Could it have *Really* Happened?
A Rejoinder to Ogden *et al.*'s "Counterfactuals" of Effects of Vaccination and Public Health Measures on COVID-19 Cases in Canada: What could have Happened?"

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Abstract

The Public Health Agency of Canada recently reviewed the public health measures it implemented to control the COVID-19 epidemic by modelling the COVID-19 infections, hospitalizations, and deaths that could have occurred had these measures, including high levels of vaccination, not been adopted. Its modelling predicts substantially higher numbers of SARS-CoV-2 cases, up to 13-times as many hospitalizations, and over 20-times more deaths from COVID-19, than actually transpired. In this commentary, we assess the justification behind the authors' proposed model and argue that few – if any – policy lessons can be drawn from their analysis.

Introduction

The article, "Counterfactuals of effects of vaccination and public health measures on COVID-19 cases in Canada: What could have happened?" by Ogden *et al.* [1] relies on simulation modelling to suggest how the COVID-19 pandemic would have affected Canada had certain public health measures not been implemented. While simulation models can be useful as "policy simulators" in artificial realities, the insights derived from them are only as valuable as the soundness of the assumptions the authors feed into them. In this commentary, we evaluate the authors' assumptions and conclude that they are problematic at-best. We first identify empirically inaccurate and conceptually ambiguous justifications supporting the article; second, we critique the model used to substantiate the article's conclusions; and finally, we elaborate on the implications of the authors' position for effective public health policy and human wellbeing in times of crisis.

The Justifications

In their abstract, the authors state that, "This study illustrates what may have happened…", and what "Canada could have experienced…" The article's title includes the clause, "What could have happened?" Put another way, the authors lay out a range of possibilities – counterfactuals – that *could* be true. But *are* they? We examine these premises below.

In their introduction, the authors assert that at the start of the COVID-19 pandemic, humans had no known immunity to SARS-CoV-2 [1]. However, if humans were truly immunologically naïve to SARS-CoV-2, then there would be no explanation for the existence of cross-reactive neutralizing antibody or memory T-cells between endemic coronaviruses and SARS-CoV-2 [2,3]. At the very least, exposure to other human coronaviruses throughout some people's lifetime appears to confer measurable levels of pre-existing immunity. Similar immune responses to the 1918 strain of influenza exist [4], and SARS-CoV-2 is unlikely to be the exception.

The authors also state that, unless the public health measures had been adopted, the consequences for Canadians and for Canada's public health system would have been "dire" [1]. They claim that, because of no effective therapies, Canada would have experienced an infection fatality rate (IFR) "approaching" 1% – contrasting it with a much lower IFR of 0.4% for the seasonal flu. While the only reference to support their claim of "dire" cites other models with no predictive value (*i.e.*, "modelling studies are not predictions…" see the Conclusion in ref. 5), empirical evidence indicates that the IFR for COVID-19 is much lower than 1%. For instance, Ioannidis [6] determined that the IFR on a global basis was 0.15-0.20% and 0.03 to 0.04% for those under 70 years of age. Similarly, the COVID-19 *Forecasting Team* showed that for most of the world population, including anyone under 50 years of age, the IFR (unadjusted for co-morbidities, and other covariates) was 0.43% (0.29–0.68) [7]. As for the alleged lack of effective therapies, early in 2020 the international literature indicated that early outpatient treatment with multidrug therapy successfully reduced hospitalization and death, even among populations considered at high risk due to exposure (*e.g.*, health workers) or physiological vulnerability (*e.g.*, elderly people) [8-12].

The article's "Chronology of the Epidemic" justifies the adoption of public health measures because of the "unrestrained SARS-CoV-2 transmission in Italy." This implies the rampant spread of the infection throughout the entire population. However, Professor Walter Ricciardi, Italy's scientific advisor, corrected this assumption when he noted that "The median age of people infected with SARS-CoV-2 who [were] dying in Italy has been 80 years, and the average age of patients requiring critical care support [was] 67 years" [13]. Ricciardi's point on risk-stratification provides an entirely different perspective on the epidemic's characteristics, and if true, nullifies a key justification for the author's model – a virus that if "unrestrained" would be an "equal opportunity" killer. As well, as shown in Table 2, Ogden *et al.* assume that the listed countries have agreed on what constitutes a COVID-19 "death." However, they overlook that until recently, a COVID-19 death was anyone dying *with*, not necessarily *from* COVID-19 (this was corrected in Ontario March 11, 2022) [14]. They also overlook the substantial differences worldwide in definitions of COVID-19 deaths (*e.g.*, China likely counts them very differently than Canada). Given these differences, the table adds little value to the authors' analysis.

