1 **COVID-19 AND ITS CARDIAC AND NEUROLOGICAL COMPLICATIONS AMONG**

2 **ONTARIO VISIBLE MINORITIES**

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41 **ABSTRACT**

42 **Background:** Due to lack of data on the epidemiology, cardiac and neurological complications

43 among Ontario visible minorities (Chinese and South Asians) affected by COVID-19, this

44 population-based retrospective study was undertaken to study them systematically.

45 **Methods:** From January 1, 2020 to September 30, 2020 using the last name algorithm to identify

46 Ontario Chinese and South Asians who were tested positive by PCR for COVID-19, their

47 demographics, cardiac and neurological complications including hospitalization and emergency

48 visit rates were analysed compared to the general population.

49 **Results:** Chinese (N= 1,186) with COVID-19 were found to be older (mean age 50.7 years)

50 compared to the general population (N= 42,547) (mean age 47.6 years) (P < .001), while South

51 Asians (N= 3,459) were younger (age of 42.1 years) (P < .001). The 30 days crude rate for

52 cardiac complications among Chinese was 169/10,000 (P = .069) while for South Asians it was

53 64/10,000 (P = .008) and for the general population it was 112/10,000. For neurological

54 complications, the 30 days crude rate for Chinese was 160/10,000 (P < .001); South Asians was

55 40/10,000 (P = .526) and general population was 48/10,000. The 30 days all-cause mortality rate

56 was significantly higher for Chinese at 8.1% vs 5.0% for the general population (P < .001) while

57 it was lower in South Asians at 2.1%. (P < .001)

58 **Conclusions:** Chinese and South Asians in Ontario affected by COVID-19 during the first wave

59 of the pandemic was found to have a significant difference in their demographics, cardiac and

60 neurological outcomes.

61 **Keywords**: COVID-19, cardiac complications, neurological complications, Chinese and South

62 Asians, clinical epidemiology

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is responsible for the global pandemic now known as coronavirus disease (COVID-19). (1, 2) Data from outside Canada suggest there are substantial disparities among different ethnic groups in who gets infected and who have adverse outcomes. In the US, according to a report by Center for Disease Control (CDC) in 2020 (13), 33% of hospitalized patients were black, compared to 18% in the community and 8% were Hispanic, compared to 14% in the community. The overall mortality rates among African Americans were much higher than that of the white and Asian persons. (13) However, the racial distribution in the impact of COVID-19 in Canada has not been studied systematically. (2, 10, 19) In Ontario and based on the 2016 Canadian census, Chinese accounts for 19.4% while South Asians accounts for 29.6% of visible minorities. (43) Therefore, these two ethnic groups account for almost 50% of visible minorities in Ontario. Despite the collected data on COVID-19 in the general population of Ontario (1), however there is a paucity of information on how these two minority ethnic groups are affected by COVID-19, in particular their rates and types of cardiac and neurological complications. Accordingly, we conducted a population-based retrospective study to evaluate the epidemiology as well as potential cardiac (31, 33, 34) and neurological complications (4, 5, 44, 45) of COVID-19 among Chinese and South Asians compared to the general population in Ontario.

METHODS

Data Sources

To identify the cohort, we used the Ontario Laboratory Information System (OLIS) database and selected those who had a positive COVID test result between January 1, 2020 and September 30, 2020 inclusive. To identify baseline demographics and health conditions, health outcomes, and health service-use, we used 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. The RPDB provides basic 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.

92 OHIP captures information of the services provided by practicing physicians in Ontario. These

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

94 Study Population

95 The cohort included individuals between the ages of 18 and 105, who had a positive COVID-19

96 test between January 1, 2020 and September 30, 2020. We excluded patients who were not

97 Ontario residents at the time of the COVID-19 test. If the person had multiple positive tests

98 within the study period, the first positive test date was chosen as the index date. Individuals'

99 ethnicities (classified into Chinese, South Asian, and all others hereby termed General) were

100 determined using an algorithm developed by Shah et al. which uses a surname-based approach to

101 identify ethnicity based on an individuals' surname (41). The use of the data in this project is

102 authorized under section 45 of Ontario's Personal Health Information Protection Act (PHIPA)

103 and does not require review by a Research Ethics Board.

104 Outcomes

105 The primary outcome of interest was death. Cardiac outcome including myocardial infarction,

106 heart failure, arrhythmia, atrial fibrillation and flutter, myocarditis, deep vein

107 thrombosis/pulmonary embolism (DVT/PE). Neurological outcomes including hemorrhagic

108 stroke, ischemic stroke, seizure, meningitis, encephalitis, encephalopathy and Parkinson 's

109 disease. Health service use includes hospitalization, emergency room visit, intensive care units

110 (ICU) admission, use of extracorporeal membrane oxygenation (ECMO), use of mechanical

111 ventilation within thirty days of having a positive COVID-19 test (Codes are listed in Appendix

112 A). The outcomes were measured at the individual level indicating whether the patient did or did

113 not experience the outcome.

114 Statistical Analysis

115 Baseline and outcome characteristics were compared between the Chinese and South Asians

116 versus the general population. In addition, Charlson comorbidity index and 30 days all-cause

117 mortality rate, cardiac and neurological complication rates were also analysed. For continuous

118 variables, descriptive statistics included mean values with standard deviation, median values

119 with interquartile range, and the p-values were calculated using one way analysis of variance

120 (ANOVA) for means and Kruskal-Wallis test for medians. Categorical variables were described

121 using proportions and p-values from a chi-squared test were provided. P-values were used to

122 compare the Chinese population to the general population, and to compare the South Asians

123 population to the general population. Multivariate logistic regression was used to determine if

124 ethnicity was associated with death, cardiac outcomes, neurological outcomes, or hospitalization

125 or emergency department visits. A separate logistic regression model was built for each binary

126 outcome with ethnicity as the main exposure categorical variable and the general population as

127 the reference group. Adjustment variables included age, sex, income quintile which is defined as

128 the quintile of neighbourhood income per person equivalent within a census metropolitan area,

129 census agglomeration or residual area (Table 1A), and long-term care placement within 90 days

130 (Table 1B) prior to positive COVID test. Odds ratios (OR) comparing Chinese and South Asian

131 ethnicities to the general population were computed for each outcome.

