CANADIAN MEDICAL ASSOCIATION JOURNAL

Research

Impact of population mixing between vaccinated and unvaccinated subpopulations on infectious disease dynamics: implications for SARS-CoV-2 transmission

David N. Fisman, Afia Amoako and Ashleigh R. Tuite

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Posted on: (29 April 2022)

Fisman et al.'s main conclusion does not follow from their model

Denis G. Rancourt [BSc, MSc, PhD (Physics)], Researcher, Ontario Civil Liberties Association (ocla.ca)
Other Contributors:
Joseph Hickey, Executive Director

Fisman et al. [1]'s main conclusion – that risk of infection among vaccinated people can be disproportionately attributed to unvaccinated people – does not follow from the model presented [2].

Their ad hoc parameter Ψ – defined as "the fraction of all infections among vaccinated people that derived from contact with unvaccinated people, divided by the fraction of all contacts [involving vaccinated people] that

occurred with unvaccinated people" – is incorrectly asserted to represent "a normalized index of the degree to which risk in one group may be disproportionately driven by contact with another."

The assertion is incorrect because the model as presented is blind as to whether the "contacts" in the normalizing denominator of Ψ are infectious or benign, irrespective of vaccination status.

In the model, most "contacts" are benign (not involving an infectious person and a susceptible person), whether vaccinated or unvaccinated. This means that the normalizing denominator of Ψ cannot be assumed to represent "contacts driving infection", as advanced by Fisman et al.

It is easy to see that the ad hoc parameter Ψ is nonsensical, from figures in their paper:
a. Fig. 2A shows Ψ dropping dramatically with increasing reproduction number. This would mean that unvaccinated people threaten vaccinated people proportionately less when the presumed pathogen is more infectious. The state should not worry about unvaccinated people if the pandemic is sufficiently virulent?
b. Fig. 2B shows Ψ approaching large values as the mixing coefficient η approaches 1. This would mean that unvaccinated people are proportionately more of a threat to vaccinated people as the two groups are more and more isolated from each other, up to complete isolation. This is an absurd result.

The obvious parameter that Fisman et al. could have reported is the numerator of Ψ, which is "the fraction of all infections among vaccinated people that derived from contact with unvaccinated people".

We plot this "numerator of Ψ", for parameters used by Fisman et al., versus the mixing coefficient η, and for different population fractions of unvaccinated people, here: https://ocla.ca/wp-content/uploads/2022/04/plot-numer-Psi-v-eta-R0-6-1.jpg

We see that there is no indication of disproportionate infections caused by unvaccinated people, and that the "the fraction of all infections among vaccinated people that derived from contact with unvaccinated people" is bound by the relative populations of vaccinated and unvaccinated susceptible individuals for random mixing, and goes more and more quickly to a value of zero as isolation between the two groups increases, as it must.

These are trivial results. The only way to get the simple model to say what Fisman et al. have said is to concoct and misinterpret an ad hoc parameter (Ψ).

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Competing Interests: None declared.

References

- [1] David N. Fisman, Afia Amoako, Ashleigh R. Tuite. Impact of population mixing between vaccinated and unvaccinated subpopulations on infectious disease dynamics: implications for SARS-CoV-2 transmission. CMAJ 2022;194:E573-E580.
- [2] Denis G. Rancourt, Joseph Hickey. OCLA Statement on CMAJ Fisman et al. Article Claiming Disproportionate Infection Risk from Unvaccinated Population, and on Negligent Media Reporting. Ontario Civil Liberties Association, 27 April 2022: https://ocla.ca

Posted on: (29 April 2022)

RE: Fundamental Error in Key Input Invalidates Model

Richard Schabas [MD MHSc FRCPC], public health physician (retired), No Current Institutional Affliation

I offer the following comments regarding the recent model published in the Canadian Medical Association Journal.1 There are several important shortcomings and concerns with this paper.

First, this is a model. It does not measure, observe or test anything. It is a prediction based on a self-described "simple" model. The predictions of this model have not been tested so, at most, this model should be regarded as an hypothesis. Like any hypothesis it needs to be tested and validated before its predictions should be considered evidence.

Second, the output of any model is totally dependent on the quality and accuracy of its inputs. This key input for this model is the vaccine effectiveness (VE) in preventing infection. The model assumes that this VE is 40-80%.

