



Original Article

Epidemiology of COVID-19 and Its Cardiac and Neurologic Complications Among Chinese and South Asians in Ontario: Waves 1, 2, and 3

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ABSTRACT

Background: Although we had previously reported the cardiac and neurologic outcomes of Chinese and South Asian Ontarians in wave 1 of COVID-19, data on subsequent waves of COVID-19 remain unexamined. This is an extension study of this cohort in waves 2 and 3.

Methods: We identified adult Ontarians with a positive COVID-19 polymerase chain reaction test from January 1, 2020 to June 30, 2021, and they were classified as being Chinese or South Asian using a validated surname algorithm; we compared their outcomes of mortality, and cardiac and neurologic complications with those of the general population using multivariable logistic regression models.

RÉSUMÉ

Contexte : Nous avons déjà présenté les issues cliniques cardiaques et neurologiques chez les Ontariens de descendance chinoise ou sud-asiatique pour la première vague de la pandémie de COVID-19, mais les données au sujet des vagues ultérieures n'avaient pas encore été analysées. Nous présentons ici une prolongation de cette étude de cohortes pour la seconde et la troisième vague de COVID-19.

Méthodologie : Notre analyse porte sur des adultes ontariens ayant obtenu un résultat positif à un test de COVID-19 par réaction en chaîne de la polymérase entre le 1^{er} janvier 2020 et le 30 juin 2021. Un algorithme validé pour l'analyse des noms de famille a été utilisé pour

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is responsible for the global pandemic known as coronavirus disease (COVID-19).^{1,2} Differences in COVID-19 infection rates and adverse outcomes following infection across different ethnic groups have been

described.³⁻¹⁰ In the US, the overall mortality rate among African Americans with COVID-19 was significantly higher than that of White and Asian people.¹¹

In Canada's most populous province—Ontario—South Asians (29.6% of the total population) and Chinese people (19.4%) represent the largest visible minorities.^{12,13} We have previously described the cardiac and neurologic complications among Chinese and South Asian Ontarians during the first wave of the pandemic (between January 15, 2020 and July 17, 2020), identifying significant differences in baseline demographics and outcomes.³ Since then, 2 subsequent waves (wave 2: July 18, 2020 to March 4, 2021; wave 3: March 5, 2021 to June 30, 2021) of COVID-19 infection in Ontario have been observed, with variation in infection rates and

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Ethics Statement: This research has adhered to the REB of University of Toronto ethical guidelines.

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See page 902 for disclosure information.

Results: Compared to the general population ($n = 439,977$), the Chinese population ($n = 15,208$) was older (mean age 44.2 vs 40.6 years, $P < 0.001$) and the South Asian population ($n = 46,333$) was younger (39.2 years, $P < 0.001$). The Chinese population had a higher 30-day mortality (odds ratio [OR] 1.44; 95% confidence interval [CI] 1.28-1.61) and more hospitalization or emergency department visits (OR, 1.14; 95% CI, 1.09-1.28), with a trend toward a higher incidence of cardiac complications (OR, 1.03; 95% CI, 0.87-1.12) and neurologic complications (OR, 1.23; 95% CI, 0.96-1.58). South Asians had a lower 30-day mortality (OR, 0.88; 95% CI, 0.78-0.98) but a higher incidence of hospitalization or emergency department visits (OR, 1.17; 95% CI, 1.14-1.20) with a trend toward a lower incidence of cardiac complications (OR, 0.76; 95% CI, 0.67-0.87) and neurologic complications (OR, 0.89; 95% CI, 0.73-1.09). There was also a significant difference in these outcomes between wave 1, 2 and 3, with a greater mortality in all groups in waves 2 and 3.

Conclusions: Ethnicity continues to be an important determinant of mortality, cardiac and neurologic outcomes, and healthcare use among patients with COVID-19, requiring further studies to understand factors driving these differences.

outcomes based on various demographic and social factors. Thus, we conducted this extension study using similar methodology to evaluate mortality, cardiac and neurologic complications, and healthcare utilization in waves 1, 2, and 3 among Chinese and South Asian Ontarians, compared to the general population and compared to these outcomes across the 3 waves.

Methods

Data sources and study population

To identify the cohort, we used the Case and Contact Management System (CCM) database and selected adults (aged 18 to 105 years) who had a positive COVID polymerase chain reaction (PCR) test result between January 1, 2020 and June 30, 2021 (inclusive). We excluded patients who were not Ontario residents at the time of the COVID test. If a person had multiple positive tests within the study period, the first positive test date was chosen as the index date. Our methodology has been previously reported.³ In brief, data from the Registered Persons Database, the Canadian Institute for Health Information Discharge Abstract Database, the National Ambulatory Care Reporting System, and the Ontario Health Insurance Plan physician claims database were used to identify demographics and health conditions, health outcomes, and health service utilization. The Registered Persons Database provides demographic information about

isoler les sujets de descendance chinoise ou sud-asiatique, et leur taux de mortalité de même que les complications cardiaques et neurologiques ont été comparés à ceux de la population générale à l'aide de modèles de régression logistique multivariée.

