An Advisory Committee Statement (ACS) National Advisory Committee on Immunization (NACI)

Guidance on COVID-19 vaccine booster doses: Initial considerations for 2023

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Preamble

The National Advisory Committee on Immunization (NACI) is an External Advisory Body that provides the Public Health Agency of Canada (PHAC) with independent, ongoing and timely medical, scientific, and public health advice in response to questions from PHAC relating to immunization.

In addition to burden of disease and vaccine characteristics, PHAC has expanded the mandate of NACI to include the systematic consideration of programmatic factors in developing evidence based recommendations to facilitate timely decision-making for publicly funded vaccine programs at provincial and territorial levels.

The additional factors to be systematically considered by NACI include: economics, ethics, equity, feasibility, and acceptability. Not all NACI statements will require in-depth analyses of all programmatic factors. While systematic consideration of programmatic factors will be conducted using evidence-informed tools to identify distinct issues that could impact decision-making for recommendation development, only distinct issues identified as being specific to the vaccine or vaccine-preventable disease will be included.

This statement contains NACI's independent advice and recommendations, which are based upon the best current available scientific knowledge. This document is being disseminated for information purposes. People administering the vaccine should also be aware of the contents of the relevant product monograph. Recommendations for use and other information set out herein may differ from that set out in the product monographs of the Canadian manufacturers of the vaccines. Manufacturer(s) have sought approval of the vaccines and provided evidence as to its safety and efficacy only when it is used in accordance with the product monographs. NACI members and liaison members conduct themselves within the context of PHAC's Policy on Conflict of Interest, including yearly declaration of potential conflict of interest.

Background

The Omicron variant of SARS-CoV-2 virus was first detected in November 2021, with its sub-variants continuing to circulate in Canada and globally, more than one year later. The epidemiology of COVID-19 is expected to continue to evolve, and the likelihood, timing, and severity of any potential future resurgence of COVID-19 is uncertain. No strong evidence of seasonality of COVID-19 has emerged to date, and it has yet to be seen whether the incidence of SARS-CoV-2 virus infections will be analogous to other respiratory viruses that increase in the fall and winter seasons, thereby increasing pressure on health systems during this period.

Since September 2021, NACI has been developing and updating guidance on the use of COVID-19 booster doses based on a decision-making framework assessing the need for, and benefit of, additional doses of COVID-19 vaccines in various populations. These decisions were supported by vaccine principles, as well as evidence where available.

The NACI Interim guidance on planning considerations for a fall 2022 COVID-19 vaccine booster program in Canada (June 29, 2022) provided jurisdictions with planning advice for a booster dose program in advance of a possible future surge of COVID-19 in Canada over the fall and winter months and included an updated decision-making framework on booster doses. More specific guidance on vaccination recommendations for the fall of 2022, including booster doses in children 5 to 11 years of age and the use of bivalent Omicron-containing mRNA COVID-19 vaccines, was provided in the following NACI statements:

- Recommendations on the use of a first booster dose of Pfizer-BioNTech Comirnaty COVID-19 vaccine in children 5 to 11 years of age (August 19, 2022)
- Recommendations on the use of bivalent Omicron-containing mRNA COVID-19 vaccines (September 1, 2022)
- Updated guidance on COVID-19 vaccine booster doses in Canada (October 7, 2022)
- Updated recommendations on the use of COVID-19 vaccine booster doses in children 5 to 11 years of age and concurrent vaccine administration (December 9, 2022)

Since then, additional NACI guidance has been requested as provinces and territories begin to consider planning for 2023.

NACI's recommendations remain aligned with the current goals of the Canadian COVID-19 Pandemic Response (as of February 14, 2022):

- To minimize serious illness and death while minimizing societal disruption as a result of the COVID-19 pandemic.
- To transition away from the crisis phase towards a more sustainable approach to long term management of COVID-19.

For further information on NACI's recommendations on the use of COVID-19 vaccines, please refer to National Advisory Committee on Immunization (NACI): Statements and publications and the COVID-19 vaccine chapter in the Canadian Immunization Guide (CIG).

Methods

On November 29, 2022, and December 13, 2022, the NACI COVID-19 Working Group and full NACI membership respectively reviewed the available evidence on epidemiology and vaccine protection, as well as planning considerations for the next steps of the COVID-19 booster program, including ethics, equity, feasibility and acceptability considerations. NACI also recommended the continued application of the existing decision-making framework for booster doses. NACI approved these recommendations on January 06, 2023.

Further information on NACI's process and procedures is available elsewhere [1, 2].

