

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

Updated guidance on COVID-19 vaccines for
individuals who are pregnant or breastfeeding

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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

On June 29, 2022, NACI published interim guidance on [planning considerations for a fall 2022 COVID-19 vaccine booster program in Canada](#). NACI identified people who are pregnant among those who are at increased risk of severe illness from COVID-19 and strongly recommended that pregnant people should be offered a fall COVID-19 booster dose regardless of the number of booster doses previously received.

The NACI recommendations for the use of COVID-19 vaccines in pregnancy and breastfeeding have evolved over time with accumulating evidence since the authorization of the first COVID-19 vaccines. Initially, in December 2020, NACI took a precautionary approach by recommending against routinely offering COVID-19 vaccines to populations excluded from clinical trials, including people who were pregnant or breastfeeding. On May 28, 2021, the committee updated their guidance to strongly recommend the use of mRNA COVID-19 vaccines in pregnant or breastfeeding populations, given the accumulated data on the safety of COVID-19 vaccines in these groups and the emerging evidence at that time on risks of SARS-CoV-2 infection in the context of pregnancy. Pregnant adults and adolescents have been recommended to receive a booster dose of mRNA COVID-19 vaccine since December 3, 2021 and January 28, 2022, respectively.

Since that time:

- Evidence has continued to emerge about the disproportionate burden of COVID-19 disease in pregnant people in Canada compared to the non-pregnant population of the same age. Compared to non-pregnant persons, SARS-CoV-2 infection in pregnancy is associated with increased risk of hospitalization and admission to an intensive care unit (ICU) ^(1, 2). SARS-CoV-2 infection during pregnancy is also associated with an increased risk of preterm birth, low birth weight and admission to a neonatal intensive care unit (NICU) ⁽²⁻⁵⁾.
- Additional evidence has accumulated further supporting the safety of mRNA COVID-19 vaccines in pregnancy and breastfeeding.
- The uptake of COVID-19 vaccine has been lower among pregnant people compared to non-pregnant people in Canada. Preliminary unpublished evidence in Ontario indicates that primary series vaccine coverage among pregnant people (71%) was 16 percentage points lower than in the general female population of reproductive age in Ontario by the end of 2021 ⁽⁶⁾.

In this statement, NACI reaffirms the importance and safety of COVID-19 vaccination during pregnancy and breastfeeding to address the disproportionate risk of severe COVID-19 disease in people who are pregnant, with the goal of reducing the incidence of adverse outcomes for pregnant persons, fetuses and newborns from COVID-19 disease.

NACI continues to strongly recommend that individuals who are pregnant or breastfeeding should be immunized with a primary series of an authorized mRNA vaccine. NACI also reiterates its existing recommendations for booster doses in these populations. For further information on these recommendations, please refer to the [COVID-19 vaccine chapter](#) in the [Canadian Immunization Guide](#) (CIG).

NACI continues to monitor the rapidly evolving scientific data, recognizing that the trajectory of the COVID-19 pandemic remains unclear. Updated recommendations will be made as needed.

METHODS

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

On June 2, 14 and 28 of 2022, the NACI COVID-19 Working Group, which included external clinical and academic experts in pregnancy and breastfeeding, reviewed data on the current epidemiology of COVID-19 in pregnancy, vaccine safety, vaccine effectiveness and immunogenicity, gestational timing of vaccination, and vaccination during breastfeeding.

NACI approved the following recommendations on July 5, 2022. Evidence released or published after this date was not included in this statement.

For further information on NACI's recommendations on the use of COVID-19 vaccines, please refer to NACI's [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 ^(7, 8).

RECOMMENDATIONS

Consistent with NACI's [Interim guidance on planning considerations for a fall 2022 COVID-19 vaccine booster program in Canada](#):

NACI strongly recommends that individuals who are pregnant should be offered a fall COVID-19 vaccine booster dose regardless of the number of booster doses previously received.

With regard to timing of vaccination during pregnancy:

1. NACI recommends that the fall COVID-19 booster dose should be offered at any stage of pregnancy (i.e., in any trimester), regardless of the number of booster doses previously received. **(Strong NACI recommendation)**
 2. NACI recommends that COVID-19 vaccine booster doses may be offered at an interval of 6 months since previous COVID-19 vaccine dose or SARS-CoV-2 infection. However, a shorter interval of at least 3 months may be warranted to optimize protection for the pregnant person in the context of heightened epidemiological risk (including increased risk of severe outcomes in pregnant people). **(Discretionary NACI recommendation)**
- An individual may receive all doses for which they are eligible during the course of a pregnancy.

Consistent with existing recommendations in NACI's [Interim guidance on planning considerations for a fall 2022 COVID-19 vaccine booster program in Canada](#):

- **Individuals who are breastfeeding may be offered** a fall COVID-19 vaccine booster dose, regardless of the number of booster doses previously received.
- **Individuals at increased risk of severe illness from COVID-19* who are breastfeeding should be offered** a fall COVID-19 vaccine booster dose regardless of the number of booster doses previously received.
*For details regarding who is considered at increased risk of severe illness, refer to NACI's [Interim guidance on planning considerations for a fall 2022 COVID-19 vaccine booster program in Canada](#).