Résultats : En comparaison de la population générale ($n = 439\,977$), les personnes de descendance chinoise ($n = 15\,208$) se sont révélées plus âgées (âge moyen de 44,2 ans contre 40,6 ans, $P < 0,001$), tandis que les personnes de descendance sud-asiatique ($n = 46\,333$) étaient plus jeunes (39,2 ans, $P < 0,001$). Dans la population de descendance chinoise, le taux de mortalité après 30 jours était plus élevé (rapport de cotes [RC] de 1,44; intervalle de confiance [IC] à 95 % de 1,28 à 1,61), et davantage d'hospitalisations ou de consultations aux urgences sont survenues (RC de 1,14; IC à 95 % de 1,09 à 1,28). L'incidence de complications cardiaques (RC de 1,03; IC à 95 % de 0,87 à 1,12) et de complications neurologiques (RC de 1,23; IC à 95 % de 0,96 à 1,58) avait également tendance à être plus élevée. Chez les personnes de descendance sud-asiatique, le taux de mortalité après 30 jours était plus faible (RC de 0,88; IC à 95 % de 0,78 à 0,98), mais l'incidence d'hospitalisations ou de consultations aux urgences était plus élevée (RC de 1,17; IC à 95 % de 1,14 à 1,20). Elles présentaient également une tendance vers une plus faible incidence de complications cardiaques (RC de 0,76; IC à 95 % de 0,67 à 0,87) et de complications neurologiques (RC de 0,89; IC à 95 % de 0,73 à 1,09). Des différences significatives ont également été observées pour ces paramètres entre les vagues 1, 2 et 3 de la maladie, et le taux de mortalité était plus élevé pour tous les groupes des vagues 2 et 3.

Conclusions : L'origine ethnique demeure un déterminant important de la mortalité, des issues cliniques cardiaques et neurologiques ainsi que de l'utilisation des ressources en santé chez les patients atteints de la COVID-19. D'autres études sont toutefois nécessaires pour mieux comprendre les facteurs qui expliquent ces différences.

anyone who has ever received an Ontario health card number. The Canadian Institute for Health Information Discharge Abstract Database contains patient-level data for hospitalizations. The National Ambulatory Care Reporting System captures information on patient visits to emergency departments (EDs). The Ontario Health Insurance Plan captures information regarding the services provided by practicing physicians in Ontario. These datasets were linked using unique encoded identifiers and analyzed at ICES. Long-term care status was ascertained using the Ontario Drug Benefit database and the Continuing Care Reporting System.

Exposure

We classified patients as being Chinese or South Asian using a validated surname algorithm with high specificity as reported by Shah et al. in 2010.¹⁴ We compared Chinese and South Asian people to the general Ontario population (those not classified as Chinese or South Asian). The cohort was stratified into 3 waves: wave 1 was from January 15, 2020 to July 17, 2020; wave 2 was from July 18, 2020 to March 4, 2021; and wave 3 was from March 5, 2021 to June 30, 2021.

Outcomes

The primary outcomes at 30 days following a positive PCR test were as follows: death, composite cardiac outcome (myocardial infarction, heart failure, arrhythmia, atrial fibrillation/flutter, myocarditis, pulmonary embolism/deep vein

