

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

Interim guidance on the use of bivalent Omicron-
containing COVID-19 vaccines for primary series

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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

Bivalent Omicron-containing mRNA COVID-19 vaccines are authorized as booster doses for those 5 years of age and older, but there is currently no bivalent vaccine authorized for a primary series in any age group or as a booster dose for those less than 5 years of age. Several regulatory submissions for the use of bivalent mRNA COVID-19 vaccines as a primary series are currently under review by Health Canada. Many original monovalent mRNA vaccines will no longer be available in the coming months, and PHAC has asked NACI to consider how jurisdictions can ensure COVID-19 product options for the primary series are available to all recommended populations. This includes consideration of off-label use of bivalent vaccines using age-based dosages that are different from those currently authorized for the primary series with the original mRNA COVID-19 vaccines. As regulatory submissions progress over the summer, vaccine schedules and/or dosages may change for some age groups. New formulations of COVID-19 vaccines that reflect changes in circulating Omicron subvariants may also become available in the fall of 2023.

Bivalent Omicron-containing mRNA COVID-19 vaccines have been recommended to be used as booster doses in Canada since September 1, 2022, when NACI published initial recommendations on their use. Currently, bivalent Omicron-containing vaccines are authorized as booster doses for individuals 5 years of age and older and NACI's recommendations cite a preference for their use over original mRNA vaccines for booster doses. For more information on COVID-19 booster doses, please refer to the [COVID-19 chapter](#) of the Canadian Immunization Guide (CIG).

Since the initial authorization and recommendations of bivalent Omicron-containing COVID-19 vaccine booster doses:

- Although there are some fluctuations in COVID-19 transmission indicators (i.e., cases reported, hospitalizations, and deaths) and variations across provinces and territories, COVID-19 activity has been relatively stable with hospitalizations remaining at a relatively high level since the widespread circulation of Omicron in early 2022, with the highest hospitalization rates among older adults.
- Additional evidence has emerged on the performance and safety of bivalent vaccines as booster doses.
- Some limited direct evidence is now available on the use of bivalent Omicron-containing vaccines for the primary series.

NACI continues to monitor the rapidly evolving scientific data recognizing that the trajectory of the COVID-19 pandemic remains unclear.

NACI's recommendations remain aligned with the goals of the Canadian COVID-19 Pandemic Response that were last updated on [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

Methods

On January 10, January 31, and April 4, 2023, the NACI COVID-19 Working Group (WG) reviewed the available epidemiology and evidence on vaccine safety and protection, including clinical trial results on bivalent Omicron-containing vaccines as the primary series and real-world evidence on bivalent Omicron-containing vaccines as booster doses. NACI also conducted an in-depth ethical analysis on this topic informed by the framework outlined by the Public Health Ethics Consultative Group (PHECG) ^(1, 2). Equity, feasibility and acceptability factors were also considered according to NACI's published, peer-reviewed framework and evidence-informed tools to support systematic assessment of ethics, equity, feasibility, and acceptability (EEFA) ⁽²⁾. On January 23, February 6, 7 and April 28 2023, NACI reviewed the evidence presented to the COVID-19 WG and approved these recommendations on May 29, 2023.

These recommendations are interim and were made considering only the currently available bivalent Omicron-containing vaccines, which are not authorized for use as a primary series. Future recommendations will consider new product options as regulatory decisions are made.

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)

Further information on NACI's process and procedures is available elsewhere ^(2, 3).

Overview of Evidence

Information available as of May 11, 2023 is summarized below.

