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

Updated guidance on the use of COVID-19 vaccines in individuals who have not previously been vaccinated against COVID-19

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Mise à jour des directives sur l'utilisation des vaccins contre la COVID-19 chez les personnes qui n'ont pas été vaccinées auparavant contre la COVID-19

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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 8programmatic 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

On September 12 and 28, 2023, Health Canada authorized XBB.1.5-containing mRNA COVID-19 vaccine products (Moderna Spikevax XBB.1.5 and Pfizer-BioNTech Comirnaty Omicron XBB.1.5 respectively) for use in individuals 6 months of age and older (see Table 1 for authorized products). The updated COVID-19 vaccine has been authorized for use in those who have never previously received a COVID-19 vaccine (also referred to as a "primary series"), and those who have previously been vaccinated with any COVID-19 vaccines.

Interim guidance on the use of bivalent Omicron-containing COVID-19 vaccines for primary series was provided in June 2023. In the NACI Addendum to the guidance on the use of COVID-19 vaccines in the fall of 2023 issued in September 2023, NACI acknowledged the use of the XBB.1.5 formulations and provided interim guidance on the use of the XBB.1.5-containing vaccines as a primary series for those who had never been vaccinated with a COVID-19 vaccine or were only partially vaccinated, with further advice to follow. The complete additional advice is provided in this October 2023 statement.

Since 2022, NACI has strongly recommended a primary series of mRNA COVID-19 vaccination for everyone 5 years of age and older, with a discretionary recommendation for children 6 months to under 5 years of age. With the recent changes to the vaccine schedules for the XBB.1.5-containing COVID-19 vaccines as outlined in the product monographs, NACI is updating its guidance on the use of COVID-19 vaccines for individuals who have not been previously vaccinated.

Methods

On July 25, August 14, September 8 and 19, 2023, the NACI COVID-19 Working Group (WG) reviewed the available epidemiology and evidence on hybrid immunity, rates of myocarditis and/or pericarditis following immunization, vaccine effectiveness (VE) of bivalent vaccines, vaccine protection for moderately to severely immunocompromised individuals, and immunogenicity of XBB.1.5-containing vaccines compared to earlier formulations.

On September 28, 2023, NACI reviewed the evidence presented to the COVID-19 WG, reached consensus on proposed recommendations, and approved the Statement on October 20, 2023. An early briefing on the recommendations was provided by NACI to provinces and territories on October 5, 2023 in order to facilitate rollout of the new vaccine products.

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

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

Overview of Evidence

Information available as of September 19, 2023 is summarized below.

Epidemiology

- Recombinant XBB* sub-lineages of SARS-CoV-2 continue to circulate in Canada and globally. From sequencing data up to the week of September 17, 2023, EG.5* and other XBB* sub-lineages comprised nearly all positive cases sampled across Canada [3].
- Seroepidemiologic studies have demonstrated high levels of infection-acquired seroprevalence in the Canadian adult population, which decreases with increased age, with older individuals having higher levels of immunity derived from vaccination alone. There have been fewer seroepidemiologic studies in the pediatric population, but Canadian studies have shown that seroprevalence due to infection is lowest in children under 2 years of age and increases with increasing age [4-9].
- Evidence on risk factors for severe COVID-19 illness in children is limited given the much lower incidence of severe outcomes (e.g., hospitalizations, ICU admissions and deaths) of COVID-19 among children overall.

Vaccine protection

- Hybrid immunity results from ≥1 exposure(s) from vaccination and ≥1 exposure(s) from SARS-CoV-2 infection (before or after vaccination). Earlier NACI statements have summarized evidence demonstrating that previous infection and vaccination may provide superior protection against variants of concern, including Omicron, compared with vaccination alone, or previous SARS-CoV-2 infection without vaccination [10-18].
- Individuals vaccinated with the updated XBB.1.5-containing COVID-19 vaccines are expected to benefit from a better immune response against currently circulating strains compared to earlier formulations, based on clinical data suggesting cross-neutralization from the XBB.1.5-containing vaccines against newer circulating variants that are descendants of the XBB lineage.

