

SOGC Statement on COVID-19 Vaccination in Pregnancy

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Pre-amble

The SOGC acknowledges the need for guidance related to the COVID-19 vaccine and pregnancy and during lactation. We recognize the difficulty facing women and their health care providers at this time, due to the absence of clinical trials that can support evidence-informed recommendations about the COVID-19 vaccine for pregnant and breastfeeding populations. Information related to COVID-19, the impact of the disease on pregnancy and data related to COVID-19 vaccines in development are rapidly evolving. The information contained herein is subject to change as further evidence becomes available.

Consensus Statement: Women who are pregnant or breastfeeding should be offered vaccination at any time during pregnancy if they are eligible and no contraindications exist.

This decision is based on the women's personal values and an understanding that the risk of infection and/or morbidity from COVID-19 outweighs the theorized and undescribed risk of being vaccinated during pregnancy or while breastfeeding. Women should not be precluded from vaccination based on pregnancy status or breastfeeding.

SARS-CoV-2 and the impact on pregnancy

Most pregnant women who become infected with SARS-CoV-2 will have mild-to-moderate symptoms and many can be asymptomatic.¹ However, both Canadian and international data from large studies spanning multiple jurisdictions demonstrate that approximately 8-11% of pregnant women will require hospitalization for COVID-related morbidity and between 2-4% of pregnant women require admission to an intensive care unit (ICU).^{2, 3, 4} Compared to non-pregnant women with COVID-19, pregnant women are at increased risk of invasive ventilation with an equivalent mortality to age-matched peers.^{2, 4} 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.^{2, 4} In addition, both Canadian and US data^{2, 3, 4} 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

There are currently three COVID-19 vaccines licensed for use in Canada: Pfizer-BioNTech COVID-19 vaccine (mRNA vaccine), Moderna COVID-19 vaccine (mRNA vaccine) and AstraZeneca COVID-19 vaccine (non-replicating viral vector vaccine).

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.⁵ 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.⁶ However, much data since then has been generated on different dosing intervals. 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

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 commonly 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

Pregnant and breastfeeding women were excluded from the available Phase II and Phase III studies for the Pfizer-BioNTech and Moderna COVID-19 vaccines. However, for Pfizer-BioNTech, there were 23 individuals (12 in the vaccine arm and 11 in the placebo arm) who reported pregnancies during the trial and are being followed for pregnancy outcomes with no reports of adverse effects to date. For the Moderna trials, there were 13 women (6 in the vaccine and 7 in the placebo group) who reported pregnancies during the trial without report of adverse effects to date. Recently V-safe CDC registry which includes pregnant women reported no differences in the rates of adverse events or pregnancy complications for those women who were pregnant and received either the Pfizer-BioNTech vaccine or the Moderna vaccine. The Developmental and Reproductive Toxicity (DART) animal studies for the Moderna and Pfizer-BioNTech vaccines are ongoing. According to the World Health Organization (WHO) and the American College of Obstetricians & Gynecologists (ACOG), no major safety signals have been identified.⁹

Similarly, breastfeeding women were also excluded from the Phase III trials available at present. Therefore, there is no 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. Because mRNA vaccines are not considered live virus vaccines, they are not hypothesized to be a risk to the breastfeeding infant.¹⁰

Non-replicating Viral Vector Vaccines

The Oxford-AstraZeneca ChAdOx1 nCoV-19 vaccine utilizes a Chimpanzee adenovirus non-replicating vector vaccine platform. The chimpanzee adenovirus does not cause disease in humans, but is used to carry part of the pathogen's DNA into human cells where it causes the human cells to make viral proteins (in this case the spike protein of SARS-CoV-2). The viral DNA does not alter human DNA.

