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Alliance canadienne pour la prévention et prise-en-charge de la covid
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Why COVID-19 Vaccine Boosters are Unnecessary and Not Recommended: A Critique from the Scientific and Medical Advisory Committee of the Canadian Covid Care Alliance – October 4, 2022.

A critical analysis on the interim guidance on planning considerations for a fall 2022 COVID-19 vaccine booster program in Canada, an Advisory Committee Statement (ACS) of the National Advisory Committee on Immunization (NACI), published on June 29, 2022.

The document produced by NACI claims in its preamble that, *"This statement contains NACI's independent advice and recommendations, which are based upon the best current available scientific knowledge."* However, when analysing in detail all the references brought forward to justify the recommendations of periodically administered boosters, there seems to be no evidence provided to support mRNA genetic vaccine boosters.

This document presents a point-by-point analysis of statements in each section of the NACI document, along with an analysis of the references when applicable, to expose the unfounded nature of these recommendations.

Key points of the analysis

- There are NO safety data regarding the administration of boosters every 3, 6 or 9 months, and this fact is openly stated on page 10 of the document. This point alone precludes any recommendation regarding boosters' administration.
- The studies used as evidence to claim the effectiveness of boosters regarding severe outcomes do not present an analysis of adverse events, without which, it is impossible to sufficiently perform a risk/benefit analysis that proves, without doubt, that the benefits of boosters outweigh the risks.
- The evidence that boosters reduce the frequency of severe outcomes (*i.e.*, hospitalizations) is weak, and the potential benefits appear to be extremely short-lived.
- There is evidence that natural immunity alone provides similar or better protection as vaccination and hybrid immunity (Altarawneh *et al.*, 2022).
- It appears assumed that immunity and protection is given almost exclusively by antibodies, with NO consideration of T cell immunity, which provides key protection against all intracellular infections, such as viral infections.
- Because antibody levels will normally decrease over time—from any infection—it is hardly evidence of diminished protection. Instead, a decline in serum antibody only shows the time elapsed since immune challenge; the further away the episode, the lower the level of antibody. With acquired immunity, memory and plasma B cells that produce the antibodies persist and generate replacement antibodies as needed.
- The T cell response of vaccinated people that encounter the virus is phenotypically different than in people who first developed immunity through infection (Rodda *et al.*, 2022). These results are disconcerting, because they show a profound change (imprinting) in the T cell functionality that does not seem to be recoverable.

NACI claim:
"The epidemiology of COVID-19 continues to change and there is still considerable uncertainty with regard to the likelihood, timing, and severity of any potential future COVID-19 wave. It is possible that, consistent with other respiratory viruses, incidence of COVID-19 may increase in the later fall and winter seasons and that new variants of concern (VOC) may emerge."

Counterargument:
The evolution of the SARS-CoV-2 virus has indeed changed over the nearly three years since it was first described in Wuhan, China, and this evolution has been marked by the occurrence of many variants due to rapid mutations of the virus. However, these mutations have not, up until now, generated more lethal variants. The latest variants, although more contagious and rapidly transmitted, are producing less severe disease. This is consistent with the evolutionary pressures of viruses to become more infectious and more benign to the host to successfully outcompete earlier variants. This fact directly challenges the recommendation of repeated boosters for the general population. There is little evidence that supports the assumption that future mutations of the virus, expected to circulate in the fall and winter, will produce more severe disease. Moreover, Omicron variants continue to be present within the Canadian population, which means that people are being exposed to the virus and are being 'naturally boosted' by this exposure without need for vaccination.

NACI claim:
"…while older adults are more likely to have been vaccinated, they are the least likely to have evidence of both vaccination and infection (i.e., hybrid immunity) among individuals 5 years of age and older [2,4]"
Note: Reference 2 is a report of the Immunity Task Force, which contains references of Brown *et al.*, 2022. Reference 4 is a report by Canadian Blood Services.

Counterargument:
The definition of hybrid immunity is based on being IgG+ to 2 antigens: IgG anti-spike (considered infection and vaccine-induced), and IgG anti-nucleocapsid (considered infection-induced). The problems in any analysis based on this definition are as follows.

1. It assumes that the higher IgG titres of spike-directed antibodies arise from principally vaccination rather than natural infection, which is not necessarily true.

2. Anti-nucleocapsid antibodies may not always be generated in naturally infected people, and this would contribute to an underestimation of natural or hybrid immunity.

3. It assumes higher IgG titres are equivalent of having better/stronger immunity, which is not necessarily true, especially since IgA and IgM antibodies located at the initial site of respiratory viral infection in the upper airways should be most protective. IgG antibody levels are low in the upper airways. Furthermore, if the generated antibodies are not neutralizing in nature, they are still expected to enhance infection by opsonisation (*i.e.,* coating the pathogen for recognition by phagocytic immune cells and proteolytic destruction by the complement system).

4. The titres of the IgG are measured without considering the time since vaccination or infection, where it is expected that infected+ 3-dosed participants will have higher titres, because the last dose is proximal to the time at which the sample was taken. However, negative efficacy may be produced by booster doses after an initial protective period of a few months due to acquisition of antigen tolerance. This effect is evident in a Government of Ontario report, for example, in which the proportion of cases of COVID-19 were highest among those who had been 'boosted', lower among the 'fully inoculated', and least among the 'not fully inoculated', which includes the 'uninoculated' (shown Public Health Ontario website on April 30, 2022 https://covid-19.ontario.ca/data). Another example is a large-scale study undertaken of BNT162b2 efficacy in children against the Omicron B1 and B2 variants in New York State by (Dorabawila *et al.* 2022), which included 365,502 participants aged 5 to 11 years old. After 41 days following full vaccination in the 5-11 years-old cohort, there was a negative 41% relative risk reduction in vaccine effectiveness (VE) compared to unvaccinated children that was statistically significant; the vaccinated children were more likely to get infected with Omicron than unvaccinated children. Since other seroprevalence studies have shown that about 75% of US children that were tested had virus-induced antibodies following Omicron infection (Clark *et al.*, 2022; Mallapaty, 2022), it is likely that most of the children in the New York State study already had natural immunity before they were vaccinated.

5. Little discussion of cell mediated immunity—which is optimal to resolving intracellular infections—has occurred.

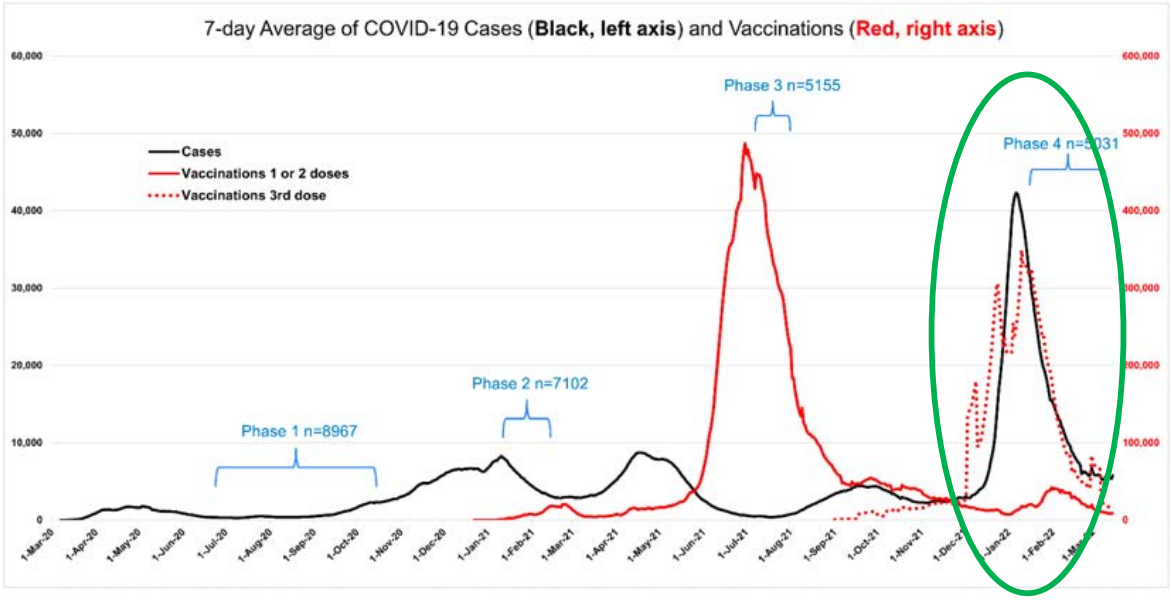
6. While Brown *et al.* (2022) mention that "…persons 60 years of age or older … have the lowest rates of combined infection and vaccination," it could simply indicate that elderly vaccinated people mount poorer immune responses due to immunoscenescence.