Vaccine protection in individuals with moderately to severely immunocompromising conditions

- Individuals with immunocompromising conditions, including those receiving immunosuppressive therapy, are at increased risk for prolonged infection, serious complications from SARS-CoV-2 infection and reduced immune responses to vaccination. Numerous studies have shown that immunogenicity after a 2-dose primary series with original SARS-CoV-2 vaccines is substantially decreased in some individuals with immunocompromising conditions when compared to healthy vaccine recipients, although evidence is predominately in adolescent and adult populations. Observational studies have also shown moderately lower VE against infection and COVID-19 disease in adults with immunocompromising conditions compared to the general population [19].

* Denoting inclusion of the sub-lineages in the overall lineage estimate.

- Evidence from observational studies in adults with or without previous SARS-CoV-2 infection who received an additional dose (i.e., third dose) after a 2-dose primary series indicates that humoral immune responses increase after the third dose although the degree of increase varies between studies and according to the type of immunocompromising condition or medication [19, 20]. Based on an evidence review, there is limited evidence on the VE of a single dose of COVID-19 vaccine compared to a multi-dose series in unvaccinated individuals with immunocompromising conditions with a prior history of SARS-CoV-2 infection [21].
- Indirect data from general adult populations (18 years of age and older) with original mRNA COVID-19 vaccines suggest Moderna Spikevax original (100 mcg) may result in higher VE after a 2-dose primary series compared to Pfizer-BioNTech Comirnaty original (30 mcg). Moderna Spikevax original (100 mcg) is also associated with a higher seroconversion rate and higher total antibody titres than Pfizer-BioNTech (30 mg) among adult patients who are immunocompromised [19, 22]. It is unknown whether this enhanced immunogenicity would also be observed with Moderna Spikevax XBB.1.5 compared to Pfizer-BioNTech Comirnaty Omicron XBB.1.5 at the different age-based dosages (see Table 1 for age-based dosages).

Risk of myocarditis and/or pericarditis following COVID-19 vaccination

- Evidence on myocarditis and/or pericarditis following COVID-19 vaccines continues to evolve as the vaccine schedule and dosages change over time.
- A higher rate of myocarditis and/or pericarditis cases has previously been reported nationally and internationally after primary series vaccination with Moderna Spikevax original (100 mcg) compared to Pfizer-BioNTech Comirnaty original (30 mcg) vaccine, especially among 12 to 29-year-old males following the second dose of vaccine. It is important to note that myocarditis can also occur as a complication of SARS-CoV-2 infection [23].
- Data on the risk of myocarditis and/or pericarditis after vaccination with Moderna Spikevax products at the 50 mcg dose (i.e., original+BA.1 bivalent, original+BA.4/5 bivalent) in a primary series are limited as until recently, only the 100 mcg dosage of original Moderna Spikevax has been used in the primary series in individuals 12 years of age and older [24]. While Moderna Spikevax original 50 mcg has been authorized and recommended for use as a primary series for individuals 6 to 11 years of age, the use of this vaccine in this population has been limited and data are not available to determine the risk of myocarditis and/or pericarditis in this context.
- Data with Moderna Spikevax 50 mcg used as a booster dose is available from safety surveillance systems in Canada and internationally [25]. The risk of myocarditis and/or pericarditis following a first booster dose of an original mRNA COVID-19 vaccine (Moderna Spikevax [50 mcg] and Pfizer-BioNTech [30 mcg]) in individuals 12 years of age and older is lower than the risk following the second dose of the primary series. In addition, longer intervals between doses appeared to be associated with a lower risk of myocarditis and/or pericarditis [26]. No statistically significant product-specific difference in the risk of myocarditis and/or pericarditis has been identified between booster doses of Moderna

Spikevax (50 mcg, original or bivalent) and Pfizer-BioNTech (30 mcg, original or bivalent). However, uptake of booster doses has been low in younger age groups. NACI removed any product preferences for its booster dose recommendations in adolescents and young adults in the fall of 2022.

