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Epidemiology of COVID-19 and its Cardiac and Neurological Complications among Chinese and South Asians in Ontario: Wave 1, 2 and 3

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Short title: COVID-19 Cardiac and Neurological Complications in Ontario

ABSTRACT

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

Methods: We identified adult Ontarians with a positive COVID-19 PCR test between January 1, 2020 to June 30, 2021 and they were classified as Chinese or South Asians using a validated surname algorithm and compared their outcomes of mortality, cardiac and neurological complications with the general population using multivariable logistic regression models.

Results: Compared to the general population (N = 439,977), Chinese (N = 15,208) were older (mean age 44.2 vs 40.6 years, $p < 0.001$) while South Asians (N = 46,333) were younger (39.2 years $p < 0.001$). Chinese had a higher 30-day mortality (Odds ratio [OR] 1.44; 95% CI 1.28-1.61) and hospitalization or emergency department (ED) visits (1.14; 1.09-1.28) and with a trend towards higher cardiac complications (1.03; 0.87-1.12) and neurological complications (1.23; 0.96-1.58). South Asians had a lower 30-day mortality (0.88; 0.78-0.98) but a higher hospitalization or ED visits (1.17; 1.14-1.20) with a trend towards lower cardiac complications (0.76; 0.67-0.87) and neurological complications (0.89; 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 neurological outcomes, and healthcare use among patients with COVID-19, requiring further studies to understand factors driving these differences.

Keywords: Epidemiology, COVID-19, cardiac and neurological complications, Chinese and South Asian Ontarians, Wave 1, 2 and 3.

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is responsible for the global pandemic known as coronavirus disease (COVID-19). [1,3] Differences in COVID-19 infection rates and adverse outcomes following infection across different ethnic groups have been described. [2,15,18,19,29,30] In the US, the overall mortality among Afro-Americans with COVID-19 was significantly higher than that of White and Asians.[14]

In Canada's most populous province Ontario, South Asians (29.6% of the total population) and Chinese (19.4%) represent the largest visible minorities.[43] We have previously described the cardiac and neurological complications among Chinese and South Asian Ontarians during the first wave (between January 15, 2020 and July 17, 2020) of the pandemic, identifying significant differences in baseline demographics and outcomes.[2] Since then, two subsequent waves (wave 2: July 18, 2020 to March 4, 2021 and wave 3: March 5, 2021 to June 30, 2021) of COVID-19 infections in Ontario have been observed with variation in infection rates and outcomes based on various demographic and social factors. Thus, we conducted this extension study using similar methodology to evaluate mortality, cardiac and neurological complications, and healthcare utilization in waves 1, 2 and 3 among Chinese and South Asian Ontarians compared to the general population and compared these outcomes across the three 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 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. [2] In brief, data from the Registered Persons Database (RPDB), Canadian Institute for Health Information (CIHI) Discharge Abstract Database (DAD), the National Ambulatory Care Reporting System (NACRS), and the Ontario Health Insurance Plan (OHIP) physician claims database were used to identify demographics and health conditions, health outcomes, and health service utilization. The RPDB provides demographic information about anyone who has ever received an Ontario health card number. The DAD contains patient-level data for hospitalizations. The NACRS captures information on patient visits to emergency departments.

OHIP captures information of 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 Ontario Drug Benefit (ODB) database and the Continuing Care Reporting System (CCRS).

Exposure

We classified patients as Chinese or South Asians using a validated surname algorithm with high specificity as reported by Shah in 2010. [41] We compared Chinese and South Asians to the general Ontario population (those not classified as Chinese or South Asians). The cohort was stratified into three waves: Wave 1 from Jan 15, 2020 to July 17, 2020, Wave 2 from July 18, 2020 to March 4, 2021 and Wave 3 from March 5, 2021 to June 30, 2021.

Outcomes

The primary outcomes at 30 days following a positive PCR test were : death, composite cardiac outcome (myocardial infarction, heart failure, arrhythmia, atrial fibrillation/flutter, myocarditis, pulmonary embolism/deep vein thrombosis); composite neurological outcome (hemorrhagic stroke, ischemic stroke, seizure, meningitis, encephalitis, encephalopathy and Parkinson's Disease), as well as healthcare utilization (hospitalization, emergency room visit [ED], ICU admission, use of ECMO, 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 between the Chinese, South Asians and the general population. For continuous variables, descriptive statistics included mean values with standard deviation, median values with interquartile range, and the p-values were calculated using one-way ANOVA for means and Kruskal-Wallis test for median. Categorical variables were described using proportions and p-values from a chi-squared test were provided.

We reported crude and age- and sex-standardized rates of outcomes. We used Ontario population from the year 2020 as the reference population. We used multivariable logistic regression to determine if 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, where the general population was the reference group. We adjusted for age, sex, income quintile, long-term care residence and Charlson index in the 90 days prior to positive COVID test. We reported odds ratios (ORs) and 95% confidence interval (CI) comparing Chinese and South Asians to the general population. Using stratified analyses, we compared the outcomes across the three waves.

Sensitivity analyses

Acknowledging age is an important predictor of outcomes, we conducted sensitivity analyses, stratifying the cohort and limiting the analyses to those below 65 years and those 65 years and older. (Figure 2A and 2B) We also evaluated the variation in outcomes among those who resided and did not reside in a long-term care facility. (Figure 3A and 3B)

RESULTS

All patients in our analyses had a positive PCR test for COVID-19. Compared to the general population (N = 439,977), Chinese (N = 25,208) were older (mean age 44.2 vs 40.6 years, $p < 0.001$) while South Asians (N = 46,333) were younger (39.2 years, $p < 0.001$). There was a significant decrease in the mean age from wave 1 to 3: Chinese (54.3, 45.9 and 40.4 years respectively); South Asians (43.9, 39.8 and 37.7 years respectively); 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 3: Chinese (93.3%), South Asians (95.1%), 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 general population, 30-day mortality was higher among Chinese (3.1 vs. 1.9%, $P < 0.001$) and lower among South Asians (0.9 vs. 1.9%, $P < 0.001$). Compared to the general population, cardiac complications were similar in Chinese (1.0% vs. 0.9%) and lower among South Asians (0.6% vs. 0.9%, $p < 0.001$) whereas neurological complications were similar among Chinese (0.4% vs. 0.3%) and South Asians (0.2% vs. 0.3%). (Figure 1) Healthcare utilization was more frequent in both Chinese and South Asians compared to the general population (Table 2).

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

Among those below 65 years, the variation in mortality rates was no longer observed, but both South Asians and Chinese patients had higher rates of healthcare utilization than the general population. (Figure 2A) For those 65 and older; mortality rates, cardiac and neurological complication rates and ICU admission rates were all increased significantly compared to those < 65 years. (Figure 2B) Mortality rates, cardiac and neurological complication rates were all increased significantly for those residing in long-term care facilities (LTC). (Figure 3A) Among those not residing in LTC, we found a higher rate of healthcare, except hospitalization, utilization among both ethnic groups compared to the general population. (Figure 3B).