- The graph of the Supplemental material of Brown *et al.* (2022) shows an almost perfect correlation between the booster dose (red dot line) and the Omicron infection peak (black line, Jan-22: last peak of the graph), marked by the green circle, indicating that boosters have no impact in preventing any infection increase, and might even favor it.

7. The claim of relatively low natural immunity in the Canadian adults prior to vaccination is also dubious. This is based on the Ab-C study performed with the University of Toronto and funded by the Angus Reid Group. By the fall of 2021, this study reported that only 5.25% of tested Canadians had nucleocapsid protein antibodies, apparently through seroreversion (Tang *et al.*, 2022). This strongly contrasts other studies have observed up to 90% seropositive reactivity of antibodies to the spike, nucleocapsid and other SARS-CoV-2 proteins in serum samples from Canadians tested in 2020 and 2021 (Majdoubi *et al.* 2021; Parsons, 2022; Pelech, Kinexus Bioinformatics, personal communication). These findings indicate that a very large proportion of Canadians already had natural seroconversion before they were even vaccinated.

Figure 1: Original Figure S1 from the supplemental material of the manuscript Brown *et al.* (2022).

Figure S1. 7-day rolling averages of confirmed COVID cases in Canada (black line) and SARS-CoV-2 vaccinations, either first or second dose (solid red line) or third dose (dotted red line), from March 2020 to March 2022



Notes: Testing and vaccination data were derived from the Public Health Agency of Canada as of April 20, 2022: https://www.canada.ca/en/public-health/services/diseases/coronavirus-disease-covid-19/epidemiological-economic-research-data.html

NOTE: Brown *et al.* (2022) used a sample of Angus Reid Survey database, to capture representatively the Canadian population.

NACI claim:
"Although the Omicron variant is associated with less severe illness compared to previous strains, it is partially evasive of immunity conferred by ancestral COVID-19 vaccines or by a previous infection with a SARS-CoV-2 variant prior to Omicron."

Counterargument:
If the Omicron variant is associated with less severe disease, the need to continually vaccinate the entire population is unwarranted.

The claim that Omicron is, "*partially evasive of immunity conferred by ancestral COVID-19 vaccines or by a previous infection with a SARS-CoV-2 variant prior to Omicron," is* not supported by any reference in the document. The structure of the Omicron variants is within 97% identity in terms of its amino acid sequence with the original Wuhan strain, and even more related in structure

to the other variants of concern that quickly replaced it. With natural infection, the antibody response is targeted to most of the 28 proteins found in the SARS-CoV-2 virus, not just the spike protein. Furthermore, antibodies that are produced from natural and vaccine induced immunity can recognize over a hundred different parts of the SARS-CoV-2 spike protein alone. There is actually little overlap between these immunogenic parts and the locations of the Omicron mutations.

Those that have drawn up the NACI guidelines have fallen into the trap thinking that only certain spike protein-directed antibodies are effective in providing protection against COVID-19. This is because most reports in the scientific literature have focused on reduced antibody recognition of the Omicron spike protein that specifically refer to lower "neutralization" activity of the vaccine-induced antibodies generated against the Wuhan version of the spike protein. Some of the mutations in Omicron fall within the ACE2 receptor binding domain of the spike protein. This region is important for the ability of the virus to attach to host cells, and antibodies that bind within or near this portion of the spike protein, upon their attachment can hinder the binding and entry of the virus to cells, slow replication, and reduce the spread of infection. However, the vast majority of the antibody protection afforded by natural immunity and COVID-19 vaccines is directed against other parts of the spike protein. The binding of these antibodies anywhere on the surface of the virus tags it for recognition and destruction by the cells of the innate immune system. Moreover, the surface of the spherical virus particle is coated with many copies of the spike protein, and only one of these spike protein complexes may be sufficient to allow attachment and entry of the virus into cells. Finally, it is also important to consider the possibility that the non-neutralizing nature of the antibodies in a focused immune response to just the spike protein might even enhance the infection rate of immune cells through antibody-dependent enhancement.

NACI claim:
"Preliminary evidence suggests infection- and/or vaccine-acquired immunity wanes over time, which supports administration of subsequent vaccine doses (especially in populations at high risk of severe disease and/or at high risk of poor immune responses to vaccination) to improve protection in case of increasing COVID-19 indicators (e.g., case incidence, test positivity, outbreaks, wastewater signals)."

Counterargument:
There are no references supporting this specific claim.

There are references in these guidelines (not specifically used for the above claim) evaluating hybrid-immunity vs. infection-immunity in relation to symptomatic infections and severe outcomes.

These references are:

- Altarawneh, H.N., Chemaitelly, H., Ayoub, H.H., Tang, P., Hasan, M.R., Yassine, H.M., *et al.* Effect of prior infection, vaccination, and hybrid immunity against symptomatic BA.1 and BA.2 Omicron infections and severe COVID-19 in Qatar. medRxiv; 2022. This paper is now published in NEJM https://www.nejm.org/doi/full/10.1056/NEJMoa2203965

This article concludes natural immunity, vaccination, or both (hybrid) are equally effective against severe COVID-19: "*Previous infection alone, BNT162b2 vaccination alone, and hybrid immunity all showed strong effectiveness (>70%) against severe, critical, or fatal COVID-19 due to BA.2 infection. Similar results were observed in analyses of effectiveness against BA.1 infection and of vaccination with mRNA-1273.*" The authors suggest that for symptomatic (non-serious) infections, natural immunity is a bit inferior (46%) to 3 doses (52%) to infection+3 doses (55%), which seems unlikely to be significantly different.

Interestingly, this article excluded participants that were PCR + within 14 days after a second dose or 7 days after a third dose of vaccine. If they had included those cases, the effectiveness in the vaccinated group could have been lower.

This report supports the excellent protection given by natural immunity.

- Cerqueira-Silva, T., Andrews, J.R., Boaventura, V.S., Ranzani, O.T., de Arújo Oliveira, V. *et al.* Effectiveness of CoronaVac, ChAdOx1 nCoV-19, BNT162b2, and Ad26.COV2.S among individuals with previous SARS-CoV-2 infection in Brazil: a test-negative, case-control study. Lancet Infect Dis. 2022. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8971277/

This report that claims better protection against re-infection in infected-vaccinated participants was not based on the recent Omicron waves, and the findings pertain to reinfection by pre-Omicron variants.

The results of this report are not relevant to the current Omicron situation.

- Nordström, P., Ballin, M., Nordström, A. Risk of SARS-CoV-2 reinfection and COVID-19 hospitalisation in individuals with natural and hybrid immunity: a retrospective, total population cohort study in Sweden. Lancet Infect Dis. 2022. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8971363/

This Swedish study, with 2,039,106 individuals, tracked natural immunity from recovery from COVID-19, which was found to reduce the risk of a SARS-CoV-2 reinfection by 95% within 3 months, and reduced the risk of hospitalization by 87% after 20 months. The authors claim that natural immunity must be considered equally to vaccination: "*The risk of SARS-CoV-2 reinfection and COVID-19 hospitalisation in individuals who have survived and recovered from a previous infection remained low for up to 20 months. Vaccination seemed to further decrease the risk of both outcomes for up to 9 months, although the differences in absolute numbers, especially in hospitalisations, were small. These findings suggest that if passports are used for societal restrictions, they should acknowledge either a previous infection or vaccination as proof of immunity, as opposed to vaccination only.*"

The results of this report are not relevant to the current Omicron situation (as the results were pre-Omicron). However, the study does recognise the value of natural immunity.

