Brief Rapid Report

COVID-19 Vaccination Prioritization on the Basis of Cardiovascular Risk Factors and Number Needed to Vaccinate to Prevent Death

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ABSTRACT

The supply limitations of COVID-19 vaccines have led to the need to prioritize vaccine distribution. Obesity, diabetes, and hypertension have been associated with an increased risk of severe COVID-19 infection. Approximately half as many individuals with a cardiovascular risk factor need to be vaccinated against COVID-19 to prevent related death compared with individuals without a risk factor. Adults with body mass index ≥ 30, diabetes, or hypertension should be of a similar priority for COVID-19 vaccination to adults 10 years older with a body mass index of 20 to < 30, no diabetes, and no hypertension.

RÉSUMÉ

Les limitations d'approvisionnement en vaccins contre la COVID-19 ont abouti à la nécessité d'établir des priorités dans la distribution des vaccins. L'obésité, le diabète et l'hypertension ont été associés à un risque accru d'infection grave par la COVID-19. Il y a approximativement deux fois moins d'individus présentant un facteur de risque cardiovasculaire qui devraient être vaccinés contre la COVID-19 pour prévenir les décès liés à cette maladie, par rapport au nombre d'individus sans facteur de risque. Les adultes ayant un indice de masse corporelle ≥ 30, un diabète ou une hypertension devraient bénéficier d'une priorité de vaccination contre la COVID-19 comparable à celle d'adultes 10 ans plus vieux et ayant un indice de masse corporelle de 20 à < 30, sans diabète et sans hypertension.

Vaccination is highly efficacious at preventing symptomatic COVID-19 infection.[1-3] There has consequently been unprecedented global demand for effective COVID-19 vaccines, which has exceeded supply. Policymakers have implemented guidance for prioritizing vaccine distribution in their countries and jurisdictions. These policies are designed to vaccinate those at highest risk of contracting COVID-19, being hospitalized, or dying from the condition. Current policy prioritizes elderly individuals, especially those who are institutionalized, with evolving guidelines for other groups. The US Centers for Disease Control and Prevention[4] and Public Health England[5] suggest that individuals with certain underlying health conditions, which are thought to be

associated with increased COVID-19 morbidity and mortality, should be prioritized for vaccination. As of February 23, 2021, Public Health England's guidance for vaccination is that adults 65 years of age and older be prioritized highest; followed by adults younger than 65 years with diabetes, body mass index ≥ 40, or other chronic disease; with healthy adults younger than 65 years of age prioritized lowest. However, the public health benefits of such guidance have not been demonstrated and in the absence of data on the population distribution of these morbidities, the value of the strategies proposed cannot be quantified and are speculative.

Younger age and male sex are associated with an increased risk of acquiring COVID-19, whereas in those who develop infection, older age and male sex are associated with a higher risk of death. Cardiovascular risk factors are recognized risk factors for acquiring COVID-19 (obesity and diabetes)[6] and have also been associated with a higher case fatality rate among those who develop COVID-19 (obesity, diabetes, and hypertension).[7,8] Therefore, adults in the general population with cardiovascular risk factors are likely to be at higher risk of acquiring COVID-19 and also having a higher mortality rate

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should they get infected. Consequently, the absolute reduction in COVID-19 risk from vaccinating these individuals might be expected to be higher than for nonobese individuals without diabetes or hypertension. The objective of this analysis was to estimate the number of middle-aged and older adults (age 40-80 years) needed to vaccinate to prevent a COVID-19 death in populations with different clinical characteristics.

Methods

The numbers of men and women stratified according to age in Canada in 2020 were obtained from estimates from the United Nations Department of Economic and Social Affairs.[9] The Canadian incidence rates of COVID-19 for the week of January 31 to February 6, 2021 were obtained from the Government of Canada's Web site on COVID-19 epidemiological and economic research data.[10] We estimated the age-stratified and overall prevalence rates of obesity, diabetes, and hypertension using data from the **P**rospective **U**rban **R**ural **E**pidemiology (PURE) study—a large, prospective cohort study including 10,462 adults from British Columbia, Ontario, and Quebec. Obesity was defined as a body mass index ≥ 30. Diabetes included self-reported diabetes, use of blood glucose-lowering medications, or a fasting blood glucose level ≥ 7 mmol/L. Hypertension included self-reported hypertension, use of a blood pressure-lowering medication, or blood pressure $\geq 140/90$ mm Hg.[11] We observed a relative risk for COVID-19 infection among obese individuals (compared with those with a body mass index of 20 to < 30) of 1.61 (95% confidence interval [CI], 1.19-2.17); a relative risk for COVID-19 infection among adults with diabetes of 1.72 (95% CI, 1.21-2.45); and a relative risk for COVID-19