132 **RESULTS**

133 Chinese (N= 1,186) infected by COVID-19 were older with a mean age of 50.7 years compared

134 to general population (N= 42,547) of 47.6 years (P< .001), while South Asians (N= 3.459) were

135 younger with a mean age of 42.1 years (P< .001). 14.0% of Chinese and only 3.8% of South

136 Asians were >80 years compared to 12.4% of the general population. (Table 1A) There was no

137 statistical difference in sex distribution for Chinese while for South Asians 53.9% were male

138 compared to 46.4% in the general population (P< .001). Income quintile showed that only 8.2%

139 of South Asians were in the highest category (quintile 5) while for general population it was

140 14.6%. The majority of both Chinese and South Asians (99.2% and 99.3%) and the general

141 population (96.1%) were from urban areas. (Table 1A) Among the components of the Charlson

142 comorbidity index (past 5 years from index), for Chinese only chronic obstructive pulmonary

143 disease or other respiratory diseases (1.0%) vs general population (2.3%) were significantly

144 different (P= .004). (Table 2A). Rate of past hospitalization was similar in Chinese (26.7% vs

145 28.3%, P = .227) while it was lower among South Asians (20.1% vs 28.3%, P< .001). (Table 1B)

146 The clinical outcomes for all 3 cohorts are shown in Figures 1-5. Compared to the general

147 population, emergency visits and ICU admission rates were both higher for Chinese while they

148 were lower in South Asians (both P < .003). These data were further dichotomised into < 65

149 years old (Figure 1) and for those ≥ 65 years old (Figure 2). In addition, the data was also

150 analysed based on those residing in long- term care facilities (Figure 3) and compared to those

151   who were not in long-term care facilities. (Figure 4) The 30 days all-cause mortality rate was

152   much higher for Chinese at 8.1% vs 5.0% of the general population while it was much lower in

153   South Asians at only 2.1% (P < .001). (Figure 5) The overall cardiac complication rate was

154   found to be higher for Chinese compared to the general population (1.7% vs 1.1%, P = .003) and

155   especially for those 65 years and older. The overall neurological complication rate for the

156   general population was very low (0.5%) but was higher in Chinese (1.6%, P = .005) and tended

157   to be lower in South Asians (0.4%, P > .05). (Figure 5) Among all the neurological

158   complications, encephalopathy was the commonest accounting for 6.4% of hospitalized and

159   14.1% of Chinese admitted to ICU but it was not statistically significant compared to the general

160   population. The 30 days crude rate for cardiac complications among Chinese was 169/10,000 (P

161   = .069) and for the general population was 112/10,000. For neurological complications, the 30

162   days crude rate for Chinese was 160/10,000 (P < .001); general population was 48/10,000.

163   (Figure 5)

164   For South Asians with COVID-19, the incidence of underlying diabetes was higher than the

165   general population (19.7% vs 17.2%, P < .001) while they were lower in the following pre-

166   morbid conditions: hypertension, heart failure, chronic obstructive pulmonary disease (COPD),

167   dementia and chronic kidney disease. (P < .001). Only 3.2% of South Asians were in long term

168   care facilities compared to 12.2% in the general population (P < .001) and their incidence of

169   hospitalization during the past 5 years from index was lower at 18.1% compared to 25.8% in the

170   general population. (P < .001) (Table 1B) These differences could be due to the younger age of

171   this cohort. (Table 1A) Their Charlson comorbidity index was significantly lower in incidence

172   for heart failure, peripheral vascular disease, cerebrovascular disease, dementia and COPD. (P <

173   .001) (Table 2A) Their overall mortality rate was much lower at 2.1% compared to the general

174   population of 5.0% (P< .001). The all cardiac complication rate was also lower at 0.6% vs 1.1%

175   for the general population (P < .001) while the all neurological complication rate was similar to

176   the general population (0.4% vs 0.5%, P = 0.526). Although their hospitalization rate was lower,

177   there were no difference in their ICU admission rate and mechanical ventilation rate when

178   compared to the general population. (P > .05) (Figure 5). The 30 days crude rate for cardiac

179   complications among South Asians was 40/10,000 (P= .526) compared to the general population

180   at 112/10,000. The 30 days crude rate for neurological complications among South Asians was

181   64/10,000 (P = .008) compared to the general population of 48/10,000. (Figure 5)

182   Multivariate logistic regression analysis demonstrated that ethnicity is a major determinant for 30

183   days overall mortality, cardiac and neurological complications, hospitalization or emergency

184   department visits. (Table 2B) Chinese ethnicity, independent of their age, sex, income quintile

185   and long-term care placement within 90 days prior to positive COVID-19 tests, was found to

186   have higher odds ratios for all these outcomes while they were lower in South Asians compared

187   to the general population. (Table 3) For Chinese, their mortality OR = 1.743; cardiac

188   complications OR = 1.433; neurological complications OR = 3.141 and hospitalization or

189   emergency department visits OR = 1.437. For South Asians, their mortality OR = 0.981; cardiac

190   complications OR = 0.707; neurological complications OR = 1.088; and hospitalization or

191   emergency department visits OR = 0.869. (Figure 6)

192   **DISCUSSION**

193   For Ontario visible minorities affected by COVID-19 during the first wave of the pandemic,

194   Chinese were older while South Asians were found to be relatively younger compared to the

195   general population. This may be attributed in part to a much larger proportions of front-line

196   health care workers and those in distribution centers are of South Asian descent and they have a

197   lower socioeconomic status compared to the general population. (2, 10) This is further evidenced

198   in our study indicating that only 8.2% of South Asians with COVID-19 was found to be in the

199   highest income quintile 5 while Chinese and the general population were higher at 15.3% and

200   14.6% respectively. (Table 1) Based on the 2016 Canadian census (43), Chinese accounts for

201   5.7% of Ontario population while only 2.5% of this studied group was found to have COVID-19

202   and this is below the expected infection rate. This could be in part an under-estimation due to the

203   sensitivity rate of 80.2% using the last-name algorithm to identify Chinese. (41) For South

204   Asians, they account for 8.7% of the Ontario population and 7.3% was found to have COVID-19

205   which is very close to the expected infection rate. (43) Chinese when tested positive for COVID-

206   19 were more than likely to be at long-term care facilities compared to the general population

207   (6.4% vs 5.0%, p = .031) while it was much lower for South Asians at 1.4%. (Table 2) History of

208   heart failure (p <.004) and COPD (p < .003) were the only two baseline characteristics found to

209   be less frequent for Chinese compared to the general population. Lower incidence of heart failure

210   was also found among Chinese Americans in a previous study. (52) The incidence of COPD was

211   also found to vary by ethnicity in London, United Kingdom. (53) Although there was no

212   significant difference in the number of Charlson comorbidity index for Chinese, their

213   hospitalization rates, emergency and ICU admission rates, cardiac and neurological complication

214   rates and overall mortality rates were much higher than the general population. (Figure 5) Since

215   many of these Chinese were residing in long-term care facilities, they were more vulnerable to be

216   infected by COVID-19 and develop fatal complications. The overall mortality rates,