NOTE: None of these manuscripts describing vaccine effectiveness of boosters analysed or presented adverse events (AEs) experienced by the cohorts. This makes any risk/benefit analysis impossible.

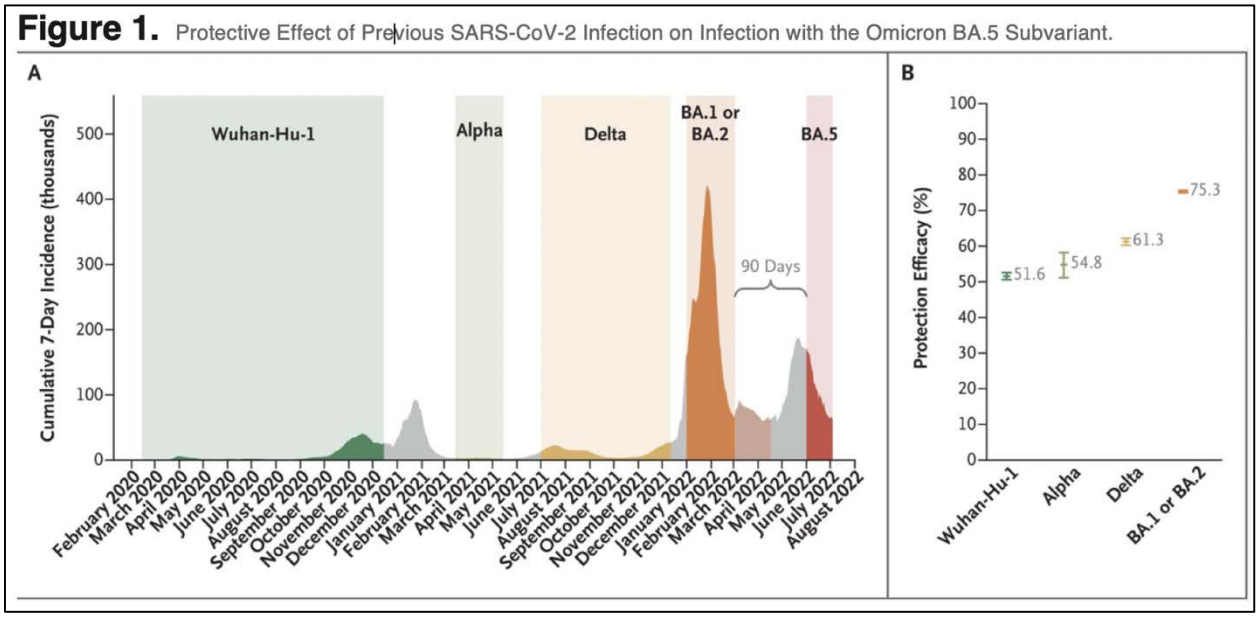
Another pre-Omicron Israeli study (Gazit *et al*., 2021) that compared natural to vaccine immunity noted that vaccinated people were at least 13-times more likely to get a symptomatic COVID-19 infection than those with natural immunity.

This particular claim by the NACI panel also discounts the persistence of naturally acquired immunity that is evident historically with other SARS coronaviruses and now amply evident with SARS-CoV-2. Individuals that have previously recovered from infection with SARS-CoV-1 in 2002 and 2003 were observed to have appreciable antibodies levels (~54% of peak levels) against SARS-CoV-1 Spike protein even three and a half years later (Wu *et al*., 2007; Cao *et al*., 2007). Following infection with MERS-CoV (the coronavirus that caused Middle East respiratory syndrome), antibody levels against this virus have also been shown to persist for up to 34 months in recovered patients (Payne *et al*., 2016).

The on-going 4000 participant Canadian study conducted by Kinexus Bioinformatics Corporation has noted that antibodies against multiple SARS-CoV-2 proteins are evident more than two and a half years after initial infection with SARS-CoV-2. Moreover, these detectable antibody levels in serum from study participants have remained appreciable likely due to continuous re-exposures to the virus during the course of the COVID-19 pandemic. This represents a natural boosting of immunity, which has happened to a large percentage of the Canadian population with the Omicron waves.

Finally, a recent nation-wide survey (9.3M individuals) of the highly vaccinated population in Portugal (more than 98% of the population above 12-year-old fully vaccinated before 2022) has reaffirmed the primacy of naturally acquired immunity for the protection against reinfection (Malato *et al*., 2022). Based on PCR and antigenic testing, it was estimated that 57% of the population over 12-year-old had been previously infected knowing well that such testing was underestimating the actual level. Seroprevalence studies detecting anti-N IgGs added another 29.2% of previously infected individual raising the overall level of infected population to 86.2%. In addition, it is possible that the seroprevalence study that relied on detection of N protein immunoreactivity also underestimated the actual level of previous infection as a few studies have found that many individuals that have recovered from SARS-CoV-2, which was confirmed by PCR tests, do not appear to produce antibodies against the N protein (Pelech, Kinexus Bioinformatics, personal communication). The study then analysed the level of protection conferred by previous infection and found 51.6% protection by original Wuhan variant, 54.8% with Alpha, 61.3% with Delta and 75.3% with Omicron BA.1 and BA.2 combined. It is unclear whether the higher level of protection conferred by the most recent infections is attributable to waning of protection over time from less recent infections, putative immune escape of the new subvariants from previous infection, or a combination of both. Further studies are required to sort this out. Nevertheless, this study clearly shows a high level of protection against reinfection with BA.5 in a population with previous SARS-CoV-2 infection history.

Figure 2: Original Figure 1 from the manuscript Malato *et al*., 2022: Protective effect of previous SARS-CoV-2 infection on infection with the Omicron BA.5 subvariant.



NACI claim:
"NACI continues to strongly recommend a primary series with an authorized mRNA vaccine in all authorized age groups"

Counterargument:
Based on safety analysis of the original trial data performed by CCCA (video "More Harm than Good" https://www.canadiancovidcarealliance.org/wp-content/uploads/2021/12/The-COVID-19-Inoculations-More-Harm-Than-Good-REV-Dec-16-2021.pdf) this recommendation has no merit. Those in the lowest age groups are clearly at much lower risk of hospitalization, ICU admissions and deaths than those that are elderly. Table 1 provides an assessment of the risks by Health Canada. The actual risks are at least a magnitude lower than these estimates, because the Health Canada numbers are based on less than 10% of Canadians recorded as having had COVID-19, whereas, serological testing indicates 50 to 90% of the population has antibodies that support prior infection with SARS-CoV-2. Furthermore, about half of recorded hospitalizations, ICU admissions and deaths were with individuals that came to hospital initially for reasons distinct from COVID-19 (https:/covid-19.ontario.ca/data/hospitalizations). On top of this, the current Omicron variants of SARS-CoV-2 induce less severe clinical disease and are accompanied by low rates of hospitalizations, ICU admissions and deaths from COVID-19 than seen with earlier variants.

Table 1. Risks of hospitalization, intensive care unit admissions and deaths in Canada by age group.

Age Group (Years)	Cases	Hospitali-zations	Hospitali-zations %	ICU Admissions	ICU Admissions %	Deaths	Deaths %
0-11	411,608	5,360	1.30	502	0.12	40	0.01
12-19	329,154	2,331	0.71	243	0.07	25	0.01
20-29	738,020	8,611	1.17	931	0.13	144	0.02
30-39	702,156	12,941	1.84	1,769	0.25	335	0.05
40-49	612,537	14,049	2.29	2,904	0.47	720	0.12
50-59	513,891	22,083	4.30	5,419	1.05	2,052	0.40
60-69	323,585	31,294	9.67	7,541	2.33	4,864	1.50
70-79	198,538	39,235	19.76	6,919	3.48	9,821	4.95
80+	251,197	56,473	22.48	3,495	1.39	27,794	11.06
All groups	**4,080,686**	**192,377**	**4.71**	**29,723**	**0.73**	**45,795**	**1.12**

Data sourced from: https://health-infobase.canada.ca/covid-19/ on September 23, 2022.