In sum, the value of the article is diminished by untested, outdated, or false assumptions to justify public health policies – such as social distancing, closures, and mask and vaccine mandates – that have resulted in significant harms to the vulnerable populations that these policies purport to protect [15,16]. However, a greater problem occurs when these justifications are merged with the modelling techniques employed by the authors.

The Model

Ogden *et al.* have created an agent-based simulation model (ABM) for understanding the benefits of Canada's pandemic response. ABMs are computational models for simulating the actions and interactions of autonomous agents (such as people) to understand the behavior of a system and the processes that govern any outcomes of interest [17]. Because ABMs maintain distinct information on every individual in a simulated population, their finer-grained nature allows them to represent certain types of activities, relationships, and interventions with greater precision and flexibility than with more traditional differential equation models used in the study of pathogen transmission [17,18]. However, the granularity of ABMs carries with it an increased cognitive burden to understand the link between a model's structure and its behaviour [18]. Ogden *et al.*, have circumvented that necessity by filling-in details of people's movements that are exogenous to the structure of the model, rather than being driven by factors or feedbacks that are internal to the current state of the model. This expanded effort in deepening their model has inhibited a critical broadening of the model boundary that will limit its validity [18].

For example, the behaviour of the model's agents has an all-or-none relationship with public health measures: when in-place, people change their behaviour in a pre-set manner that is proportional to the value Oxford Stringency Index; when not in-place, agents maintain their status quo. This forced dependence on government orders is contrary to other research demonstrating that people's inherent fear of infection, alone, will cause them to alter their behaviour rapidly [19], and often before strict rules are in-place [20].

One consequence of guessing at what drives people's behaviour is that two metrics of the calibrated model have diverged substantially from nationally recorded data. Cumulative case and death rates reported by April 2022 were approximately 9,000 cases and 98 deaths per 100,000 population, respectively. When compared to the estimated values in their "S1" scenario in Table 3, both empirical values lie outside the 95th percentiles of their modelled counterparts. This directional bias is indicative of structural errors that have likely translated into exaggerated comparisons between the calibrated model and its counterfactual scenarios.

Thus, when Ogden *et al*. discuss Canada's experience with SARS-CoV-2 without restrictive measures or high levels of vaccination, they failed to note two problems. First, "up to 800,000" COVID-19 deaths are greater than any other historic event in Canada over the last 108 years. When mortality estimates [21] are adjusted to the 2020 population, the number of Canadians that died in WWI, WWII, and from the Spanish Flu pandemic – *combined* – is still lower than 800,000 (at approximately 655,500). Second, the addition of 800,000 deaths would have large implications for all-cause mortality, more than doubling it from approximately 640,000 deaths to 1.4 million. However, it is an amazing coincidence that all the pandemic responses, which were

applied at different times, have produced such a large effect that all-cause mortality has been reduced to nearly what can be predicted historically [22] — before March 2020 — when there was no pandemic and no measures, whatsoever. The counterfactual scenarios in Table 3 require that we subscribe to an imagined story [23] of Canada's pandemic that is pre-determined by the structure of Ogden *et al*.'s model.

Conclusion

The article's justifications and conclusions, which are derived from a single model with questionable assumptions, leads us to wonder: "what was its point"? Was it to showcase an evidence-based analysis of actual policies and their alternatives? Or was it an attempt to justify government policies, despite other evidence of their limited benefit [24]? We leave these questions for readers to ponder.

That said, the article does have two redeeming features. The authors admit that Canada's response to the pandemic was not perfect, and that the unintended consequences of the adopted public health measures need to be investigated. It will be a measure of the honesty, courage, and integrity of the Public Health Agency of Canada, if the latter is ever realized.

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