infection among adults with hypertension of 1.17 (95% CI, 0.77-1.42) on the basis of our analysis of 12,599 individuals from the PURE data (unpublished). We used Public Health Ontario's estimates of the COVID-19 case fatality ratio, which included data up to May, 2020.[12] The effects of obesity on COVID-19 case fatality rates were estimated using data from a systematic review in which body mass index ≥ 30 was associated with an odds ratio for death of 1.67 (95% CI, 1.43-1.96).[13] On the basis of another systematic review of the effects of comorbidities on COVID-19 outcomes, we assumed that those with diabetes and COVID-19 had a relative risk of death of 1.94 and that those with hypertension and COVID-19 had a relative risk of death of 2.10 compared with infected individuals without diabetes or hypertension, respectively.[7] We estimated the protective effect of vaccination by pooling (using random effects models) the estimates from 3 randomized trials that evaluated the Pfizer (New York, NY), Moderna (Cambridge, MA), and ChAdOx1 nCoV-19 (AZD1222, AstraZeneca, Oxford) COVID-19 vaccines, respectively.[1-3]

We estimated the number needed to vaccinate (NNV) in each stratum of the Canadian population as $NNV = \frac{1}{ARR}$ where the absolute risk reduction (ARR), $ARR = (COVID19$ *mortality rate assuming no vaccination*$) - (COVID19$ *mortality rate assuming complete vaccination*$)$.

Results

In Canada, in 2020, there were 2,414,000 men aged 40-50 years; 2,597,000 men aged 50-60 years; 2,322,000 men aged 60-70 years; and 1,435,000 men aged 70-80 years. The respective numbers of women in these age categories were 2,433,000; 2,585,000; 2,390,000; and 1,583,000. In
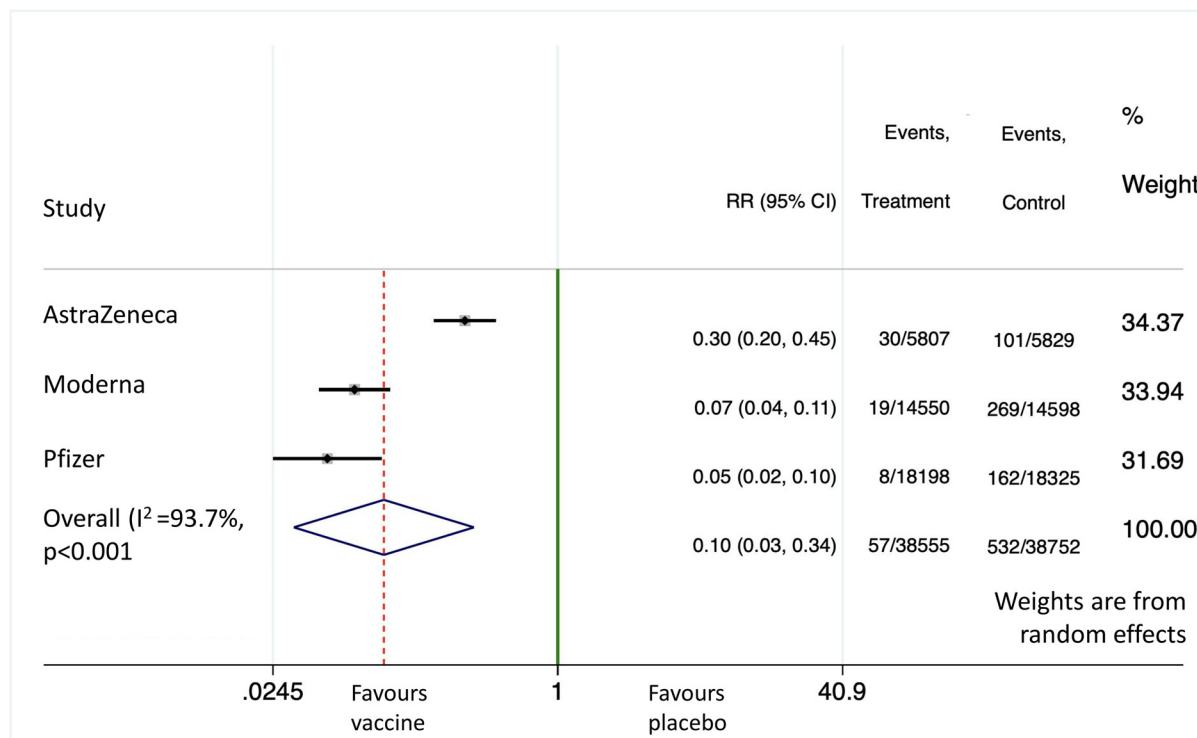