- There are no data on the risk of myocarditis and/or pericarditis following the monovalent XBB.1.5-containing COVID-19 vaccines at this time. NACI will continue to monitor the safety and effectiveness of COVID-19 vaccines and will update recommendations as needed.

Ethics, equity, feasibility, and acceptability (EEFA)

- NACI continues to simplify and streamline the COVID-19 vaccine recommendations to facilitate the implementation of vaccine programs and ease of communication for both provincial and territorial vaccination programs and individual health care providers.
- Lower parental acceptability for pediatric COVID-19 vaccines (as compared with adult acceptability) has been observed. While most children may have mild or no symptoms, some may still experience severe disease due to COVID-19 and some can develop post-COVID-19 condition. Young children will continue to become eligible for the COVID-19 vaccine program at 6 months of age and are more likely to be SARS-CoV-2 naïve than older children. A better understanding of risk factors for severe disease in young children in the context of more recent SARS-CoV-2 variants and prior infection is needed [27].

Recommendations

Please see Table 4 for an explanation of strong versus discretionary NACI recommendations.

For individuals 5 years of age and older who are previously unvaccinated:

1. **NACI recommends that individuals 5 years of age and older who are previously unvaccinated against COVID-19 should be vaccinated. The latest formulations of mRNA COVID-19 vaccines are recommended. (*Strong NACI Recommendation)***
   - 1 dose is recommended as per the authorized schedule in the product monograph. An additional dose is recommended for individuals who are moderately to severely immunocompromised (see Recommendation #4).
   - For the number of doses and schedules, see Table 2 for those not previously vaccinated and Table 3 for those who started a primary series with a non-XBB.1.5 vaccine.

   Considerations:

   - The latest formulations of Health Canada authorized mRNA COVID-19 vaccines available as of fall 2023 are monovalent XBB.1.5, with vaccine products from Moderna (Spikevax) and Pfizer-BioNTech (Comirnaty). See Tables 1 and 2 for dosages.
   - The recommendations for those 5 years of age and older take into account the high levels of seroprevalence due to infection in the population at this time.

- There is no longer a product preference between Moderna Spikevax and Pfizer-BioNTech Comirnaty with the use of XBB.1.5-containing COVID-19 vaccines for unvaccinated individuals 12 to 29 years of age. Please see "Additional considerations" for more information.
- The reduced dose schedule for unvaccinated individuals 5 years of age and older is applied going forward for those receiving the XBB.1.5-containing COVID-19 vaccine as their first dose.
    - Individuals 5 year of age and older who started a primary series with earlier formulations (i.e., original monovalent, original+BA.1 bivalent or original+BA.4/5 bivalent) but did not complete the series are recommended to complete the series with an XBB.1.5-containing vaccine based on the total number doses previously recommended (i.e., they should receive a total of 2 COVID-19 vaccine doses in the primary series if not immunocompromised and 3 doses in the primary series if they are moderately to severely immunocompromised). See Table 3.

For children 6 months to under 5 years of age who are previously unvaccinated:

2. **NACI recommends that children 6 months to under 5 years of age who are previously unvaccinated against COVID-19 and who are at high risk of severe illness due to COVID-19 should be vaccinated. The latest formulations of mRNA COVID-19 vaccines are recommended. (*Strong NACI Recommendation)***

3. **NACI recommends that children 6 months to under 5 years of age who are previously unvaccinated against COVID-19 and who are not known to be at high risk of severe illness due to COVID-19 may be vaccinated. The latest formulations of mRNA COVID-19 vaccines are recommended. (*Discretionary NACI Recommendation*)**