With regard to the use of [authorized bivalent Omicron-containing mRNA COVID-19 vaccine](#) products for people who are pregnant or breastfeeding:

- Reformulations of previously-recommended mRNA vaccines can be recommended for use in pregnant or breastfeeding individuals without contraindications to the vaccine, based on reassuring published data regarding the safety of mRNA vaccines in pregnancy.
- Individuals [eligible for a fall booster](#) dose, particularly those in groups at a higher risk of severe outcomes from COVID-19, should not delay their planned vaccination in anticipation of a bivalent Omicron-containing mRNA vaccine if it is not yet available. Individuals choosing to delay a booster dose in anticipation of a new vaccine formulation should carefully assess their individual risks (i.e., risks of SARS-CoV-2 infection and severe outcomes from COVID-19) and benefits associated with deferring a booster dose.
- If the bivalent Omicron-containing mRNA COVID-19 vaccine is not readily available, an original mRNA COVID-19 vaccine should be offered to ensure timely protection.
- There are currently no data on the use of bivalent Omicron-containing mRNA COVID-19 vaccines as part of a primary series and therefore NACI continues to recommend that a primary series be completed using original mRNA COVID-19 vaccines. NACI will continue to monitor the evidence as it emerges and update recommendations as needed.

NACI also reiterates its existing recommendations:

- Individuals who are pregnant or breastfeeding who have not yet begun or completed their primary vaccine series should be offered the recommended doses. Administration of the COVID-19 primary vaccine series remains a top priority in Canada as unvaccinated or partially vaccinated individuals continue to be disproportionately affected by severe COVID-19 disease.
- If individuals who are pregnant or breastfeeding have not yet received a first booster dose, NACI continues to strongly recommend that a first booster dose be offered.
- COVID-19 vaccines may be administered concurrently with (i.e., same day), or at any time before or after other [vaccines recommended during pregnancy or while breastfeeding](#).

SUMMARY OF EVIDENCE

Severity of COVID-19 in pregnant people and their infants

- For people who are pregnant, the evidence consistently shows that pregnancy is associated with increased disease severity with SARS-CoV-2 infection. Compared to non-pregnant persons, SARS-CoV-2 infection in pregnancy was associated with at least two times higher risk of hospitalization, approximately five times higher risk of admission to an ICU ^(1, 2), and at least two times higher odds of requiring invasive ventilation ⁽⁹⁾. Emerging studies of the impact of Omicron variant infection on outcomes in pregnant persons suggest that Omicron may be less severe than prior variants; however, moderate to severe infection continues to be observed in symptomatic pregnant persons, particularly among those who are unvaccinated ⁽¹⁰⁻¹³⁾.
- SARS-CoV-2 infection in pregnancy is also associated with a higher risk of adverse neonatal outcomes including premature delivery, low birth weight and admission to a NICU ^(2-5,9). Additionally, the risks for preterm delivery, low birth weight and admission to a NICU increase with disease severity in the pregnant person ⁽¹⁴⁾.
- Preliminary evidence has also found that SARS-CoV-2 infection in pregnancy is associated with increased odds of diagnosis with a neurodevelopmental disorder in the first year of life, particularly among infants who were exposed during third trimester infections ⁽¹⁵⁾.
- Pregnant people are strongly recommended to receive booster doses because of the increased risks of severe disease ⁽²⁾. Healthcare providers should be aware of the disproportionate burden of disease among racialized pregnant people ⁽²⁾ and lower vaccine uptake among people who are pregnant ⁽¹⁶⁾, especially those who are younger or reside in rural areas or neighbourhoods with the lowest income ⁽⁶⁾. Culturally safe care should be provided to encourage equitable impact of this vaccination program.

Safety of COVID-19 vaccine in pregnancy

- Pregnant persons vaccinated with an mRNA COVID-19 vaccine during pregnancy experience the same rates of expected local and systemic adverse events as non-pregnant persons ⁽¹⁷⁻¹⁹⁾. Vaccination during pregnancy does not increase risk for miscarriage, stillbirth, low birth weight, preterm birth, NICU admission, or other adverse pregnancy/birth outcomes ⁽²⁰⁻²⁶⁾.

Safety of COVID-19 vaccine during breastfeeding

- No safety concerns have been identified with mRNA COVID-19 vaccination during lactation. People who are breastfeeding experience the same rates of side effects as do those who are not breastfeeding, and studies have not found any impacts of mRNA COVID-19 vaccination on the infant/child being fed human milk or on milk production or excretion ⁽²⁷⁾.

