

SOGC Statement on COVID-19 Vaccination in Pregnancy

POLIQUIN, V; CASTILLO, E; BOUCOIRAN, I; WONG, J; WATSON, H; YUDIN, M; MONEY, D; VAN SCHALKWYK, J; ELWOOD, C on behalf of the Infectious Disease Committee of the Society of Obstetricians and Gynaecologists of Canada

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CONSENSUS STATEMENTS:

- 1. COVID-19 vaccination is *recommended* during pregnancy in any trimester and while breastfeeding**
- 2. All available COVID-19 vaccines approved in Canada can be used during pregnancy and breastfeeding, but the SOGC recommends following provincial and territorial guidelines on type of vaccine to prioritize for pregnant and breastfeeding individuals.**
- 3. Individuals should not be precluded from vaccination based on pregnancy status or breastfeeding.**
- 4. Given that pregnant people are at increased risk of morbidity from COVID-19 infection, all pregnant persons should be prioritized to receive a COVID-19 vaccination.**

Vaccinations are an important part of primary and preventative healthcare for pregnant women. The benefit of vaccination during pregnancy for the infant (e.g. pertussis and influenza) is recognized and recommendation of these vaccinations is part of routine prenatal care. No vaccine has ever been associated with teratogenicity or adverse pregnancy outcomes.

SARS-CoV-2 and the impact on pregnancy

Compared to non-pregnant women with COVID-19, pregnant women are at increased risk of admission to hospital, critical care and invasive ventilation compared to age-matched peers.^{1,2} Canadian and international data from large studies spanning multiple jurisdictions demonstrate that approximately 7-11% of pregnant women will require hospitalization for COVID-related morbidity and between 1-4% of pregnant women require admission to an intensive care unit (ICU).¹⁻³ Most recently, a prospective cohort study of 5183 pregnant women compared to 175 905 non-pregnant women demonstrated that pregnancy conferred an increased risk of death from COVID-19 (OR 1.84, CI 1.60-2.16). The risk of severe morbidity from COVID-19 in pregnant women appears to be associated with risk factors including age \geq 35 years old, asthma, obesity, preexisting diabetes, preexisting hypertension and heart disease.^{1,2} In addition, both Canadian and US data.¹⁻³ show an increased risk of preterm birth associated with COVID-19 infection in pregnancy which will cause consequent morbidity to the infant related to prematurity.

COVID-19 vaccines approved for use in Canada

In Canada, the dominant vaccines in use to prevent infection with SARS-CoV-2 are the mRNA vaccine platforms. This model consists of messenger RNA (mRNA) encapsulated by a lipid nanoparticle (LNP), which allows the mRNA entrance into host (human) cells. The mRNA in the vaccine codes for the SARS-CoV-2 spike protein utilized by the virus to bind to human receptors and promote viral replication. The vaccine provides the host cell instructions to manufacture only this spike protein and express it on its surface. Recognizing the spike protein as a foreign antigen, the host immune system is then activated to produce an immune response.⁴ The mRNA does not enter the nucleus or alter human DNA and human cells do not have the machinery to allow it to do so.

The Pfizer-BioNTech and Moderna COVID-19 vaccines were originally evaluated in licensure trials as a series of two intramuscular injections given 21-28 days apart.⁵ However, since then, considerable data has been generated on different dosing intervals.⁶ The efficacy of the Pfizer-BioNTech COVID-19 vaccine has been demonstrated for adults 16 years and older in Phase II and Phase III trials involving the randomization of approximately 44,000 individuals.⁷ These trials demonstrated a vaccine efficacy of 94.6% for preventing symptomatic COVID-19 cases at least 7 days following the second dose.⁷ In Phase III trials for the Moderna COVID-19 vaccine involving the randomization of 30,000 individuals, the vaccine was reported to have 94.1% efficacy against symptomatic COVID-19 with no serious safety concerns identified during the initial 2 month follow-up period.⁸ Since the initial clinical trials, numerous population-based studies have reported on real-world vaccine efficacy. Among these, Canadian data from Quebec and British Columbia have demonstrated vaccine efficacy greater than 80-90% for infection for at least 4 months after the 2nd dose and including against infections with Delta variant.^{6,9} Vaccine efficacy data specific to pregnant women are emerging and suggest that COVID-19 mRNA vaccine efficacy is comparable to the vaccine efficacy observed in non-pregnant persons.^{10,11}