Study	RR (95% CI)	Events, Treatment	Events, Control	% Weight
AstraZeneca	0.30 (0.20, 0.45)	30/5807	101/5829	34.37
Moderna	0.07 (0.04, 0.11)	19/14550	269/14598	33.94
Pfizer	0.05 (0.02, 0.10)	8/18198	162/18325	31.69
Overall ($I^2 =93.7\%$, p<0.001)	0.10 (0.03, 0.34)	57/38555	532/38752	100.00

Weights are from random effects

.0245   Favours vaccine   1   Favours placebo   40.9

Figure 1. Forest plot showing the relative risk (RR) with 95% confidence interval (CI) for COVID-19 in each of 3 vaccine trials, as well the pooled RR.
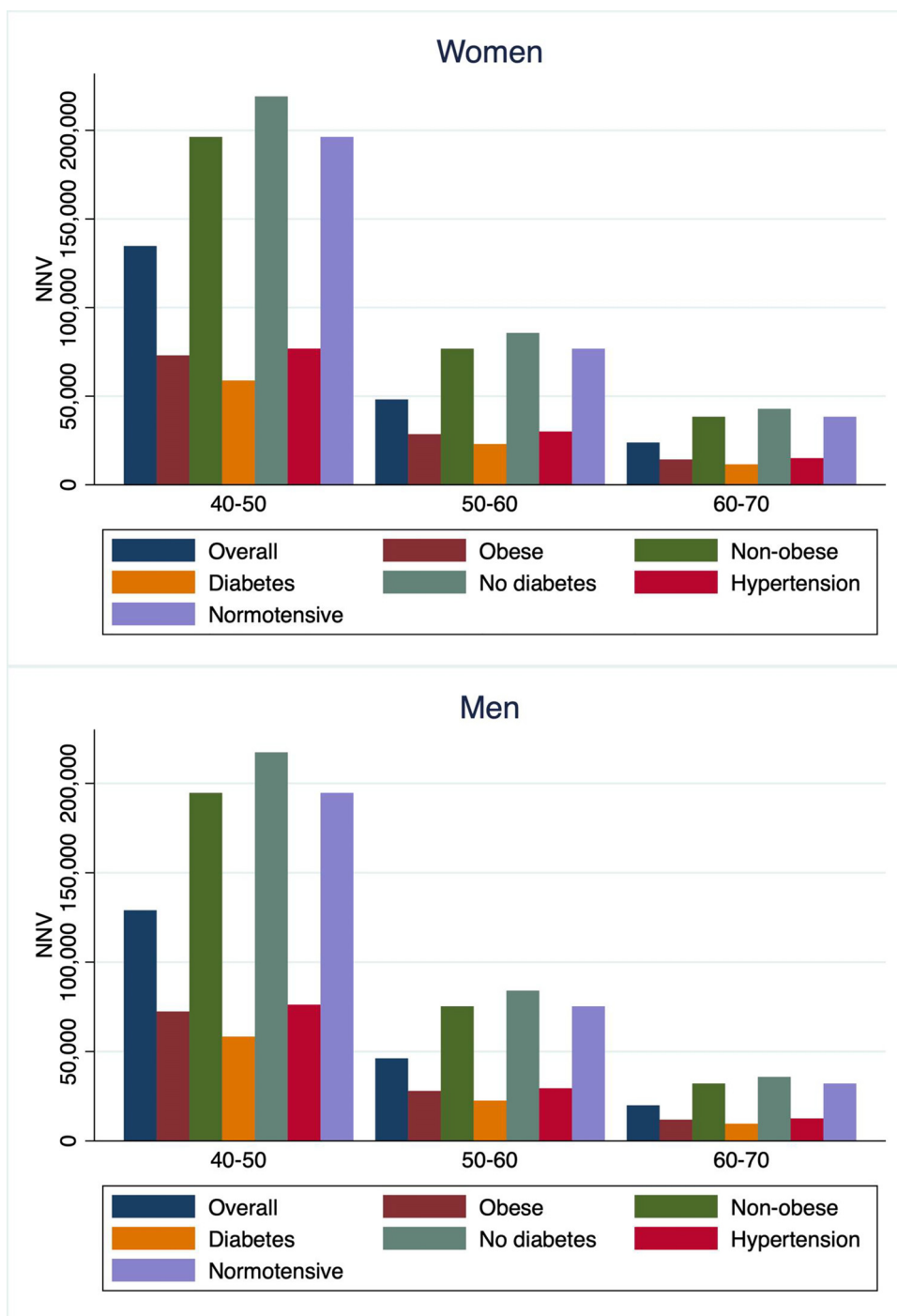
Figure 2. The estimated number needed to vaccinate (NNV) to prevent 1 COVID-19 death stratified according to sex, age in years, and cardiovascular risk factor presence.