Evolving epidemiology

- The evolutionary trajectory of SARS-CoV-2, including the emergence of novel variants of concern (VOCs), remains uncertain ^(4, 5).
- Omicron XBB1.5 sub-lineage is currently the dominant strain circulating in Canada and has gradually replaced the previously dominant BA.5-related sub-lineages (e.g., BQ.1 and BQ.1.1) ⁽⁶⁾. New XBB recombinant strains, such as XBB.1.16 and XBB.1.9, are also increasing nationally ⁽⁶⁾.
- Omicron is antigenically and genomically quite different from previous VOCs and hence is able to partially evade the immune response induced by COVID-19 vaccines formulated with only original SARS-CoV-2 and also previous pre-Omicron infections. Recently circulating sub-lineages of Omicron (e.g., BQ*, XBB*) are more immune evasive than previous Omicron sub-lineages (e.g., BA.2, BA.4/5) based on the ability of recent sub-lineages to more efficiently evade neutralizing antibodies elicited from vaccination and past infection ^(5, 7-13).
- Rates of hospitalizations and deaths in Canada continue to be highest for adults 60 years of age and older, with risk increasing with age and highest among those 80 years of age and older and those who are unvaccinated, and lowest for those recently vaccinated and those with hybrid immunity, particularly if the previous infection was with an Omicron strain ⁽¹⁴⁻¹⁶⁾.

- Seroepidemiologic studies demonstrate high levels of antibodies due to infection in the Canadian population overall (76.9%; 95% credible interval: 70.2 to 82.8%), with the estimates of seropositivity due to infection decreasing with increasing age⁽¹⁷⁾.
- The proportion of individuals who have completed the primary series for COVID-19 is high in Canada among individuals 12 years of age and older (>85%). Uptake for the primary series has been low among children 5 to 11 years of age and 0 to 4 years of age (approximately 40% and 6% respectively)⁽¹⁸⁾.
- In Canada, hybrid immunity (resulting from ≥ 1 exposure(s) from vaccination and ≥ 1 exposure(s) from SARS-CoV-2 infection) also 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.

Summary of evidence on bivalent Omicron-containing vaccines for primary series

Primary series of Moderna Spikevax bivalent BA.1 in children 6 months to 5 years of age

- The safety and immunogenicity of Moderna Spikevax bivalent BA.1 (25 mcg) as a primary series was evaluated in a Phase 3 open-label study in 179 unvaccinated children 6 months to 5 years of age. The vaccine contains equal parts (12.5 mcg each) of mRNA encoding for the spike protein of original SARS-CoV-2 and that of the Omicron BA.1 variant. Study participants were vaccinated with 2 doses 28 days apart. Neutralizing antibody responses and reactogenicity were compared to 6 month- to 5-year-old participants who had received a Moderna Spikevax original (25 mcg) primary series in an earlier study. Due to the different time frames for vaccination with each product, a substantially higher proportion of participants who received Moderna Spikevax bivalent BA.1 had serological evidence of prior SARS-CoV-2 infection compared to participants who received Moderna Spikevax original (63% vs. 8%)⁽¹⁹⁾.
- In all participants and the subset without evidence of prior SARS-CoV-2 infection, neutralizing antibody responses against BA.1 28 days after dose 2 of Moderna Spikevax bivalent BA.1 were superior compared to those after dose 2 in participants who received Moderna Spikevax original (geometric mean ratio [GMR] of titres were 25.4 [95% confidence interval (CI): 20.1 to 32.1%] in all participants and 15.8 [95% CI: 11.4 to 21.9%] in the subgroup without prior infection). In all participants, neutralizing antibody responses against original SARS-CoV-2 were non-inferior after dose 2 of Moderna Spikevax bivalent BA.1 compared to dose 2 of Moderna Spikevax original (GMR 0.83 [95% CI: 0.67 to 1.02%]). In the subgroup of participants without evidence of prior SARS-CoV-2 infection, neutralizing antibody responses against original SARS-CoV-2 did not meet non-inferiority criteria compared to responses after dose 2 of Moderna Spikevax original (GMR 0.4 [95% CI: 0.3 to 0.5%]).
- Local and systemic reactogenicity after dose 1 and dose 2 of Moderna Spikevax bivalent BA.1 (25 mcg) were similar compared to those after dose 1 and dose 2 of Moderna Spikevax original (25 mcg). In an analysis conducted for Moderna Spikevax bivalent BA.1 recipients only, the frequency of fever was higher after dose 1 for those with prior SARS-CoV-2 infection compared to those without evidence of prior SARS-CoV-2 infection (12% vs. 2%). There were no reports of vaccine-related serious adverse events, myocarditis and/or pericarditis or deaths. Given the number of participants enrolled in the trial, it is

unlikely that uncommon, rare or very rare adverse events would be detected. NACI will continue to monitor post-market safety surveillance data as it emerges.