217   hospitalization rates, ICU admission rates, cardiac and neurological complication rates were all

218   much higher among those 65 years or older in all three cohorts. This would indicate that age is a

219   very important prognostication factor in patients infected with COVID-19, as reported

220   previously. (6, 15, 16, 26)

221   CARDIAC COMPLICATIONS

222   One of the biggest risk factors for severe COVID19 and fatality from COVID19 is underlying

223   cardiovascular (CV) disease comorbidity. (40) However, in the current study, compared to the

224   general population, the frequencies of CV disease comorbidity such as heart failure, COPD and

225   asthma in Chinese was significantly lower than in the general population while in the South

226   Asians, these conditions were less frequent except for asthma. We assessed for acute MI, heart

227   failure, arrhythmia in general, atrial fibrillation and flutter, myocarditis and DVT/PE. The

228   incidence was too low in our study to draw conclusions regarding any potential differences

229   between groups. The heart can be affected in diverse ways by COVID-19. (31, 34-38) and

230   mechanisms of myocardial injury (39) in patients with COVID-19 include oxygen supply–

231   demand imbalance, direct viral myocardial invasion (33), inflammation, coronary plaque rupture

232   with acute MI, microvascular thrombosis, and adrenergic stress (32). The recent North American

233   Cardiovascular COVID-19 Myocardial Infarction (NACMI) Registry (49, 50) that the primary

234   outcome — a composite of in-hospital death, stroke, recurrent MI, or repeat unplanned

235   revascularization —occurred in 36% of COVID-positive patients, compared with 13% of

236   COVID-negative patients and 5% of control subjects (P <.001 relative to controls). This

237   difference was driven largely by a high in-hospital death rate in COVID-positive patients. (40)

238   ST-segment elevation MI in COVID-positive patients disproportionately affects ethnic

239   minorities (23% Hispanic and 24%Black) with diabetes, which was present in 46% of COVID-

240   positive patients. Importantly, 23% have no culprit vessel on angiography and this may represent

241   different aetiologies of ST-segment elevation, including microemboli, myocarditis (33), and

242   stress cardiomyopathy. It is noteworthy that Asians only comprised of 6% of the study

243 population and this underscores the importance of following the cause-specific outcomes in the

244 Asian population.

245 NEUROLOGICAL COMPLICATIONS

246 Neurological complications of COVID-19 can be divided into two major categories: *de novo*

247 neurological complications as a direct result of COVID-19 infections and exacerbation of pre-

248 existing neurological conditions when patients were infected by SARS-CoV-2 virus. (7) In our

249 current study, Chinese had no significant difference in the prevalence of pre-morbid conditions

250 based on the Charlson comorbidity index compared to the general population. This would

251 suggest that excessive neurological complication rate of Chinese could be due to a direct result

252 of COVID-19 infection rather than exacerbation of their pre-existing neurological conditions in

253 addition to being older in their mean age. Among all the neurological complications,

254 encephalopathy was the commonest accounting for 6.4% of hospitalized and 14.1% of Chinese

255 patients admitted to ICU but it was not statistically significant compared to the general

256 population. Encephalopathy in COVID-19 patients could be due to a combination of etiological

257 factors: hypoxemia secondary to respiratory failure, toxic and metabolic factors secondary to

258 acute illness and as well recently recognized inflammatory brain diseases. (4, 51)

259 Encephalopathy of admitted COVID-19 patients in a large cohort study was associated with

260 increased the risk of death by 5.5 times (OR= 4.01 – 7.57, p < .001). (46) In our current study,

261 there were very few cases of hemorrhagic (21) and ischemic stroke (20, 24, 30), seizures and

262 Parkinson's Disease among Chinese but this could be due to the relatively small number in this

263 cohort. The estimated incidence of stroke as a complication of COVID-19 varies between 2.5%

264 to 5% found in various recent publications. (5, 8) In addition, there were no cases reported with

265 encephalitis, meningitis, Guillain-Barre syndrome and inflammatory myositis in both the

266 Chinese and South Asians. Ongoing pathological studies will be required to examine if there are

267 direct invasion of the SARS-CoV-2 virus in neural tissues of the central and peripheral nervous

268 system. (4, 12, 48) These clinical-pathological studies would be vital in discovering if there are

269 different pathophysiological mechanisms in explaining the difference in neurological

270 complications between these 3 cohorts. (47) Although these are very rare neurological

271 complications of COVID-19 (3, 4, 15, 22, 25, 46), we hope that with increasing number of

272 patients in our future studies, the true incidence of these unusual neurological complications of

273 COVID-19 among Chinese and South Asians in Ontario will be discovered.

274 LIMITATIONS

275 We used surname algorithm to classify surnames as Chinese, South Asian, or General. The

276 dataset excludes surnames which are not unique to one of these populations such as Khan,

277 Ahmed or Fernandes from the South Asian list, or Lee or Young from the Chinese list. As a

278 result, the South Asian list includes predominantly Hindu surnames and is therefore most

279 representative of Indian surnames; Muslim surnames from Pakistan and Bangladesh are often

280 shared with Muslim populations from other world regions and are not included in the list. These

281 exclusions resulted in an algorithm with a high specificity (99.7% for both ethnicities) but lower

282 sensitivity (50.4% for South Asians, 80.2% for Chinese). (41) Another limitation is the surname

283 algorithm cannot be used to identify Blacks and other visible minorities and this study period

284 covered mainly the first wave of COVID-19 in Ontario with limited data on ethnicity/race. Since

285 we used only 30 days all-cause mortality rates, cardiac and neurological complication rates, the

286 current study is not able to capture patients with "long-haul" COVID-19 symptoms (7, 12) even

287 though they may have recovered from the acute illness. Another limitation relates to that hospital

288 administrative records may not capture all complications and hence the true incidence of cardiac

289 and neurological complications may be under-estimated in this study. 46), we hope that with

290 increasing number of patients in our future studies, the true incidence of these unusual

291 neurological complications of COVID-19 among Chinese and South Asians in Ontario will be

292 discovered.

293 **CONCLUSIONS**

294 In this preliminary cohort study, using multivariate logistic regression analysis, ethnicity was

295 found to be the most important determinant for mortality, cardiac and neurological outcomes and

296 hospitalization rates for those Ontarians infected by COVID-19. (Figure 6) These data have

297 significant implications for health care policy makers regarding resource allocation and

298 vaccination priority (42) in order to provide proper prevention and appropriate medical care for

299 those Chinese and South Asians who are residing in long term care facilities. These elderly

300 patients are more vulnerable to be infected by COVID-19 and develop fatal complications. For

301 South Asians infected by COVID-19, even though they were relatively younger than the general

302 population, their overall mortality rate was still of importance particular for those 65 years and

303 older and for those residing in long-term facilities. In addition, these findings would be of

304 importance to Ontario public health units and health care authorities when dealing with the

305 second and third wave of this pandemic in Ontario.

