Mathematical Models on COVID-19

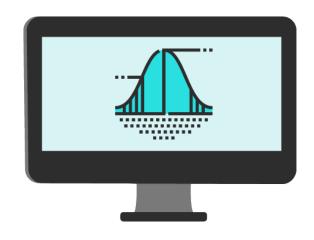
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Counterfactuals of effects of vaccination and public health measures on COVID-19 cases in Canada: What could have happened?

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In March 2020, Canada was faced with a highly transmissible and virulent pathogen (SARS-CoV-2) for which there was no natural immunity, no vaccine, and no effective antivirals. Therefore, in March 2020 and until vaccines were developed, the only available interventions were non-pharmaceutical interventions.

This study illustrates what could have happened, in terms of infections, hospitalizations and deaths related to coronavirus disease 2019 (COVID-19) in Canada, if public health (PH) measures had not been used



to control the COVID-19 epidemic and if restrictions had been lifted with low levels of vaccination, or no vaccination, of the Canadian population. The timeline of the outbreak in Canada and the PH interventions used to control the outbreak are reviewed.

In the absence of vaccines, two possible control strategies were considered: 1) eradication and prevention of importation, often referred to as the Zero-COVID strategy largely carried out by Atlantic provinces and territories for most of the pandemic; or 2) suppression of transmission so that health care capacity is not overwhelmed (the strategy applied in large provinces for most of the pandemic).

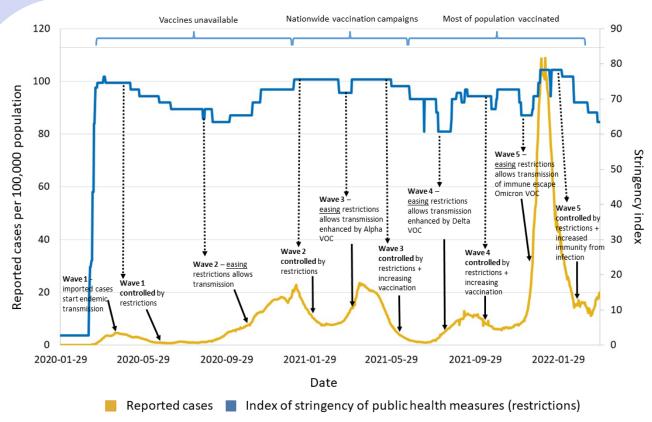


Figure 1. Chronology of the coronavirus disease 2019 epidemic, and public health responses, in Canada up to April 1, 2022^a.

a The timeline is curtailed due to reductions in national surveillance.

In larger provinces, the cycle of lifting of PH restrictions, followed by resurgence, followed by reintroduction of restrictions has been a feature of control **(Figure 1)**, during which the necessity for mandatory restrictions has been debated. Although Canada did not adopt a Zero-COVID approach as a whole, mandatory restrictions have contributed to a lower death rate during the pandemic compared to other high-income countries.

Few therapeutics had been developed to treat or prevent COVID-19, but the turning point was the arrival of mRNA vaccines that have been highly effective against both infection and severe outcomes for Wild type, Alpha and Delta variant. The emergence of the Omicron variant changed the landscape of the role of vaccines, but they continue to protect against severe outcomes from infections with all variants.

The Public Health Agency of Canada (PHAC) used a <u>previously developed agent-based model</u> to compare the outcomes of different PH and vaccination strategies (counterfactual scenarios). <u>This study</u> examines the additional COVID-19 infections, hospitalizations, and deaths which may have occurred if PH measures and vaccination had not been implemented to control the spread of COVID-19 epidemic in Canada.

Methods

The agent-based model was developed to simulate the pandemic in Canada up to the time of writing (April 2022), and to project the clinical incident cases and hospital prevalence up to March 2022. The model of a representative 100,000 individuals of the Canadian population incorporated the PH measures used, vaccination rollout (first, second and third doses by age groups and priority groups), and emergence of the Alpha, Delta, and Omicron BA.1 variants. The model also accounted for vaccine effectiveness and severe outcomes specific to each variant, protection against reinfections of the same or a different variant, and waning immunity following vaccination and natural infection.

The eight simulated scenarios (including the baseline, Scenario 1) were as follows:

Scenario 1: Baseline Scenario; implementation and lifting of PH measures and vaccinations as observed (Figure 1).

Scenario 2: Worst case scenario; no PH measures or vaccinations were implemented.

Scenario 3: Implementation and lifting of PH measures but there were no vaccinations.

Scenario 4: No PH measures but vaccines were administered as observed.

Scenario 5: PH measures lifted July 1, 2020 (after the 2nd wave) and vaccines administered as observed.

Scenario 6: PH measures lifted March 1, 2021 (after the 3rd wave) and vaccines administered as observed.