Effectiveness of COVID-19 vaccination during pregnancy

- COVID-19 vaccination during pregnancy is effective at protecting against severe or critical COVID-19 disease ⁽²⁸⁾, hospitalization and ICU admission from COVID-19 infection ⁽²⁹⁾ and intubation and maternal mortality in those with severe disease ⁽³⁰⁾. Limited evidence available for the Omicron variant suggests that the proportion of pregnant people who had moderate to severe infection was lower among those who were fully vaccinated ⁽¹³⁾ and those who received a booster dose ⁽¹¹⁾ compared to pregnant people who were unvaccinated or partially vaccinated. A booster dose in pregnancy has been shown to increase antibody levels in the pregnant person and umbilical cord blood at birth ⁽³¹⁻³³⁾, including against the Omicron BA.1 variant ⁽³⁴⁾. As of the date that NACI reviewed the evidence, there were no specific data on effectiveness of a second booster dose in

pregnancy. Evidence on the effectiveness of second booster doses in the general population is described in NACI's [Interim guidance on planning considerations for a fall 2022 COVID-19 vaccine booster program in Canada](#).

- Infants of people who were vaccinated with a second or third dose of COVID-19 vaccine during pregnancy experienced lower rates of Delta and Omicron infection in the first 4 months of life compared to infants born to individuals who were unvaccinated ⁽³⁵⁾. Infants of people who received a 2-dose primary series during pregnancy had a lower risk of hospitalization with COVID-19 (including Omicron) in the first 6 months of life compared to infants born to individuals who were unvaccinated ⁽³⁶⁾.
- Similar to the general adult population, it is expected that pregnant people who have received a primary series and a first booster dose will experience waning of protection against infection (and to a lesser extent, severe disease) with increased time since their previous dose.

Considerations for gestational timing of a booster dose

- Booster dose vaccination at any stage of pregnancy is recommended to optimize protection of the pregnant person, given the higher risk of severe illness ^(2, 37) and adverse neonatal and obstetrical outcomes ⁽³⁷⁾, particularly when infected during the second and third trimesters.
- A booster dose in pregnancy increases antibody levels in both the pregnant person and the infant cord blood, as measured at birth ^(31-33, 38). Protecting the pregnant person may indirectly protect the fetus from adverse outcomes associated with COVID-19, including premature birth ⁽²⁾. The correlate of protection from cord blood antibodies in the neonate is unknown. Available evidence suggests that antibody levels in the cord blood may be higher at birth following a primary series in the third trimester of pregnancy; however, antibodies were detectable in cord blood following primary series vaccination at any time during pregnancy ^(31, 39). Evidence in the area of optimal gestational timing of booster doses in pregnancy is limited. Based on the known risks of COVID-19 to the pregnant person, vs. benefits to the newborn that are less well known, booster dose vaccination should not be delayed with the intention of optimizing transfer of transplacental antibodies to the neonate.
- There is evidence of waning antibody levels in pregnant people following primary series immunization in the first trimester ^(31, 33). Given the safety of mRNA vaccination during pregnancy, NACI recommends that an individual may receive all doses for which they are eligible during the course of a pregnancy.

Vaccination and breastmilk antibodies

- Studies demonstrate that vaccination during lactation induces anti-SARS-CoV-2 antibodies in human milk. There is a weak-to-moderate positive correlation between serum and milk antibody levels following vaccination of the lactating person ⁽⁴⁰⁻⁴²⁾ and milk antibody levels can remain stable for up to 60 days ⁽⁴³⁾. However, limited evidence indicates that exposure to antibodies in human milk does not lead to detectable antibodies in infants. Infants born to pregnant individuals who were vaccinated during pregnancy had detectable plasma antibodies at birth, whereas no antibodies were detected in the blood ^(44, 45) or nasal mucosa ⁽⁴⁵⁾ of nursing infants whose mothers were vaccinated postpartum.

RESEARCH PRIORITIES

1. Continuous monitoring of the burden of disease among people who are pregnant and infants in future COVID-19 waves as SARS-CoV-2 evolves.
2. Continuous monitoring of data on the safety, immunogenicity, efficacy, and effectiveness of the COVID-19 vaccines in pregnancy and breastfeeding, including booster doses and new COVID-19 vaccine products, through clinical trials and studies in real-world settings. This should include 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 (including longer-term outcomes) after vaccination or infection in pregnant or breastfeeding individuals and neonates.
3. Further characterization of vaccine confidence and acceptability among people who are pregnant, including in racialized and other groups that experience higher burden of disease in pregnancy and lower vaccine uptake, in order to develop strategies to reduce health inequities in these populations.
4. Further evaluation of the optimal gestational timing of boosters in people who are pregnant, with respect to the safety profile, duration or waning of protection against infection and severe disease for both pregnant people and their infants, and the potential for immune interference in infants ≥ 6 months with transplacentally-acquired antibodies who are subsequently vaccinated with a COVID-19 vaccine.

Table 1. 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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