Finally, the work by Fraiman *et al.* (2022), which presents a reanalysis of adverse events of special interest ("AESI"), casts serious doubts on the alleged "safety" of the mRNA vaccine as initially estimated at the time of the emergency authorisation. The precautionary principle would advise not to recommend vaccination before a more rigorous assessment of harm-benefit is updated. As the authors emphasized in their study:
"*These results raise concerns that mRNA vaccines are associated with more harm than initially estimated at the time of emergency authorization… The excess risk of serious adverse events found in our study points to the need for formal harm-benefit analyses, particularly those that are stratified according to risk of serious COVID-19 outcomes. These analyses will require public release of participant level datasets.*"

This study has to be put in the context of the recent advice from the Danish Health Authorities that prohibit vaccination for people under 18-year-old, **banni**ng the first dose as of July 1, 2020 and the second dose as of September 2022, unless recommended by personalised medical advice (https://www.sst.dk/da/corona/vaccination). Moreover, the Danish Health Authorities no longer recommend COVID-19 booster vaccination for otherwise healthy individuals under age 50 years. https://www.sst.dk/en/English/Corona-eng/Vaccination-against-COVID-19).

NACI claim:
"NACI also strongly recommends a booster dose for all adults, and for adolescents who are at high risk for severe disease…a fall booster dose in advance of a potential future wave of COVID-19 will be most important for older adults and other populations at increased risk of severe

COVID-19 disease, regardless of the number of booster doses previously received. Evidence to date suggests that while protection against symptomatic disease wanes over time, protection against severe disease is better maintained."

Counterargument:
There has not been any safety study regarding repeated administration of mRNA genetic vaccines. The guideline document admits to the lack of safety data on page 10.

Moreover, there is evidence pointing to a correlation between boosters and the occurrence of higher COVID-19 cases, presented by Brown *et al*. (2022) (see Figure 1 on page 4 of this document).

There is also evidence of increase serious AEs (including death) after the administration of a first booster in the elderly, particularly in those previously infected (Zhang *et al*., 2022).

Finally, there is evidence from Quebec hospitalization data, showing a higher frequency of hospitalization in boosted patients (even when looking at cases/millions of the corresponding vaccination-status group) [https://vaccintrackerqc.ca/cas_et_hospitalisations/#selon-le-statut-vaccinal].

Figure 3: Absolute numbers of new hospitalization in Quebec (website consulted on August 08, 2022). Note the higher number of 3-dose hospitalized patients represented by the purple line.

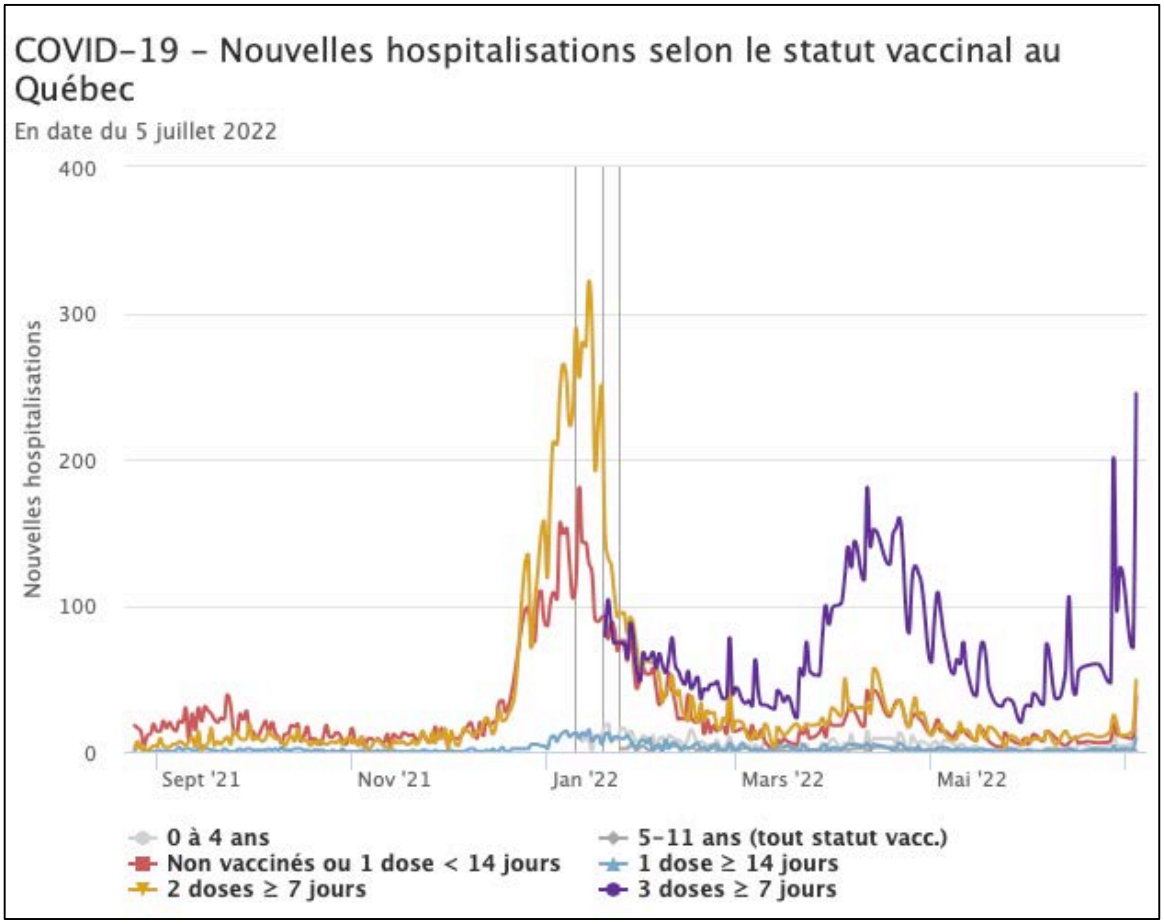
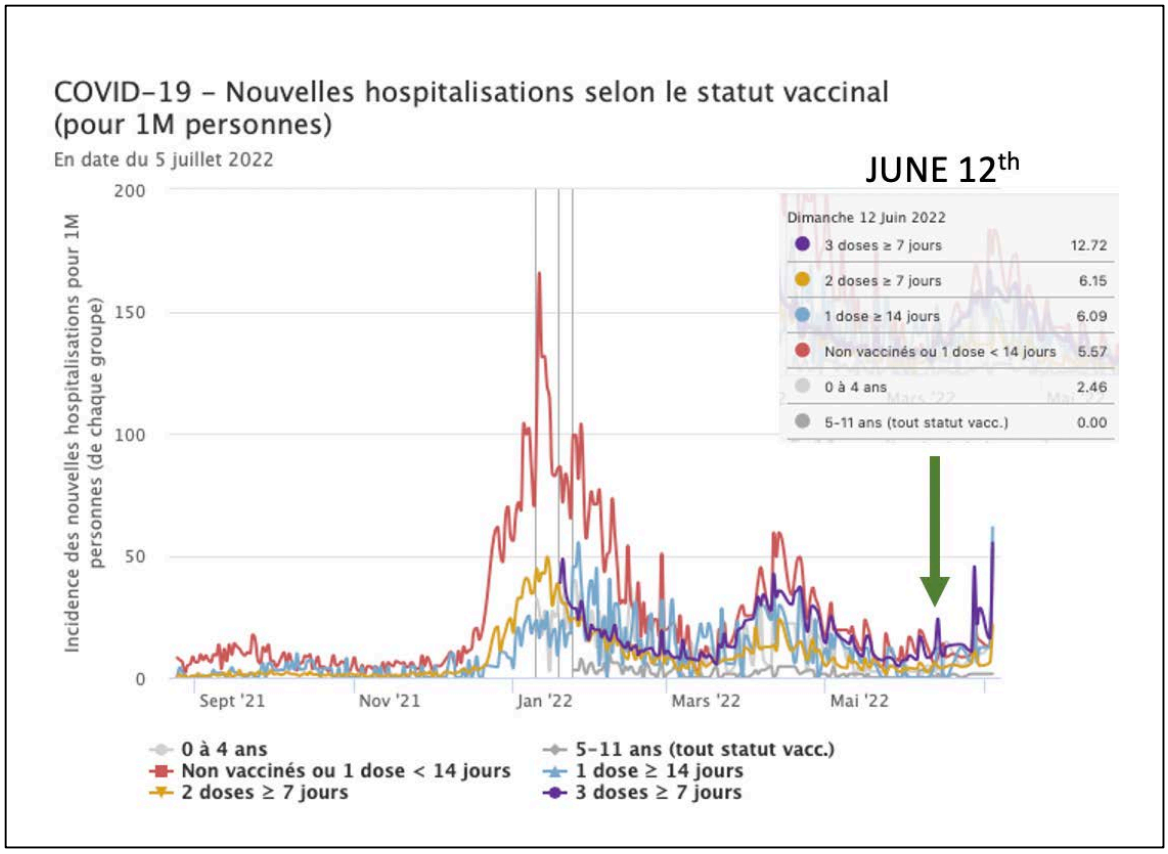


Figure 4: Numbers/million of the corresponding group: boosted patients (purple line) represent the highest number of hospitalized cases starting on June 12th (the website stopped adding new data on July 4th).