Canada, the incidence rate of COVID-19 per 100,000 people from January 31 to February 6, 2021, was 85.2 among men aged 40-50 years; 72.7 among men aged 50-60 years; 53.1 among men aged 60-70 years; and 40.3 among men aged 70-80 years. Respective rates among women were 84.5, 71.3, 44.4, and 39.2. In the PURE study, rates of obesity, diabetes, and hypertension among Canadian participants (older than 35 years of age) were respectively 26%, 9%, and 38%. Rates of these risk factors stratified according to age and sex are

presented in Supplemental Table S1. The pooled effect of COVID-19 vaccination on the risk of acquiring COVID-19 (Fig. 1) was a relative risk of 0.10 (95% CI, 0.03-0.34). Among those who are infected with COVID-19, the case fatality ratio (ie, the proportion of identified cases that succumb to the infection adjusted for censoring bias) according to Public Health Ontario data is 0.67% for those aged 40-50 years; 2.03% for those aged 50-60 years; 6.52% for those aged 60-70 years; and 20.89% for those aged 70-80 years.
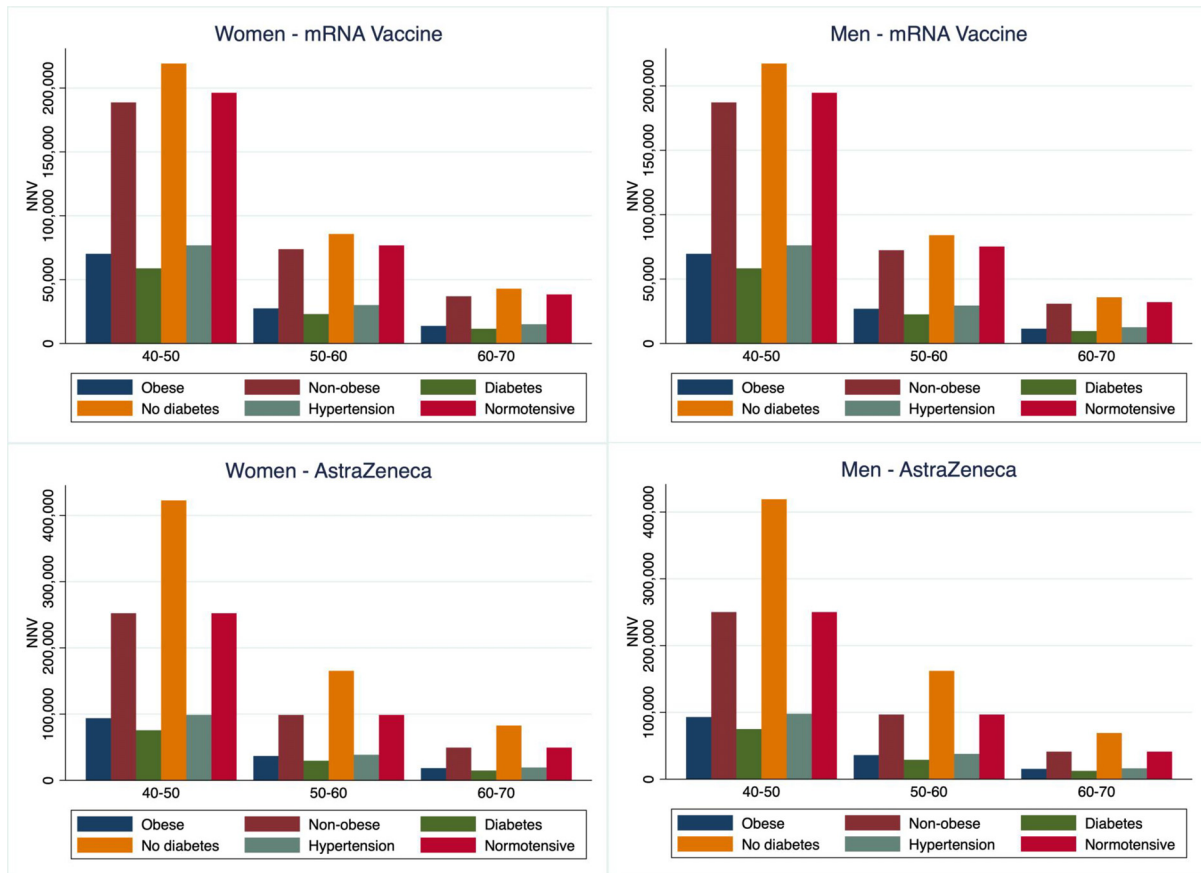
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Figure 3. The estimated number needed to vaccinate (NNV) to prevent 1 COVID-19 death stratified according to vaccine type, sex, age in years, and cardiovascular risk factor presence.