REFERENCES

1. Public Health Ontario: COVID-19 in Ontario—A Focus on Diversity: January 15, 2020, to May 14, 2020.

2. Subedi R, Greenberg L, Turcotte M. Statistics Canada: StatCan COVID-19: COVID-19 mortality rates in Canada's ethno-cultural neighbourhoods, October 28, 2020.

3. Nepal G, Rehrig JH, Shretha GS etal. Neurological manifestations of COVID-19: a systematic review. Critical Care 24, Article number: 421 (2020).

4. Ellul MA, Benjamin L, Singh B etal. Neurological associations of COVID-19: The Lancet Neurology, July 02, 2020.

5. 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-e586.

6. O'Brien K, St-Jean M, Wood P, Willbond S etal. StatCan COVID-19 death comorbidities in Canada, November 16, 2020.

7. Narth A. Neurologic complications of coronavirus infections. Neurology 2020;94:809-810.

8. Wang L, Shen Y, Li M etal. Clinical manifestations and evidence of neurological involvement in 2019 novel coronavirus SARS-CoV-2: a systematic review and meta-analysis. J Neurol 2020 Jun11: 1-13.

9. Niazkar HR, Zibaee B, Nasimi A etal. The neurological manifestations of COVID-19: a review article. Neurol Sci 2020 Jun 1: 1-5.

10. StatCan: Impacts on Immigrants and People Designated as Visible Minorities, October 20, 2020.

11. Dhamoon MS, Thaler A, Gururangan K etal. Acute Cerebrovascular Events With COVID-19 Infection. Stroke 2021;52:48-56.

12. 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. Frontiers in Neurology January 2021;Vol. 11, article 615061.

13. CDC: COVID-19 in Racial and Ethnic Minority Groups, June 4, 2020.

14. Suleyman G, Fadel RA, Malette K etal. Clinical Characteristics and Morbidity Associated With Coronavirus Disease 2019 in a Series of Patients in Metropolitan Detroit. JAMA Netw open. 2020 Jun 1;3(6):e2012270.

15. Wang D, Yin Y, Hu C etal. 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 Apr 30;24(1):188.

16. Hooper MW, Napoles AM, Perez-Stable EJ. COVID-19 and Racial/Ethnic Disparities. JAMA May 11, 2020.

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

354 18. Haynes N, Cooper LA, Albert MA. At the Heart of the Matter: Unmasking and
355   Addressing   COVID-19's   Toll   on   Diverse   Populations.
356   10.1161/CIRCULATIONAHA.120.048126.

357 19. Laurencin C, McClinton A. The COVID-19 Pandemic: a Call to Action to Identify and
358   Address Racial and Ethnic Disparities. Journal of Racial and Ethnic Health Disparities,
359   April 3, 2020.

360 20. Van der Worp B, Sandset EC, Caso V. Likely Increase in the Risk of Death or Disability
361   from Stroke during the COVID-19 Pandemic, European Stroke Organization, May 9,
362   2020.

363 21. Oxley TJ, Mocco J, Majidi S etal. Large-Vessel Stroke as a Presenting Feature of
364   COVID-19 in the Young. NEJM; May 10, 2020.

365 22. Tu H, Tu S, Gao S etal. The epidemiological and clinical features of COVID-19 and
366   lessons from this global infectious public health event. Journal of Infection, April 11,
367   2020.

368 23. Lodigiani C, Iapichino G, Carenzo L etal. Venous and arterial thromboembolic
369   complications in COVID-19 patients admitted to an academic hospital in Milan, Italy.
370   Thromb Res. 2020 Apr 23,191:9-14.

371 24. Qureshi A, Abd-Allah F, Alsenani F etal. Management of acute ischemic stroke in
372   patients with COVID-19 infection: Report of an international panel. Int J. Stroke. 2020
373   May 3:1747493020923234.

374 25. Zhou, Y, Li W, Wang D etal. Clinical time course of COVID-19, its neurological
375   manifestation and some thoughts on its management. Stroke Vasc Neurol 2020 May4.
376   Pii: svn-2020-000398.

377 26. Guo T, Fan Y, Chen M etal. Cardiovascular Implications of Fatal Outcomes of Patients
378   With Coronavirus Disease 2019 (COVID-19). JAMA Cardiol. 2020 Mar 27.

379 27. Shi S, Qin M, Shen B etal. Association of Cardiac Injury with Mortality in Hospitalized
380   Patients with COVID-19 in Wuhan, China. JAMA Cardiol 2020 Mar 25.

381 28. DataSF. Demographics of COVID-19 Cases and Deaths, City and Country of San
382   Francisco.

383 29. Warrior L, Kim CY, Burdick DJ etal. Leading with inclusion during the COVID-19
384   pandemic. Neurology 2020;95:537-542.

385 30. Khosravani H, Rajendram P, Notario L etal. Protected Code Stroke: Hyperacute Stroke
386   Management During the Coronavirus Disease 2019 (COVID-19) Pandemic. Stroke.
387   2020;51:00-00.

388 31. Canadian Cardiovascular Scoiety, Guidance from the CCS COVID-19 Rapid Response
389   Team: Is it COVID-19 or Is it Heart Failure? Management of Ambulatory Heart Failure
390   Patients.

391 32. Giustino G, Pinney S, Lala A etal, Coronavirus and Cardiovascular Disease, Myocardial
392   Injury, and Arrhythmia, JAAC Focus Seminar, JACC Vol.76, No. 17, October 27,
393   2020:2011-23.