Method Section

NACI claim:
"NACI's recommendations on booster doses are based on the decision-making framework…. This framework has been updated with evolving evidence (e.g., including consideration of population level cumulative immunity and vaccine coverage) as outlined in Table 1. Recommendations are based on evidence of the need for (e.g., increased risk of severe illness from COVID-19 and/or increased risk of decreased protection, and waning protection due to increased time since last dose or infection) and benefit of (e.g., safety and effectiveness) booster doses in the Canadian context."

Counterargument:
There is not a single specific reference for this paragraph, nor for Table 1 in this document.

"Cumulative Immunity" should be defined in the document, since all the references that appear in other sections of the guidelines consider exclusively the level of antibodies, which does not mean that the person will mount an optimal immune response when challenged by the pathogen. Also,

antibody titres decreasing over time is not a marker of decrease immune response, but merely an indicator of the time elapsed since the encounter with the antigen/pathogen. For example, natural immunity results in the production of plasma and memory B cells that become inactive until the body is re-exposed to the pathogen once again, and resume production of the specific antibodies for this target.

NACI claim:
"On May 24, 2022, and June 7, 2022, NACI reviewed data on the current epidemiology of COVID-19, the level and duration of protection conferred by vaccine-induced immunity, SARS-CoV-2 infection-induced immunity and hybrid immunity (i.e., induced by vaccination and infection); as well as considered future multivalent COVID-19 vaccines."

Counterargument:
There is no specific reference for this claim.

This claim may point to the references of the Background Section: report of the Immunity Task Force Report: Brown *et al.* (2022); and Altarawneh *et al.* (2022), Cerqueira-Silva *et al.* (2022), Nordström *et al.* (2022). As commented above (pages 2-5), these references do not support the NACI's claim.

Recommendations Section

NACI recommendation 1
*"NACI recommends that **individuals who are at increased risk of severe illness from COVID-19 should be offered** a fall COVID-19 vaccine booster dose* regardless of the number of booster doses previously received…… (Strong NACI Recommendation)."*

Counterargument:
There are **no safety data** for repeated administration of these products, which are not standard vaccines. This is not acceptable for a 'strong recommendation.' Traditional vaccines rarely require more than two injections for immunity that last for years.

The recommendation always uses the word "offer", which implies people can refuse it. For a medical guideline this is a very odd choice of words. Why did they not say that people should take a booster? Is there a legal implication?

NACI recommendation 2
"NACI recommends that all other individuals 12 to 64 years of age may be offered a fall COVID-19 booster dose regardless of the number of booster doses previously received. (Discretionary NACI Recommendation)."*

Counterargument:
There are **no safety data** for administration of these products repeatedly, which are not standard vaccines. This is not acceptable either for a 'discretionary recommendation'; with each booster injection, the risk of vaccine injury increases.

NACI recommendation 3
"NACI recommends that COVID-19 booster doses may be offered at an interval of 6 months since previous COVID-19 vaccine dose or SARS-CoV-2 infection. However, a shorter interval of at least 3 months may be warranted in the context of heightened epidemiologic risk, as well as operational considerations for the efficient deployment of the program. (Discretionary NACI Recommendation.)"

Counterargument:
There are **no safety data** for administration of these novel genetic vaccine products repeatedly. This is not acceptable either for a 'discretionary recommendation.'

NACI claim:
"Given the uncertainties, the planning of a forthcoming COVID-19 booster program should include sufficient resilience and flexibility (e.g., emerging epidemiological trends may alter the timing of an upcoming booster program, triggering an earlier or later roll-out than currently anticipated). Timely, close and ongoing monitoring and assessment of national and international data will be required to ensure adaptability of response."

Counterargument:
We acknowledge the fact that science evolves and changes over time. However, if scientific results are to be used to enforce policies that affect all members of the population, should not these policies be based on validated, level 1 evidence? 'Freshly' produced data is susceptible to have more inaccuracies, simply because it has not been replicated and sufficiently scrutinized. Moreover, analysis of safety signals seemed to have been minimized, when it should, instead, remain at the forefront. Is this the type of data that is suitable as the base of policies to repeatedly inject boosters to the population?

Summary of the Evidence Section: Evolving epidemiology and vaccine coverage

NACI claim:
"It is possible that consistent with other respiratory viruses, incidence of COVID-19 will increase in the later fall and winter seasons thus posing a risk for individuals/communities and increasing pressure on health systems."

Counterargument:
So far, the incidence of COVID-19 in seven distinct waves is not seasonal. It is also surprising that the historic trends of, increasing use of healthcare resources of the previous decade was not mentioned in this context (Canadian Institute for Health Information. Care in Canadian ICUs, 2016 (Ottawa, Ontario); ISBN 978-1-77109-476-4 (PDF)). Does NACI believe that a vaccine will relieve that pressure? While vaccination might help prevent some chronically critically ill people from becoming an acute problem for a slowly suffocating healthcare system, it seems speculative that a vaccine can realistically prevent healthcare from being over-burdened. During the first three waves of COVID-19, when there were little or no COVID-19 vaccines available, there were no increases in net hospitalizations, ICU admissions or deaths in Canadian hospitals.
Despite the insistence that health care workers become vaccinated, the healthcare system has been stretched due to stringent healthcare worker isolation guidelines following exposure and the occurrence of SARS-CoV-2 infections in these very workers (pointing to inefficient capacity of the vaccine to stop infection and transmission amongst those who were vaccinated). In addition, the firing, early retirement, resignation, and/or relocation of a significant number of health care workers who have chosen to not disclose their personal medical information or receive the COVID-19 genetic vaccine has negatively impacted the workforce, decreasing the acute and long-term care capacity of the healthcare system.

NACI claim:
"Data from Canadian Blood Services (donors aged 17 years and older) suggest that about 37% of Canadians were infected with SARS-CoV-2 by the end of April 2022 with variation by jurisdiction and higher infection rates among children, young adults, racialized communities and those residing in lower-income neighbourhoods (7). Preliminary unpublished data suggest that seroprevalence in individuals less than 17 years of age is higher compared to older age groups."

Counterargument:
Blood donor data is unlikely to be representative of the entire population. As studied by Golding *et al.* (2013), "*Blood donors are a poor control group for non-genetic studies of diseases related to environmentally, behaviourally, or socially patterned exposures.*" Thus, the measure of antibodies in donor serum, such as that presented by the COVID seroprevalence report of Canadian Blood Services (reference #7 of the NACI guidelines), is also unlikely to represent the population from which the donors originate. In addition, the blood test utilized by Canadian Blood Services relied on the presence of antibodies against the nucleocapsid protein to serve as a marker of natural immunity. However, studies performed by Kinexus Bioinformatics have found that more than half of individuals that have recovered from SARS-CoV-2, which was confirmed by PCR tests, do not appear to produce antibodies against the nucleocapsid protein of the virus, but do have antibodies against the membrane and other SARS-CoV-2 viral proteins.