Using these data, we estimated the numbers of individuals (1) in each age, sex, and body mass index stratum; (2) among those with and without diabetes; and (3) among those with and without hypertension who would develop and die from COVID-19 in the absence of vaccination vs the numbers expected to develop and die from COVID-19 after vaccination. On the basis of these data, the estimated NNV to prevent 1 COVID-19 death in Canadian adults overall is 33,595 and in men aged 70-80 years is 8722, and in women aged 70-80 years is 9060. The estimated NNV to prevent 1 COVID-19 death in different subgroups of the adult population are presented in Figure 2. We undertook separate analyses of the AstraZeneca vaccine (relative risk, 0.30; 95% CI, 0.20-0.45) and the 2 mRNA vaccines (pooled relative risk, 0.064; 95% CI, 0.043-0.094). Whereas the NNV differed according to vaccine type, the proportionate reduction in NNV among those with obesity, diabetes, or hypertension was similar between vaccine types (Fig. 3).

Discussion

The major finding from this analysis of Canadian data on middle-aged and older adults is that the NNV to prevent COVID-19 death among those with cardiovascular risk factors (obesity, diabetes, or hypertension) is approximately half the NNV among adults without these cardiovascular risk factors. Consequently, the NNV of obese, diabetic, and

hypertensive adults in any age group is similar to the NNV of nonobese, nondiabetic, and normotensive adults 10 years older.

In most regions within Canada, COVID-19 vaccination is offered to the elderly population first (along with long-term care residents and frontline health care workers), followed by members of the public in cohorts of successively decreasing age. Our analysis supports this approach by showing that vaccinating elderly individuals first is a highly efficient way of preventing COVID-19 deaths. After elderly individuals have been vaccinated, there remains uncertainty as to how to prioritize vaccination of the remaining population. It has been recognized that cardiovascular risk factors including obesity, diabetes, and hypertension are risk factors for the acquisition of COVID-19 infection as well as for a fatal outcome in the event of COVID-19 infection. Our analysis, which has been conducted using contemporary data to inform the prevalence of these cardiovascular risk factors in the Canadian population, suggests that preferentially vaccinating individuals with 1 or more cardiovascular risk factors might be an efficient way to prevent COVID-19 mortality.

This analysis has several limitations. We assumed that COVID-19 vaccines are equally effective among individuals with cardiovascular risk factors as among those without cardiovascular risk factors. Although there was no evidence from the randomized, controlled trials of COVID-19 vaccinations to indicate that the efficacy of these vaccines varies according

to the recipient's age, sex, or cardiovascular risk factors, data that have yet to be peer-reviewed suggest that among 248 health care workers who received the BNT 162b2 vaccine, the humoral immune response was larger among those with a "normal" body mass index compared with a higher body mass index.[14] Also, although we showed a reduction in the NNV to reduce mortality if those with cardiovascular risk factors are vaccinated earlier, we did not estimate the number of quality-adjusted life-years gained by such a strategy. If individuals without cardiovascular risk factors gain more quality-adjusted life-years through COVID-19 vaccination, this might attenuate the apparent advantages of preferentially vaccinating those with cardiovascular risk factors earlier. We have not evaluated the potential effect of preferentially vaccinating adults with chronic diseases other than obesity, diabetes, and hypertension because there were limited numbers of these diseases in the PURE data. Public Health England guidance includes diseases such as dementia, kidney disease, and recent cancer as conditions warranting earlier vaccination, in part on the basis of data from the United Kingdom National Health Service showing individuals with these diseases to be at higher risk of COVID-19 death.[15,16] Last, our analysis is on the basis of the Canadian adult population distribution and characteristics. These findings might not be generalizable to populations with substantially different distributions of cardiovascular risk factors, although the general principles are likely to hold.