Variations across the three waves

Figure 4 shows the variation in age and sex-standardized rates of our outcomes of interest across the 3 waves for all three groups. In contrast to wave 1, higher age and sex-standardized rates of mortality, cardiac and neurological outcomes, and healthcare use was observed in all three groups. Across all waves, Chinese patients were found to have highest rates of mortality and cardiac and neurological complications whereas South Asians had the lowest rates. In contrast, healthcare use of South Asians 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 Asians being younger than the general population. Despite adjusting for baseline differences in age, income and comorbidities, Chinese patients with COVID-19 had higher OR of COVID-19-related mortality and healthcare utilization; while South Asians had lower OR of mortality, but higher OR of healthcare utilization compared to the general population. (Table 3)

The younger age at the time of COVID-19 infection among South Asians could be, in part, attributed to a larger proportion of South Asians being frontline health care workers or working in distribution centers or other at-risk workplaces compared to the general population. [3,11]. Other factors driving these differences could also 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.

A higher mortality 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 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 persisted when we studied outcomes of those not residing in a long-term care facility. A higher proportion of Chinese had dementia compared to the general population in our cohort which could be one explanation. In contrast, South Asians were younger at the time of COVID-19, yet in adjusted analyses, the COVID-19-related mortality was lower in South Asians. The reasons for this remain unexplained and future work including information on vaccination status and its timing will be required to understand the implications of these findings.

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

Cardiac and neurological complications

In the current study, there was a decline in deaths as well as cardiac complications from wave 1 to wave 2 and 3, from 2.6% to 0.7% and 1.0% ($p < 0.001$), respectively. Data from 40 health care systems participating in a large healthcare network found that the risk for cardiac complications [70] including myocarditis [34] and pericarditis was significantly higher after SARS-CoV-2 infection than after mRNA COVID-19 vaccination for both sexes in all age groups. [78] These findings therefore support vaccination among all at-risk populations, including Chinese and South Asians.

We found that a history of myocardial infarction, heart failure and chronic obstructive pulmonary disease [53] or other respiratory diseases were less frequent in the Chinese compared to the general population. The recently published CAPACITY-COVID registry and LEOSS study have demonstrated

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. [36-39] On the other hand, serious cardiac complications are rare during hospitalization. [28,76]

The risk of COVID-19 may be higher in patients with chronic heart failure [32,35], in part due to the advanced age and presence of multiple comorbidities, as evident in this study. These patients with COVID-19 also have a significantly higher risk of adverse outcomes. [33,50-53,56,57,60,74] As such, guideline-directed medical therapy should be continued in patients with heart failure, regardless of COVID-19. [79] In a comparison of COVID-19 patients treated in the intensive care unit versus those not treated in the unit in Shenzhen, China [77]; troponin elevation [40], ventricular wall thickening, pulmonary hypertension, and cardiac complications including myocardial injury, arrhythmia [71], and heart failure were 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.

Neurological complications of COVID-19 [4,5,16,23,25,26,46] can be divided into two major categories: de novo neurological complications as a direct result of COVID-19 infections or exacerbation of preexisting neurological conditions when patients were infected by SARS-CoV-2 virus. [8,10,44,47,58,59, 61-69] In our current study, Chinese had no significant difference in the prevalence of pre-morbid conditions compared to the general population. This would suggest that excessive neurological complication rate of Chinese could be due to a direct effect of COVID-19 infection rather than exacerbation of their preexisting neurological conditions in addition to being older in their mean age. Among all the neurological complications, encephalopathy was the commonest accounting for 6.4% of hospitalized and 14.1% of Chinese patients admitted to ICU but it was not statistically significant compared to the general population. (Table 1) Encephalopathy in COVID-19 patients could be due to a combination of etiological factors: hypoxemia secondary to respiratory failure, toxic and metabolic factors secondary to acute illness and as well recently recognized inflammatory brain diseases.[5,51] Encephalopathy of admitted COVID-19 patients in a large cohort study was associated with increased risk of death by 5.5 times (OR 4.01 – 7.57, $p < 0.001$).[46] In our current study, there were very few cases of hemorrhagic stroke [11,21] and ischemic stroke [20,24,30,31] seizures and Parkinson's Disease among Chinese but this 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% found in various recent publications. [6,9,12,22,75]. Ongoing clinical-pathological studies including examining the angiotensin converting enzyme receptor (ACER-2) will be required to examine if there are direct invasion of the SARS-CoV-2 virus in neural tissues of the central and peripheral nervous system [6,14,49]. These future studies would be vital in explaining why there are differences in neurological and cardiac complications between different ethnic groups.[48]

LIMITATION

Although using surname algorithm to identify Chinese and South Asians has a high specificity of 99.7% for both ethnicities, it has a much lower sensitivity of 50.4% for South Asians and 80.2% for Chinese.[41] Since we used only 30-day all-cause mortality rates, cardiac and neurological complication rates, the current study is not able to capture “long-haul” COVID-19 patients and their eventual outcomes.

[8,13,73,74] 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. [45, 72] Massive COVID-19 vaccination in Ontario started in December,2020 and vaccination status data from that point onwards were not available for this study. The datasets from CIHI are finalized on an annual basis and hospitalization datasets may be incomplete. 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, patients of Chinese and South Asian ethnicity based on surname algorithm was found to be independently associated with mortality and healthcare use among Ontarians with COVID-19 infection in wave 1, 2 and 3. These findings would be of importance to health care authorities across Canada when dealing with subsequent waves of this pandemic [55,72]. Furthermore, our findings have implications for healthcare policy makers on how to allocate limited resources and vaccinations for at-risk populations. [40-42]

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STATEMENT OF AUTHORSHIP

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Data collection and analysis: MK, YK.

Writing of manuscript: Drs. JYC, GWM; MK and YK.

Critical review of manuscript: Drs. JYC, GWM, DTK, MVV, MG

SUPPLEMENTARY MATERIAL

Supplementary table S1

REFERENCES

1. Public Health Ontario: COVID-19 in Ontario—A Focus on Diversity: January 15, to May 14, 2020.
2. Chu JY, Kaliwal Y, Koh M, et al. COVID-19 and its Cardiac and Neurological Complications among Ontario Visible Minorities. *CJNS* June 24,2021: 1-10. doi:10.1017/cjn.2021.148
3. Subedi R, Greenberg L, Turcotte M. Statistics Canada: StatCan COVID-19: COVID-19 mortality rates in Canada’s ethno-cultural neighborhoods, October 28, 2020.
4. Nepal G, Rehrig JH, Shretha GS, et al. Neurological manifestations of COVID-19: a systematic review. *Critical Care*.2020;24:421.
5. Ellul MA, Benjamin L, Singh B, et al. Neurological associations of COVID-19. *Lancet Neurol*. 2020; 19:767–83.
6. Frontera JA, Sabadia S, Lalchan R. A prospective study of neurologic disorders in hospitalized patients with COVID-19 in New York City: *Neurology*. 2021;96: e575–86.
7. O’Brien K, St-Jean M, Wood P, et al. StatCan COVID-19 death comorbidities in Canada, November 16, 2020.
8. Narth A. Neurologic complications of coronavirus infections. *Neurology*. 2020; 94:809–10.
9. Wang L, Shen Y, Li M, et al. Clinical manifestations and evidence of neurological involvement in 2019 novel coronavirus SARS-CoV-2: a systematic review and meta-analysis. *J Neurol*.2020; 267:2777–89.
10. Niazkar HR, Zibae B, Nasimi A, et al. The neurological manifestations of COVID-19: a review article. *Neurol Sci*. 2020; 41:1667–71.
- 11 StatCan: Impacts on Immigrants and People Designated as Visible Minorities, October 20, 2020.
12. Dhamoon MS, Thaler A, Gururangan K, et al. Acute cerebrovascular events with COVID-19 infection. *Stroke*. 2021; 52:48–56.
13. Troxel AB, Frontera JA, Mendoza-Puccini C. The National Institutes of Health COVID-19 NeuroDatabank and NeuroBiobank: A National Resource for Learning, Discovery, and Progress. *Front Neurol*. 2021;11: 615061.
14. CDC: COVID-19 in Racial and Ethnic Minority Groups, June 4, 2020.
15. Suleyman G, Fadel RA, Malette K, et al. Clinical characteristics and morbidity associated with Coronavirus disease 2019 in a series of patients in Metropolitan Detroit. *JAMA Netw Open*. 2020;3: e2012270.
16. Wang D, Yin Y, Hu C, et al. Clinical course and outcome of 107 patients infected with the novel

Coronavirus, SARS-CoV-2, discharged from two hospitals in Wuhan, China. *Crit Care*.