Effectiveness and safety of bivalent Omicron-containing mRNA vaccines

- While there is currently no clinical evidence on the safety, immunogenicity or efficacy of a primary series with bivalent BA.1-containing vaccines in individuals 6 years of age and older, and no data on the use of a primary series with bivalent BA.4/5 vaccines from either manufacturer in any age group, there is evidence on the safety and protection of bivalent BA.1 and BA.4/5 vaccines when used as a booster dose in individuals 5 years of age and older that has been described in NACI's [Guidance on an additional COVID-19 booster dose in the spring of 2023 for individuals at high risk of severe illness due to COVID-19](#). Briefly:

Vaccine effectiveness

- Real-world effectiveness data from the United States (US) and Europe suggest that in children and adults, a booster dose of a bivalent BA.4/5 mRNA COVID-19 vaccine provides increased protection against infection, symptomatic disease and severe outcomes, compared to those who only received doses of original monovalent mRNA vaccines in the past ⁽²⁰⁻²⁸⁾. In some of the studies from the US, the relative vaccine effectiveness (VE) of the bivalent booster increased with increased time since the original vaccine group received their last dose, due to increased waning over time in this group. From most of these observational studies, it cannot be determined if the benefit is due to the recent receipt of a booster dose and/or specifically the receipt of a bivalent booster. For a more detailed description of some of these studies, please see NACI's [Guidance on an additional COVID-19 booster dose in the spring of 2023 for individuals at high risk of severe illness due to COVID-19](#).
- Preliminary data from Ontario demonstrate that short-term (<90 to 119 days) VE against severe outcomes in community dwelling adults 50 years of age and older was similar between those receiving original and bivalent mRNA vaccine booster doses and between the available vaccine products (Moderna Spikevax original or bivalent BA.1 and Pfizer-BioNTech Comirnaty original or bivalent BA.4/5) during a period when BA.5 was the predominant Omicron sub-lineage and BQ.1 was emerging ⁽²⁹⁾.
- In studies where bivalent Omicron-containing booster recipients were compared to those who received an original booster dose in the same time period, the protection of a bivalent booster against symptomatic disease was similar to or slightly higher than that offered by original boosters against symptomatic disease.
 - A randomized clinical trial conducted by Moderna in the United Kingdom compared those 16 years of age and older randomized to receive a bivalent BA.1 booster to those randomized to receive an original monovalent booster. Although the primary endpoint was immunogenicity, exploratory analyses revealed that the efficacy against symptomatic disease was somewhat higher for the bivalent booster than the original booster against sub-lineages BA.2 (relative VE of bivalent booster compared to original booster vaccine of 32.6%; 95% CI: -15.1 to 60.5%) and BA.4 (41.6%; 95% CI: -5.1 to 67.5%), but not against BA.5 (4.4%; 95% CI: -27.2 to 28.2%) ⁽³⁰⁾.