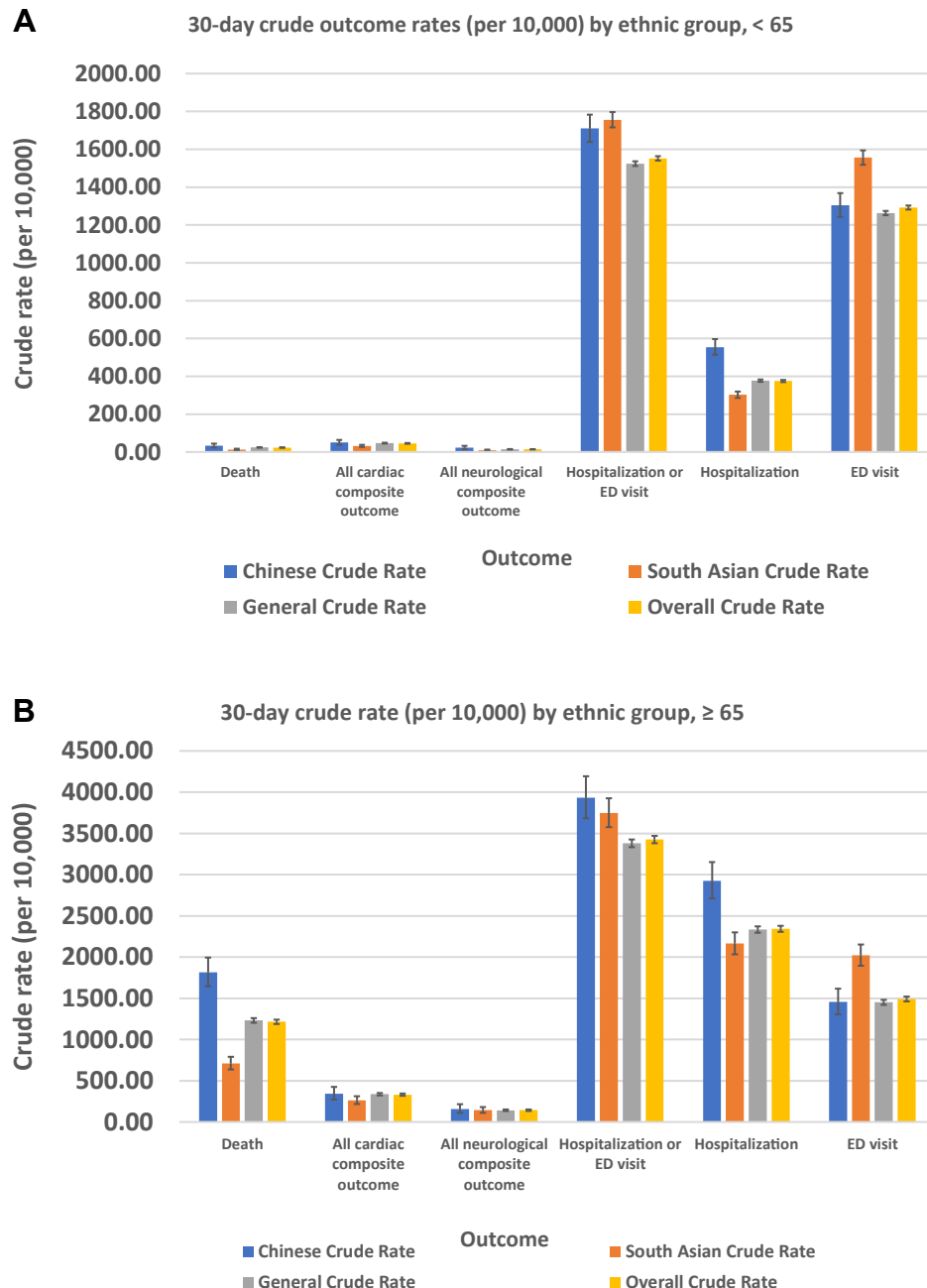


Figure 1. 30-day outcome crude rates, by ethnic group, for patients aged (A) < 65 years and (B) ≥ 65 years. ED, emergency department.

thrombosis); composite neurologic outcome (hemorrhagic stroke, ischemic stroke, seizure, meningitis, encephalitis, encephalopathy, and Parkinson's Disease); and healthcare utilization (hospitalization, ED visit, intensive care unit [ICU] admission, use of extracorporeal membrane oxygenation, use of mechanical ventilation). Codes are listed in [Supplemental Table S1](#). Outcomes were measured at the individual patient level. The final follow-up date was July 31, 2021.

Statistical analysis

Baseline and outcome characteristics were compared among the Chinese, South Asian, and general populations.

For continuous variables, descriptive statistics included mean values with standard deviation, and median values with interquartile range; the *P* values were calculated using 1-way analysis of variance for means, and the Kruskal-Wallis test for medians. Categorical variables were described using proportions, and *P* values from a χ^2 test were provided.

We reported crude and age- and sex-standardized rates of outcomes. We used the Ontario population from the year 2020 as the reference population. We used multivariable logistic regression to determine whether ethnicity was associated with our outcomes of interest. A separate logistic regression model was built for each binary outcome, with ethnicity as the main exposure categorical variable, and the general population

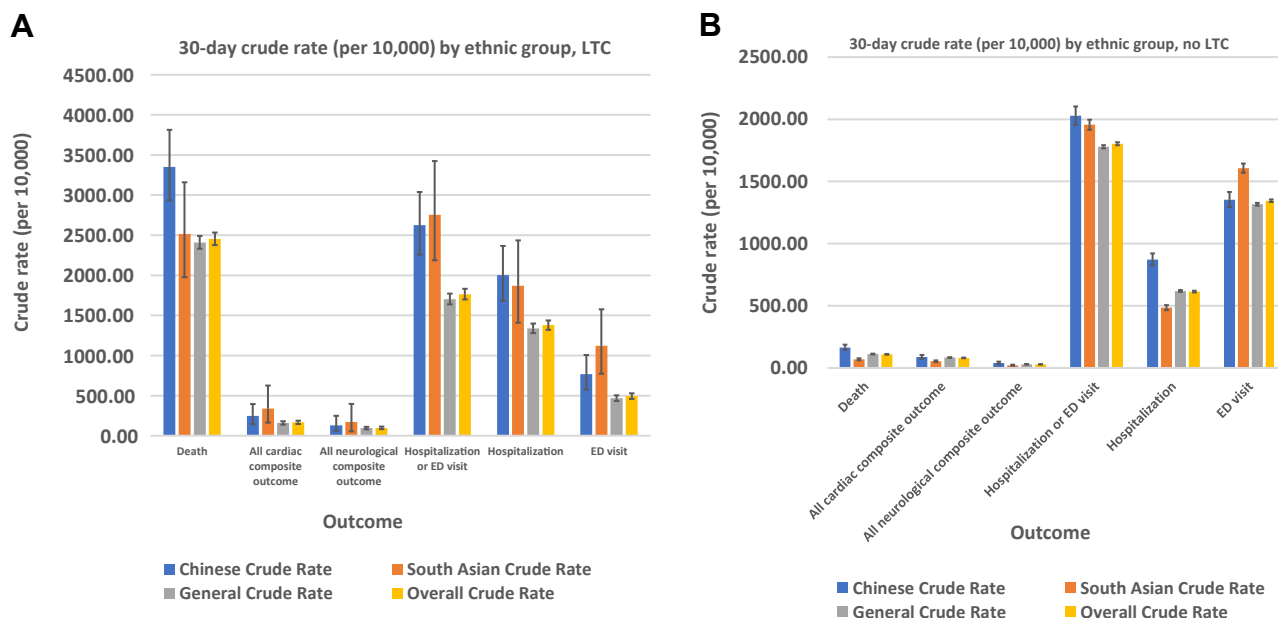


Figure 2. 30-day outcome crude rates, by ethnic group, for patients (A) in long-term care (LTC) and (B) not in LTC. ED, emergency department.

as the reference group. We adjusted for age, sex, income quintile, long-term care residence, and Charlson Index in the 90 days prior to a positive COVID test. We reported odds ratios (ORs) and 95% confidence intervals (CIs) comparing Chinese people and South Asian people to the general population. Using stratified analyses, we compared the outcomes across the 3 waves.

Sensitivity analyses

Recognizing that age is an important predictor of outcomes, we conducted sensitivity analyses, stratifying the cohort and limiting the analyses to those aged < 65 years and those aged ≥ 65 years (Figure 1). We also evaluated the variation in outcomes among those who did reside vs did not reside in a long-term care facility (Figure 2).