Key considerations for booster dose decisions

The following sections outline key considerations to monitor over time with regard to future booster dose recommendations, as reflected in NACI's decision-making framework on booster doses. Available information as of December 19, 2022 is summarized below.

Epidemiology

- Previous waves of SARS-CoV-2 in Canada have occurred over the spring, summer, fall and winter months, with some regional variability. The evolutionary trajectory of SARS-CoV-2, including the emergence of novel variants of concern (VOCs), is uncertain, and the seasonality of SARS-CoV-2 has not been established.
- COVID-19 hospitalizations, ICU admissions and deaths continue to occur at a higher baseline frequency since the appearance of Omicron in late 2021 compared to the pre-Omicron period.
- Some populations are at increased risk of severe outcomes of COVID-19 due to biological factors (e.g., advanced age, pre-existing medical conditions, pregnancy) and social factors (e.g., socioeconomic status, belonging to a racialized population) that may intersect. However, age continues to be the single greatest risk factor for severe outcomes of COVID-19. Older adults are the most likely to experience severe disease, with hospitalizations, ICU admissions and death rates highest in those 80 years of age and over, and ICU admission rates also high in those 70 to 79 years of age (see the PHAC COVID-19 epidemiology update).
- Previously dominant BA.5.2 and BA.5.2.1 Omicron sublineages are decreasing, with more immune-evasive sublineages increasing (e.g., BQ.1, BQ.1.1 and BF.7).

Duration of protection from booster doses against severe outcomes due to COVID-19

- Thus far, vaccine protection has been shown to wane over time, with protection against severe outcomes persisting longer than protection against symptomatic disease.
- For BA.1 and BA.2 sublineages of Omicron, the duration of protection against severe disease such as hospitalization has remained high, with most estimates above 70% out to 26 weeks following receipt of an original (non-bivalent) COVID-19 vaccine booster dose [3-16].
- Duration of protection against severe disease for more recent variants and new vaccine formulations is not known at this time and continues to be monitored.

- When vaccine programs are implemented, data on duration of protection from the vaccine are often lacking and it is with ongoing monitoring that we determine whether and how often booster doses are required for the population (e.g., booster doses for pertussis in adolescents and adults and no booster doses for either HPV or hepatitis B vaccines).

Hybrid immunity

- Evidence to date shows that vaccine effectiveness (VE) against BA.1 and BA.2 Omicron sublineages is higher in those who have been both vaccinated and infected with SARS-CoV-2 (i.e., in those who have hybrid immunity to SARS-CoV-2) when compared to those with prior infection alone or vaccination alone [4-10]. The duration of protection from hybrid immunity has not yet been fully characterized, but is likely to have an impact on the need for and timing of additional booster doses.
- In Canada, the hybrid immunity profile differs by age group. A greater proportion of older adults are protected by vaccination only and have not been infected, as compared to younger ages. Adolescents and young adults have the highest proportion of hybrid immunity, and a large proportion of children have been infected but not vaccinated [17].
- Potential vaccination- and/or infection-induced protection against severe outcomes due to infection or reinfection from emerging Omicron sublineages have yet to be determined and the impact of various immunity profiles on protection against future VOCs is unknown.
- There are Canadian data suggesting that vaccine protection may reach a plateau for adults with hybrid immunity, and the benefit of additional mRNA COVID-19 vaccine booster doses may be marginal [18]. This study assessed VE of the original mRNA COVID-19 vaccine against BA.2 among healthcare workers, and whether the findings would apply broadly to other COVID-19 vaccines (i.e., Omicron-containing bivalent mRNA vaccines), other VOCs, and populations has yet to be determined.

Immunogenicity and VE of booster doses of Omicron-containing bivalent mRNA COVID-19 vaccine

- Clinical trials show that a booster dose of Omicron-containing bivalent mRNA COVID-19 vaccine produce higher neutralizing antibody responses against Omicron sublineages than the original vaccines, although preliminary results from small real-world studies have been somewhat variable. The immune response against the ancestral strain is similar after a booster dose of the original or Omicron-containing bivalent mRNA COVID-19 vaccine.
- Neutralization of more recent Omicron sublineages such as BQ.1 is reduced compared to neutralization of earlier Omicron sublineages such as BA.1 or BA.5 after booster vaccination with either an original or Omicron-containing bivalent vaccine [19-25].
- Preliminary data from Ontario demonstrates that short-term (<90 days) VE against severe outcomes in community dwelling adults aged 50 years and older was similar between original and bivalent mRNA COVID-19 vaccine booster doses and between the available vaccine products (Moderna or Pfizer-BioNTech) during a period when BA.5 was the predominant Omicron sublineage and BQ.1 was emerging [26].
- A study from the United States in adults who had received at least 2 doses of an original mRNA COVID-19 vaccine reported improved VE against symptomatic SARS-CoV-2 infection after a subsequent booster dose of BA.4/5 bivalent mRNA vaccine compared to adults who did not receive a bivalent Omicron-containing mRNA COVID-19 vaccine [27]. The relative increase in VE was also larger for individuals with a longer interval since receipt of their previous original dose. A similar trend was observed for protection against

COVID-19-associated emergency department/urgent care encounters and hospitalizations [28].