- A retrospective, observational study in France matched and compared those 60 years of age and older who had received a booster dose of Pfizer-BioNTech Comirnaty bivalent BA.4/5 with those who received a booster dose with an original COVID-19 vaccine (mostly Pfizer-BioNTech original) in the same time period. At a median of 77 days of follow-up, the bivalent booster offered minimal advantage over an original booster for protection against symptomatic disease (relative VE of bivalent booster compared to original booster of 8%; 95% CI: 0 to 16%). A subgroup analysis in participants without evidence of previous SARS-CoV-2 infection showed no significant difference between bivalent and original boosters (VE calculated using adjusted hazard ratio for infection was 4%; 95% CI: -6 to 12%)⁽³¹⁾.
- Preliminary data comparing bivalent BA.1 and BA.4/5 boosters are available from four Scandinavian countries using linked administrative data to evaluate the VE of original, bivalent BA.1 and bivalent BA.4/5 boosters. Bivalent BA.4/5 and BA.1 boosters (manufacturer not specified) were administered during the same time period and the bivalent BA.4/5 vaccine was associated with a somewhat lower relative risk of hospitalization compared to the bivalent BA.1 vaccine. However, this observation was based primarily on the comparative VE from Denmark. The VE estimate was not significant for Norway, and not estimable in the other two countries⁽²⁴⁾.

Safety

- Available evidence from Canada and internationally show that overall, the safety profile of the bivalent mRNA COVID-19 vaccine boosters is comparable to that of original mRNA COVID-19 vaccine boosters among individuals 5 years of age and older⁽³²⁻³⁸⁾.
- The safety profile appears to be similar in those with or without previous SARS-CoV-2 infections.
- Post-market surveillance data from Canada and the US indicates that the risk of myocarditis and/or pericarditis after mRNA COVID-19 vaccines (primary series or first booster) in children 5 to 11 years (who were predominantly vaccinated with Pfizer-BioNTech Comirnaty original [10 mcg]) is lower compared to adolescents and young adults who received Pfizer-BioNTech Comirnaty original (30 mcg) or Moderna Spikevax original (100 mcg)⁽³⁹⁻⁴¹⁾.
- A possible association between Pfizer-BioNTech Comirnaty bivalent BA.4/5 booster and ischemic stroke in persons 65 years of age and older was identified by the US Vaccine Safety Datalink (VSD) in January 2023^(42, 43). This potential safety signal has not been identified with the Moderna Spikevax bivalent BA.4/5 mRNA COVID-19 vaccine and has not been replicated in other surveillance systems used to monitor vaccine safety in the US or in other countries. To date, the totality of the US data suggests that it is very unlikely that the potential signal in VSD represents a true clinical risk⁽⁴²⁻⁴⁴⁾. This is supported by international data including from Canada, Israel, Europe, and Singapore where a similar signal has not been identified. Monitoring of the potential safety signal is ongoing. NACI will update its recommendations as needed.

Ethics, equity, feasibility, and acceptability (EEFA)

- NACI evaluated the following ethical considerations when making its recommendations: promoting well-being and minimizing risk of harm, maintaining trust, respect for persons and fostering autonomy, and promoting justice and equity. NACI considered the available

evidence on bivalent, Omicron-containing mRNA vaccines used for primary series and accumulating real-world evidence on effectiveness and safety of bivalent Omicron-containing mRNA vaccine booster doses.

- It will not be feasible to continue using original monovalent mRNA vaccines for the primary series in Canada, as the supply of most original formulations is not expected to be available beyond summer 2023.
- Streamlining of products recommended for primary series and booster doses simplifies the storage and handling required for vaccination programs and reduces the risk of vaccine administration errors.
- Primary series recommendations are particularly important for infants who age into vaccine eligibility at 6 months and are less likely to be previously infected than older children and adults, and for young children for whom vaccine uptake has been low compared to individuals 12 years of age and older.
- Given the current prevalence of Omicron sub-lineages and preferential recommendation for bivalent Omicron-containing vaccines for booster doses, those who may be hesitant to receive an original monovalent mRNA vaccine for a primary series now have another option recommended by NACI.
- Despite the limited evidence on the use of bivalent vaccines as a primary series, the precautionary principle indicates that scientific uncertainty should not prevent decision makers from taking action to reduce risks associated with COVID-19.
- Informed consent of those receiving a bivalent vaccine as a primary series and clear communication on the rationale will be important given the limited direct evidence regarding use of the bivalent vaccines for the primary series compared to original mRNA vaccines, and limited product options for children 6 months to 4 years of age for whom only a bivalent Moderna Spikevax product can be administered at the appropriate dosage. The off-label use of the bivalent products for the primary series should also be included as part of the informed consent process.
- COVID-19 vaccines have evolved over the pandemic and will continue to change as science and research progresses. Recommendations will evolve as well to ensure equitable access to products that can be used for primary series for those who are unvaccinated.