Moreover, the assumption that higher antibody titres are equivalent of having better/stronger immunity, is not necessarily true. Antibody levels are always meant to decrease, in any type of infection, since the blood stream cannot sustain the continual/indefinitely increase of protein levels. Their decrease (maybe below a threshold of detection of a given test) it is hardly evidence of diminished protection, and it only shows the relation to the time elapsed since infection (*i.e.,*

the further away, in time, the infection occurred, the lower the level of antibody will be). This reduction is necessary, because very high concentrations of antibodies, due to potential non-specific, cross-reactivities may induce or exacerbate autoimmune diseases. Indeed, antibodies generated following these COVID-19 genetic vaccines could be related to the occurrence of a variety of autoimmune diseases (Chen *et al.*, 2022).

Furthermore, as antibodies are amongst the most abundant serum proteins, continued production of antibodies well beyond the elimination of the infectious target would lead to hypergammaglobulinemia with much higher blood viscosity and adverse effects of hemodynamic function (Sloop *et al*., 2020).

Finally, given that cell mediated immunity is the optimal response for resolving intracellular infections, such as that of viruses, it is difficult to claim that immunity of the population is accurately assessed by exclusively measuring antibody titres. Sekine *et al.* (2020) have shown that "*SARS-CoV-2-specific T cells were detectable in antibody-seronegative exposed family members and convalescent individuals with a history of asymptomatic and mild COVID-19*", stressing the importance of avoiding the false equivalence of antibodies and immunity

NACI claim:
"The evolution of seroprevalence rates over time suggests that the majority of infected individuals were infected by the Omicron variant."

Counterargument:
Since natural immunity provides very effective protection against Omicron BA.2 (Carazo *et al.* 2022, reference #12 of NACI guidelines) and the additional protection given by a second booster has been shown to be very short-lived: 22% at week 10 (Gazit *et al.* 2022, reference #28 of NACI guidelines), the evidence to support boosters claiming that they increase protection against Omicron is very weak.
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Hybrid immunity

NACI claim:
"Available evidence shows that hybrid immunity is more robust than immunity due to infection or vaccination alone…"

Counterargument:
'Hybrid immunity' is a newly developed term aiming to assess a mixed type of immunity, generated by, 1) encountering a microorganism via natural exposure, and 2) encountering the microorganism, or a portion of it, in the form of a vaccine. This concept was probably never explored before, because vaccines have always been designed to imitate the 'natural encounter' ideally with the whole microorganism against which we want to develop immune memory. While the natural immune response generates the most diverse repertoire (Kundu *et al*., 2022), 'hybrid immunity,' for some unexplained reason, has become the new gold standard.

Almost all references cited by the NACI guidelines have exclusively focused on antibody-mediated response to viral antigens, completely ignoring T cell immune response. It bears emphasizing the importance of falsely equating antibodies with immunity. Sekine *et al.* (2020) for example, showed that "*SARS-CoV-2-specific T cells were detectable in antibody-seronegative exposed family members and convalescent individuals with a history of asymptomatic and mild COVID-19*."

It is worrisome that 'hybrid immunity' has been reduced to: 1) measuring serum antibodies against anti-spike (exclusive to the vaccine) and anti-nucleocapsid (absent in the vaccinated only); and 2) that levels of these two antibodies constitutes proof of clinical protection.

Antibody titres are dynamic. They increase after exposure with antigen, reach a peak, and subsequently decline, sometimes to an undetectable level. Therefore, titers merely reflect the time that has elapsed since the original exposure. It does not mean the population of memory and plasma B cells for any subsequent response has vanished. However, what remains unclear is how this dynamic behavior translates to clinically relevant outcomes, such as a reduction in hospitalization. Any established correlation between neutralizing antibody titers and severe clinical outcomes occurred in the Johnson & Johnson and Novavax vaccines (Khoury *et al.* (2021) as cited in Wratil *et al.* (2022), which are not widely used in Canada. Other trials of Pfizer and Moderna only evaluated PCR-confirmed symptomatic COVID-19, using 1 or 2 symptoms, such as fever, headache, or sore throat, and not hospitalization and deaths. In our opinion, the assumption that higher neutralizing antibodies, elicited by Pfizer or Moderna vaccines, are responsible for fewer severe COVID-19 outcomes is not based on robust evidence. Often in these clinical studies, prior natural immunity in the vaccinated participants is poorly assessed if at all.

Finally, there is no consideration of how previous infections from other human CoVs produce cross-reactive T cells to SARS-CoV-2 (Kundu *et al.* 2022).

NACI claim:
"The duration of protection from hybrid immunity has not yet been fully characterized, and it is unclear whether hybrid immunity will continue to provide strong protection against some Omicron sub-lineages (e.g. BA.4, BA.5) or potential new variant."

Counterargument:
If there is no established duration for hybrid immunity, any claim regarding periodicity of booster series is not evidence-based and has no merit. The same applies to any evidence of effectiveness against Omicron sub-lineages.

NACI claim:
"Hybrid immunity resulting from three or more exposures to the virus antigen (i.e., ≥1 exposure[s] from vaccination and ≥1 exposure[s] from SARS-CoV-2 infection before or after vaccination) may provide superior protection (as measured by neutralization capacity) against VOCs, including Omicron, compared with primary vaccination only, or previous SARS-CoV-2 infection without vaccination."

Counterargument:
There will most-certainly be measurable differences between multiple exposures to the antigen when it is compared to a single infection event. However, this is hardly an argument to perpetuate repeated vaccinations, since inevitable multiple re-exposures achieved naturally prevents severe disease, especially in healthy young adults (Chemaitelly *et al*., 2022).

NACI claim:
"...protection against Omicron BA.2 conferred by prior infection (with or without vaccination) is higher following prior infection with Omicron BA.1 compared to prior infection with pre-Omicron strains."

Counterargument:
Considering the wide circulation of Omicron sub-lineages in the population, it is likely most of the population has now developed some degree of naturally acquired immunity (Fowlkes *et al*., 2022). When this information is combined with evidence of increased serious AEs (Zhang *et al*., 2022), it is then unclear what added benefit repeated boosters would confer.

NACI claim:
"The protection against Omicron BA.2 conferred by a prior SARS-CoV-2 infection was increased by vaccination with 1 and 2 doses but did not seem to increase with a third dose. At about 4 months (132 days) of follow up, protection against Omicron BA.2 reinfection was 72% in individuals with prior BA.1 infection without vaccination and 96-97% among those with Omicron BA.1 infection and vaccination with 2 or 3 doses."

Counterargument:
This claim does not appear to favor repeated booster doses, at all. The NACI claim is based on the work of Carazo *et al.* (2022) (reference #12 of the NACI guidelines). Instead, the pre-print manuscript indicates that primary infection with Omicron BA.1, alone (and without vaccination), was associated with a risk reduction of symptomatic reinfection of 86% (95%CI: 79-91). This is a comparable estimate to the 'hybrid immunity' conferred by pre-Omicron primary infection plus two or three vaccine doses and is nearly 2-times higher than the estimated 3-dose vaccine effectiveness 46% (95%CI: 40-52) among the previously non-infected.

Vaccine effectiveness (VE) and duration of protection following a first or second booster dose

NOTE:
All NACI claims in this section explore vaccines/boosters' effectiveness (VE) to reduce infection and severe clinical outcomes. We will present some of NACI's claims below, analysing the references used to sustain those claims. However, it is very worrisome that NACI has not performed a Safety Analysis prior, or in parallel, to the study of VE.
If the repeated administration of these products has not been tested for safety, their effectiveness is irrelevant to the public.

NACI claim:
"Current data suggest that COVID-19 vaccines offer higher protection against hospitalization and severe disease than against infection."

Counterargument:
This is an implied admission that the vaccines are neither preventing transmission, nor the occurrence of disease, which nullifies the recommendations for the general population. Furthermore, with a background of prevalent existing natural immunity in the population and the emergence of more benign SARS-CoV-2 variants such as the Omicron variants, it is difficult to establish that the COVID-19 vaccines actually reduce severe COVID-19 and hospitalizations.

NACI claim:
"VE against severe disease with Omicron infection is approximately 90% shortly after a first booster dose and remains above 75% in most studies, up to 20 weeks from the first booster (17-20)."