Results

All patients in our analyses had a positive PCR test for COVID-19. Compared to the general population (n = 439,977), the Chinese population (n = 25,208) was older (mean age 44.2 vs 40.6 years, $P < 0.001$), whereas the South Asian population (n = 46,333) was younger (mean age 39.2 years, $P < 0.001$). The mean age decreased significantly from wave 1 to wave 3: Chinese population (54.3, 45.9, and 40.4 years, respectively); South Asian population (43.9, 39.8, and 37.7 years, respectively); and general population (52.9, 41.6, and 37.4 years, respectively) ($P < 0.001$). The majority of COVID-19 cases in Ontario for all 3 cohorts were from wave 2 and wave 3: Chinese population, 93.3%; South Asian population, 95.1%; and general population, 92.7%. Further differences in baseline characteristics are described in Table 1.

Table 2 shows the crude rates of each outcome of interest. Compared to the rate in the general population, 30-day mortality was higher in the Chinese population (3.1 vs 1.9%, $P < 0.001$) and lower in the South Asian population

(0.9 vs 1.9%, $P < 0.001$). Compared to that in the general population, the incidence of cardiac complications was similar in the Chinese population (1.0% vs 0.9%) and lower in the South Asian population (0.6% vs 0.9%, $P < 0.001$), whereas the incidence of neurologic complications was similar in the Chinese population (0.4% vs 0.3%) and the South Asian population (0.2% vs 0.3%; Fig. 3). Healthcare utilization was more frequent in both the Chinese and South Asian populations, compared to that in the general population (Table 2).

In multivariable logistic regression analyses, the odds ratio (OR) of 30-day mortality was higher in the Chinese population (1.44; 95% confidence interval [CI] 1.28-1.61) and lower in the South Asian population (OR, 0.88; 95% CI, 0.78-0.98) compared to that in the general population (Table 3). The OR for cardiac complications was similar between the Chinese and the general populations (OR, 1.03; 95% CI, 0.87-1.22) and lower in the South Asian population (OR, 0.76; 95% CI, 0.67-0.87). Neurologic complications were numerically more frequent in the Chinese population than in the general population (OR, 1.23; 95% CI, 0.96-1.58) and were less likely in the South Asian population (OR, 0.88; 95% CI, 0.72-1.08), but the confidence intervals included null values. The OR for hospitalization or ED visit was higher in the Chinese population (OR, 1.13; 95% CI, 1.09-1.18) and the South Asian population (OR, 1.17; 95% CI, 1.14-1.20) compared to that in the general population (Table 3).

Among those aged < 65 years, the variation in mortality rate was no longer observed, but both South Asian and Chinese patients had higher rates of healthcare utilization than the general population (Fig. 1A). For those aged ≥ 65 years, mortality rates, cardiac and neurologic complication rates, and ICU admission rates were all increased significantly compared to the rates among those aged < 65 years (Fig. 1B). The mortality rate, and the cardiac and neurologic complication

Table 1. Baseline characteristics of patients with positive COVID test, by ethnic group, in Ontario: waves 1, 2, and 3