In Phase III trials for both Pfizer-BioNTech and Moderna COVID-19 vaccines, there were no clinically meaningful differences in adverse events or severe adverse events in the vaccine group compared to control except for lymphadenopathy which occurred in approximately 0.3% of the vaccine group compared to <0.1% of the placebo group for the Pfizer-BioNTech COVID-19 vaccine. The most reported side effects from the mRNA COVID-19 vaccines were pain at the injection site, fatigue and headache. Fever was reported in 11-16% of patients, particularly following the second dose.⁷ Data from the US v-safe pregnancy registry demonstrates that pregnant women are more likely than non-pregnant women to report injection site pain following administration of COVID-19 mRNA vaccines, but are less likely to report headache, myalgia, chills and fever.¹²

While pregnant and breastfeeding individuals were excluded from the available Phase II and Phase III studies for the Pfizer-BioNTech and Moderna COVID-19 vaccines a growing body of data demonstrates no difference in rates of spontaneous abortion, stillbirth, preterm birth nor other pregnancy complications. The V-Safe registry in the US has reported on over 7,000 vaccinated pregnant women (including a robust representation of women vaccinated in the early pregnancy) who received either the Pfizer-BioNTech vaccine or the Moderna vaccine and identified no differences in the rates of adverse pregnancy and neonatal outcomes for those women who were pregnant and compared to pre-pandemic rates.^{11,12} Additional US data from the University of Washington, demonstrated that COVID-19 vaccination in pregnant and lactating individuals can induce an immunogenic response, does not raise significant vaccine-related adverse events or obstetrical and neonatal outcomes, and is effective in preventing COVID-19 disease.^{13,14} Most recently, analysis of US and Norwegian population-level data reporting on 105,446 and

18,477 pregnancies, respectively, have demonstrated no evidence of increased risk for early pregnancy loss following Covid-19 vaccination.^{15,16}

Canadian data on vaccines in pregnancy are now available from Ontario and have been published as 2 online reports. (Better Outcomes Registry & Network (BORN) Ontario. COVID-19 Vaccination During Pregnancy in Ontario: Surveillance Report #2, Reporting Interval December 14, 2020 to June 30, 2021. Ottawa, ON: BORN Ontario; July 30, 2021.) During this entire reporting period, there were 39,985 women who received at least one dose of COVID-19 vaccine during pregnancy. Of note 26,381 had received 1 dose and 13,604 had received 2 doses. Monthly uptake of vaccine increased over this time period from 0.02% to 45.4% by June 2021. There was no evidence of any pregnancy specific increase in any risks associated with vaccine uptake. The second source of Canadian data will be the Canadian COVID-19 Vaccine Registry for Pregnant & Lactating Individuals (COVERED) whose objective is to assess the safety and effectiveness of vaccination against COVID-19 in pregnancy (registration is open and available on the website: <https://covered.med.ubc.ca/>).

Data on the safety of COVID-19 vaccines in lactating women or the effects of mRNA vaccines on the breastfed infant or on milk production is limited, however because mRNA vaccines are not live virus vaccines, they are not hypothesized to be a risk to the breastfeeding infant.¹⁷

Considerations for COVID-19 vaccination during pregnancy

Decades of experience with other vaccines administered during pregnancy would suggest that we could expect a similar efficacy for the COVID-19 vaccines in pregnant women compared to non-pregnant women. Vaccines in general are immunogenic, safe, and efficacious when delivered to pregnant persons. Recently COVID-19 vaccination has been shown to be efficacious in preventing infection in pregnant women.¹⁸ While further primary prospective clinical data on safety and efficacy of COVID-19 vaccines in pregnant populations is forthcoming, growing post-marketing surveillance has identified no signals for adverse pregnancy or neonatal outcomes associated with administration of COVID-19 vaccinations.

What *is* known is that an unvaccinated pregnant woman remains at risk of COVID-19 infection and remains at heightened risk of severe morbidity if infected compared to non-pregnant counterparts. Severe infection with COVID-19 carries risks to maternal, fetal and neonatal health. While pregnancy itself does not appear to increase the risk of becoming infected with SARS-CoV-2, pregnant individuals may be in work-related (e.g. health-care worker, front line workers etc.) or community situations (e.g. caregiver, Indigenous communities, outbreak setting, etc.) where the risk of infection is considerable. Owing to maternal age, underlying comorbidities, or social marginalization, some pregnant individuals are at higher risk of severe COVID-related morbidity.

We recommend pregnant individuals should be offered vaccination against COVID-19 at any time during pregnancy or while breastfeeding if no contraindications exist.

In Canada, NACI has preferentially advised that “a complete vaccine series with an mRNA COVID-19 vaccine should be offered to individuals in the authorized age group who are pregnant or breastfeeding. Informed consent should include discussion about emerging evidence on the safety of mRNA COVID-19 vaccines in these populations. (Strong NACI Recommendation). Contraindications to vaccination are few and a complete description is available within the National Advisory Committee on Immunization guidance document.¹⁹

Anticipatory guidance for vaccination during pregnancy

Individuals should be informed of the expected side effects following vaccination. While pain at the injection site, fatigue and headache are the most commonly reported symptoms following vaccination, fever was reported 16% of the time for younger, non-pregnant individuals.⁸ Pregnant individuals can be counselled to treat mild post-vaccination fevers with antipyretics (e.g. acetaminophen).