Recommendations

NACI continues to recommend that unvaccinated individuals receive a primary series of COVID-19 vaccines as recommended in the [COVID-19 vaccine chapter](#) of the Canadian Immunization Guide and current NACI [statements and publications](#). Regarding the product offered,

- 1. NACI recommends that when mRNA vaccines are used for the primary series, bivalent Omicron-containing vaccines can be used, as outlined in [Table 1](#).**
- Consistent with current NACI recommendations on vaccine interchangeability, regardless of which product is offered to start a primary series, the previous dose should be counted; the series should be continued and not restarted. If a primary series is started with an original mRNA vaccine, a bivalent Omicron-containing vaccine can be used to complete the series. If a primary series is started with a bivalent Omicron containing mRNA vaccine and the same product is not readily available to complete the series, another bivalent Omicron-containing mRNA vaccine may be used to complete the series. For more

information on interchangeability with other COVID-19 vaccines, please refer to the COVID-19 vaccine chapter in the Canadian Immunization Guide.

- The current recommendation for the primary series is for the bivalent vaccine products authorized to date, as these are the products currently available for use in Canada (see [Table 1](#) for more details). If there are changes to the authorized schedules and/or dosages or if new formulations of COVID-19 vaccines become available for the fall 2023 vaccination program, these interim recommendations will be reviewed and updated as appropriate.
- Please see the [COVID-19 chapter](#) of the Canadian Immunization Guide and [Table 1](#) for information on recommended intervals and number of doses for the primary series for the [general population](#) and individuals who are [moderately to severely immunocompromised](#).

Additional considerations and rationale

Table 1. Interim recommended bivalent Omicron-containing mRNA vaccines, dosages and schedules for primary series^a

| Population | Vaccine type and dosage | Number of doses and optimal interval for individuals who are not moderately to severely immunocompromised | Number of doses and recommended intervals for individuals who are moderately to severely immunocompromised |
|---------------------------------------|---|---|--|
| Children 6 months to 4 years of age | <ul style="list-style-type: none"> • Moderna Spikevax bivalent 25 mcg (0.25 mL)^b | 2 doses at least 8 weeks apart | 3 doses 4 to 8 weeks apart |
| Children 5 to 11 years of age | <ul style="list-style-type: none"> • Pfizer-BioNTech Comirnaty bivalent 10 mcg (0.2 mL) • Moderna Spikevax bivalent 25 mcg (0.25 mL)^c | 2 doses at least 8 weeks apart | 3 doses 4 to 8 weeks apart |
| Individuals 12 years of age and older | <ul style="list-style-type: none"> • Pfizer-BioNTech Comirnaty bivalent 30 mcg (0.3 mL) (Preferred for those 12 to 29 years of age^c) • Moderna Spikevax bivalent 50 mcg (0.5 mL)^c | 2 doses 8 weeks apart | 3 doses 4 to 8 weeks apart |

- Products referred to include Moderna Spikevax bivalent BA.1 or BA.4/5, and Pfizer-BioNTech Comirnaty bivalent BA.4/5.
- There is no bivalent Pfizer-BioNTech product available in Canada to provide an appropriate dosage (3 mcg) for children 6 months to 4 years of age.
- Individuals who are moderately to severely immunocompromised may benefit more from a primary series with Moderna Spikevax bivalent (50 mcg in ≥12 years of age and 25 mcg in 6 months to 11 years of age) compared to Pfizer-BioNTech Comirnaty bivalent BA.4/5 (30 mcg in ≥12 years of age and 10 mcg in 5 to 11 years of age).