- Early estimates of VE against hospitalization in immunocompetent adults 65 years of age and older from the United States, reported that a booster dose using a BA.4/5 bivalent Omicron-containing mRNA vaccine provided an additional 73% protection against COVID-19 hospitalization compared with past vaccination with original mRNA COVID-19 vaccines only (≥2 doses given ≥2 months previously) [29]. As original mRNA COVID-19 vaccines are no longer authorized for use in the United States, the effectiveness of bivalent versus original vaccines when used as booster doses in the same time period could not be compared. Of note, the VE studies from the United States were released following NACI deliberations and were not considered as part of decision-making [28, 29].

Ethics, equity, feasibility and acceptability

- Although age is the greatest risk factor for severe outcomes of COVID-19, intersecting equity factors continue to create disproportionate risk for some key populations. Any future booster program should continue to support reducing the impact on those at highest risk of severe disease.
- COVID-19 vaccine uptake in Canada has been highest in older age groups, and decreases with younger age and with each subsequent dose. As of December 4th 2022, less than 50% of individuals 65 years of age and older have received a COVID-19 vaccine in the last 6 months, which includes the fall 2022 booster program period. (PHAC COVID-19 vaccination in Canada)
- Given the uncertainties around the future epidemiological context, any planning of a forthcoming COVID-19 booster program should include flexibility. Emerging epidemiological trends may alter the timing of any upcoming booster program, triggering an earlier or later roll-out. Timely, close and ongoing monitoring and assessment of national and international data will be required.
- Planning vaccination ahead of a future surge of COVID-19 could facilitate access to vaccines, reduce inequities, and decrease the burden on healthcare systems. The timing of the next surge is unknown.
- For all currently vaccine-eligible age-groups (i.e., 6 months of age and older), concurrent administration of any dose of a COVID-19 vaccine with other vaccines (e.g., seasonal inactivated influenza vaccine) has the potential to increase program efficiency and may also increase immunization rates.
- There may be variability in how each province, territory and community assesses risk and responds to the needs of their respective jurisdictions, with a focus on protecting those at highest risk for serious outcomes from COVID-19 infection.

Recommendations

At this time, NACI is reinforcing existing recommendations for COVID-19 vaccines including suggested timing of doses following a previous SARS-CoV-2 infection. The fall 2022 booster program is being used as the reference point to consolidate booster guidance that has been published to date. A summary of recommendations for the primary series and booster doses is also provided in Table 1.

It is noted that the start date of the fall 2022 booster program varied across Canadian jurisdictions from August to September 2022.

Please see Table 2 for an explanation of strong versus discretionary NACI recommendations.

NACI continues to recommend a COVID-19 vaccine primary series as follows:

1) **Individuals 5 years of age and older should be immunized with a primary series of an authorized mRNA vaccine. (*Strong NACI recommendation*)**

2) **Children 6 months to under 5 years of age may be immunized with a primary series of an authorized mRNA vaccine. (*Discretionary NACI recommendation*)**

Additional details including those pertaining to alternative vaccine products are available in the COVID-19 vaccine chapter in the Canadian Immunization Guide and NACI statements and publications.

NACI continues to recommend COVID-19 vaccine booster doses as follows:

3) **At least one booster dose should be offered to all adults 18 years of age and over and adolescents 12 to 17 years of age who are at increased risk of severe illness. (*Strong NACI recommendation*)**

    - This recommendation predates guidance issued in the fall of 2022. The individuals identified above who have not yet received any booster dose should receive one.