394   33. Kawakami R, Sakamoto A, Kawai K etal, Pathological Evidence for SARS-CoV-2 as a
395   Cause of Myocarditis: JACC Review Topic of the Week, JACC Vol 77, No. 3, 2021.
396   34. Panjrath G, Krepp J. COVID-19 and Heart Failure: Harsh Reality of Pre-existing
397   Conditions, JACC Vol. 76, No. 20, 2020.
398   35. Alvarez-Garcia J, Lee S, Gupta A etal, Prognostic Impact of Prior Heart Failure in
399   Patients Hospitalized with COVID-19, JACC Vol. 76, No. 20, 2020.
400   36. Mehra MR, Ruschitzka F. COVID-19 Illness and Heart Failure, JACC HEART
401   FAILURE, 2020.
402   37. Bhatt AS, Jering KS, Vaduganathan M etal. Clinical Outcomes in Patients With Heart
403   Failure Hospitalized With COVID-19, JACC HEART FAILURE Vol. 9, No. 1, 2021.
404   38. Freaney PM, Shah SJ, Khan SS. COVID-19 and Heart Failure With Preserved Ejection
405   Fraction. JAMA September 30, 2020.
406   39. Tersalvi G, Vicenzi M, Calabretta D etal. Elevated troponin in patients with Coronavirus
407   Disease 2019 (COVID-19): possible mechanisms, Journal of Cardiac Failure (2020).
408   40. Gao T, Fan Y, Chen M etal. Cardiovascular Implications of Fatal Outcomes of Patients
409   With Coronavirus Disease 2019(COVID-19), JAMA Cardiology, March 27, 2020.
410   41. Shah BR, Chiu M, Amin S, Ramani M, Sadry S, Tu JV. Surname lists to identify South
411   Asian and Chinese ethnicity from secondary data in Ontario, Canada: a validation
412   study. BMC Med Res Methodol. 2010;10:42. doi:10.1186/1471-2288-10-42
413   42. Wang C, Wang Z, Wang G, Lau JY-N, Zhang K, Li W. COVID-19 in early 2021:current
414   status and looking forward. Signal Transduction and Targeted Therapy (2021)6:114;
415   https//doi.org/10.1038/s41392-021-00527-1
416   43. StatCan Census Profile 2016: Ontario (Province) and Canada.
417   https//:www12.stacan.gc.ca
418   44. Needham EJ, Chou SH-Y, Coles AJ, Menon DK Neurological Implications of COVID-
419   19 Infections, Neurocrit Care, 2020 Apr 28 : 1-5. Doi: 10.1007/s12028-020-00978-4
420   45. Mao, L, Wang M, Chen S et al. 2020 Neurological Manifestations of Hospitalized
421   Patients with COVID-19in Wuhan, China: a retrospective case series study. medRxiv.
422   Doi: 10.1101/2020.02.22.20026500
423   46. Chou S. AAN-2021 Conference: Hot Topics: Neuro-COVID Plenary Session,
424   Neurological Complications of COVID-19. April 17, 2021
425   47. Vinciguerra M, Greco E. Sras-CoV-2 and black population: ACE2 as shield or blade ?
426   Infect Genet Evol. 2020 Oct; 84: 104361
427   48. Normandin E, Bhattacharyya S, Mukerji S, et al. Neuropathological features of COVID-
428   19. https://index.mirasmart.com/AAN2021/PDFfiles/AAN2021-004641.html.
429   49. Kornowski R, Orvin K. The Clinical Challenge of ST-Segment Elevation Myocardial
430   Infarction and COVID-19. JACC. https://doi.org/10.1016/j.jacc.2021.03.231
431   50. Garcia S, Dehghani P, Grines C, et al. Initial Findings From the North American COVID-
432   19 Myocardial Infarction Registry. JACC. https://doi.org/10.1016/j.jacc.2021.02.055

433   51. Remsik J, Wilcox JA, Babady NE et al. Inflammatory leptomeningeal cytokines mediate
434   COVID-19 neurological symptoms in cancer patients. Cancer Cell 2021;39(2):276-283.
435   52. Bahrami H, Kronmal R, Bluemke DA et al. Differences in the incidence of Congestive
436   Heart Failure by Ethnicity: The Multi-Ethnic Study of Atherosclerosis. Arch Intern Med.
437   2008 Ocotber 27; 168(19): 2138-2145. Doi:10.1001/archinte. 168.19.2138
438   53. Gilkes A, Ashworth M, Schofield P et al. Does COPD risk vary by ethnicity? A
439   retrospective cross-sectional study. International Journal of COPD 201611 739-746.
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LEGENDS FOR TABLES AND FIGURES

442   **Table 1A:** Baseline characteristics of patients by ethnic group.

Characteristics	Chinese	South Asian	General	Overall	P-values	P-values
					Chinese vs General	South Asian vs General
	N=1,186	N=3,459	N=42,547	N=47,192		
Age, mean (SD)	50.7 ± 21.9	42.1 ± 19.2	47.6 ± 23.0	47.3 ± 22.8	<.001	<.001
Age, median (IQR)	51 (32-64)	40 (27-56)	46 (28-63)	46 (28-62)	<.001	<.001
Age groups					<.001	<.001
19 and under	58 (4.9%)	320 (9.3%)	3,737 (8.8%)	4,115 (8.7%)		
20 to 39	355 (29.9%)	1,402 (40.5%)	13,830 (32.5%)	15,587 (33.0%)		
40 to 59	403 (34.0%)	1,059 (30.6%)	12,479 (29.3%)	13,941 (29.5%)		
60 to 79	204 (17.2%)	546 (15.8%)	7,208 (16.9%)	7,958 (16.9%)		
80+	166 (14.0%)	132 (3.8%)	5,293 (12.4%)	5,591 (11.8%)		
Sex					0.808	<.001
Male	546 (46.0%)	1,865 (53.9%)	19,739 (46.4%)	22,150 (46.9%)		
Female	640 (54.0%)	1,594 (46.1%)	22,808 (53.6%)	25,042 (53.1%)		
Income Quintile					0.365	<.001
Income Quintile 1 (lowest)	335 (28.2%)	659 (19.1%)	12,066 (28.4%)	13,060 (27.7%)		
Income Quintile 2	268 (22.6%)	935 (27.0%)	8,990 (21.1%)	10,193 (21.6%)		

Income Quintile 3	205 (17.3%)	1,012 (29.3%)	8,340 (19.6%)	9,557 (20.3%)		
Income Quintile 4	194 (16.4%)	560 (16.2%)	6,778 (15.9%)	7,532 (16.0%)		
Income Quintile 5 (highest)	181 (15.3%)	284 (8.2%)	6,205 (14.6%)	6,670 (14.1%)		
Residence					<.001	<.001
Rural	6 (0.5%)	15 (0.4%)	1,528 (3.6%)	1,549 (3.3%)		
Urban	1,177 (99.2%)	3,435 (99.3%)	40,867 (96.1%)	45,479 (96.4%)		

443

444 **Table 1B:** Baseline characteristics of patients by ethnic group: comorbidities, long term care

445 status and hospitalization.