- Omicron and its sub-lineages are antigenically distinct from the original SARS-CoV-2 virus. Recent and currently dominant strains circulating in Canada are some of the most antigenically distinct sub-lineages observed to date ^(5, 45). Exposure to diverse antigens through vaccination and subsequent expansion of the immune repertoire against COVID-19 is expected to be beneficial in the long term, especially for unvaccinated individuals who have not been infected with SARS-CoV-2 (e.g., infection naïve young children who have not been vaccinated or infection naïve infants who are newly eligible for vaccination). Use of bivalent vaccines for the primary series primes naïve individuals with both Omicron and original SARS-CoV-2, which will help to maximize the breadth of immunity at the earliest opportunity.
- The safety profile of bivalent Omicron-containing vaccines as boosters has been observed to be similar to that of original mRNA vaccine boosters.
- Available evidence on the effectiveness of bivalent vaccines as boosters suggest they provide protection that is similar to, or somewhat better than that with original mRNA vaccines as boosters, particularly with regard to preventing SARS-CoV-2 infection or symptomatic disease. The limited available evidence assessing the immunogenicity of Moderna Spikevax bivalent BA.1 and original vaccines as a primary series in children 6 months to 5 years of age indicate a better immune response of the bivalent vaccine against the Omicron subvariant BA.1.
- Given the potential for substantial virus evolution and uncertainty about the emergence of future variants/subvariants, further modification of the strain composition of COVID-19 vaccines over time is anticipated and this is expected to increase the immune response and possibly also protection against divergent SARS-CoV-2 spike protein antigens.

Rationale for the recommended bivalent Omicron-containing mRNA vaccines and dosages for the primary series (as described in [Table 1](#)):

- Seroprevalence due to SARS-CoV-2 infection in Canada is high in adults (although somewhat lower in older adults), adolescents and school-aged children, but relatively lower in young children and infants who may not yet have been exposed to SARS-CoV-2. As such, the dosage of Moderna Spikevax bivalent BA.1 or BA.4/5 currently authorized for use as a booster dose (i.e., 50 mcg for adults and adolescents, 25 mcg for children 6 to 11 years of age) is expected to be sufficient for primary series doses with Moderna Spikevax bivalent vaccines for children 6 years of age and older, as well as adolescents and adults. The standard dose for Pfizer-BioNTech Comirnaty bivalent vaccines, according to age, is recommended for use in the primary series.
- Individuals with a decreased response to vaccination, such as those who are moderately to severely immunocompromised, may benefit from a primary series with Moderna Spikevax bivalent using the dosages outlined above (50 mcg in individuals 12 years of age and older, and 25 mcg in children 6 months to 11 years of age) compared to Pfizer-BioNTech Comirnaty bivalent BA.4/5 (30 mcg in individuals 12 years of age and older, and 10 mcg in children 5 to 11 years of age). For the original COVID-19 vaccines, NACI preferentially recommended the use of Moderna Spikevax original (25 mcg) for moderately to severely immunocompromised children 6 months to 4 years of age, as this product required one fewer dose than the Pfizer-BioNTech original (3 mcg) product and may therefore be more acceptable and feasible for this group.
- For individuals 12 to 29 years of age, Pfizer-BioNTech Comirnaty bivalent BA.4/5 is preferred to Moderna Spikevax bivalent BA.1 or BA.4/5 due to a lower risk of myocarditis and/or pericarditis observed after dose 1 and dose 2 of the primary series with Pfizer-BioNTech Comirnaty original (30 mcg) compared to Moderna Spikevax original (100 mcg)

in this age group. For some moderately to severely immunocompromised individuals 12 to 29 years of age, administration of Moderna Spikevax bivalent (50 mcg) may be considered based on clinical judgement.