4) **All adults 65 years of age and older, and individuals 5 to 64 years of age who are at increased risk of severe illness from COVID-19 should have received a booster dose since the start of fall 2022. For individuals who have not yet received the fall 2022 booster dose, it should be offered, as per the recommended intervals (see recommendation #7). (*Strong NACI recommendation*)**

    - Individuals 12 years of age and older who are considered at increased risk of severe illness from COVID-19 include those with underlying medical conditions (including those who are moderately to severely immunocompromised and who therefore received a three-dose primary series), and racialized and marginalized populations who have been disproportionately affected due to a number of intersecting factors. Other groups considered at increased risk are identified in NACI's Interim guidance on planning considerations for a fall 2022 COVID-19 vaccine booster program in Canada.
    - There is limited evidence on clinical risk factors for severe COVID-19 disease in pediatric populations younger than 12 years of age. Children at increased risk for severe outcomes may include children: with obesity, who are medically fragile/have medical complexities, who have more than one comorbidity or neurological disorders, or who have Down syndrome or immunocompromising conditions.

5) **In addition, a booster dose may be offered to individuals 5 to 64 years of age without risk factors for severe illness from COVID-19 if one has not already been received since the start of fall 2022. For individuals who have not yet received a fall 2022 booster dose, it may be offered, as per the recommended intervals (see recommendation #7). (*Discretionary NACI recommendation*)**

6) **There are no authorized booster dose products for children 6 months to under 5 years of age at this time. NACI has not issued recommendations on booster doses for this age group.**

7) **When COVID-19 booster doses are offered, they should be provided using the recommended interval of 6 or more months since the previous COVID-19 vaccine dose or SARS-CoV-2 infection (whichever is later), as more time between exposures to vaccine or infection may result in a better immune response.**

8) **Bivalent Omicron-containing mRNA COVID-19 vaccines are the preferred booster products for all individuals 5 years of age and older.**

    - Since October 2022, NACI has recommended that bivalent Omicron-containing mRNA COVID-19 vaccines are the preferred booster products for the authorized age groups (at the time, the bivalent vaccine was authorized for individuals 12 years of age and older). This authorization was expanded to all individuals 5 years of age and older following Health Canada's authorization of the bivalent Pfizer-BioNTech Comirnaty mRNA 10 microgram product for children 5 to 11 years of age in December 2022.

    - The first booster dose program for children 5 to 11 years of age coincided with the fall booster dose campaign that targeted individuals 12 years of age and older. To integrate booster dose guidance for both of these age groups, current booster dose recommendations for individuals 5 years of age and older are summarized in Table 1. Children 5 to 11 years of age are recommended to receive only one booster dose at this time. However, at the provider's discretion, an additional booster dose using the bivalent vaccine (as per the recommended interval – see recommendation #7) could be offered to children considered at high risk of severe COVID-19 who have previously received a fall booster dose with the original Pfizer-BioNTech Comirnaty mRNA vaccine.

Table 1. Summary table of mRNA COVID-19 vaccine recommendations by age group

Population by age	NACI Recommendation	
	Primary Series	**Booster Dose(s)[a,b]**
Adults 65 years of age and older	Should be offered[c]	At least one booster dose continues to be recommended for all adults 18 years of age and over. Regardless of previous booster doses, a booster since the start of fall 2022 should be offered as per the recommended interval[b] if not already received.

Adults 18 to 64 years of age	Should be offered[c]	***Those at increased risk for severe illness from COVID-19:*** At least one booster dose continues to be recommended for all adults 18 years of age and over. Regardless of previous booster doses, a booster since the start of fall 2022 should be offered as per the recommended interval[b] if not already received. ***Those NOT at increased risk for severe illness from COVID-19:*** At least one booster dose continues to be recommended for all adults 18 years of age and over. A booster since the start of fall 2022 may be offered as per the recommended interval[b] if not already received.
Adolescents 12 to 17 years of age	Should be offered[c]	***Those at increased risk for severe illness from COVID-19:*** At least one booster dose continues to be recommended for adolescents 12 to 17 years of age who are at increased risk of severe illness from COVID-19. Regardless of previous booster doses, a booster since the start of fall 2022 should be offered as per the recommended interval[b] if not already received[d]. ***Those NOT at increased risk for severe illness from COVID-19:*** A booster since the start of fall 2022 may be offered as per the recommended interval[b] if not already received.
Children 5 to 11 years of age	Should be offered[c]	***Those at increased risk for severe illness from COVID-19:*** A booster since the start of fall 2022 should be offered as per the recommended interval[b] if not already received[d].