2020;24: 188.

17. Hooper MW, Napoles AM, Perez-Stable EJ. COVID-19 and racial/ethnic disparities. *JAMA*.

2020;323: 2466–7. *LE JOURNAL CANADIEN DES SCIENCES NEUROLOGIQUES*

Volume 00, No. 00 – Month 2021 9 <https://www.cambridge.org/core/terms>.

<https://doi.org/10.1017/cjn.2021.148>

Downloaded from <https://www.cambridge.org/core>. IP address: 99.225.112.67, on 20 Aug 2021 at

17:17:23, subject to the Cambridge Core terms of use, available at

18. APM Research Lab. The Color of Coronavirus: COVID-19 Deaths by Race and Ethnicity in the U.S. May 12, 2020.

19. Haynes N, Cooper LA, Albert MA. At the heart of the matter: unmasking and addressing COVID-19's toll on diverse populations. *Circulation*. 2020;142: 105–7.

20. Laurencin C, McClinton A. The COVID-19 pandemic: a call to action to identify and address racial and ethnic disparities. *J Racial and Ethnic Health Disparities*. 2020;7: 398–402.

21. Van der Worp B, Sandset EC, Caso V. Likely Increase in the Risk of Death or Disability from Stroke during the COVID-19 Pandemic, European Stroke Organization, May 9, 2020.

22. Oxley TJ, Mocco J, Majidi S, et al. Large-Vessel Stroke as a Presenting Feature of COVID-19 in the Young. *N Engl J Med*. 2020;382: e60.

23. Tu H, Tu S, Gao S, et al. The epidemiological and clinical features of COVID-19 and lessons from this global infectious public health event. *J Infecti*. 2020; 81:1–9.

24. Lodigiani C, Iapichino G, Carenzo L, et al. Venous and arterial thromboembolic complications in COVID-19 patients admitted to an academic hospital in Milan, Italy. *Thromb Res*. 2020; 191:9–14.

25. Qureshi A, Abd-Allah F, Alsenani F, et al. Management of acute ischemic stroke in patients with COVID-19 infection: Report of an international panel. *Int J Stroke*. 2020; 15:540–54.

26. Zhou, Y, Li W, Wang D, et al. Clinical time course of COVID-19, its neurological manifestation and some thoughts on its management. *Stroke Vasc Neurol*. 2020;5: 177–9.

27. Guo T, Fan Y, Chen M, et al. Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19). *JAMA Cardiol*. 2020;5: 811–8.

28. Shi S, Qin M, Shen B, et al. Association of cardiac injury with mortality in hospitalized patients with

- COVID-19 in Wuhan, China. *JAMA Cardiol.* 2020;5: 802–10.
29. DataSF. Demographics of COVID-19 Cases and Deaths, City and Country of San Francisco.
30. Warrior L, Kim CY, Burdick DJ, et al. Leading with inclusion during the COVID-19 pandemic. *Neurology.* 2020;95: 537–42.
31. Khosravani H, Rajendram P, Notario L, et al. Protected code stroke: hyperacute stroke management during the coronavirus disease 2019 (COVID-19) pandemic. *Stroke.* 2020;51: 1891–5.
32. Canadian Cardiovascular Society. Guidance from the CCS COVID-19 rapid response team: is it COVID-19 or is it heart failure? Management of ambulatory heart failure patients.
33. Giustino G, Pinney S, Lala A, et al. Coronavirus and cardiovascular disease, myocardial injury, and arrhythmia. *Focus Seminar. J Am Coll Cardiol.* 2020;76: 2011–23.
34. Kawakami R, Sakamoto A, Kawai K, et al. Pathological evidence for SARS-CoV-2 as a cause of myocarditis. *JACC review topic of the week. J Am Coll Cardiol.* 2021;77: 314–25.
35. Panjra G, Krepp J. COVID-19 and heart failure: harsh reality of pre-existing conditions. *J Am Coll Cardiol.* 2020;76: 349–51.
36. Alvarez-Garcia J, Lee S, Gupta A, et al. Prognostic impact of prior heart failure in patients hospitalized with COVID-19. *J Am Coll Cardiol.* 2020;76: 2334–48.
37. Mehra MR, Ruschitzka F. COVID-19 illness and heart failure: a missing link? *JACC Heart Fail.* 2020;8: 512–4.
38. Bhatt AS, Jering KS, Vaduganathan M, et al. Clinical outcomes in patients with heart failure hospitalized with COVID-19. *JACC Heart Fail.* 2021;9: 65–73.
39. Freaney PM, Shah SJ, Khan SS. COVID-19 and heart failure with preserved ejection fraction. *JAMA.* 2020;324: 1499–500.
40. Tersalvi G, Vicenzi M, Calabretta D, et al. Elevated troponin in patients with Coronavirus Disease 2019 (COVID-19): possible mechanisms. *J Card Fail.* 2020;26: 470–5.
41. Shah BR, Chiu M, Amin S, Ramani M, Sadry S, Tu JV. Surname lists to identify South Asian and Chinese ethnicity from secondary data in Ontario, Canada: a validation study. *BMC Med Res Methodol.* 2010; 0:42. doi: 10.1186/1471-2288-10-42
42. Wang C, Wang Z, Wang G, Lau JY-N, Zhang K, Li W. COVID-19 in early 2021: current status and looking forward. *Signal Transduct Target Ther.* 2021;6: 114.