The authors cite two references to support the lower bound (40%) estimate. The first is a surveillance report from the United Kingdom at a time (December 2021) when Omicron Variant was just emerging.2 The data in this report are based on Delta Variant but the report makes it clear that lower VE with Omicron is anticipated. The second reference is simply another unvalidated model.3

The authors cite only a single reference to support an upper bound (80%) estimate of VE.4

The authors' use of this single reference is highly problematic for three reasons. First, the reference only covers data up until October 20, 2021 - six months ago! It does not take into account the impact of new Variants (Omicron and B.2) or continuing waning immunity. Second, the reference study does not support a VE estimate of 80%. The reference study measured VE for three vaccines between July 1, 2021 and October 20, 2021 at 49%, 52% and 70%. Third, the authors have failed to acknowledge abundant new evidence5,6, including some from Ontario,7,8, showing little or no persistent (and perhaps even negative) VE against infection.

In summary, this paper describes an untested hypothesis based on flawed assumptions, invalidating its conclusions.

Richard Schabas MD MHSc FRCPC

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Competing Interests: None declared.

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- David N. Fisman, Afia Amoako, Ashleigh R. Tuite. Impact of population mixing between vaccinated and unvaccinated subpopulations on infectious disease dynamics: implications for SARS-CoV-2 transmission. CMAJ 2022;194:E573-E580.

Posted on: (28 April 2022)

RE: Impact of population mixing between vaccinated and unvaccinated subpopulations on infectious disease dynamics: implications for SARS-CoV-2 transmission

James C Doidge [PhD], Medical statistician, Intensive Care National Audit and Research Centre; and London School of Hygiene and Tropical Medicine
Other Contributors:
Alex de Figueiredo, Statistician
Trudo Lemmens, Professor and Scholl Chair in Health Law and Policy
Kevin Bardosh, Applied medical anthropologist

Fisman and colleagues[1] present a oversimplification of a complex epidemiological, social, and bioethical issue. The findings are predetermined by the authors' own model design choices; something that should never occur in science. That the authors make strong ethical and political claims that feed existing social polarization makes the flawed design even more problematic.

The authors use a compartmental SIR model to compute the infection burden in vaccinated and unvaccinated population subgroups and assess contribution of the unvaccinated group to the cumulative rate of infection among the vaccinated. The study's main conclusion—that mixing with unvaccinated people increases the risk of infection among the vaccinated—is predetermined by the authors choice of model and parameters. By ignoring waning immunity (from both vaccination and prior infection), the authors have constructed a model in which herd immunity always occurs, leaving some residual proportion of the population uninfected indefinitely. In this hypothetical scenario, it is a foregone conclusion that if one group with high baseline immunity is mixed with another group of lower baseline immunity then a greater proportion of the high-immunity group will become infected before herd immunity is achieved, than if they had not mixed. This is nothing more than dilution. The model[2] contains two crucial parameters: 'vaccine efficacy' and 'baseline immunity in unvaccinated'. If these are set to any combination where the latter is higher, then the findings are reversed; the vaccinated increase risk for the unvaccinated. Obviously, both conclusions are similarly flawed. In the context of observed waning of vaccine efficacy against infection[3], even the authors acknowledge that "it is unlikely that SARS-CoV-2 will be eliminated". Why then is their analysis based on an assumption that it will be?

It is especially problematic that a modelling paper so detached from reality contains such explicit and strong condemnation of 'the unvaccinated'. The authors discuss the theoretical risk that the unvaccinated pose vaccinated via their disproportionate demand for healthcare resources–something not considered in the model–without any acknowledgement of the vast difference in healthcare demands of, say, a healthy 18-year-old compared with a comorbid 80-year-old. The potential for this work to foster social division and misplaced anger and blame is at odds with public health ethics. The authors claim support for Canada's vaccine mandates without any acknowledgment that these policies helped to ignite nation-wide protest. The combination of deeply flawed modelling, moral condemnation and politicisation should be sufficient to retract a paper published in Canada's preeminent medical journal. Unfortunately, the damage has already been done, with many media outlets added fuel to the fire through uncritical reporting of this study. Trust in public health and science has been further eroded.

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Competing Interests: None declared.