		Those NOT at increased risk for severe illness from COVID-19: A booster since the start of fall 2022 may be offered as per the recommended interval[b] if not already received.
Children 6 months to less than 5 years of age	May be offered[c]	No authorized product; not recommended

a. Bivalent Omicron-containing products are preferred for booster doses for the authorized ages.
b. The recommended interval between the previous COVID-19 vaccine dose (previous booster or completion of the primary series) and a booster dose is 6 months, and between infection and a booster dose is 6 months (whichever is longer). A shorter interval of at least 3 months may be considered in the context of heightened epidemiologic risk, evolving SARS-COV-2 epidemiology, as well as operational considerations for efficient deployment.
c. Those who are moderately to severely immunocompromised are recommended to receive an additional dose in the primary series.
d. Children 5 to 11 years of age who already received a booster dose with an original COVID-19 mRNA vaccine are not recommended to receive a bivalent Omicron-containing booster. However, at the provider's discretion, a bivalent booster dose (as per the recommended interval[b]) could be offered to children considered at high risk of severe COVID-19 who have previously received a booster dose with the original Pfizer-BioNTech Comirnaty mRNA vaccine.

Additional details are available in the COVID-19 vaccine chapter in the Canadian Immunization Guide and NACI statements and publications.

Considerations regarding potential future booster programs and planning

With the inherent uncertainties around the evolution of the pandemic, it is unclear when the need for additional COVID-19 vaccine booster doses will arise, or to whom booster doses should be offered in the event that they are needed. NACI will continue to monitor the evidence, including SARS-CoV-2 epidemiology and duration of vaccine protection, particularly with regard to severe outcomes, in the coming months to provide recommendations on the timing of subsequent booster doses if warranted. Product options for booster doses could include additional vaccines as they become available.

There are a number of options for the timing of possible future booster doses if additional booster doses are required, and these include the following:

- Offer additional booster doses at a fixed interval from the previous booster dose
- Offer additional booster doses at fixed time(s) of year
- Offer additional booster doses based on evolving epidemiology
- Some combination of the above

In addition to monitoring epidemiology, duration of protection from current booster doses and previous infection, safety, immunogenicity, and vaccine effectiveness of bivalent Omicron-containing vaccines or alternative vaccine products, future booster dose decisions should consider ethics, equity, and acceptability of future booster dose recommendations in addition to feasibility considerations of delivering booster dose campaigns. NACI acknowledges that significant preparations occur every year for the seasonal influenza campaign and will endeavour to provide further advice to inform the potential integration of COVID-19 immunization in advance of the fall of 2023.

RESEARCH PRIORITIES

1. Continuous monitoring of data on the safety, immunogenicity, efficacy, and effectiveness of COVID-19 vaccines, including booster doses, through clinical trials and studies in real-world settings, including the degree and duration of protection conferred by each booster dose against circulating variants. The research should also consider the clinical implications of previous SARS-CoV-2 infection; repeated immunization; and outcomes after any infection such as MIS-C, post-COVID-19 condition/post-acute COVID syndrome (long COVID), or infection-induced myocarditis or pericarditis in adult, adolescent, and pediatric populations.
2. Further evaluations of the optimal interval between dose administration, as well as further evaluations of the optimal interval between previous SARS-CoV-2 infection and vaccine dose administration.
3. Vigilant monitoring and reporting of adverse events of special interest, including myocarditis and/or pericarditis, in order to accurately inform potential risks associated with any future booster doses. Global collaboration should be prioritized to enable data sharing so decision makers around the world can weigh benefits and risks of additional booster doses of COVID-19 vaccines.
4. Continuous monitoring of COVID-19 epidemiology and VE in special populations at high risk of severe outcomes or long-term consequences of infection with COVID-19.
5. Further evaluation on the optimal timing and trigger for the initiation of potential future booster dose recommendations, as well as evaluation of potential risks associated with providing booster doses earlier than necessary.
6. Continuous monitoring of vaccine coverage in Canada, for COVID-19 vaccines and other routine vaccines, particularly in the context of COVID-19 vaccine booster doses and including consideration of measures that may reduce the risk of disparities in vaccine confidence and uptake across different sub-populations.

Table 2. Strength of NACI Recommendations

Strength of NACI Recommendation *based on factors not isolated to strength of evidence* (e.g., public health need)	**Strong**	**Discretionary**
Wording	"***should/should not be*** offered"	"***may/may not be*** offered"
Rationale	Known/anticipated advantages outweigh known/anticipated disadvantages ("should"), **OR** Known/Anticipated disadvantages outweigh known/anticipated advantages ("should not")	Known/anticipated advantages are closely balanced with known/anticipated disadvantages, **OR** uncertainty in the evidence of advantages and disadvantages exists
Implication	A strong recommendation applies to most populations/individuals and should be followed unless a clear and compelling rationale for an alternative approach is present.	A discretionary recommendation may be considered for some populations/individuals in some circumstances. Alternative approaches may be reasonable.

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