Characteristic	Chinese population	South Asian population	General population	Overall	<i>P</i>	<i>P</i>
	n = 15,208	n = 46,333	n = 439,977	N = 501,518	Chinese vs general	South Asian vs general
Age, y, mean (SD)	44.15 ± 21.20	39.19 ± 18.87	40.63 ± 21.37	40.60 ± 21.16	< 0.001	< 0.001
Age, y, median (IQR)	43 (29–58)	37 (26–53)	39 (24–56)	39 (24–55)	< 0.001	< 0.001
Age groups, y					< 0.001	< 0.001
≤ 19	1766 (11.6)	6454 (13.9)	74,096 (16.8)	82,316 (16.4%)		
20–39	5010 (32.9)	18,523 (40.0)	150,481 (34.2)	174,014 (34.7%)		
40–59	5008 (32.9)	14,204 (30.7)	130,576 (29.7)	149,788 (29.9%)		
60–79	2414 (15.9)	6150 (13.3)	62,009 (14.1)	70,573 (14.1%)		
≥ 80	1010 (6.6)	1002 (2.2)	22,815 (5.2)	24,827 (5.0%)		
Sex					0.93	< .001
Female	7741 (50.9)	21,684 (46.8)	223,793 (50.9)	253,218 (50.5%)		
Male	7467 (49.1)	24,649 (53.2)	216,184 (49.1)	248,300 (49.5%)		
Income quintile					< 0.001	< 0.001
Missing	51 (0.3)	66 (0.1)	1396 (0.3)	1513 (0.3%)		
1 (lowest)	3882 (25.5)	8073 (17.4)	112,051 (25.5)	124,006 (24.7%)		
2	3876 (25.5)	12,177 (26.3)	91,786 (20.9)	107,839 (21.5%)		
3	2673 (17.6)	13,988 (30.2)	90,032 (20.5)	106,693 (21.3%)		
4	2666 (17.5)	7808 (16.9)	79,019 (18.0)	89,493 (17.8%)		
5 (highest)	2060 (13.5)	4221 (9.1)	65,693 (14.9)	71,974 (14.4%)		
Residence					< 0.001	< 0.001
Missing	51 (0.3)	65 (0.1)	1205 (0.3)	1321 (0.3%)		
Rural	58 (0.4)	247 (0.5)	19,580 (4.5)	19,885 (4.0%)		
Urban	15,099 (99.3)	46,021 (99.3)	419,192 (95.3)	480,312 (95.8%)		
Asthma	1781 (11.7)	7279 (15.7)	72,043 (16.4)	81,103 (16.2%)	< 0.001	< 0.001
Diabetes	1943 (12.8)	8010 (17.3)	56,669 (12.9)	66,622 (13.3%)	0.707	< 0.001
Hypertension	3241 (21.3)	9691 (20.9)	93,533 (21.3)	106,465 (21.2%)	0.876	0.086
Heart failure	284 (1.9)	639 (1.4)	11,057 (2.5)	11,980 (2.4%)	< 0.001	< 0.001
COPD	205 (1.3)	320 (0.7)	8674 (2.0)	9199 (1.8%)	< 0.001	< 0.001
Dementia	631 (4.1)	446 (1.0)	16,319 (3.7)	17,396 (3.5%)	0.005	< 0.001
LTC	689 (4.5)	294 (0.6)	14,578 (3.3)	15,561 (3.1%)	< 0.001	< 0.001
LTC time of test	337 (2.2)	120 (0.3)	5646 (1.3)	6103 (1.2%)	< 0.001	< 0.001
Hospitalization in previous 5 y	2985 (19.6)	7591 (16.4)	97,427 (22.1)	108,003 (21.5%)	< 0.001	< 0.001
Chronic kidney disease	426 (2.8)	1127 (2.4)	12,847 (2.9)	14,400 (2.9%)	0.392	< 0.001
Charlson comorbidity index (past 5 y from index)						
Acute myocardial infarction	76 (0.5)	333 (0.7)	3459 (0.8)	3868 (0.8%)	< 0.001	0.116
Congestive heart failure	143 (0.9)	311 (0.7)	5696 (1.3)	6150 (1.2%)	< 0.001	< 0.001
Peripheral vascular disease	49 (0.3)	40 (0.1)	1631 (0.4)	1720 (0.3%)	0.332	< 0.001
Cerebrovascular disease	171 (1.1)	210 (0.5)	4189 (1.0)	4570 (0.9%)	0.032	< 0.001
Dementia	280 (1.8)	193 (0.4)	7006 (1.6)	7479 (1.5%)	0.016	< 0.001
COPD or other respiratory diseases	98 (0.6)	223 (0.5)	5119 (1.2)	5440 (1.1%)	< 0.001	< 0.001
Rheumatic-like diseases	17 (0.1)	37 (0.1)	641 (0.1)	695 (0.1%)	0.279	< .001
Ulcers of the digestive system	63 (0.4)	58 (0.1)	1223 (0.3)	1344 (0.3%)	0.002	< .001
Liver disease—mild	41 (0.3)	57 (0.1)	1096 (0.2)	1194 (0.2%)	0.619	< .001
Diabetes with no chronic complications	236 (1.6)	591 (1.3)	6086 (1.4)	6913 (1.4%)	0.081	0.058
Diabetes with chronic complications	290 (1.9)	794 (1.7)	9760 (2.2)	10,844 (2.2%)	0.01	< 0.001
Hemiplegia or paraplegia	56 (0.4)	56 (0.1)	1267 (0.3)	1379 (0.3%)	0.071	< 0.001
Renal (kidney) disease	94 (0.6)	181 (0.4)	3078 (0.7)	3353 (0.7%)	0.235	< 0.001
Cancer (no secondary found)	138 (0.9)	234 (0.5)	4352 (1.0)	4724 (0.9%)	0.316	< 0.001
Liver disease—moderate or severe	14 (0.1)	38 (0.1)	451 (0.1)	503 (0.1%)	0.692	0.186
Cancer (metastatic—secondary)	55 (0.4)	56 (0.1)	1316 (0.3)	1427 (0.3%)	0.166	< 0.001
HIV / AIDS*	0 (0.0)	3 (0.0)	118 (0.0)	121 (0.0%)	0.043	0.008
Mean ± SD	0.18 ± 0.78	0.11 ± 0.60	0.19 ± 0.81	0.18 ± 0.79	0.1	< 0.001
Median (IQR)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0.049	< 0.001
Charlson category						
0	14,101 (92.7)	44,135 (95.3)	406,041 (92.3)	464,277 (92.6%)	0.141	< 0.001
1	421 (2.8)	865 (1.9)	12,991 (3.0)	14,277 (2.8%)		
≥ 2	686 (4.5)	1333 (2.9)	20,945 (4.8)	22,964 (4.6%)		
Wave (χ ² test)					< 0.001	< 0.001
1	1024 (6.7)	2274 (4.9)	32,147 (7.3)	35,445 (7.1%)		
2	7810 (51.4)	25,648 (55.4)	216,165 (49.1)	249,623 (49.8%)		
3	6374 (41.9)	18,411 (39.7)	191,665 (43.6)	216,450 (43.2%)		

Values are n (%), unless otherwise indicated. Waves: 1 = January 15, 2020 to July 17, 2020; 2 = July 18, 2020 to March 4, 2021; 3 = March 5, 2021 to June 30, 2021 (end of cohort selection).

COPD, chronic obstructive pulmonary disease; HIV/AIDS, human immunodeficiency virus/acquired immune deficiency syndrome; IQR, interquartile range; LTC, long-term care; SD, standard deviation.

*Very low number of cases.

Table 2. Crude rates of 30-day mortality, cardiac and neurological complications, and healthcare use of patients with COVID-19 in Ontario