    - Risk factors for severe illness due to COVID-19: There is limited evidence on clinical risk factors for severe COVID-19 disease in pediatric populations. Children at increased risk for severe outcomes may include children who are medically fragile/have medical complexities, children with more than one comorbidity, children with neurological disorders, children with chronic lung disease, and children with Down syndrome (Trisomy 21), and other immunocompromising conditions.
    - 2 doses of Moderna Spikevax or 3 doses of Pfizer-BioNTech Comirnaty are recommended, with an 8-week interval between doses. An additional dose is recommended for individuals who are moderately to severely immunocompromised (see Recommendation #4).
    - For the number of doses and schedules, see Table 2 for those not previously vaccinated and Table 3 for those who started a primary series with a non-XBB.1.5 vaccine.

    Considerations:

- The latest formulations of Health Canada authorized mRNA vaccines available as of fall 2023 are monovalent XBB.1.5, with vaccine products from Moderna (Spikevax) and Pfizer-BioNTech (Comirnaty). See Tables 1 and 2 for dosages.
- A mixed product schedule using vaccines from different manufacturers can be offered for the primary series; however, if both Pfizer-BioNTech Comirnaty and Moderna Spikevax vaccine products are used in the same primary series for an individual 6 months to under 5 years of age, the total number of doses in the series should follow the Pfizer-BioNTech Comirnaty schedule (see Table 3).
- If children 6 months to under 5 years of age started the primary series with a non-XBB.1.5 vaccine but did not complete the series, they should complete the primary series with an XBB.1.5-containing vaccine (see Table 3).
- Children who started the primary series at less than 5 years of age and turn 5 years of age before completing the series, should receive the number of XBB.1.5 vaccine doses recommended as per Table 3 for those 5 years of age and older and using the age-appropriate dosage for their current age.

For individuals 6 months of age and older who are moderately to severely immunocompromised and are previously unvaccinated:

4. **NACI recommends that individuals 6 months of age and older who are previously unvaccinated and are moderately to severely immunocompromised should receive an additional dose of COVID-19 vaccine above the number of doses recommended for those who are not immunocompromised. (*Strong NACI Recommendation*)**

- For individuals **6 months to under 5 years of age who are moderately to severely immunocompromised**, NACI recommends a schedule consisting of 3 doses of Moderna Spikevax (preferred) or 4 doses of Pfizer-BioNTech Comirnaty, with a 4- to 8-week interval between doses. **Product preference** for children 6 months to under 5 years of age who are moderately to severely immunocompromised: 3 doses of the Moderna Spikevax (25 mcg) vaccine is preferred over 4 doses of Pfizer-BioNTech Comirnaty (3 mcg) because there is likely higher acceptability and more feasible implementation due to fewer doses in the schedule using Moderna Spikevax.
- For individuals **5 years of age and older who are moderately to severely immunocompromised**, 2 doses are recommended by NACI, with a 4- to 8-week interval between doses.
    - The reduced dose schedule for unvaccinated individuals 5 years of age and older is applied going forward for those receiving the XBB.1.5-containing COVID-19 vaccine as their first dose.
    - If the primary series was started with non-XBB1.5 COVID-19 vaccine(s) but the series was not completed, those 5 years of age and older who are moderately to severely immunocompromised are recommended to receive a total of 3 doses of COVID-19 vaccines for the primary series (see Table 3).

- For the number of doses and schedules, see Table 2 for those not previously vaccinated and Table 3 for those who started a primary series with a non-XBB.1.5 vaccine.
- For more information on individuals with moderately to severely immunocompromising conditions, please see the COVID-19 Vaccine Chapter in the CIG.