The AstraZeneca COVID-19 vaccine was initially evaluated as a series of two intramuscular injections given 4-12 weeks apart; however, similar to the mRNA vaccines, considerable data on different dosing intervals has accrued. In addition, less restrictive storage and handling requirements may facilitate logistics for widespread administration of this vaccine platform. Preliminary Phase III data from 11,636 participants demonstrates an overall vaccine efficacy of 70.4% against symptomatic COVID-19 disease.¹¹ Pregnant and breastfeeding women

were excluded from the Phase III AstraZeneca Trials, however 21 inadvertent pregnancies (12 in the vaccine arm and 9 in the placebo arm) were reported without adverse effects to date. Preclinical trials did not demonstrate adverse effects on fertility, pregnancy, fetal or postnatal outcomes.

In Phase III trials for the AstraZeneca COVID-19 vaccine, there were no clinically meaningful differences in adverse events or severe adverse events in the vaccine group compared to control. Three cases of transverse myelitis were detected (2 in the treatment group and 1 in the control group) and were determined to be unrelated to the vaccine study based on a review by an expert panel of neurologists. Side effects following the AstraZeneca vaccine were reported as mild to moderate and commonly included: pain at the site of injection, fatigue, myalgias and feeling feverish.

Considerations for COVID-19 Vaccination During Pregnancy and Breastfeeding

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 women. While there have been no red flags or hypothesized mechanisms for potential harm associated with the administration of an mRNA non-replicating viral vector vaccine during pregnancy, until more data is available, the potential risks of vaccination to a pregnant woman and her fetus remain unknown and only theoretical. What *is* known, however, 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 both 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 or underlying comorbidities, some pregnant women are at high risk of severe COVID-related morbidity.

NACI has advised “that a complete vaccine series with a COVID-19 vaccine may be offered to pregnant individuals in the authorized age group, without contraindications to the vaccine, if a risk assessment deems that the benefits outweigh the potential risks for the individual and the fetus, and if informed consent includes discussion about the absence of evidence on the use of COVID-19 vaccine in this population (Discretionary NACI Recommendation)⁵.

We **recommend** that pregnant and breastfeeding women who are eligible for the COVID-19 vaccine due to exposure risk, medical status, or other circumstances should be able to make an informed decision by having access to up-to-date information about the safety and efficacy of the vaccine (including clear information about the data that is not yet available) and information about the risks of COVID-19 infection for them. The concern around vaccination in the absence of evidence of safety in pregnancy has been debated in the literature. The PREVENT Working Group state, “the absence of evidence and the mere theoretical or even documented risk of fetal harm is generally not sufficient to justify denying pregnant women access to a vaccine in an outbreak or epidemic.” During an epidemic, the default should be to offer vaccines to pregnant women alongside other affected populations.^{9, 12, 13}

Universal exclusion of pregnant women from receipt of the COVID-19 vaccine based on an undocumented and hypothetical risk to the fetus would leave pregnant women vulnerable to severe morbidity and their infant to preterm birth risk, which would compromise fetal health.

Pregnant and breastfeeding women will likely look to their prenatal care provider to assist in making decisions weighing the risks and benefits so that they might arrive at a well informed and autonomous decision that is right for them as an individual. Such a discussion should prioritize patient autonomy and should include, but not be limited to assessment of:

- Local epidemiology and risk of community acquisition of COVID-19
- Workplace situation and risk of work-related acquisition of COVID-19
- Individual risk for COVID-related morbidity including consideration for comorbidities such as advanced maternal age, immunosuppressive conditions, pre-existing diabetes, pre-existing hypertension, obesity or chronic respiratory/cardiac conditions
- Available data related to the safety of the vaccine during pregnancy and lactation
- Data that is not yet available related to the safety and efficacy of the vaccine for pregnant and breastfeeding women
- Individual beliefs and personal risk assessment of the available data

Individuals who proceed with vaccination

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 women can be counselled to treat mild post-vaccination fevers with antipyretics (e.g., acetaminophen).

A registry to track pregnancy outcomes for those women that receive any vaccine doses in pregnancy is being planned for Canada. Women can participate here (<http://med-form-ridprogram.sites.olt.ubc.ca/vaccine-surveillance/>).