Outcome	Chinese patients	South Asian patients	General population of patients	P	
	N = 15,208	N = 46,333	N = 439,977	Chinese vs general	South Asian vs general
Death	471 (3.1)	394 (0.9)	8280 (1.9)	< 0.001	< 0.001
All cardiac composite outcome	145 (1.0)	257 (0.6)	3789 (0.9)	0.227	< 0.001
AMI	11 (0.1)	29 (0.1)	237 (0.1)	0.337	0.445
HF	20 (0.1)	52 (0.1)	684 (0.2)	0.46	0.023
Arrhythmia—excluding atrial fibrillation and flutter	43 (0.3)	67 (0.1)	919 (0.2)	0.051	0.003
Atrial fibrillation and flutter	52 (0.3)	54 (0.1)	1174 (0.3)	0.079	< 0.001
Myocarditis	1–5*	1–5*	12–16*	0.56	0.609
DVT/PE	43 (0.3)	82 (0.2)	1183 (0.3)	0.746	< 0.001
All neurological composite outcome	66 (0.4)	106 (0.2)	1385 (0.3)	0.01	0.001
Stroke	19 (0.1)	29 (0.1)	367 (0.1)	0.084	0.135
Ischemic stroke	12 (0.1)	20 (0.0)	290 (0.1)	0.541	0.065
Hemorrhagic stroke	7 (0.0)	10 (0.0)	85 (0.0)	0.023	0.74
Seizure	4–8*	6–10*	165 (0.0)	0.772	0.05
Meningitis	0 (0.0)	0 (0.0)	1–5*	0.71	0.516
Encephalitis	0 (0.0)	0 (0.0)	1–5*	0.853	0.746
Encephalopathy	33 (0.2)	50 (0.1)	712 (0.2)	0.098	0.005
Viral meningitis not specified elsewhere	0 (0.0)	0 (0.0)	1–5*	0.853	0.746
GBS	0 (0.0)	0 (0.0)	9 (0.0)	0.577	0.33
Inflammatory myositis/myalgia	0 (0.0)	0 (0.0)	0 (0.0)	n/a	n/a
Parkinson’s Disease	10 (0.1)	20 (0.0)	169 (0.0)	0.095	0.621
Health services					
Hospitalization or ED visit	3126 (20.6)	9086 (19.6)	78,166 (17.8)	< 0.001	< 0.001
Hospitalization	1404 (9.2)	2288 (4.9)	28,300 (6.4)	< 0.001	< 0.001
ED visit	2019 (13.3)	7430 (16.0)	56,685 (12.9)	0.156	< 0.001
ICU admission	414 (2.7)	613 (1.3)	7315 (1.7)	< 0.001	< 0.001
ECMO	6 (0.0)	22 (0.0)	139 (0.0)	0.593	0.074
Mechanical ventilation	224 (1.5)	358 (0.8)	3908 (0.9)	< 0.001	0.011

Values are n (%), unless otherwise indicated.

AMI, acute myocardial infarction; DVT, deep vein thrombosis; ECMO, extracorporeal membrane oxygenation; ED, emergency department; GBS, Guillain Barre syndrome; HF, heart failure; ICU, intensive care unit; n/a, not applicable; PE, pulmonary embolus.

* Small number of reported cases.

rates were all increased significantly for those residing in long-term care facilities (Fig. 2A). Among those not residing in long-term care facilities, we found a higher rate of healthcare utilization, except hospitalization, among both ethnic groups compared to that in the general population (Fig. 2B).

Variations across the 3 waves

Figure 4 shows the variation in age- and sex-standardized rates of our outcomes of interest across the 3 waves for all 3 groups. In contrast to wave 1, higher age- and sex-

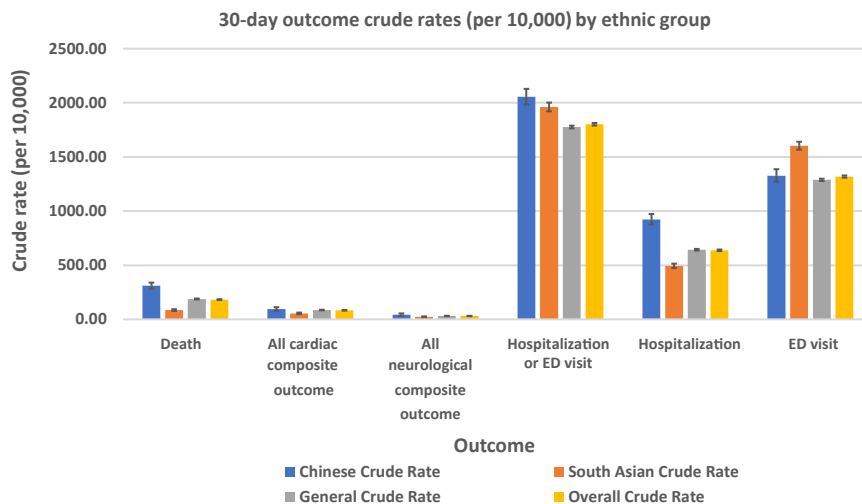


Figure 3. 30-day outcome crude rates (per 10,000), by ethnic group. ED, emergency department.

Table 3. Results of multivariable logistic regression analyses evaluating outcomes in patients with COVID-19 infection in Ontario

Outcome	Chinese vs general population	South Asian vs general population
	Adjusted* OR (95% CI)	Adjusted* OR (95% CI)
30-day mortality	1.44 (1.28–1.61)	0.88 (0.78–0.98)
All cardiac complications	1.03 (0.87–1.12)	0.76 (0.67–0.87)
All neurologic complications	1.23 (0.96–1.58)	0.89 (0.73–1.09)
All hospitalization or ED visits	1.14 (1.09–1.28)	1.17 (1.14–1.20)

CI, confidence interval; ED, emergency department; OR, odds ratio.
* Adjusted Odds Ratio (aOR).

standardized rates of mortality, cardiac and neurologic outcomes, and healthcare use were observed in all 3 groups. Across all waves, Chinese patients were found to have the highest rates of mortality and cardiac and neurologic complications, whereas South Asian patients had the lowest rates.

In contrast, healthcare use by the South Asian population was highest during wave 2, whereas that of Chinese patients was highest in wave 3.

Interpretation

We found variations in COVID-19-related outcomes among the Chinese and South Asian populations in Ontario, with Chinese patients being older and South Asian patients being younger than the general population. Despite adjusting for baseline differences in age, income, and comorbidities, Chinese patients with COVID-19 had a higher OR of COVID-19-related mortality and healthcare utilization, and the South Asian population had a lower OR of mortality, but a higher OR of healthcare utilization compared to those in the general population (Table 3).