43. StatCan Census Profile 2016: Ontario (Province) and Canada. [https://: www12.statcan.gc.ca](https://www12.statcan.gc.ca)
44. Needham EJ, Chou SH-Y, Coles AJ, Menon DK. Neurological implications of COVID-19 infections. *Neurocrit Care*. 2020;32: 667–71. doi: 10.1007/s12028-020-00978-4
45. Mao, L, Wang M, Chen S, et al. Neurological manifestations of hospitalized patients with COVID-19 in Wuhan, China: a retrospective case series study. medRxiv. 2020. doi: 10.1101/2020.02. 22.20026500
46. Chou S. AAN-2021 conference: hot topics: neuro-COVID plenary session. *Neurol Complicat COVID-19*. 2021.
47. Vinciguerra M, Greco E. Sras-CoV-2 and black population: ACE2 as shield or blade? *Infect Genet Evol*. 2020;84: 104361.
48. Normandin E, Bhattacharyya S, Mukerji S, et al. Neuropathological features of COVID-19. <https://index.mirasmart.com/AAN2021/PDFfiles/AAN2021-004641.html>.
49. Kornowski R, Orvin K. The Clinical Challenge of ST-Segment Elevation Myocardial Infarction and COVID-19. *J Am Coll Cardiol*. 2021; 77:2004–6.
50. Garcia S, Dehghani P, Grines C, et al. Initial Findings From the North American COVID-19 Myocardial Infarction Registry. *J Am Coll Cardiol*. 2021;77: 1994–2003.
51. Remsik J, Wilcox JA, Babady NE, et al. Inflammatory leptomeningeal cytokines mediate COVID-19 neurological symptoms in cancer patients. *Cancer Cell*. 2021;39: 276–83.
52. Bahrami H, Kronmal R, Bluemke DA, et al. Differences in the incidence of congestive heart failure by ethnicity: the multi-ethnic study of atherosclerosis. *Arch Intern Med*. 2008;168: 2138–45. doi: 10.1001/archinte.168.19.2138
53. Gilkes A, Ashworth M, Schofield P, et al. Does COPD risk vary by ethnicity? A retrospective cross-sectional study. *Int J COPD*. 2016;11: 739–46.
54. Chung MK, Zidar DA, Bristow MR, et al. COVID-19 and Cardiovascular Disease From Bench to Bedside. *Circulation Research*. 2021; 128:1214-1236. doi: 10.1161/CIRCRESAHA. 121.317997
55. Public Health of Ontario: Coronavirus Disease 2019 (COVID-19): 03/11/2022
56. European Society of Cardiology guidance for the diagnosis and management Of cardiovascular disease during the COVID-19 pandemic: part 1—epidemiology, pathophysiology, and diagnosis. doi:10.1093/eurheartj/ehab696
57. ESC guidance for the diagnosis and management of cardiovascular disease

During the COVID-19 pandemic: part 2—care pathways, treatment, and follow-up.

doi:10.1093/eurheartj/ehab697

58. Xiong W, Mu J, Guo J, et al. New onset neurologic events in people with COVID-19

in 3 regions in China. *Neurology* 2020 Sep 15;95(11): e1479-e1487

59. Xie J, Wu W, Li S et al. Clinical characteristics and outcomes of critically ill patients

With novel coronavirus infectious disease (COVID-19) in China: a retrospective multicenter study.

Intensive care Med. 2020 Oct;46(10):1863-1872

60. Lim SL, Woo KL, Lim E, et al. Impact of COVID-19 on health-related quality of life in patients

With cardiovascular disease: a multi-ethnic Asian study. *Health Qual Life Outcomes.* 2020 Dec

14;18(1):387. doi: 10.1186/s12955-020-01640-5

61. Wan D, Du T, Hong W, et al. Neurological complications and infection mechanism of SARS-CoV-2

Signal Transduct Target Ther. 2021 Nov 23;6(1):406

62. Serrano-Castro PJ, Estvill-Torius G, Cabezudo-García P, et al. Impact of SARS-CoV-2 infection on

Neurodegenerative and neuropsychiatric diseases: a delayed pandemic? *Neurologia (Engl Ed).* 2020

May;35(4):245-251. doi:10.1016/j.nrl.2020.04.002

63. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with

COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* 2020 28 March-3 April; 395(10229):

1054-1062. doi: 10.1016/S0140-6736(20)30566-3

64. Tsigoulis G, Palaiodimou L, Zand R, et al. COVID-19 and cerebrovascular diseases: a comprehensive

Overview. *Ther Adv Neurol Disord.* 2020, 13: 1756286420978004. Doi:10.1177/1756286420978004

65. Orru G, Conversano C, Malloggi E, et al. Neurological Complications of COVID-19 and Possible

Neuroinvasion Pathways: A Systematic Review. *Int J Environ Res Public Health.* 2020 Sep. 17 (18): 6688

doi: 10.3390/ijerph17 186688

66. Shehata GA, Lord KC, Grudzinski MC, et al. Neurological Complications of COVID-19: Underlying

Mechanisms and Management. *Int J Mol Sci.* 2021 Apr 15;22(8):4081. Doi: 10.3390/ijms22084081

67. Sharifian-Dorche M, Huot P, Oshero M, et al. Neurological complications of coronavirus

Infection; a comparative review and lessons learned during the COVID-19 pandemic. *J Neurol Sci.*

2020 Oct 15;417: 117085. doi: 10.1016/j.jns.2020.117085

68. Whittaker A, Anson M, Harky A. Neurological Manifestations of COVID-19: A systematic review and

- current update. *Acta Neurol Scand.* 2020 Jul;142(1):14-22. Doi: 10.1111/ane.13266. Epub 2020 June 2.
69. Maury A, Lyoubi A, Peiffer-Smadja N, et al. Neurological manifestations associated with SARS-CoV-2 And other coronaviruses: A narrative review for clinicians. *Rev Neurol (Paris)*. Jan-Feb 2021;177(1-2):51-64. doi: 10.1016/j.neurol.2020.10.001
70. Chang W-T, Toh HS, Liao C-T, et al. Cardiac Involvement of COVID-19: A Comprehensive Review. *Am J Med Sci.* 2021 Jan;361(1):14-22. doi: 10.1016/j.amjms.2020.10.002.
71. Kochi AN, Tagliari AP, Forleo GB, et al. Cardiac and arrhythmic complications in patients with COVID-19. *J Cardiovasc Electrophysiol.* 2020 May;31(5): 1003-1008. doi: 10.1111/jce.14479
72. Bouzid D, Visseaux B, Kassaseya C, et al. Compariosn of Patients Infected With Delta Versus Omicron COVID-19 Variants Presenting to Paris Emergency Departments: A Retrospective Cohort Study. *Ann Intern Med* 2022; Mar 15.
73. Katsoularis I, Fonseca-Rodriguez O, Farrington P, et al. Risks of deep vein thrombosis, pulmonary embolism, and bleeding after covid-19: nationwide self-controlled cases series and matched cohort study. *BMJ* 2022;376: e069590. doi:10.1136/bmj-2021-069590
74. Abbasi J. The COVID Heart—One Year After SARS-CoV-2 Infection, Patients Have an Array of Increased Cardiovascular Risks. *JAMA* March22/29, 2022 Volume 327, Number 12
75. Misra S, Kolappa K, Prasad M, et al. Frequency of Neurologic Manifestations in COVID-19: A Systematic Review and Meta-Analysis. *Neurology*, 2021;97 (23): e2269-e2281
76. The CAPACITY-COVID Collaborative Consortium and LEOSS Study Group *Eur Heart J* 2022;43:1104-20.
77. Zhang JH, Wu W-B, Qu J-X, et al. Cardiac manifestations of COVID-19 in Shenzhen, China. *Infection* 2020; 48:861-70, <https://doi.org/10.1007/s15010-020-01473-w>
78. Block JP, Boehmer TK, Forrest CB, et al. Cardiac Complications After SARS-CoV-2 Infection and mRNA COVID-19 Vaccination - PCORnet, United States, January 2021-January 2022 *MMWR* 2022;71:51723.
<https://doi.org/10.15585/mmwr.mm7114e1>
79. Roifman I, Arora RC, Bewick D, et al. Cardiovascular Care Delivery During the Second Wave of COVID-19 in Canada
Can J Cardiol 2021; 37:790-3. <https://doi.org/10.1016/j.cjca.2020.11.016>

Table 1: Baseline characteristics of patients with positive COVID test by ethnic groups in Ontario: Wave 1,2 and 3