Despite these limitations, this analysis represents an important estimation of the effects of prioritized vaccination strategies. In the context of a novel disease that is causing enormous morbidity and mortality, such models, using the best available data (even if limited) are important to guide public health decision-making.[17] Importantly, this analysis does not address the role of vaccines in preventing community spread of COVID-19. We are unable to make inference on the plausible population benefits of prioritizing the vaccination of people, such as younger adults who are at high risk of acquiring and therefore transmitting the infection.

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Disclosures

The authors have no conflicts of interest to disclose.

References

1. Baden LR, El Sahly HM, Essink B, et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. N Engl J Med 2021;384:403–16.

2. Polack FP, Thomas SJ, Kitchin N, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. N Engl J Med 2020;383:2603–15.

3. Voysey M, Clemens SAC, Madhi SA, et al. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. Lancet 2021;397:99–111.

4. CDC. Centers for Disease Control and Prevention. How CDC Is Making COVID-19 Vaccine Recommendations. Available at: https://www. cdc.gov/coronavirus/2019-ncov/vaccines/recommendations.html. Accessed April 7, 2021.

5. Gov.UK. COVID-19: The Green Book, Chapter 14a. Available at: https://www.gov.uk/government/publications/covid-19-the-green-book-chapter-14a. Accessed April 7, 2021.

6. Ho FK, Celis-Morales CA, Gray SR, et al. Modifiable and non-modifiable risk factors for COVID-19, and comparison to risk factors for influenza and pneumonia: results from a UK Biobank prospective cohort study. BMJ Open 2020;10: e040402.

7. Ng WH, Tipih T, Makoah NA, et al. Comorbidities in SARS-CoV-2 patients: a systematic review and meta-analysis. mBio 2021;12. e03647-20.

8. Bae S, Kim SR, Kim MN, Shim WJ, Park SM. Impact of cardiovascular disease and risk factors on fatal outcomes in patients with COVID-19 according to age: a systematic review and meta-analysis. Heart 2021;107:373–80.

9. United Nations. Department of Economic and Social Affairs. Population Dynamics. Download Files. Available at: https://population.un.org/wpp/Download/Standard/Population/. Accessed April 7, 2021.

10. Government of Canada. COVID-19 Epidemiological and Economic Research Data. Available at: https://www.canada.ca/en/public-health/services/diseases/coronavirus-disease-covid-19/epidemiological-economic-research-data.html. Accessed April 7, 2021.

11. Yusuf S, Joseph P, Rangarajan S, et al. Modifiable risk factors, cardiovascular disease, and mortality in 155 722 individuals from 21 high-income, middle-income, and low-income countries (PURE): a prospective cohort study. Lancet 2020;395:795–808.

12. Public Health Ontario. COVID-19 Case Fatality, Case Identification, and Attack Rates in Ontario. Available at: https://www.publichealthontario.ca/-/media/documents/ncov/epi/2020/06/covid19-epi-case-identification-age-only-template.pdf?la=en. Accessed April 7, 2021.

13. Huang Y, Lu Y, Huang YM, et al. Obesity in patients with COVID-19: a systematic review and meta-analysis. Metabolism 2020;113: 154378.

14. Pellini R, Venuti A, Pimpinelli F, et al. Obesity may hamper SARS-CoV-2 vaccine immunogenicity [e-pub ahead of print]. medRxiv https://doi.org/10.1101/2021.02.24.21251664. Accessed April 7, 2021.

15. Williamson EJ, Walker AJ, Bhaskaran K, et al. Factors associated with COVID-19-related death using OpenSAFELY. Nature 2020;584:430–6.

16. Clift AK, Coupland CAC, Keogh RH, et al. Living risk prediction algorithm (QCOVID) for risk of hospital admission and mortality from coronavirus 19 in adults: national derivation and validation cohort study. BMJ 2020;371:m3731.

17. Tam DY, Naimark D, Natarajan MK, et al. The use of decision modelling to inform timely policy decisions on cardiac resource capacity during the COVID-19 pandemic. Can J Cardiol 2020; 36:1308–12.

Supplementary Material

To access the supplementary material accompanying this article, visit the online version of the *Canadian Journal of Cardiology* at www.onlinecjc.ca and at https://doi.org/10.1016/j.cjca.2021.04.012.