The younger age at the time of COVID-19 infection among the South Asian population could be, in part, attributed to a larger proportion of the South Asian population being frontline

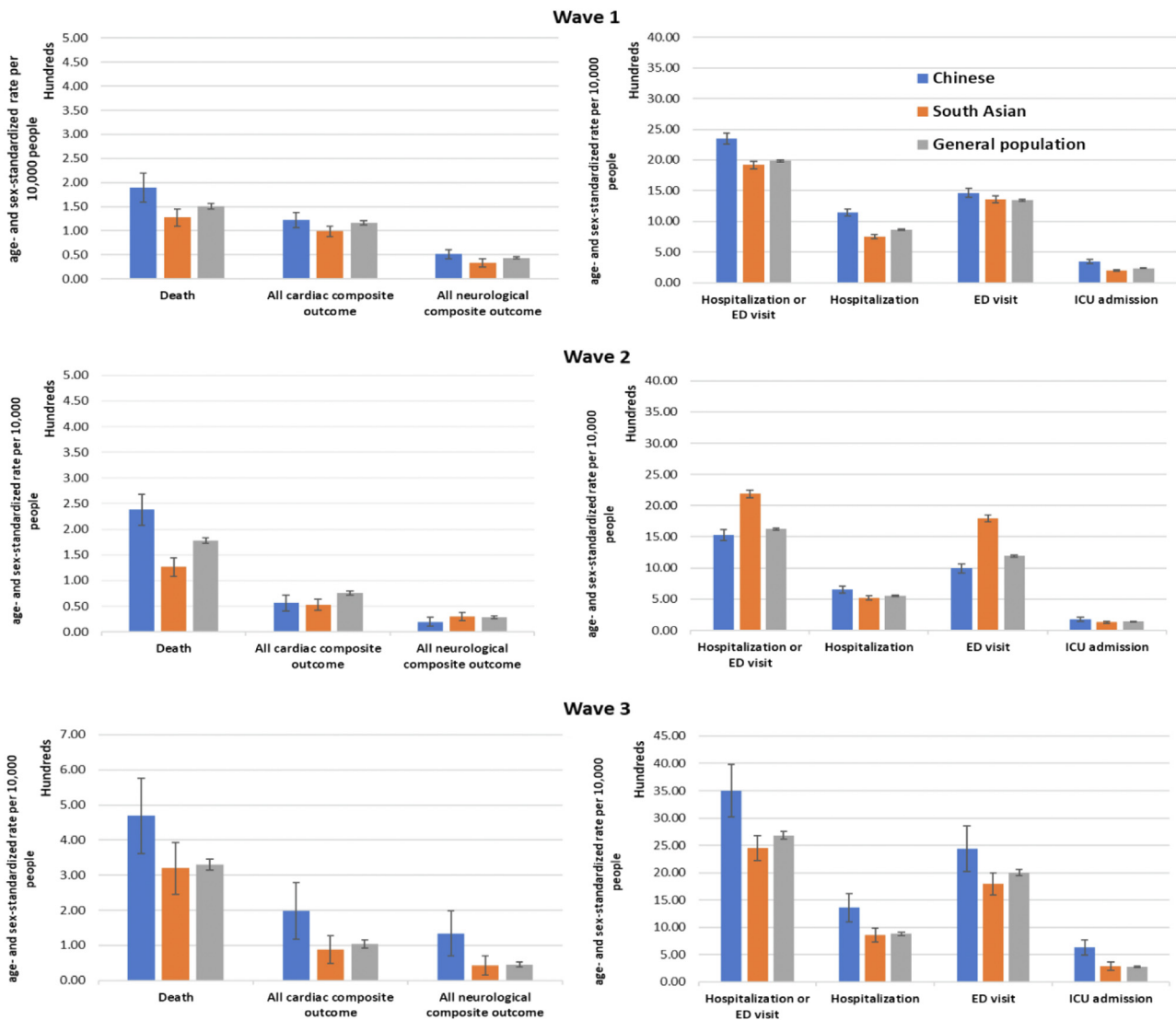


Figure 4. Age- and sex-standardized (per 10,000 people) rates (with 95% confidence intervals as vertical lines) of COVID-19-related outcomes among various ethnic groups in Ontario during waves 1, 2, and 3. ED, emergency department; ICU, intensive care unit.

healthcare workers or working in distribution centers or other at-risk workplaces, compared to that in the general population.^{2,13} Other factors driving these differences could include variation in vaccination rates or the use of masks or other public health measures by different age and ethnic groups. Future work should evaluate the impact of these factors on the observed differences and across different jurisdictions in Canada.

The higher mortality rate in Chinese patients with COVID-19, despite adjusting for baseline differences, remains unexplained (Table 3). A greater proportion of Chinese patients in our cohort resided in a long-term care facility compared to that of the general population (2.2% vs 1.3%), with the latter being associated with higher COVID-19 mortality (Table 1). Yet, in our sensitivity analyses, the higher odds of mortality among Chinese patients persisted when we studied outcomes of those not residing in a long-term care facility. A higher proportion of the Chinese population had dementia compared to that of the general population in our cohort, which could be one explanation. In contrast, the South Asian population was younger at the time of COVID-19, yet in adjusted analyses, COVID-19-related mortality was lower in this population. The reasons for this finding remain unclear, and further work, including information on vaccination status and its timing, is required to understand the implications of these findings.

COVID-19-related healthcare use was higher among the South Asian population in wave 2, and it was higher for the Chinese population in wave 3; this finding was driven mostly by a higher rate in ED visits in both these groups. Despite relatively similar baseline comorbidity status, the higher ICU admission rate among Chinese patients, especially in wave 3, may suggest that a greater number of ED visits was due to greater COVID-19 severity in this population, but the lack of a similar increase in ICU admission rates for South Asian patients in wave 2 could suggest that the greater number of ED visits by the South Asian population may be due to lack of access to primary care physicians or use of the ED for routine medical care.