Characteristics	Chinese	South Asian	General	Overall	P-values	P-values
					Chinese vs	South Asian vs
	N=1,186	N=3,459	N=42,547	N=47,192	General	General
Asthma	135 (11.4%)	542 (15.7%)	6,823 (16.0%)	7,500 (15.9%)	<.001	0.571
Diabetes	209 (17.6%)	683 (19.7%)	7,302 (17.2%)	8,194 (17.4%)	0.679	<.001
Hypertension	389 (32.8%)	884 (25.6%)	12,987 (30.5%)	14,260 (30.2%)	0.093	<.001
Heart Failure	40 (3.4%)	93 (2.7%)	2,243 (5.3%)	2,376 (5.0%)	0.004	<.001
COPD	23 (1.9%)	43 (1.2%)	1,521 (3.6%)	1,587 (3.4%)	0.003	<.001
Dementia	140 (11.8%)	107 (3.1%)	4,881 (11.5%)	5,128 (10.9%)	0.723	<.001
Chronic kidney disease	55 (4.6%)	100 (2.9%)	2,159 (5.1%)	2,314 (4.9%)	0.498	<.001
LTC within 90 days from testing date	162 (13.7%)	110 (3.2%)	5,207 (12.2%)	5,479 (11.6%)	0.141	<.001
LTC status on testing date	76 (6.4%)	48 (1.4%)	2,136 (5.0%)	2,260 (4.8%)	0.031	<.001
Hospitalization (last 5 years from index)	317 (26.7%)	696 (20.1%)	12,054 (28.3%)	13,067 (27.7%)	0.227	<.001

446 COPD = chronic obstructive pulmonary disease, LTC = long-term care

Table 2A: Baseline characteristics of patients by ethnic group: Charlson comorbidity index.

Characteristics	Chinese	South Asian	General	Overall	P-value Chinese vs General	P-value South Asian vs General
	N=1,186	N=3,459	N=42,547	N=47,192		
Charlson comorbidity index (past 5 years from index)						
Acute Myocardial Infarction	14 (1.2%)	32 (0.9%)	515 (1.2%)	561 (1.2%)	0.926	0.137
Congestive Heart Failure	27 (2.3%)	46 (1.3%)	1,123 (2.6%)	1,196 (2.5%)	0.441	<.001
Peripheral Vascular Disease	8 (0.7%)	8 (0.2%)	309 (0.7%)	325 (0.7%)	0.836	<.001
Cerebrovascular Disease	33 (2.8%)	32 (0.9%)	963 (2.3%)	1,028 (2.2%)	0.237	<.001
Dementia	62 (5.2%)	48 (1.4%)	2,136 (5.0%)	2,246 (4.8%)	0.747	<.001
Chronic Obstructive Pulmonary Disease or other Respiratory diseases	12 (1.0%)	27 (0.8%)	965 (2.3%)	1,004 (2.1%)	0.004	<.001
Rheumatic-like Diseases	≤5	≤5	119 (0.3%)	124 (0.3%)	0.365	0.002
Ulcers of the Digestive System	7 (0.6%)	11 (0.3%)	230 (0.5%)	248 (0.5%)	0.818	0.081
Liver Disease - Mild	≤5	≤5	150 (0.4%)	158 (0.3%)	0.382	0.004
Diabetes - No Chronic	41 (3.5%)	73 (2.1%)	1,020	1,134	0.019	0.287

Complications			(2.4%)	(2.4%)		
Diabetes with Chronic Complications	47 (4.0%)	100 (2.9%)	1,845 (4.3%)	1,992 (4.2%)	0.533	<.001
Hemiplegia or Paraplegia	8 (0.7%)	13 (0.4%)	315 (0.7%)	336 (0.7%)	0.794	0.014
Renal (Kidney) Disease	14 (1.2%)	20 (0.6%)	661 (1.6%)	695 (1.5%)	0.304	<.001
Cancer (No secondary found)	16 (1.3%)	26 (0.8%)	615 (1.4%)	657 (1.4%)	0.784	<.001
Liver Disease - Moderate or Severe	*3-8	*3-8	70 (0.2%)	80 (0.2%)	0.499	0.191
Cancer (Metastatic - secondary)	*8-12	≤5	166 (0.4%)	181 (0.4%)	0.004	0.01
Mean +-SD	0.38 ± 1.14	0.19 ± 0.80	0.37 ± 1.11	0.36 ± 1.09	0.676	<.001
Median (IQR)	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)	0.918	<.001
Charlson category					0.995	<.001
0	1,011 (85.2%)	3,181 (92.0%)	36,290 (85.3%)	40,482 (85.8%)		
1	64 (5.4%)	113 (3.3%)	2,268 (5.3%)	2,445 (5.2%)		
≥2	111 (9.4%)	165 (4.8%)	3,989 (9.4%)	4,265 (9.0%)		

448   IQR= interquartile range, SD = standard deviation

449 **Table 2B:** Absolute number of events by ethnic groups.

Outcomes	Chinese N=1,186	South Asian N=3,459	General N=42,547	Overall N=47,192
Death	96 (8.1%)	71 (2.1%)	2,118 (5.0%)	2,285 (4.8%)
All cardiac composite outcome	20 (1.7%)	22 (0.6%)	476 (1.1%)	518 (1.1%)
All neurological composite outcome	19 (1.6%)	14 (0.4%)	205 (0.5%)	238 (0.5%)
Hospitalization or ED visits	370 (31.2%)	715 (20.7%)	9,981 (23.5%)	11,066 (23.4%)

450 ED= emergency department

451   **Table 3:** Summary of odds ratios for death, cardiac complications, neurological complications,

452   hospitalization or emergency visits.

Comparison	Odds Ratio Estimate	Lower CL	Upper CL
Death: Chinese vs General	**1.743**	**1.344**	**2.262**
Death: South Asian vs General	0.981	0.753	1.280
Cardiac: Chinese vs General	**1.433**	**0.903**	**2.274**
Cardiac: South Asian vs General	0.707	0.458	1.092
Neurological: Chinese vs General	**3.141**	**1.943**	**5.080**
Neurological: South Asian vs General	1.088	0.628	1.887
Hospitalization or ED: Chinese vs General	**1.437**	**1.263**	**1.635**
Hospitalization or ED: South Asian vs General	0.869	0.796	0.949

453   Odds ratios were obtained from logistic regression. Each ethic group was compared to the

454   general population (General). Odds ratios that are significantly different from 1 are in bold. CL =