Timing of vaccination during pregnancy and neonatal protection

The primary indication for administration of COVID-19 vaccination is for **maternal protection**. In theory, immunization of a pregnant woman may confer benefit to a newborn infant through a mechanism of maternal vaccination similar to what is seen for pertussis and influenza vaccination during pregnancy. While natural COVID-19 infection does appear to result in placental antibody transfer, vaccination negates the fundamental risk of COVID-19 in pregnancy while conferring the same neonatal benefit.²⁰ Evidence demonstrates that vaccine-generated antibodies are present in umbilical cord blood following maternal vaccination with a rapid rise in titres occurring by 15d post-vaccination.^{14,21} There appears to be efficient antibody transfer via the placenta, similar to pertussis vaccination which does confer neonatal protection.^{14,21-23} In general maternal antibody transfer via the placenta is a more efficient way to confer neonatal protection than breast feeding. Antibodies are also transferred to breast milk post vaccination.²⁴⁻²⁹ However, until such time when a clinical benefit to the newborn is confirmed, the primary indication for administration of a COVID-19 vaccine to a pregnant individual remains for maternal protection, therefore, vaccination should occur at anytime and not be administered for optimization of potential neonatal protection.

Vaccine Spacing

There is no clear evidence to direct whether spacing of other vaccines is required, relative to the COVID-19 vaccine. Recently NACI has changed its recommendation to support simultaneous vaccination of COVID-19 with any other vaccine. This is uniquely applicable to pregnant persons in that there is no required delay of any vaccine (e.g. Tdap or influenza vaccination) or Rh-immunoglobulin for COVID-19 vaccination and *vice versa*. Of note, pregnant women and infants remain at increased risk of morbidity and mortality from seasonal influenza compared to general population and the vaccinating pregnant women against influenza remains part of routine prenatal care during the pandemic.

Vaccination of the pregnant patient in the context of limited vaccine supply

Given that pregnant women are at higher risk of severe COVID-related morbidity and mortality, they represent a population that should be prioritized for vaccination in situations where vaccine supply is limited. Specifically, the WHO has recommended that pregnant women be prioritized in stage II, representing a situation where the supply is only sufficient to immunize 11-20% of a population. Importantly, the WHO recommendation is upheld in all epidemiologic situations including community transmission, sporadic cases as well as no cases.³⁰

Inadvertent pregnancy following vaccination

Individuals who are discovered to be pregnant during their vaccine series or shortly afterward should *not* be counselled to terminate pregnancy based on having received the vaccine. If conception is presumed to predate the first dose, it is recommended to follow the same procedures for active surveillance (as available) as would be activated if the pregnancy was known at the time of vaccination. A registry to track pregnancy outcomes for individuals receiving any vaccine doses during pregnancy is being planned for Canada. Pregnant individuals can get more information here: <http://med-fom-ridprogram.sites.olt.ubc.ca/vaccine-surveillance/>.

Where pregnancy is detected during the vaccine series (i.e. following the first dose, but ahead of the second dose), pregnant individuals should continue to be offered the opportunity to complete their vaccination series. Pregnant individuals should not be precluded or forced to delay the vaccine series in any trimester.

Individuals contemplating pregnancy

Ideally, an individual would be immunized against COVID-19 ahead of pregnancy to benefit from maximal vaccine efficacy throughout the entire pregnancy. There is no reason to delay pregnancy upon receipt of vaccination.

Booster doses

Pregnant women mount immune responses comparable to the non-pregnant population and vaccine efficacy of the COVID vaccines among cohorts of pregnant women are comparable to non-pregnant women. There is no data to suggest that pregnant women who meet criteria for a booster dose should be treated differently than the non-pregnant population. While timing and criteria for booster doses may vary by jurisdiction, pregnant women should receive a booster dose when recommended.

Future research

As the evidence evolves, it is becoming clear that pregnant and postpartum individuals represent a population at increased risk of COVID-related morbidity. Severe COVID-19 infection during pregnancy has important implications for both maternal and fetal health. NACI acknowledges that people of reproductive age constitute a substantial proportion of the Canadian population, yet limited data on the use of COVID-19 vaccine in pregnancy are available. We support NACI's recommendation for the inclusion of pregnant individuals in clinical trials of COVID-19 vaccines. This will help to ensure that this population has equitable access to COVID-19 vaccine options, and that vaccination decisions can be informed by robust safety, immunogenicity, and efficacy data.³¹

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