Scenario 7: PH measures lifted July 1, 2021 (after the 4th wave) and vaccines administered as observed.

Scenario 8: PH measures lifted November 1, 2021 (after the 5th wave) and vaccines administered as observed.

Results

The simulations showed that the combination of PH measures and vaccination that were implemented in Canada (Scenario 1) resulted in fewer clinical and asymptomatic infections, hospitalizations, intensive care unit (ICU) admissions, and deaths compared to the seven counterfactual scenarios (Table 3). Only the baseline scenario modelling the actual vaccination and PH measures which were implemented in Canada resulted in hospitalizations consistently below hospital bed threshold.

Compared to the baseline scenario, the following differences were observed in the clinical incident cases per 100,000 in the simulated counterfactual scenarios:

Scenario 2: Increased initial wave (wild-type) and subsequent Delta wave

Scenario 3: Increased Delta wave

Scenario 4: Increased initial and Omicron waves, but the Delta wave was prevented

Scenario 5: Increased initial wave and increased Omicron wave

Scenario 6: Increased Alpha and Omicron waves

Scenario 7: Increased Delta and Omicron waves

Scenario 8: Increased Omicron wave

Table 3. Key metrics (median and 95 percentiles for 100 model runs) of casesa, hospitalizations and deaths estimated by the agent-based model simulations for the observed baseline and seven counterfactual scenarios for the period February 7, 2020 to March 31, 2022.

	Counterfactual scenarios							
Transmission control methods in the scenarios and outputs of modelling	S1 Observed Baseline	S2 No PH measures or vaccination	No vaccination (PH measures maintained)	S4 No PH measures (vaccination maintained)	S5 No PH measures after July 1, 2020 (vaccination maintained)	S6 No PH measures after March 1, 2021 (vaccination maintained)	S7 No PH measures after July 1, 2021 (vaccination maintained)	S8 No PH measures after November 1, 2021 (vaccination maintained)
Vaccination rollout	Yes	No	No	Yes	Yes	Yes	Yes	Yes
Lifting of PH measures	April 1, 2022	No PH measures	April 1, 2022	No PH measures	July 1, 2020	March 1, 2021	July 1, 2021	November 1, 2021
Clinical cases per 100,000*	12001 (10028- 15306)	90154 (89299-91277)	38858 (29438- 43633)	59574 (58509-61940)	44746 (43783-45556)	47472 (39046-52298)	25368 (22115-27848)	17983 (16139-20842)
Asymptomatic cases per 100,000*	47638 (44775- 51455)	113752 (110854-117951)	58754 (52099- 60876)	108293 (107001- 111504)	90302 (89493-91334)	92660 (74662-103826)	84869 (81558-87347)	81098 (79752-83044)
Hospitalisations per 100,000	256 (182-387)	4715 (4572-4918)	2529 (1541-3225)	2246 (2136-2348)	1619 (1541-1722)	1469 (871-2150)	601 (500-710)	324 (240-438)
ICU admissions per 100,000	74 (48-111)	1428 (1360-1489)	779 (455-988)	681 (626-724)	498 (452-557)	446 (249-681)	174 (140-212)	93 (66-134)
Deaths per 100,000	48 (32-76)	2034 (1938-2115)	947 (563-1301)	849 (803-899)	583 (538-634)	350 (182-603)	131 (101-163)	70 (47-92)

^{*} Cases include reinfections and vaccine breakthrough cases, which occurred particularly during the Omicron-driven waves. Cases are higher than the model population (100,000) in some scenarios due to reinfections in the population.

Discussion, limitations, and conclusion

The relative effectiveness of the response to COVID-19 in Canada is illustrated by the substantially lower death rate in Canada compared to other similar countries. Canada's relative success in managing COVID-19 is also supported by the counterfactual scenarios modelled in this study. The results of the simulated counterfactual scenarios suggest that it was the combination of non-pharmaceutical PH measures and vaccination which limited morbidity and mortality in the Canadian population.

It is important to note that the modelled population represents an "average Canadian community" and does not account for regional variations in demography, contact rates, and sensitivity to infection. Additionally, the model is conservative in predicting cases but underestimated the number of deaths in the baseline scenario. The model did not consider outbreaks with high transmission and case fatality rates in healthcare and long-term care settings; therefore, infections, hospitalizations and deaths were underestimated in the counterfactual scenarios.

Although the response to COVID-19 in Canada was not perfect, these results show that not having restrictions in place early in the pandemic, lifting these public health measures early and the absence of an effective vaccine may have led to catastrophic outcomes in terms of deaths and the burden on the healthcare system. Further regional analysis for Canada which includes an examination of the broader public health impacts of COVID-19 (particularly long COVID) will be key to learn more from this pandemic moving forward.



