that areas with a higher proportion racially minoritized groups experienced increased hazard of COVID-19–related mortality but not higher case fatality confirmed findings in other settings [3, 10]. A systematic review of 52 US studies found that African-American/Black and non-White Hispanic populations experienced a disproportionate burden of infections, hospitalization, and COVID-19–related mortality, but not higher in-hospital case fatality, compared with similarly aged White non-Hispanic populations [10]. Studies in the United Kingdom found that minority ethnic groups experienced elevated risk of COVID-19–related mortality [3], higher prevalence of COVID-19 antibodies [46], but similar infection fatality ratio [46] compared with White counterparts. Taken together, the findings suggest that inequalities in COVID-19–related mortality by racially minoritized groups are more likely to stem from disproportionate exposure risks leading to disproportionate risks of acquisition/transmission and barriers to reach/access preventive interventions, as opposed to differences post-diagnosis [3, 10, 12].

In Canada, racially minoritized groups are more likely to work in essential services and more likely to live in larger and higher-density households [30], all of which have been identified as mechanistic risk factors for heightened exposure risk [12, 14]. Prior to COVID-19 and similar to our findings regarding non–COVID-19 mortality during the COVID-19 pandemic, mortality rates in Canada were lower in racially minoritized groups [47]. Similar to findings from the United Kingdom and Sweden [3, 48], COVID-19 has reversed the dose–response pattern of lower non–COVID-19 mortality among racially minoritized groups vs their counterparts.

The nonmonotonic relationship between area-level household size and COVID-19–related mortality might be partially explained by the positive correlation between income and household size (data not shown) and by different contact patterns (eg, individuals who live by themselves might have increased contacts outside the household). Our findings suggest that large household size, regardless of the housing density, might be an independent risk factor for household transmission. In epidemic theory, contact rates are conceptualized as density-dependent or frequency-dependent. Transmissions outside households may be influenced by population density (density-dependent transmission) [49]. Within the same household, contact rates may be better reflected by the frequency-dependent transmission (thus, household size; ie, assuming close interactions among all household members, regardless of the household density) [49].

Strengths of our study include limiting collider bias [20] and leveraging high-quality linked health administrative, surveillance, and health registries data to examine the influence of various confounders, including comorbidities, on the relationship between COVID-19–related mortality and area-level SDOH. Another strength is the competing risk survival analysis approach that allowed us to correctly estimate the marginal probability of COVID-19–related death in the presence of competing events. Our estimates of marginal probability of COVID-19–related death by area-level SDOH provided important insights into the health of each subgroup and permitted the quantification of inequalities on an absolute scale with adjustment of covariates [3, 5, 50], which are meaningful for public health decision-making, including informing strategies such as geographically focused vaccination [51–53].

Limitations include the potential for misclassification due to lack of data on the cause of death. Based on Ontario COVID-19 surveillance data, 92% of recorded all-cause deaths among individuals diagnosed with COVID-19 occurred within 30 days following or 7 days prior to a positive test (Supplementary Figure 3). Other settings have adopted similar definitions of COVID-19–related death to capture the immediate impact of COVID-19 on death [54]. Our estimates of COVID-19–related mortality might be underestimated if missed diagnosis occurs due to lack of testing or false-negative antigen tests [55]. Individuals who do not have provincial health insurance were not captured. If they were more likely to be socially and structurally vulnerable, our estimates might have underestimated the inequalities. We were restricted to area-level SDOH measures in the absence of individual-level measures, which might result in an underestimation of the SDOH–mortality associations [56]. Almost all areas with the highest quintile proportion racially minoritized groups were urban areas. However, stratified analysis by rural/urban revealed that inequalities in COVID-19–related mortality by racially minoritized groups were present in both settings (Supplementary Table 5). We lacked data on the severity of comorbidities and COVID-19 infection, and individuals’ exposures related to contact patterns and physical networks (eg, mobility, physical distancing) and masking, information that could help further explain the relationship between SDOH and COVID-19–related mortality. We did not determine if the associations between SDOH and COVID-19–related mortality differed across age groups or regions or if they changed over time (eg, between pandemic waves or in the context of vaccination) [3, 13], which will be an important next step of research. Indeed, examination of
proportional hazard assumptions suggests a time-varying relationship between proportion racially minoritized group and hazard of COVID-19–related mortality (Supplementary Table 2).

Our study demonstrated that area-level social and structural inequalities are associated with COVID-19–related mortality after accounting for age, sex, and clinical factors. The majority of inequalities stem from proximal exposures and reach of, and access to, prevention interventions. COVID-19 has reversed existing patterns of mortality by race/ethnicity, with higher COVID-19–related mortality for racially minoritized groups. Tailored strategies that specifically address and are designed around the risk pathways related to SES, racism, and housing contexts include, but are not limited to, paid sick leave and improved workplace health and safety protocols; outbreak management; and community-led and community-tailored outreach for testing, effective isolation and quarantine, and vaccine programs. Moving forward, the goal of pandemic responses should include improving overall population health by addressing disproportionate acquisition and transmission risks and inequitable coverage of prevention interventions associated with SDOH.

Supplementary Data
Supplementary materials are available at Clinical Infectious Diseases online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes
Author contributions. L. W., J. C. K., and S. M. conceptualized the study. A. C. conducted the data cleaning and statistical analyses. L. W. drafted the manuscript. A. C., S. B., J. S., A. K. C., B. S., P. C. A., J. C. K., and S. M. provided critical input into the results interpretation and preparation of the manuscript.

Acknowledgments. The authors thank IQVIA Solutions Canada for use of their Drug Information File. The authors are grateful to the 14.7 million Ontario residents, without whom this research would be impossible.

Data sharing. The dataset from this study is held securely in coded form at ICES. While legal data-sharing agreements between ICES and data providers (eg, healthcare organizations and government) prohibit ICES from making the dataset publicly available, access may be granted to those who meet prespecified criteria for confidential access, available at https://www.ices.on.ca/DAS (email: das@ices.on.ca). The full dataset creation plan and underlying analytic code are available from the authors upon request, understanding that the computer programs may rely upon coding templates or macros that are unique to ICES and are therefore either inaccessible or may require modification.

Disclaimer. Some of the material presented here is based on data and/or information compiled and provided by the Canadian Institute for Health Information (CIHI) and Ontario Health (OH) (previously known as Cancer Care Ontario). The opinions, results, view, and conclusions reported in this paper are those of the authors and do not necessarily reflect those of the funding sources. No endorsement by ICES, the Ontario Ministry of Health (MOH), Ministry of Long-Term Care (MLTC), CIHI, or OH is intended or should be inferred. The study sponsors did not participate in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; or the decision to submit the manuscript for publication.

Financial support. This work was supported by the Canadian Institutes of Health Research (grant VR5-172683) and the St. Michael’s Hospital Foundation. This study was also supported by ICES, which is funded by an annual grant from the MOH and the MLTC. S. M. is supported by a Tier 2 Canada Research Chair in Mathematical Modelling and Program Science. J. K. is supported by a Clinician–Scientist Award from the University of Toronto Department of Family and Community Medicine.

Potential conflicts of interest. S. B. has participated on National Institutes of Health–funded data and safety monitoring boards. A. K. C. is a board member of Partner in Health Canada. All other authors report no potential conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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