Additional considerations for all populations

- Individuals whose primary series includes the XBB.1.5-containing COVID-19 vaccine do not require further doses at this time once the series is complete.
- Previously, Pfizer-BioNTech Comirnaty had been preferred over Moderna Spikevax for the primary series among individuals 12 and 29 years of age due to the higher risk of myocarditis and/or pericarditis observed following the Moderna Spikevax 100 mcg original monovalent vaccine primary series (especially after the second dose). However, this product preference is no longer being recommended. Compared to the original monovalent primary series, the risk of myocarditis and/or pericarditis is now expected to be lower due to the use of a 1-dose schedule in most individuals and potentially due to a lower dosage of the available Moderna Spikevax vaccine (50 mcg in the XBB.1.5 formulation compared to 100 mcg in the original monovalent formulation).
    - All vaccine recipients should be informed and counselled on the rare risk of myocarditis and/or pericarditis following COVID-19 vaccination, regardless of the product received.
- Individuals will likely be unaware of their recent infection status as testing is no longer widespread and many individuals, particularly children, may experience mild or no symptoms. Those who do have a known recent SARS-CoV-2 infection who are not previously vaccinated or have not completed a primary series may consider delaying COVID-19 vaccination by 8 weeks if the individual is not moderately to severely immunocompromised, or by 4 to 8 weeks if the individual is moderately to severely immunocompromised. These suggested intervals serve as a guide and are based on immunological principles and expert opinion and may change as evidence emerges. Clinical discretion is advised for immunizers.
- For individuals who have previously been vaccinated with a complete primary series that did not include an XBB.1.5-containing COVID-19 vaccine, a dose of XBB.1.5-containing COVID-19 vaccine is recommended 6 months following previous COVID-19 vaccination or SARS-CoV-2 infection (whichever is later). Shorter intervals (i.e., 3 months to less than 6 months) following previous vaccination or infection have also not been shown to pose a safety risk. (See Table 3)
- A submission for Novavax Nuvaxovid containing XBB.1.5 is currently being reviewed by Health Canada. NACI will review the use of the Novavax Nuvaxovid vaccine in light of the updated recommendations for individuals who have never received a COVID-19 vaccine when more information becomes available.
- NACI will continue to monitor the evidence, including SARS-CoV-2 epidemiology and duration of vaccine protection, particularly with regard to severe outcomes, to provide recommendations on the timing of subsequent doses if warranted.

Table 1. Summary of available XBB.1.5-containing mRNA COVID-19 products by age

Moderna Spikevax XBB.1.5				
Age group	**Dosage (volume)**	**Description**	**Dilution required**	**Number of doses per vial**
6 months to under 12 years	25 mcg (0.25 ml)	0.1 mcg / mL cap color: royal blue: label color: coral blue	No	10 doses
12 years of age and older	50 mcg (0.5 ml)			5 doses
Pfizer- BioNTech Comirnaty Omicron XBB.1.5				
Age group	**Dosage (volume)**	**Description**	**Dilution required**	**Number of doses per vial**
6 months to under 5 years	3 mcg (0.2 ml)	Cap and label colour: maroon	Yes (with 2.2 mL sterile 0.9% Sodium Chloride)	10 doses after dilution
5 years to under 12 years	10 mcg (0.3 ml)	Cap and label colour: blue	No	6 doses
12 years of age and older	30 mcg (0.3 ml)	Cap and label colour: grey	No	6 doses

See product monographs for Moderna Spikevax XBB.1.5 and Pfizer-BioNTech Comirnaty Omicron XBB.1.5 for storage and handling requirements.

Table 2. Immunization schedule for previously unvaccinated individuals by age starting their vaccinations with XBB.1.5-containing mRNA COVID-19 vaccines

Age group	Immunization schedule [a]	Products	Recommended interval [b]
Schedule for those not moderately or severely immunocompromised			
6 months to under 5 years of age	• 2-dose (Moderna Spikevax) or • 3-dose (Pfizer-BioNTech Comirnaty)	• 25 mcg Moderna Spikevax • 3 mcg Pfizer-BioNTech Comirnaty	8 weeks
5 years of age and older	• 1-dose	Moderna Spikevax • 25 mcg (5 to less than 12 years) • 50 mcg (12 years of age and older) Pfizer-BioNTech Comirnaty • 10 mcg (5 to less than 12 years) • 30 mcg (12 years of age and older)	Not applicable
Schedule for individuals who are moderately to severely immunocompromised			
6 months to under 5 years of age	• 3-dose (Moderna Spikevax) [c] or • 4-dose (Pfizer-BioNTech Comirnaty)	As above	4 to 8 weeks