Cardiac and neurologic complications

In the current study, a decline in deaths, as well as in cardiac complications, occurred from wave 1 to waves 2 and 3, from 2.6% to 0.7% and 1.0% ($P < 0.001$), respectively. Data from 40 healthcare systems participating in a large healthcare network indicate that the risk for cardiac complications,¹⁵ including myocarditis¹⁶ and pericarditis, was significantly higher after SARS-CoV-2 infection than after mRNA COVID-19 vaccination for both sexes in all age groups.¹⁷ These findings therefore support vaccination among all at-risk populations, including the Chinese population and the South Asian population.

We found that a history of myocardial infarction, heart failure, and chronic obstructive pulmonary disease¹⁸ or other respiratory diseases was less frequent in the Chinese population, compared to the general population. The recently Cardiac Complications in Patients With SARS Corona Virus 2 (COVID-19) Registry (CAPACITY-COVID) registry and the Lean European Open Survey on SARS-CoV-2 (LEOSS) study demonstrated that significant heterogeneity exists in the intensity of association between the types of heart disease and in-hospital mortality. Of all patients with heart disease, those

with heart failure are at greatest risk of death when hospitalized with COVID-19.¹⁹⁻²² On the other hand, serious cardiac complications are rare during hospitalization.²³⁻²⁵

The risk of COVID-19 may be higher in patients with chronic heart failure,^{26,27} in part due to advanced age and the presence of multiple comorbidities, as was evident in this study. These patients with COVID-19 also have a significantly higher risk of adverse outcomes.^{18,28-36} These findings indicate that guideline-directed medical therapy should be continued in patients with heart failure, regardless of their COVID-19 status.³⁷ In a comparison of COVID-19 patients treated in the ICU vs those not treated in the ICU in Shenzhen, China,³⁸ troponin elevation,³⁹ ventricular wall thickening, pulmonary hypertension, and cardiac complications including myocardial injury, arrhythmia,⁴⁰ and heart failure, were found to be more common in ICU patients with COVID-19. Cardiac injury in COVID-19 patients may be related more to the systemic response after infection rather than direct damage to the heart by coronavirus, at least in the Chinese population.

Neurologic complications of COVID-19⁴¹⁻⁴⁷ can be divided into 2 major categories: de novo neurologic complications as a direct result of COVID-19 infections, or exacerbation of preexisting neurologic conditions when patients were infected by the SARS-CoV-2 virus.⁴⁸⁻⁶² In our current study, the Chinese patients did not differ significantly in the prevalence of premorbid conditions, compared to the general population. This finding suggests that the excessive neurologic complication rate among the Chinese patients could be due to a direct effect of COVID-19 infection rather than exacerbation of their preexisting neurologic conditions and their having a higher mean age. Among all the neurologic complications, encephalopathy was the most common, accounting for 6.4% of hospitalized patients and 14.1% of Chinese patients admitted to ICU, but this incidence was not statistically different compared to that in the general population (Table 1). Encephalopathy in COVID-19 patients could be due to a combination of etiologic factors—hypoxemia secondary to respiratory failure, toxic and metabolic factors secondary to acute illness, and as recently recognized, inflammatory brain diseases.^{30,42} Encephalopathy of admitted COVID-19 patients in a large cohort study was associated with 5.5 times increased risk of death (OR 4.01-7.57, $P < 0.001$).⁴⁷ In our current study, very few cases of hemorrhagic stroke,^{63,64} ischemic stroke,^{10,65-67} seizures, and Parkinson's disease occurred among the Chinese population, but this low incidence could be due to the relatively small number of reported cases in this cohort. The estimated incidence of stroke as a complication of COVID-19 varies between 2.5% and 5%, according to various recent publications.^{64,68-71} Ongoing clinical-pathologic studies, including examining the angiotensin converting enzyme receptor (ACER-2), are required to determine whether the SARS-CoV-2 virus directly invades neural tissues of the central and peripheral nervous system.^{11,68,72} Such future studies would be vital in explaining why differences occur in neurologic and cardiac complications among various ethnic groups.⁷³

Limitations

Although using a surname algorithm to identify those who are Chinese or South Asian has a high specificity—99.7% for both ethnicities—it has a much lower sensitivity of 50.4% for

the South Asian population and 80.2% for the Chinese population.¹⁴ Since we used only 30-day all-cause mortality rates, and cardiac and neurologic complication rates, the current study is not able to capture “long-haul” COVID-19 patients and their eventual outcomes.^{36,48,74,75} In addition, the vaccination status of this cohort had not been ascertained, although it is a very important determinant of the risk of infection and its complications.^{76,77} A mass COVID-19 vaccination effort began in Ontario in December, 2020, and vaccination status data from that point onward were not available for this study. The datasets from the Canadian Institute for Health Information are finalized on an annual basis, and hospitalization datasets may be incomplete. A majority of the hospitals report on a monthly basis, but a few institutions may report on an annual basis. The number of hospitalizations may be an underestimate of the true volume.

Conclusions

In this very large, population-based retrospective cohort study in Ontario, being of Chinese or South Asian ethnicity, based on a surname algorithm, was found to be independently associated with mortality and healthcare use among Ontarians with COVID-19 infection in waves 1, 2, and 3. These findings are relevant to healthcare authorities across Canada when dealing with subsequent waves of this pandemic.^{77,78} Additionally, our findings have implications for healthcare policymakers regarding how limited resources and vaccinations should be allocated for at-risk populations.^{14,39,79}

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Supplementary Material

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