- NACI previously recommended the preferential use of Pfizer-BioNTech original (10 mcg) over Moderna Spikevax original (25 mcg or 50 mcg) in children 5 to 11 years of age based on the precautionary principle and limited data on the risk of myocarditis and/or pericarditis after COVID-19 vaccination that was available at the time for this age group. However, the risk of myocarditis and/or pericarditis after a primary series dose of an original mRNA COVID-19 vaccine in this age group is now known to be substantially lower compared to the risk following mRNA COVID-19 vaccines in individuals 12 to 29 years of age (in whom the risk of myocarditis and/or pericarditis is the highest) and individuals 30 to 49 years of age (in whom there is no preference between Pfizer-BioNTech Comirnaty original or Moderna Spikevax original for the primary series). Based on this, there is no preferred product between Pfizer-BioNTech Comirnaty bivalent BA.4/5 (10 mcg) and Moderna Spikevax bivalent BA.1 or BA.4/5 (25 mcg) for the primary series in children 5 to 11 years of age. It should be noted that the low rates of myocarditis and/or pericarditis with the primary series in children 5 to 11 years of age have been in the context of the predominant use of Pfizer-BioNTech Comirnaty original (10 mcg) in this age group.
- For children 6 months to 4 years of age, Moderna Spikevax bivalent BA.1 or BA.4/5 (25 mcg) is recommended for the primary series as:
 - It is not feasible to administer Pfizer-BioNTech Comirnaty bivalent BA.4/5 (3 mcg) with the products that are currently available in Canada.
 - There is a greater likelihood that children in this age group are immunologically naïve compared to older children. Thus, the same dose used for the primary series with Moderna Spikevax original is recommended for the primary series with Moderna Spikevax bivalent BA.1 or BA.4/5.
- None of the authorized bivalent mRNA COVID-19 vaccines in Canada are currently indicated for use as a primary series by Health Canada; they are currently authorized for booster doses. Regulatory review has been initiated for some products, but at this time all recommendations for use of bivalent mRNA vaccines for the primary series are considered off-label. NACI encourages manufacturers to submit modifications to current COVID-19 vaccine authorizations to the Canadian regulator in a timely manner.

Additional details on primary series vaccination for COVID-19 and bivalent Omicron-containing mRNA vaccines are available in the [COVID-19 vaccine chapter](#) in the Canadian Immunization Guide and NACI [statements and publications](#).

NACI continues to monitor and assess the evidence as it emerges and will update its recommendations as needed.

Research Priorities

1. Continuous monitoring of data on the safety, immunogenicity, efficacy, and effectiveness of COVID-19 vaccines, including bivalent mRNA vaccines for primary series and booster doses, 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 the impacts of vaccination on outcomes after any infection such as multisystem inflammatory syndrome in children (MIS-C), post-COVID-19 condition/post-acute COVID syndrome (long COVID), or infection-induced myocarditis and/or pericarditis in older and younger adult, adolescent, and pediatric populations.
2. Ongoing monitoring of research related to any proposed change in the formulation for both the primary series and the booster doses.
3. Vigilant monitoring and reporting of adverse events of special interest to support the rapid identification of potential vaccine safety signals and accurately inform potential risks associated with any future primary series or booster doses. Global collaboration should be prioritized to enable data sharing so decision makers around the world can weigh benefits and risks of COVID-19 vaccines.
4. Continuous monitoring of COVID-19 epidemiology and vaccine effectiveness in special populations at high risk of severe outcomes or long-term consequences of infection with COVID-19, including but not limited to those with co-morbidities (including immunocompromising conditions) and pregnant populations.
5. Continuous monitoring of vaccine coverage in Canada, for COVID-19 vaccines and other routine vaccines, particularly in the context of COVID-19 vaccines for the primary series (particularly for children) and booster doses and including consideration of measures that may reduce the risk of disparities in vaccine confidence and uptake across different sub-populations.

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