Characteristics	Chinese
	N=15,208
Age, mean (SD)	44.15 ± 21.20
Age, median (IQR)	43 (29-58)
Age groups	
19 and under	1,766 (11.6%)
20 to 39	5,010 (32.9%)
40 to 59	5,008 (32.9%)
60 to 79	2,414 (15.9%)
80+	1,010 (6.6%)
Sex	
Female	7,741 (50.9%)
Male	7,467 (49.1%)
Income Quintile	
Missing	51 (0.3%)
Income Quintile 1 (lowest)	3,882 (25.5%)
Income Quintile 2	3,876 (25.5%)
Income Quintile 3	2,673 (17.6%)
Income Quintile 4	2,666 (17.5%)
Income Quintile 5 (highest)	2,060 (13.5%)
Residence	
Missing	51 (0.3%)
Rural	58 (0.4%)
Urban	15,099 (99.3%)

Asthma	1,781 (11.7%)
Diabetes	1,943 (12.8%)
Hypertension	3,241 (21.3%)
Heart Failure	284 (1.9%)
COPD	205 (1.3%)
Dementia	631 (4.1%)
LTC	689 (4.5%)
LTC time of test	337 (2.2%)
Hospitalization in previous 5 years	2,985 (19.6%)
Chronic kidney disease	426 (2.8%)
Charlson comorbidity index (past 5 years from index)	
Acute Myocardial Infarction	76 (0.5%)
Congestive Heart Failure	143 (0.9%)
Peripheral Vascular Disease	49 (0.3%)
Cerebrovascular Disease	171 (1.1%)
Dementia	280 (1.8%)
Chronic Obstructive Pulmonary Disease or other Respiratory diseases	98 (0.6%)
Rheumatic-like Diseases	17 (0.1%)
Ulcers of the Digestive System	63 (0.4%)
Liver Disease - Mild	41 (0.3%)
Diabetes - No Chronic Complications	236 (1.6%)
Diabetes with Chronic Complications	290 (1.9%)
Hemiplegia or Paraplegia	56 (0.4%)
Renal (Kidney) Disease	94 (0.6%)
Cancer (No secondary found)	138 (0.9%)
Liver Disease - Moderate or Severe	14 (0.1%)
Cancer (Metastatic - secondary)	55 (0.4%)
HIV / AIDS†	0 (0.0%)

Mean +-SD	0.18 ± 0.78
Median (IQR)	0 (0-0)
Charlson category	
0	14,101 (92.7%)
1	421 (2.8%)
>=2	686 (4.5%)
Wave (Chi-squared test)	
1 (Jan 15, 2020 to July 17, 2020)	1,024 (6.7%)
2 (July 18, 2020 to March 4, 2021)	7,810 (51.4%)
3 (March 5, 2021 to June 30, 2021 (end of cohort selection))	6,374 (41.9%)

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

Outcomes, n (%)	Chinese N=15, 208	South Asian N=46, 333	General N=439, 977	P- value Chin ese vs Gene ral	P- val ue Sou th Asi an vs Gen eral
				General	General
Death	471 (3.1%)	394 (0.9%)	8,280 (1.9%)	<.001	<.001
All cardiac composite outcome	145 (1.0%)	257 (0.6%)	3,789 (0.9%)	0.227	<.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%)	1,174 (0.3%)	0.079	<.001
Myocarditis	*1 - 5	*1 - 5	*12 - 16	0.56	0.609
DVT/PE	43 (0.3%)	82 (0.2%)	1,183 (0.3%)	0.746	<.001
All neurological composite outcome	66 (0.4%)	106 (0.2%)	1,385 (0.3%)	0.01	0.001

Stroke	19 (0.1%)	29 (0.1%)	367 (0.1%)	0.13 0.084	5
Ischemic stroke	12 (0.1%)	20 (0.0%)	290 (0.1%)	0.541	0.06 5
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	0.51 6
Encephalitis	0 (0.0%)	0 (0.0%)	*1 - 5	0.853	0.74 6
Encephalopathy	33 (0.2%)	50 (0.1%)	712 (0.2%)	0.098	0.00 5
Viral meningitis not specified elsewhere	0 (0.0%)	0 (0.0%)	*1 - 5	0.853	0.74 6
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	0.62 1
Health services					
Hospitalization or ED visit	3,126 (20.6%)	9,086 (19.6%)	78,166 (17.8%)	<.001	<.001 1
Hospitalization	1,404 (9.2%)	2,288 (4.9%)	28,300 (6.4%)	<.001	<.001 1
ED visit	2,019 (13.3%)	7,430 (16.0%)	56,685 (12.9%)	0.156	<.001 1
ICU admission	414 (2.7%)	613 (1.3%)	7,315 (1.7%)	<.001	<.001 1
ECMO	6 (0.0%)	22 (0.0%)	139 (0.0%)	0.593	0.07 4
Mechanical ventilation	224 (1.5%)	358 (0.8%)	3,908 (0.9%)	<.001	0.01 1

Abbreviations: AMI—acute myocardial infarction, HF – heart failure, DVT – deep vein thrombosis, PE – pulmonary embolus,

GBS – Guillain Barre syndrome, ED – emergency department, ICU – intensive care unit, ECMO – extracorporeal membrane oxygenation.

* Small number of reported cases

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

Outcome	Chinese vs. general population Adjusted* OR (95% CI)	South Asian vs. general population 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 neurological 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)

Legends for tables and figures:

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

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

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

Figure 1. 30-day outcome crude rates (per 10,000) by ethnic groups.

Figure 2A-B. 30-day outcome crude rates by ethnic groups, < 65 and \geq 65.

Figure 3A-B. 30-day outcome crude rates by ethnic groups, LTC and no LTC.

Figure 4. Age- and sex-standardized rates (with 95% confidence intervals as vertical lines) of COVID-19 related outcomes among different ethnic groups in Ontario during waves 1, 2 and 3.