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- David N. Fisman, Afia Amoako, Ashleigh R. Tuite. Impact of population mixing between vaccinated and unvaccinated subpopulations on infectious disease dynamics: implications for SARS-CoV-2 transmission. CMAJ 2022;194:E573-E580.
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Posted on: (27 April 2022)

RE: Impact of population mixing between vaccinated and unvaccinated subpopulations on infectious disease dynamics: implications for SARS-CoV-2 transmission

York N. Hsiang [MB ChB, MHSc., FRCSC], Vascular surgeon, University of British Columbia

Dear Sir,

The article by Fisman et al.1 has garnered much medical and societal attention. The authors used a mathematical model to simulate COVID-19 infection risk across various patterns of interactions amongst vaccinated and vaccine-free individuals. The authors conclude that individuals who avoid vaccination contribute to negative health consequences for others. Such an assertion is incorrect and biased for the following reasons:

1. Uses problematic mathematical modeling as a surrogate for real-world data. Mathematical modeling has been used throughout the COVID-19 response to justify lockdown measures while promoting unscientific public health edicts. As there is abundant real world data, why they would choose a mathematical model is unclear.

2. Overestimates vaccine effectiveness against symptomatic infection. The range of vaccine effectiveness against symptomatic infection was 40-80%. The upper bound limit of 80% may apply to the old Delta variant but the lower bound limit of 40% does not apply to the Omicron variant. Current data shows that vaccine effectiveness against Omicron symptomatic infection ranges from 0% to 75% independent of vaccine type, duration since primary series, or duration since booster(s).2

3. Overestimates the risk of transmission (secondary attack rate). The authors overstate the ability of vaccines to reduce the risk of transmission. Kampf has shown that the proportional rate of symptomatic Covid-19 among fully vaccinated patients >60 years old has been increasing since July 2021. In the week of Octo 27, 2021, it was 58.9%.3 If anything, COVID-19 vaccines do a poor job at reducing transmission of disease.

4. Underestimates the percentage of the unvaccinated population with natural immunity. The authors assume a baseline of previous infection of 20% in the unvaccinated population. Even before vaccinations were available, about 60% of Canadians had clear evidence of prior SARS-CoV-2 infection.4 The longevity of protection from natural immunity against symptomatic infection has been repeatedly proven superior to vaccination alone, meaning that the underestimation of those with natural immunity skews the model towards vaccination and away from current clinical evidence.

5. Does not account for waning vaccine immunity. The authors overestimate vaccine effectiveness and fail to account for the primary reason for the ongoing and relentless Omicron waves, namely waning vaccine immunity. Studies using real-world data demonstrate rapidly waning immunity in the fully vaccinated population.5

6. Conflict of interest. The lead author has multiple conflicts of interest and receives financial compensation from COVID-19 vaccine companies including Pfizer and AstraZeneca.

Promotion of poor research such as this leads to further stigmatization and division in society. We challenge the CMAJ to retract this study or issue a correction in their next publication.

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Competing Interests: None declared.

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- 1. Fisman DN, Amoako A, Tuite AR. Impact of population mixing between vaccinated and unvaccinated subpopulations on infectious disease dynamics: implications for SARS-CoV-2 transmission. CMAJ 2022;194:E573-E580.
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Posted on: (27 April 2022)

RE: Impact of population mixing between vaccinated and unvaccinated subpopulations on infectious disease dynamics: implications for SARS-CoV-2 transmission

Dena L. Schanzer [M.Sc., P.Stat.], Statistician, infectious diseases, Public Health Agency of Canada (retired)

Noting that once the Omicron variant started to dominate over Delta in late December 2021, infection rates started to increase faster among the vaccinated than the unvaccinated and the rate ratio (RR) of unvaccinated/vaccinated quickly dropped below 1.0, I'd suggest that the main finding of this study "We found that the risk of infection was markedly higher among unvaccinated people than among vaccinated people under all mixing assumptions" should be reviewed (See Ontario Public Health data available at https://c 19.ontario.ca/data/case-numbers-and-spread for rates by vaccination status and https://data.ontario.ca/en/dataset/covid-19-vaccine-data-in-ontario to download data).