Counterargument:
This NACI claim of vaccine effectiveness (VE) against Omicron being 75% seems to contradict the evidence of Carazo *et al.* (2022), where the VE of a three-dose vaccine course is estimated at 46%.

The references supporting the claim are:

- Ferdinands, J.M., Rao, S., Dixon, B.E., Mitchell, P.K., DeSilva, M.B. *et al.* Waning 2-dose and 3-dose effectiveness of mRNA vaccines against COVID-19-associated emergency department and urgent care encounters and hospitalizations among adults during periods of Delta and Omicron variant redominance - VISION Network, 10 States, August 2021-January 2022. MMWR Morb Mortal Wkly Rep. 2022 Feb 18;71(7):255-263. doi: 10.15585/mmwr.mm7107e2.

This report presents VE related to Emergency visits and hospitalizations after a third dose or first booster in the Delta and Omicron period. The data shows rapid decline in VE after a third dose during the Omicron period for both Emergency visits (31% at 5 months) and hospitalizations (78% at 4 months). However, there is no consideration of natural immunity, which according to Carazo *et al*. (2022) provides comparable or better protection. Also, there is no analysis in this cohort of adverse events related to the vaccine, so it is impossible to perform a risk/benefit analysis.

- Stowe, J., Andrews, N., Kirsebom, F., Ramsay, M., Bernal, J.L. Effectiveness of COVID-19 vaccines against Omicron and Delta hospitalisation: test negative case-control study. medRxiv 2022. doi: https://doi.org/10.1101/2022.04.01.22273281

This report presents VE in relation to disease severity of hospitalized patients (requiring oxygen/ventilation and ICU); it seems VE for milder forms is low (53% at week 15). The design

of the report is complex. They use two sources of testing, testing in the community (pillar 2) and related to hospital patients and personnel (pillar 1), which may imply large differences in exposure. There was a calendar criterion of when the booster was administered to be included in the study, but there seems to be no clear rationale explained behind that choice.

The absolute number of patients ending in ICU is very low (<500 ICU for more than 1.5 million cases considered in the study). This questions the power analysis (statistical power and effect size) which should be reported along with the results to be able to interpret the impact of VE.
There is no consideration of natural immunity, which according to Carazo *et al.* (2022) provides comparable or better protection. Also, there is NO analysis in this cohort of adverse events related to the vaccine, so it is impossible to perform a risk/benefit analysis.

- Chemaitelly, H., Ayoub, H.H., AlMudad, S., Coyle, P., Tang, P *et al.* Duration of mRNA vaccine protection against SARS-CoV-2 Omicron BA.1 and BA.2 subvariants in Qatar. *Nature Commun.* 2022,13, 3082 doi: 10.1038/s41467-022-30895-3.

This article reports rapidly waning VE for infection, but higher VE for severe outcomes, including deaths. However, the absolute number of patients reported as severe, critical, or fatal disease is very low in the non-vaccinated (between 110 and 143 of non-vaccinated cases considered for all categories of doses and vaccine brand); this questions the power analysis (statistical power and effect size), which should be reported along with the results to be able to interpret the impact of VE. Also, there is NO analysis in this cohort of adverse events related to the vaccine, so it is impossible to perform a risk/benefit analysis.

NACI claim:
"Preliminary data indicates that a second booster dose provides additional protection compared to a first booster, including against severe disease. The duration of protection is currently unknown (28)."

Counterargument:
This NACI claim is supported by reference 28:

- Gazit, S., Saciuk, Y., Perez, G., Peretz, A., Pitzer, V.E., Patalon, T. Relative effectiveness of four doses compared to three doses of the BNT162b2 vaccine in Israel. medRxiv. 2022 Mar 24.

This article presents evidence regarding of VE of 3-doses-recipients vs 4-doses-recipients but not against double dosed, nor unvaccinated with naturally acquired immunity. The length of the study was a mere 10 weeks, with effectiveness against infection quickly decreasing to 22% at week 10. Also, the absolute number of severe outcomes (hospitalization and death) was very low in both 3 doses and 4 doses, less than 1% of the participants. This questions the power analysis (statistical power and effect size), which should be reported along with the results to be able to interpret the impact of VE.

This is very weak evidence to justify boosters. More importantly, NACI acknowledges that the duration of a second booster effectiveness is unknown. There was no analysis of AE in the cohort to perform a risk/benefit analysis.

NACI claim:
"Longer intervals between doses have been shown to result in a stronger and more durable immune response (30, 31) and somewhat better VE than shorter intervals (30, 32, 33). A longer interval between doses provides the opportunity for antibody levels to wane, which may result in a more robust immune memory response after the next dose, as it allows time for the immune response to mature in both breadth and strength."

Counterargument:
The references supporting the claim are:

- Amirthalingam, G., Bernal, J.L., Andrews, N.J., Whitaker, H., Gower, C., Stowe, J., *et al.* Serological responses and vaccine effectiveness for extended COVID-19 vaccine schedules in England. Nature Communications. 2021 Dec 10;12(1):7217. doi: 10.1038/s41467-021-27410-5

This article presents pre-Omicron results using serology of 750 participants in relation to VE. These data are not translatable to multiple boosters and different variants in circulation now.

- Ireland, G., Whitaker, H., Ladhani, S.N., Baawuah, F., Subbarao, V., Linley, E., *et al*. Serological responses to COVID-19 booster vaccine in England. medRxiv. 2021 Nov 24. doi**:** https://doi.org/10.1101/2021.11.22.21266692. Currently published in Euro Surveill. 2022 Jan;27(1):2101114.

This is a serologic study on 750 participants; it seems to be the same cohort as that used in reference 30, Amirthalingam *et al*. (2021), because it is written by the same authors and the cohort has the same demographic characteristics showing IgG increase. Serum antibody levels are not proof of protection.
It was also a pre-Omicron variants study. These data are not translatable to multiple boosters and different variants in circulation now.

- Hulme, W.J., Williamson, E.J., Horne, E., Green, A., Nab, L., Keogh, R., *et al.* Effectiveness of BNT162b2 booster doses in England: an observational study in OpenSAFELY-TPP. medRxiv. 2022 Jun 06. doi: https://doi.org/10.1101/2022.06.06.22276026

This study reports superior protection with a 1st booster compared to those that had only two doses of COVID-19 vaccines. The study does not consider Omicron variants of concern, nor the role of natural immunity. The follow-up only lasted 10 weeks. Even though the difference of VE between boosted and non-boosted was statistically significant, the absolute number of participants with severe outcomes was low (3,672 hospitalisations in 6,990,219 participants). This questions the power analysis (statistical power and effect size), which should be reported along with the results

to be able to interpret the impact of VE. Also, there is no analysis of adverse events related to the vaccine, so it is impossible to perform a risk/benefit analysis.

This is very weak data and non-translatable to the current epidemiologic situation with Omicron to justify repeated boosters that are not tested for safety.

- Skowronski DM, Setayeshgar S, Febriani Y, Ouakki M, Zou M, Talbot D, *et al.* Two-dose SARS-CoV-2 vaccine effectiveness with mixed schedules and extended dosing intervals: test-negative design studies from British Columbia and Quebec, Canada. medRxiv. 2021 Oct 26.

This study is not about boosters, or Omicron, or its variants. There is no relevant information that can be translated to the current epidemiologic situation. This study did not investigate AE in the cohorts studied. A proper risk/benefice analysis was not performed.

Safety

NACI claim:
"…second booster doses have generally been administered in specific populations (e.g., LTC residents, older adults) or in small groups, therefore evidence of their safety is currently limited."

Counterargument:
NACI admits their lack of safety data. However, other groups, including analysis done by the vaccine manufacturers (Pfizer), present concerning results regarding safety even following the primary vaccinee series.

Based on this claim alone, boosters must not be recommended.

- Section 5.3.6 Cumulative Analysis of Post-authorization Adverse Event Reports submitted by Pfizer, on Table 1 of their report (see below) there were 1223 deaths over only a 3-month period from December 1, 2020 until February 28, 2021 (Table 2). Any other medicinal product would have been taken off the market immediately. Therefore, the question should be asked, why aren't the mRNA vaccines taken off the market. From Pfizer's own data we already know that they are not safe.