Figure 1: 30-day outcome crude rates (per 10,000) by ethnic group

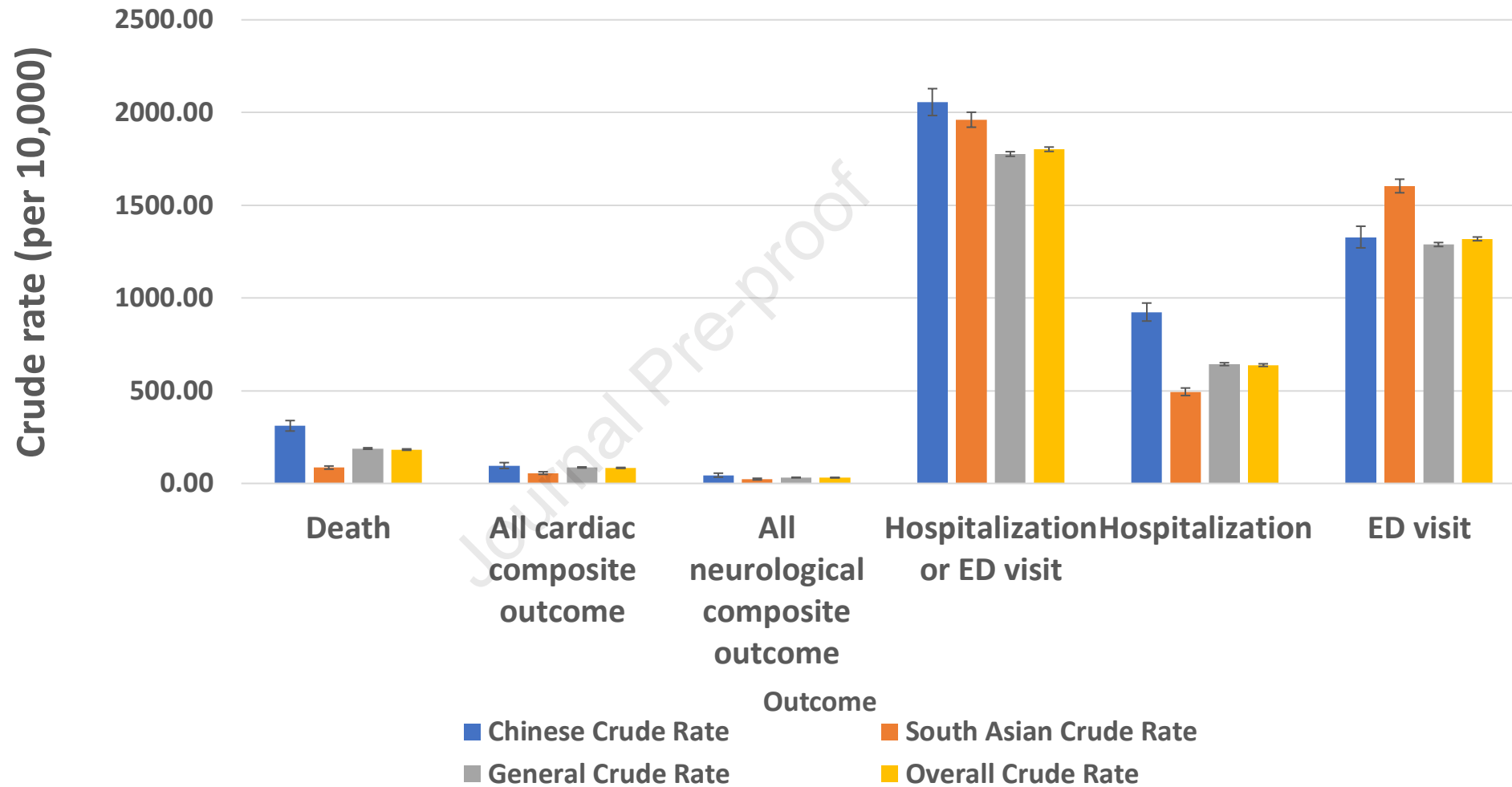


Figure 2A: 30-day crude outcome rates (per 10,000) by ethnic group, < 65

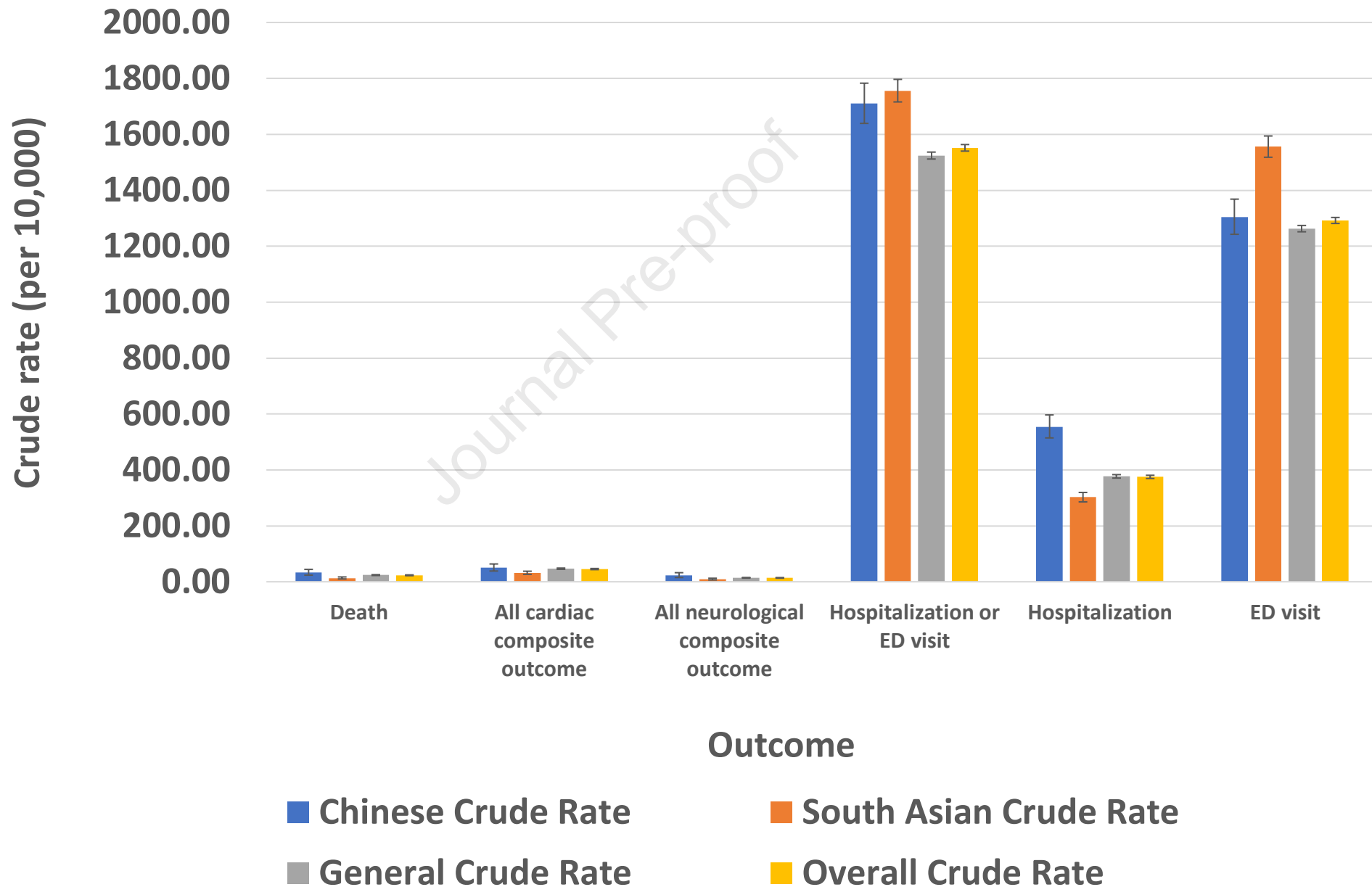