At this time vaccine passports granted the vaccinated access to high-risk venues such as restaurants bars and gyms and the vaccine effectiveness (VE) of 2 doses was much lower for Omicron than Delta. My interpretation of the diverging trends in rates at the time was that the privileges provided by vaccine passports increased the rate of high-risk contacts among the vaccinated more than the protection against infection offered by the vaccine – that is, the vaccinated rather than the unvaccinated had become the main drivers of Omicron wave. The policy decision to shut down the high-risk venues after Christmas seemed to have worked in reducing hospitalizations (however, case counts declined rapidly as access to PCR testing in Ontario became severely limited).

While the RR is typically used to calculate VE, trends in the RR could be due to waning immunity, differences in exposure risk, or differences in access to testing between the two groups, or some combination of these

factors. Would monitoring the diverging trends in the rates and RR not be informative on which sub-group or sub-groups are likely driving the epidemic wave?

It would seem quite helpful to informing public health policy in a timely manor if the authors could explore informing their model based on near real time trends in rates or RRs. Perhaps monitoring trends in rates for divergence would be helpful to identify changes in drivers of pandemic growth!

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Competing Interests: None declared.

References

- David N. Fisman, Afia Amoako, Ashleigh R. Tuite. Impact of population mixing between vaccinated and unvaccinated subpopulations on infectious disease dynamics: implications for SARS-CoV-2 transmission. CMAJ 2022;194:E573-E580.

Posted on: (27 April 2022)

All models are wrong. Some are useful.

Stephenson B Strobel [MD MA Msc], PhD Candidate; Emergency Physician, Brooks School of Public Policy, Cornell University; Niagara Health

Some are not though. A good model approximates the real world, and its assumptions reflect reality. The recent modeling by Fisman et al. published in the CMAJ is an example of a model presented in such a way that does not well represent the real world. Moreover, the interpretation of the model does not necessarily lead to the policy conclusions the authors present.

Of note, the authors make a major unrealistic assumption which is non-waning immunity among the cohort of individuals who are vaccinated. This means that these persons cannot transmit COVID19 to each other or to unvaccinated individuals. Where immunity wanes as it seems it does in the real world [2], or where there is not sterilizing immunity, the disproportionate impact that is reflected in the authors' models does not necessarily hold. This very seriously calls the authors' conclusion that the choices of the unvaccinated affect everyone “in a manner that is disproportionate to the portion of unvaccinated people in the population.” While not a perfect reflection of waning immunity, one suggestive result from the authors that reflects this is the sensitivity analysis that changes the effectiveness of the vaccine (fig 2 panel 4). Where the vaccine effectiveness d to 40% the outcome is a much lower contribution of the unvaccinated to infection risk than their headline results suggest.

This issue aside, the authors then proceed to outline policy recommendations that do not necessarily follow from their results. In the parlance of economics what the authors have outlined is an externality. The unvaccinated impose costs on the vaccinated. The goal of any good policy is to “internalize” these externalities in whatever way is effective; if possible given medicines primary dictum of “first do no harm” this should be done in a non-coercive manner unless there are exigent circumstances. However, the authors leap directly to the idea that non-vaccinated individuals should be banned from public spaces and regulation should be enacted that may violate individual freedoms. Instead, of these coercive policy recommendations, the economics literature provides guidance on how to internalize these negative externalities via taxes and subsidies. In many cases the welfare implications of these policies are often superior to the complete bans

and mandates that the authors seem to suggest [3]. These policies are much less coercive than this papers recommendations.

I am sympathetic to the idea that COVID19 is a disease that imposes externalities; vaccinated patients should not have to suffer because of the choices of unvaccinated persons. Moreover, vaccination continues to provide the best way to prevent bad outcomes from COVID19 and policy should attempt to ensure that the greatest number of people possible are vaccinated against it. However the model that the authors propose does not approximate the real world well and does not support the coercive measures that are suggested in this paper.

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Competing Interests: None declared.

References

- David N. Fisman, Afia Amoako, Ashleigh R. Tuite. Impact of population mixing between vaccinated and unvaccinated subpopulations on infectious disease dynamics: implications for SARS-CoV-2 transmission. CMAJ 2022;194:E573-E580.
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Posted on: (27 April 2022)

RE: Unvaccinated Subpopulation Assumption

Edward E. Rylander [MD], Physician, IHI Family Medicine Residency

It seems your making the assumption that the unvaccinated are also previously uninfected, in your infection and transmission numbers calculation. At this point in the pandemic it would be almost impossible to locate any sizable population of individuals who were both unvaccinated and previously uninfected (most now with multiple infections). It would seem that your calculations should be adjusted for the natural immunity that multiple infection events confer, to more accurately reflect a “real world” experience?