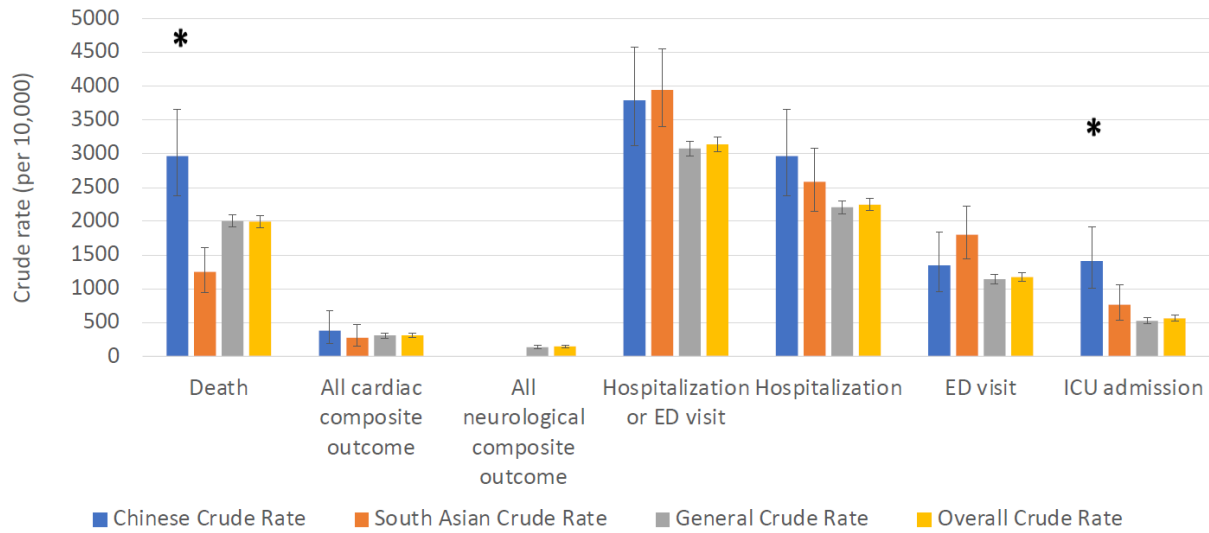455   confidence limit, ED = Emergency department visit

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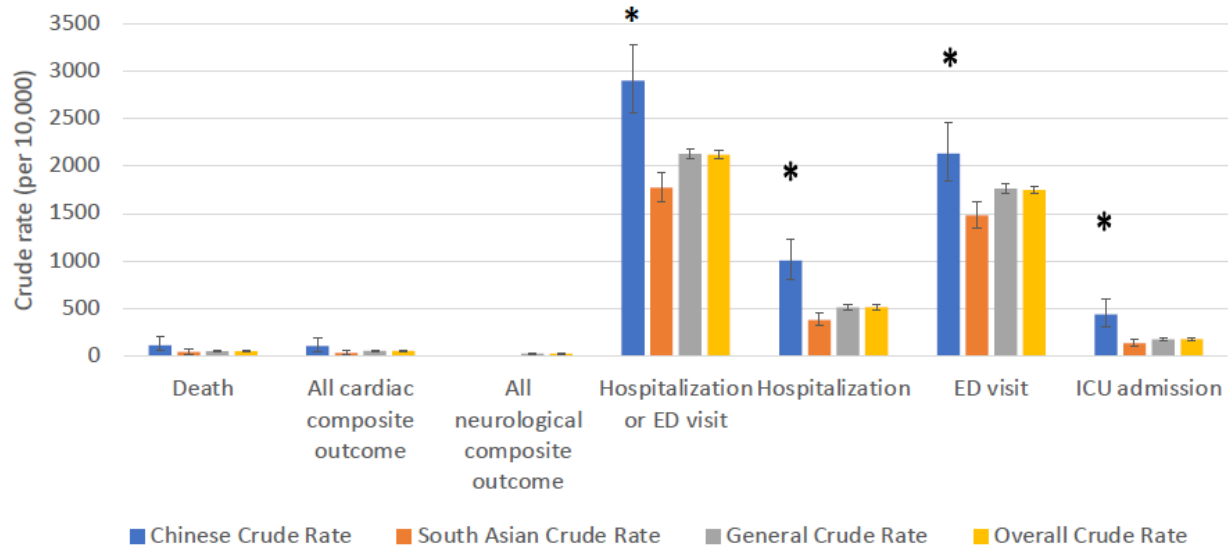
Figure 1. 30 days crude rates by ethnic groups for under age 65 years.

Error bars represent standard deviation. Asterisks indicate significant difference compared to the general crude rate. Abbreviations: ED, emergency department; ICU, intensive care unit.
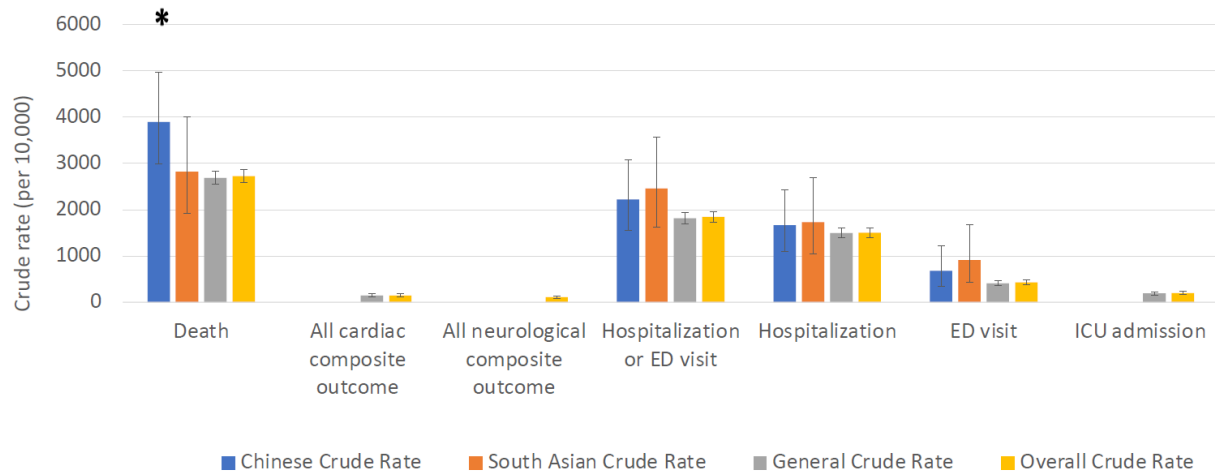
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462 **Figure 2**. 30 days crude rates by ethnic groups for age 65 years or older.