Figure 2B: 30-day crude rate (per 10,000) by ethnic group, >=65

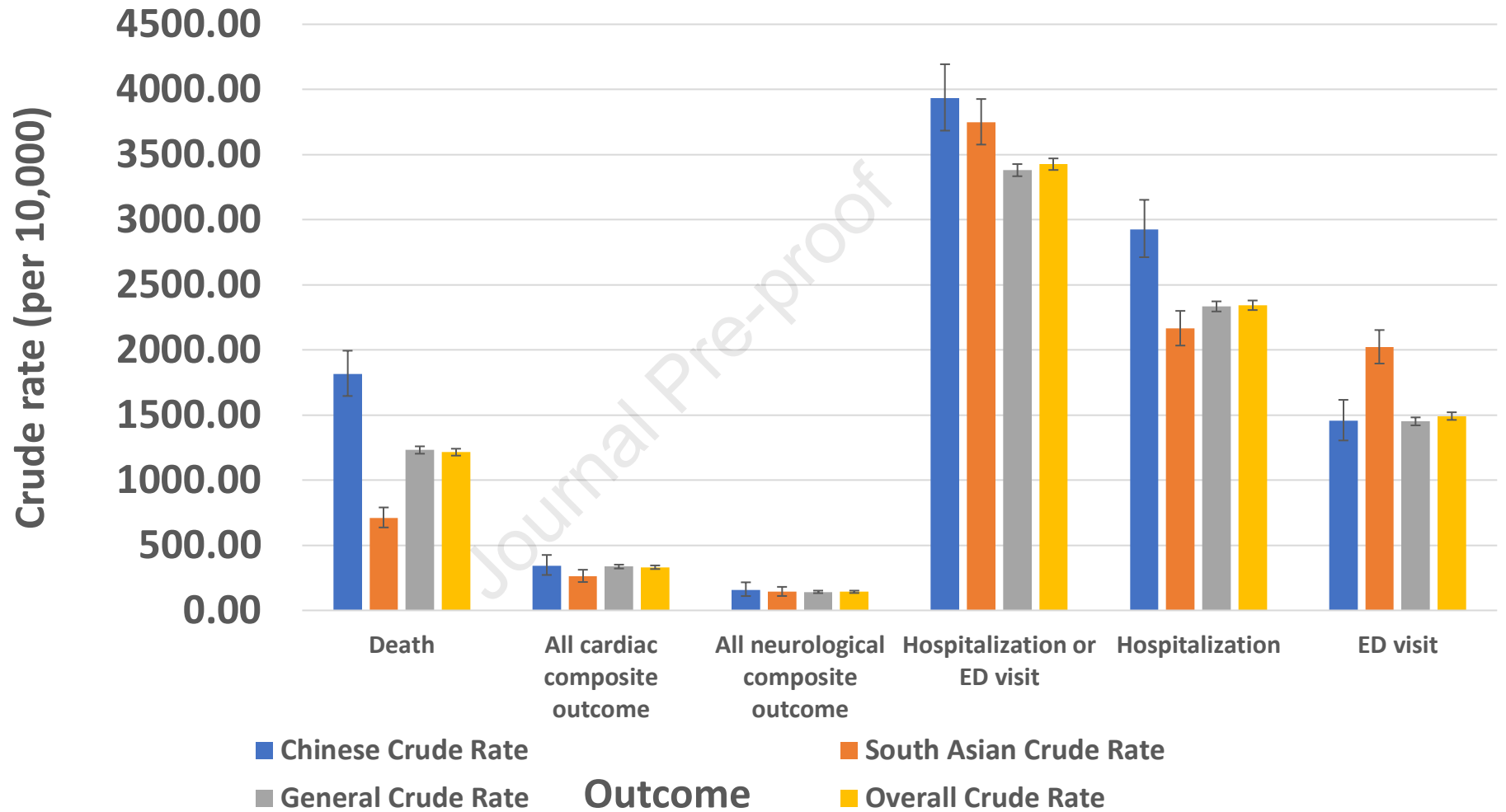
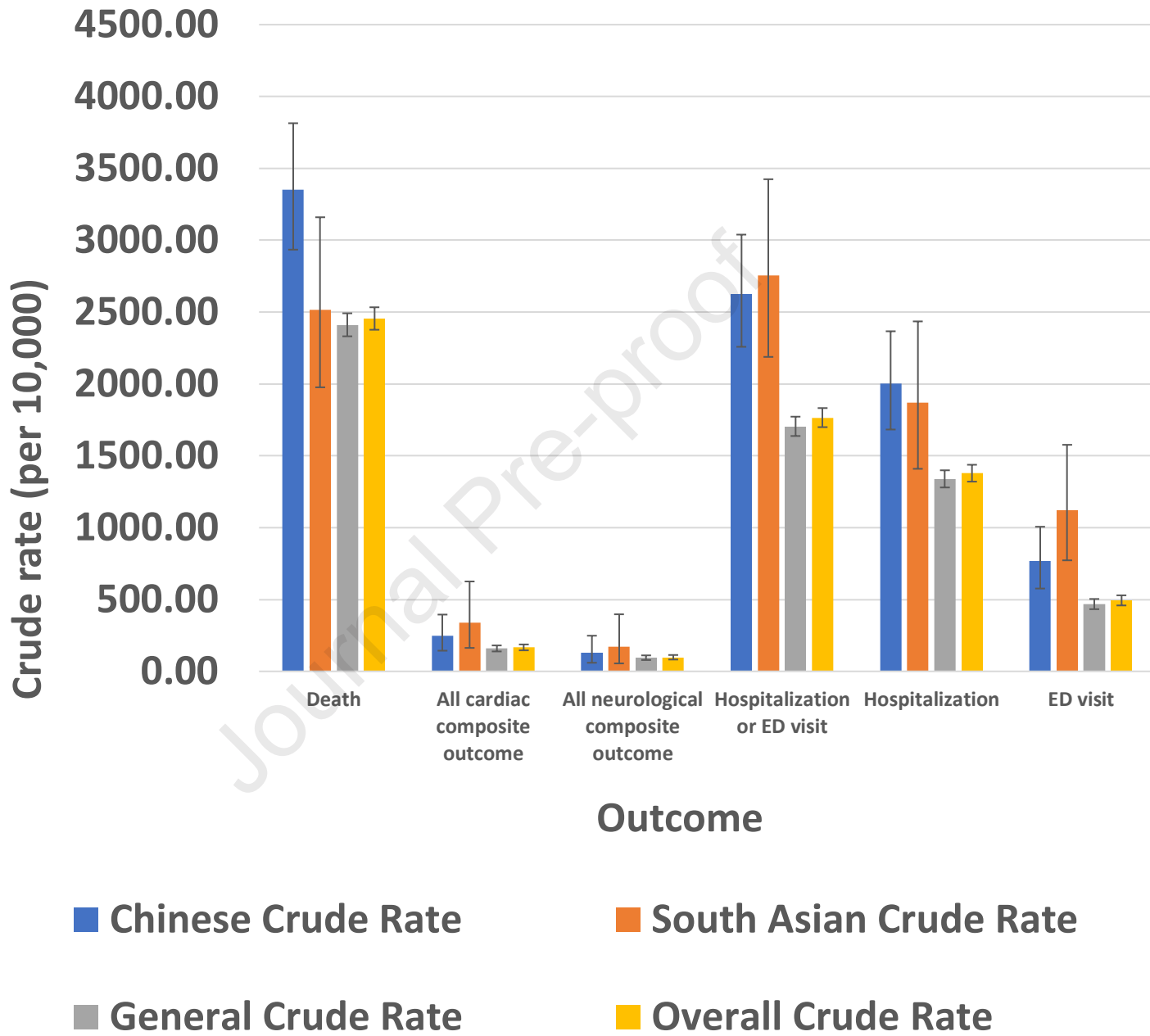
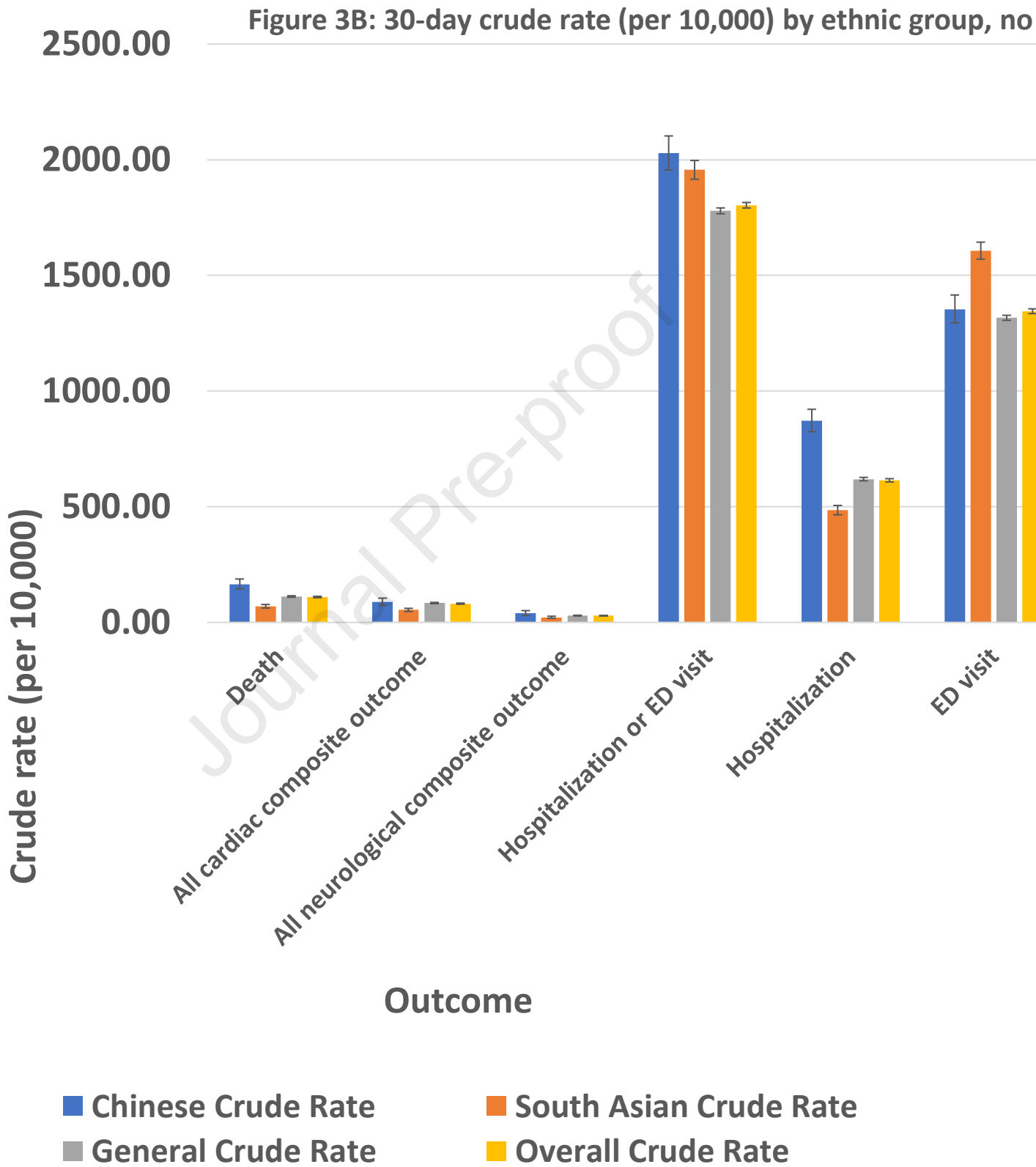