Competing Interests: None declared.

References

- David N. Fisman, Afia Amoako, Ashleigh R. Tuite. Impact of population mixing between vaccinated and unvaccinated subpopulations on infectious disease dynamics: implications for SARS-CoV-2 transmission. CMAJ 2022;194:E573-E580.

Posted on: (26 April 2022)

Your title and the presentation of the findings in mass-media is misleading

Ovidiu Lungu [PhD], scientist, this reply is done in my own name

You should have included the word 'model' in your title and the authors should have been very clear that the findings represent the result of mathematical modelling, not a real-life study of people mixing with other people. Any model is a simplified representation of the word and - more importantly - it is greatly affectedby its assumptions and its capacity to account for a host of other variables. The sensationalism in science is something that it will ruin us all in the long run. It is really sad to see that you contribute to it by not making very clear, from the title, that this is mathematical modelling, so the vulgarization of its results is misinterpreted as being based on data collected from real people.

Competing Interests: None declared.

References

- David N. Fisman, Afia Amoako, Ashleigh R. Tuite. Impact of population mixing between vaccinated and unvaccinated subpopulations on infectious disease dynamics: implications for SARS-CoV-2 transmission. CMAJ 2022;194:E573-E580.

Posted on: (25 April 2022)

RE: covid transmission mathematical model.

Steve Blitzer [MD], Physician, Medical Centre / Mackenzie Health

I would comment on a potential flaw with this mathematical model.
It does imply unvaccinated individuals in groups would result in more spread.
But unvaccinated individuals are more likely to be significantly symptomatic if infected. So then they would be more likely to stay home, isolate , and then not spread.
Conversely a vaccinated indivudual may be more likely minimally symptomatic or asymptomatic if infected.
They would thus mingle more in groups and potentially spread more infection.
Signed Dr Steve Blitzer MD da math nerd.

Competing Interests: None declared.

References

- David N. Fisman, Afia Amoako, Ashleigh R. Tuite. Impact of population mixing between vaccinated and unvaccinated subpopulations on infectious disease dynamics: implications for SARS-CoV-2 transmission. CMAJ 2022;194:E573-E

Posted on: (25 April 2022)

RE: Erroneous parameters in study

Jesse Aumond-Beaupre [BASc], Engineer, Université du Québec en Abitibi-Témiscamingue

In their conclusions they state : "We found that the risk of infection was markedly higher among unvaccinated people than among vaccinated people under all mixing assumptions."

This is clearly not the case with Omicron according to public data from UK, Scotland, Sweden, Denmark, Ontario, Quebec, Iceland, etc.

The vaccine efficacy against infection they used is 80%.

This is not realistic, even against Delta, the vaccine efficacy eventually becomes negative. This whole population study from Sweden show the vaccine efficacy became negative after ~240 days : https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3949410

This was also shown in the UKSHA reports before Omicron, you can see it in any of their Covid Vaccine Surveillance Report before the arrival of Omicron.
https://assets.publishing.service.gov.uk/government/uploads/system/uploa... (Table 2)

And now with Omicron, it's even worse. The Week 13 report raw data showed a vaccine efficacy against infection of around MINUS 300% for the triple vaccinated above 18 years old. Now they simply stopped publishing this inconvenient data.
https://assets.publishing.service.gov.uk/government/uploads/system/uploa... (Table 14)

The data from Scotland showed an efficacy against infection of minus 140% among the double vaccinated, and a higher, age adjusted, death rate. They also stopped publishing this inconvenient data.
https://www.publichealthscotland.scot/media/11089/22-01-12-covid19-winte... (Table 14)

The data from Iceland covid dashboard on January 5th 2022 showed an efficacy against infection of minus 90%.
https://www.covid.is/data (old data may be accessed using internet archive)

Negative efficacy against Omicron after 3 months, Denmark study :
https://www.medrxiv.org/content/10.1101/2021.12.20.21267966v2

Negative efficacy against Omicron after 2 months, Ontario study :
https://www.medrxiv.org/content/10.1101/2021.12.30.21268565v1.full.pdf

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Competing Interests: None declared.

References

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