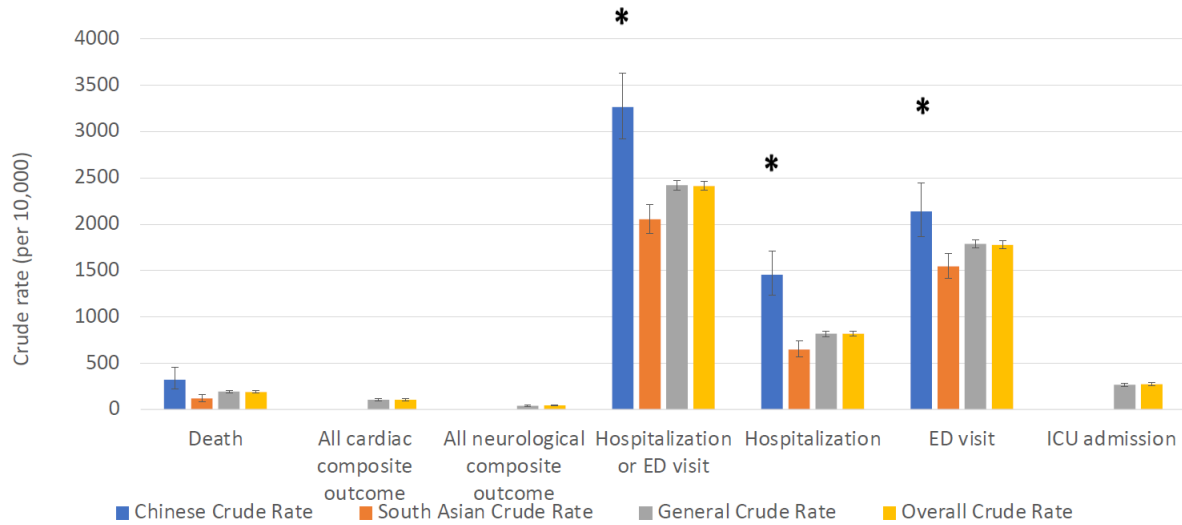463 Error bars represent standard deviation. Asterisks indicate significant difference compared to the

464 general crude rate. Abbreviations: ED, emergency department; ICU, intensive care unit

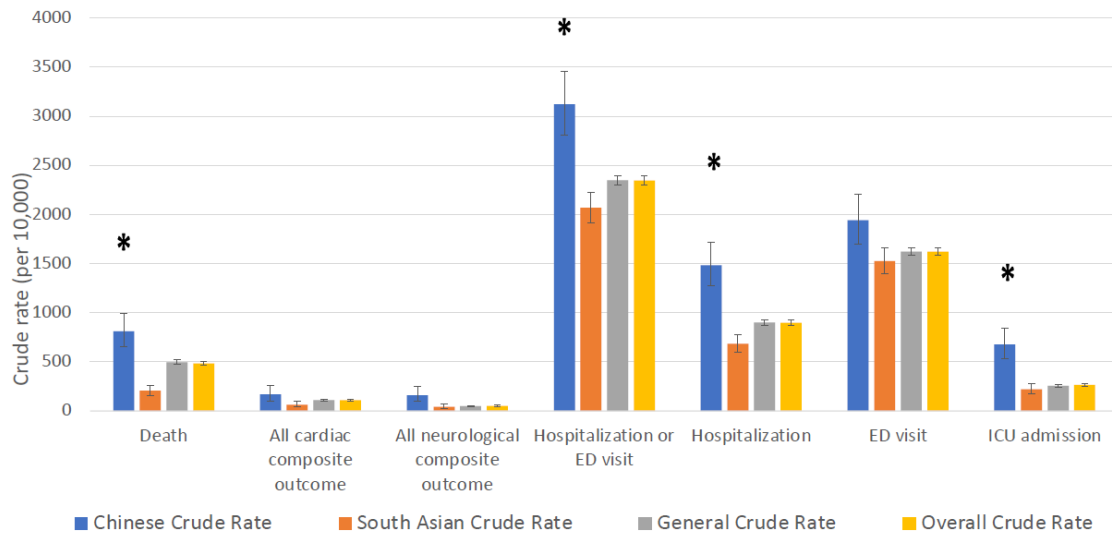**Figure 3**. 30 days crude rates by ethnic groups for patients in long-term care.

Data for patients where were in long-term care in the 90 days period before being tested positive for COVID-19. Error bars represent standard deviation. Asterisks indicate significant difference compared to the general crude rate. Abbreviations: ED, emergency department; ICU, intensive care unit

Figure 4: 30 days crude rates 19 by ethnic groups for patients not in long-term care. Data for patients where were not in long-term care in the 90 days period before being tested positive for COVID-19. Error bars represent standard deviation. Asterisks indicate significant difference compared to the general crude rate. Abbreviations: ED, emergency department; ICU, intensive care unit
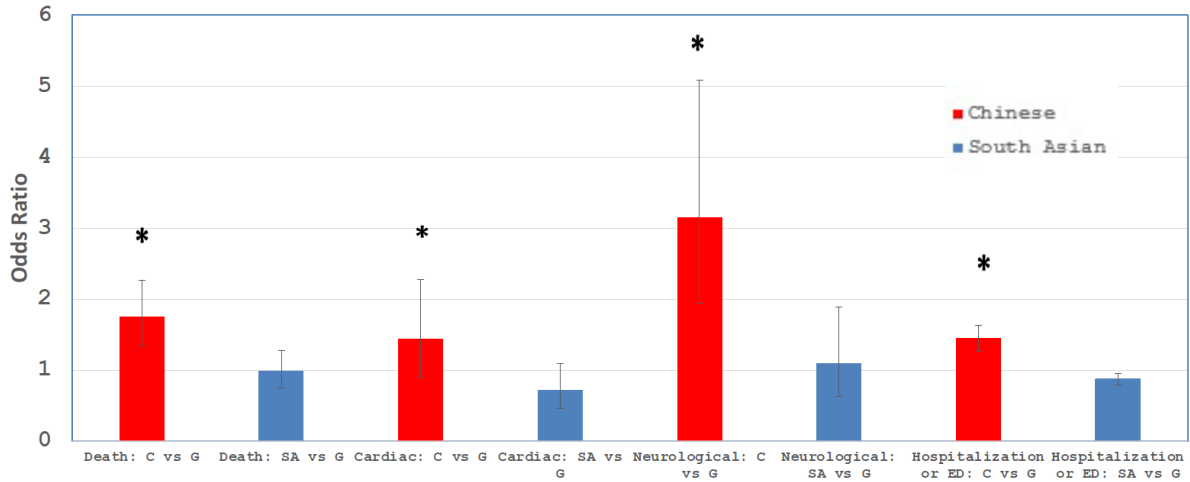
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Figure 5: 30 days crude rates for by ethnic groups.

479 Error bars represent standard deviation. Asterisks indicate significant difference compared to the

480 general crude rate. Abbreviations: ED, emergency department; ICU, intensive care unit.

481

Figure 6: Odds ratios for 30 days outcome in Chinese and South Asian compared to the general

population.

Red bars represent odd ratios for Chinese compared to the general population and blue bars

represent odd rations for South Asian compared to the general population. Error bars represent

standard deviation. Asterisks indicate odd ratios that are significantly greater than 1.

Abbreviations: ED, emergency department; ICU, intensive care unit.