Figure 3A: 30-day crude rate (per 10,000) by ethnic group, LTC





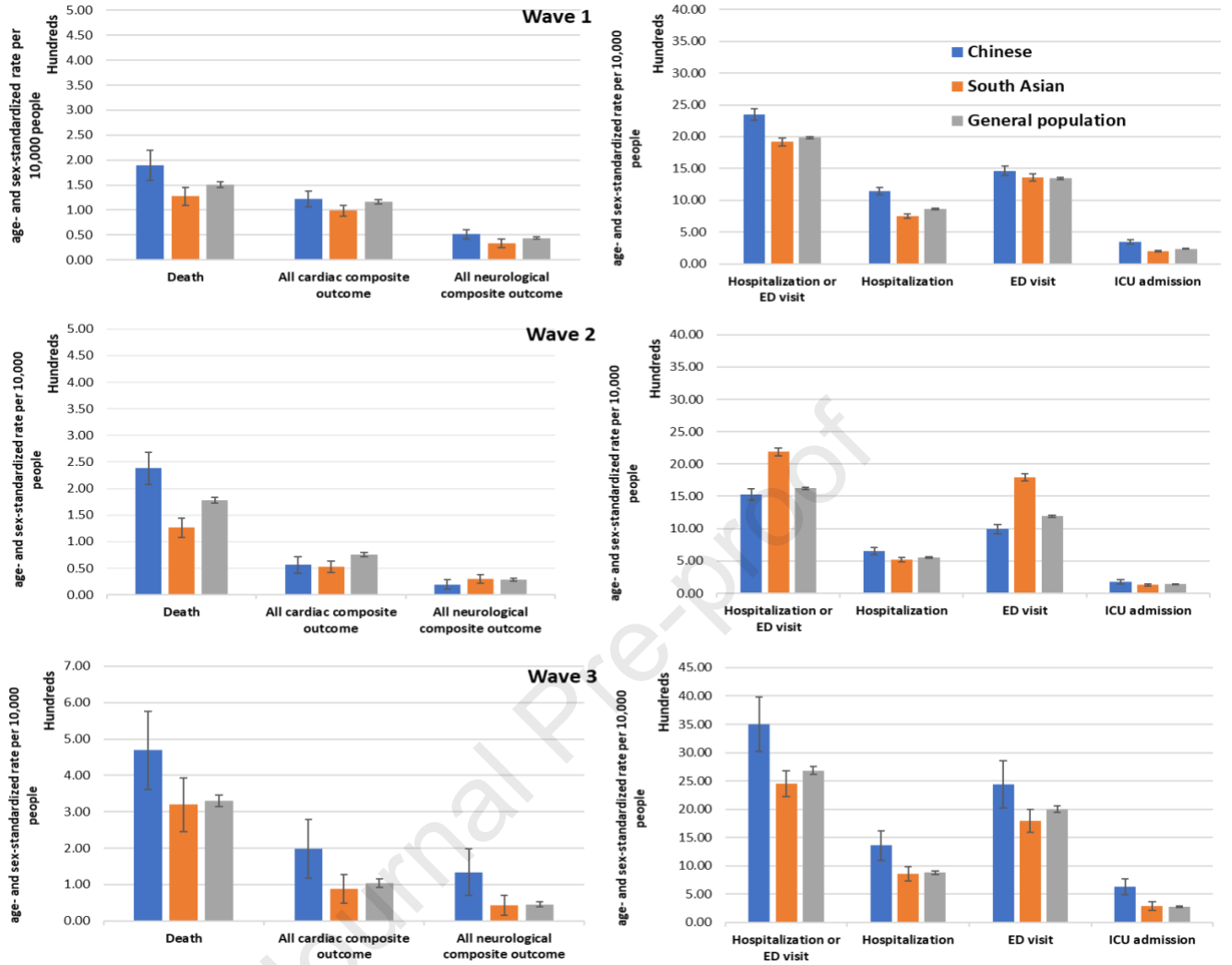


Figure 4: Age- and sex-standardized rates (with 95% confidence intervals as vertical lines) of COVID-19 related outcomes among different ethnic groups in Ontario during waves 1, 2 and 3.