5 years of age and older	• 2-dose		4 to 8 weeks

[a] See "Considerations" and Table 3 regarding individuals who started but did not complete a primary series with a vaccine that was not an XBB.1.5 formulation.
[b] For individuals with recent SARS-CoV-2 infection, these are also the suggested intervals between SARS-COV-2 infection and COVID-19 vaccination (see "Additional considerations" section).
[c] Moderna Spikevax is the preferred product in children 6 months to under 5 years of age who are moderately to severely immunocompromised due to acceptability and feasibility considerations of only requiring 3 doses instead of 4 doses for Pfizer-BioNTech Comirnaty.

Table 3. Summary of number of recommended XBB.1.5-containing mRNA COVID-19 vaccine doses based on previous non-XBB.1.5 vaccination history (i.e., previously received original monovalent or original+BA.1 bivalent or original+BA.4/5 bivalent vaccines [non-XBB.1.5])[a]

Age	Previous vaccination with only non-XBB.1.5-containing mRNA COVID-19 vaccines	Number of doses and interval of XBB.1.5-containing mRNA COVID-19 vaccines to be administered	
		Moderna Spikevax XBB.1.5 schedule **Note for the primary series for children 6 months to under 5 years of age:** Follow this column if all past vaccine doses have been Moderna Spikevax vaccines and now also administering Moderna Spikevax XBB.1.5	**Pfizer-BioNTech Comirnaty Omicron XBB.1.5 schedule** **Note for the primary series for children 6 months to under 5 years of age:** Follow this column if now administering Pfizer-BioNTech Comirnaty Omicron XBB.1.5, or if one or more past vaccine doses have been Pfizer-BioNTech Comirnaty vaccines (whether giving Pfizer-BioNTech Comirnaty Omicron XBB.1.5 or Moderna Spikevax XBB.1.5 now).
For those NOT moderately to severely immunocompromised			
6 months to under 5 years [b]	**3 or more doses**	*See 2 or more doses*	**1 dose** **6 months** from last dose Shorter intervals (i.e., 3 months to less than 6 months) have also not been shown to pose a safety risk.
	2 or more doses	**1 dose** **6 months** from last dose Shorter intervals (i.e., 3 months to less than 6 months) have also not been shown to pose a safety risk.	*See 2 doses or 3 or more doses, as applicable*
	2 doses	*See 2 or more doses*	**1 dose** **8 weeks** from last dose
	1 dose	**1 dose** **8 weeks** from last dose	**2 doses** **8 weeks** from last dose and between doses
5 years of age and older	**2 or more doses**	**1 dose** **6 months** from last dose Shorter intervals (i.e., 3 months to less than 6 months) have also not been shown to pose a safety risk.	**1 dose** **6 months** from last dose Shorter intervals (i.e., 3 months to less than 6 months) have also not been shown to pose a safety risk.