Timing of vaccination during pregnancy and vaccine interval

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. However, until such time when a newborn benefit is confirmed, the primary indication for administration of a COVID-19 vaccine to a pregnant individual remains for maternal protection. As such, for now, there is no data to guide administration at a particular gestational age and it may be considered at any gestational age including the first trimester.

There is no clear evidence to direct if vaccine spacing is required. In the absence of evidence NACI recommends spacing any other vaccines 28 days from completion of the COVID-19 vaccines, however other jurisdictions do not recommend any specific spacing and simultaneous administration of other vaccines can occur. COVID-19 vaccines, out of prudence, can be spaced 14 days from any other vaccines. The spacing recommendation is due to the theoretical risk of an increased inflammatory response, and the confusion of vaccine adverse events between different vaccines and not from data which shows a direct effect on efficacy of adverse events. In addition, administration of immunoglobulins is thought to interfere with vaccine efficacy due to circulating levels of antibody to live attenuated vaccines within the population. However, the rates of circulating antibodies to COVID-19 are low therefore the impact on vaccine efficacy of COVID-19 is unclear.

Given this, the following can be recommended:

- Wait 14 days after any other vaccine before receiving a COVID-19 vaccine. However, given the context of the global pandemic, simultaneous or closer interval of administration may be considered
- After receiving a COVID-19 vaccine dose, where possible wait 28 days before receiving any other vaccine, unless a vaccine is required urgently due to an exposure to a virus such as Hepatitis B. Again, given the global pandemic and condensed timelines of pregnancy this may not be possible.
- Time-sensitive interventions such as administration of anti-D immunoglobulin and blood products should not be delayed on account of recent COVID-19 vaccination and could be given simultaneously.

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

Certain jurisdictions may manage interruptions of vaccine supply chain by delaying administration of the second dose of a COVID-19 vaccine. There are no physiologic reasons to anticipate that the effect of delaying the second dose of the COVID-19 vaccine would be different for a pregnant individual compared to a non-pregnant individual. Pregnant individuals may resume their vaccine series akin to the non-pregnant population in situations of supply chain interruptions.

In the context of limited vaccine supply, distribution of vaccination will be prioritized differently in each jurisdiction depending on local epidemiology and public health priorities. Decisions made regarding prioritization of pregnant women should reflect that pregnancy carries an increased risk for COVID-related hospitalization, ICU admission and mechanical ventilation. Other additional factors in pregnancy such as advanced maternal age, immunosuppressive conditions, pre-existing diabetes, pre-existing hypertension, obesity or chronic cardiac and respiratory conditions may provide additional risk to pregnant women and could be considered for further prioritization in the context of limited vaccine supply.

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 those women that receive any vaccine doses in pregnancy is being planned for Canada. Women can participate 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), the decision of whether to complete the vaccine series during pregnancy should be based on an assessment of the potential risks of not being completely vaccinated during pregnancy vs. the potential risks of receiving the vaccine during pregnancy (as discussed above) and women should not be precluded or forced to delay the vaccine series in any trimester.

Individuals contemplating pregnancy

For an individual planning a pregnancy, it is recommended to complete the entire COVID-19 vaccination series (where possible) to achieve maximal vaccine efficacy ahead of pregnancy. It is not known whether an individual should delay pregnancy following receipt of the vaccine and a risk-benefit discussion for those planning pregnancy should occur similar to the discussion for pregnant and breastfeeding women.

Future research

As the evidence evolves, it is becoming clear that pregnant and postpartum women 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 no data on the use of COVID-19 vaccine in pregnancy are available. We support NACI's recommendation for the inclusion of pregnant women in clinical trials of COVID-19 vaccines to ensure that this population has equitable access to COVID-19 vaccine options informed by robust safety, immunogenicity, and efficacy data.¹⁴

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