Table 2. Original Table 1 in the Pfizer's Cumulative Analysis of Post-authorization Adverse Events Reports. Reproduced from https://phmpt.org/wp-content/uploads/2021/11/5.3.6-postmarketing-experience.pdf.

Table 1. General Overview: Selected Characteristics of All Cases Received During the Reporting Interval

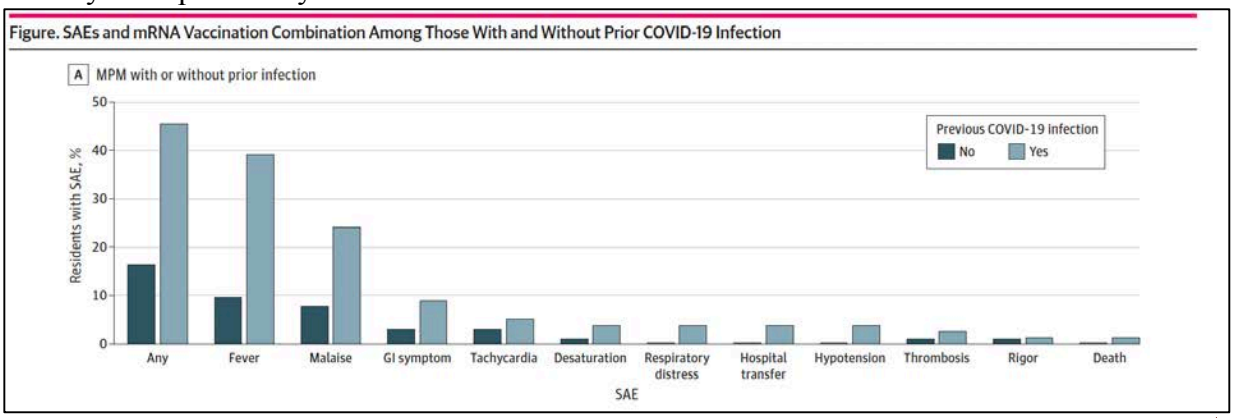
Characteristics		Relevant cases (N=42086)
Gender:	Female	29914
	Male	9182
	No Data	2990
Age range (years): 0.01 -107 years Mean = 50.9 years n = 34952	≤ 17 18-30 31-50 51-64 65-74 ≥ 75 Unknown	175[a] 4953 13886 7884 3098 5214 6876
Case outcome:	Recovered/Recovering	19582
	Recovered with sequelae	520
	Not recovered at the time of report	11361
	Fatal	1223
	Unknown	9400

a. in 46 cases reported age was <16-year-old and in 34 cases <12-year-old.

- Zhang, X.S., Moreau, A., Cruz-Santiago, D., Langevin, S., Nguyen, Q.D. Safety and adverse events among long-term care residents receiving a third COVID-19 mRNA vaccine booster dose in Quebec. JAMA Netw Open. 2022 Jul 1;5(7):e2223401. https://pubmed.ncbi.nlm.nih.gov/35862047/

This article presents severe AEs in residents of long-term care facilities in Quebec, showing that these residents may be at greater risk of post-third-dose severe AEs (including death), especially those that were previously infected. This demonstrates that prior serological testing may be advisible in residents that have recovered already from COVID-19 before they are subject to triple vaccination.

Figure 5. Original Figure A from Zhang *et al.* (2022) that shows more severe adverse effects in those that were triple vaccinated with the Moderna, then Pfizer and then Moderna RNA vaccines if they have previously recovered from COVID-19.



- Fraiman, J., Erviti, J., Jones, M., Greenland, S., Whelan, P., Kaplan, R. M., Doshi, P. (2022). Serious adverse events of special interest following mRNA vaccination in randomized trials. https://papers.ssrn.com/abstract=4125239
  This manuscript is currently published in Vaccine. 2022 Aug 30:S0264-410X(22)01028-3

This article (as already mentioned on page 9 of this document) reanalyzes the original trial data, showing that "*the excess risk of serious adverse events of special interest surpassed the risk reduction for COVID-19 hospitalization relative to the placebo group in both Pfizer and Moderna trials*."

Other considerations

NACI claim:
"As protection against infection and severe disease is highest soon after vaccine administration, vaccination at a time of low disease incidence may have limited benefit, particularly if there is an extended period of time before the next wave of COVID-19."

Counterargument:
This claim is worrisome, since it implies changing the basic paradigm of when vaccines are given, which is ideally before the pathogens start circulating, so the population builds immunity before the start of the period of high incidence of infections. The type of schedule that NACI proposes is closer to that of a therapy, which seems to be what they are doing, *i.e.*, administration of an injection that increases antibodies, at shorter and shorter intervals (note that recommendation #3 proposes 6- or 3-months intervals). In fact, similar results might be obtained by preventively administering monoclonal antibodies to target populations. In both cases protection is short-lived thus requiring repeat treatments. Except that, in the case of monoclonal antibodies administration, we can control the dose and the schedule, whereas with these antibodies generated by genetic vaccines, not only do we not control the dose but, in addition, the long-term effects of these repeated immune stimulations are unknown. What could possibly go wrong? Generation of IgG4 antibodies by class switching as recently documented by a preprint German study: "Class switch towards non-inflammatory IgG isotypes after repeated SARS-CoV-2 mRNA vaccination" (https://www.medrxiv.org/content/10.1101/2022.07.05.22277189v1.full.pdf), clearly raises the prospect of generating immune tolerance to the vaccinal spike protein in some individuals, similar to repeated allergen administration to mitigate allergies, with disturbing consequences for the control of future SARS-CoV-2 infections.

These products do not behave like traditional vaccines.

Ethics, equity, feasibility, and acceptability

Canada should follow what was already outlined in The Nuremberg Code (1947),

"*The judgment by the war crimes tribunal at Nuremberg laid down 10 standards to which physicians must conform when carrying out experiments on human subjects in a new code that is now accepted worldwide."* The objective was to ensure that crimes like these would never happen again.

1. "*The voluntary consent of the human subject is absolutely essential. This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, overreaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision. This latter element requires that before the acceptance of an affirmative decision by the experimental subject there should be made known to him the nature, duration, and purpose of the experiment; the method and means by which it is to be conducted; all inconveniences and hazards reasonably to be expected; and the effects upon his health or person which may possibly come from his participation in the experiment. The duty and responsibility for ascertaining the quality of the consent rests upon each individual who initiates, directs, or engages in the experiment. It is a personal duty and responsibility which may not be delegated to another with impunity.*
2. *The experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study, and not random and unnecessary in nature.*
3. *The experiment should be so designed and based on the results of animal experimentation and a knowledge of the natural history of the disease or other problem under study that the anticipated results justify the performance of the experiment.*
4. *The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury.*
5. *No experiment should be conducted where there is an a priori reason to believe that death or disabling injury will occur; except, perhaps, in those experiments where the experimental physicians also serve as subjects.*
6. *The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment.*
7. *Proper preparations should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability or death.*
8. *The experiment should be conducted only by scientifically qualified persons. The highest degree of skill and care should be required through all stages of the experiment of those who conduct or engage in the experiment.*
9. *During the course of the experiment the human subject should be at liberty to bring the experiment to an end if he has reached the physical or mental state where continuation of the experiment seems to him to be impossible.*
10. *During the course of the experiment the scientist in charge must be prepared to terminate the experiment at any stage, if he has probable cause to believe, in the exercise of the good faith, superior skill and careful judgment required of him, that a continuation of the experiment is likely to result in injury, disability, or death to the experimental subject.*"

(The text in quotes was extracted from British Medical Journal 1996;313(7070):1445-75).

In summary: At least 8 out of the 10 standards laid down to which physicians must conform when carrying out experiments on human subjects following judgment by the war crimes tribunal at Nuremberg in 1947 were violated in Canada during the COVID-19 pandemic. In the British Medical Journal article in 1996 it stated: *"…10 standards to which physicians must conform when carrying out experiments on human subjects in a new code that is now accepted worldwide*."

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