	1 dose	**1 dose** **8 weeks** from last dose	**1 dose** **8 weeks** from last dose
For those who ARE moderately to severely immunocompromised			
6 months to under 5 years [c]	**4 or more doses**	*See 3 or more doses*	**1 dose** **6 months** from last dose Shorter intervals (i.e., 3 months to less than 6 months) have also not been shown to pose a safety risk.
	3 or more doses	**1 dose** **6 months** from last dose Shorter intervals (i.e., 3 months to less than 6 months) have also not been shown to pose a safety risk.	*See 3 doses or 4 or more doses, as applicable*
	3 doses	*See 3 or more doses*	**1 dose** **4 to 8 weeks** from last dose
	2 doses	**1 dose** **4 to 8 weeks** from last dose Moderna is preferred [c]	**2 doses** **4 to 8 weeks** from last dose and between doses
	1 dose	**2 doses** **4 to 8 weeks** from last dose and between doses Moderna is preferred [c]	**3 doses** **4 to 8 weeks** from last dose and between doses
5 years of age and older [d]	**3 or more doses**	**1 dose** **6 months** from last dose Shorter intervals (i.e., 3 months to less than 6 months) have also not been shown to pose a safety risk.	**1 dose** **6 months** from last dose [e] Shorter intervals (i.e., 3 months to less than 6 months) have also not been shown to pose a safety risk.
	2 doses	**1 dose** **4 to 8 weeks** from last dose	**1 dose** [e] **4 to 8 weeks** from last dose
	1 dose	**2 doses** **4 to 8 weeks** from last dose and between doses	**2 doses** **4 to 8 weeks** from last dose and between doses

[a] Further details on the recommendations on the use of the XBB.1.5-containing COVID-19 vaccines in previously vaccinated individuals are available in the NACI Guidance on the use of COVID-19 vaccines in the fall of 2023 and the subsequent Addendum.

[b] Children 6 months to under 5 years of age who are at high risk for severe illness due to COVID-19 should be vaccinated against COVID-19 and other children in this age group may be vaccinated.

[c] For those 6 months to under 5 years of age who are moderately to severely immunocompromised, Moderna Spikevax is preferred because it requires only 3 doses, while Pfizer-BioNTech Comirnaty requires 4 doses.

[d] If the primary series was started with non-XBB1.5 COVID-19 vaccine(s), those 5 years of age and older who are moderately to severely immunocompromised are recommended to receive a total of 3 doses of COVID-19 vaccines for the primary series.

[e] Children who are moderately to severely immunocompromised and started their primary series with 2 or 3 doses of a non-XBB.1.5 Pfizer-BioNTech product (not the preferred product) when they were less than 5 years of age and are completing their primary series at 5 years of age or older, are recommended to receive a total of 4 doses of COVID-19 vaccine in their primary series (i.e., an additional dose of XBB.1.5-containing vaccine than what is listed in this cell, at 4 to 8 weeks from the previous dose).

Table 4. Strength of NACI Recommendations

Strength of NACI Recommendation	STRONG	DISCRETIONARY

based on factors not isolated to strength of evidence (e.g., public health need)		
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.

Research priorities

- Continuous monitoring of data on the safety, immunogenicity, efficacy, and effectiveness of COVID-19 vaccines, including with the new formulations, through clinical trials and studies in real-world settings, including the degree and duration of protection conferred against circulating variants. The research should also consider the clinical implications of previous SARS-CoV-2 infection; repeated immunization; and outcomes after infection such as post-COVID-19 condition.
- Further evaluations of the optimal interval between dose administration in children and adults, as well as further evaluations of the optimal interval between previous SARS-CoV-2 infection and vaccine dose administration.
- Continuous monitoring of COVID-19 epidemiology in children, including risk factors for severe outcomes and long-term consequences of infection with SARS-CoV-2, especially in the context of prior infection, prior vaccination and new SARS-CoV-2 variants.
- Continuous monitoring of COVID-19 epidemiology and VE in special populations at high risk of severe outcomes and on the long-term consequences of infection with SARS-CoV-2.
- Further evaluations on the safety, immunogenicity, and effectiveness on the concurrent administration of COVID-19 vaccines with other vaccines across different age groups, including concurrent administration with high-dose or adjuvanted influenza vaccine.
- Continuous monitoring of vaccine coverage in Canada, for COVID-19 vaccines and other routine vaccines, including consideration of measures that may reduce the risk of disparities in vaccine confidence and uptake across different sub-populations.
- Continuous monitoring of the epidemiology of COVID-19, including SARS-CoV-2 variants and seasonal trends, to inform future programs.

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