

### **SOGC Statement on COVID-19 Vaccination in Pregnancy**

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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. Presently, preference is given for the use of mRNA vaccinations during pregnancy as more data on safety and efficacy during pregnancy is available for these vaccines.**
- 3. The SOGC recommends following provincial and territorial guidelines on type of vaccine to prioritize for pregnant and breastfeeding individuals.**
- 4. Individuals should not be precluded from vaccination based on pregnancy status or breastfeeding.**
- 5. Given that pregnant patients 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.

### **SARS-CoV-2 and the impact on pregnancy**

Both Canadian and international reports have highlighted increased risk of severe illness, including hospitalization and admission to an Intensive Care Unit (ICU), among pregnant persons/women diagnosed with SARS-CoV-2, compared to their non-pregnant counterparts. Canadian data from a 6-province analysis of population outcomes in pregnancy reveals that hospitalization and ICU admission are both increased in pregnant women over non-pregnant women. Canadian data estimates that among pregnant women infected with SARS-CoV-2 the rate of hospitalization was 7.8% and the rate of ICU admission was 2.0%.<sup>1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11</sup>

Comorbidities including greater gestational age at diagnosis, obesity, pre-existing diabetes mellitus and hypertension put pregnant women/persons at increased risk of severe COVID-19 disease. These medical comorbidities are strongly tied to the social determinants of health.

Increased risk of preterm birth has also been documented among pregnant women/persons diagnosed with COVID-19. This finding is not only true among severe cases but milder cases as well.<sup>5, 12, 13, 14</sup> In the Canadian data the rate of preterm birth was 11.05% which is approximately 2-fold the background rate in the population.<sup>1</sup>

## COVID-19 vaccines approved for use in Canada

### mRNA Vaccine Platforms

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.<sup>15</sup> 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.<sup>16</sup> However, since then, considerable data has been generated on different dosing intervals.<sup>17</sup> 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.<sup>18</sup> These trials demonstrated a vaccine efficacy of 94.6% for preventing symptomatic COVID-19 cases at least 7 days following the second dose.<sup>18</sup> 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.<sup>19</sup> 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 2<sup>nd</sup> dose and including against infections with Delta variant.<sup>17, 20</sup> 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.<sup>21, 22</sup>

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.<sup>18</sup> 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.<sup>23</sup>

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 or other pregnancy complications. The V-Safe registry in the US has reported on over 7,000 pregnant women (including a robust representation of women vaccinated in 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 in vaccinated women compared to pre-pandemic rates.<sup>22, 23</sup> 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.<sup>24, 25</sup> Most recently, analyses 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.<sup>26, 27</sup>

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 vaccines 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 is 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/>). A recent analysis of this registry demonstrated that reactogenicity among pregnant patients receiving a COVID-19 vaccination during pregnancy was comparable to reports among non-pregnant patients. Further, the analysis compared 2879 participants who received 1-3 doses of a COVID-19 vaccine during pregnancy to 1660 unvaccinated pregnant participants and found not statistically significant difference in self-reported adverse pregnancy outcomes including preterm birth, fetal growth restriction and admission to neonatal intensive care.<sup>28</sup>

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.<sup>29</sup>

### Recently approved vaccine platforms

In early 2022, two new vaccines platforms were approved for use in Canada. Novavax Nuvaxovid contains a recombinant SARS-CoV-2 spike protein vaccine and Medicago Covifenz contains a plant-based virus-like particle of the SARS-CoV-2 spike protein. The adjuvants contained in both vaccine platforms are oil-in-water emulsion adjuvants that have been used widely and in diverse populations including pregnant women and children, most notably during the 2009-2010 H1N1 influenza pandemic.<sup>30</sup> Both vaccine platforms use technology that is well established and used for other vaccines that are administered safely to pregnant women (e.g. hepatitis, pertussis and tetanus vaccines). There is no theoretical reason why the Novavax Nuvaxois or the Medicago Covifenz vaccines should not be administered to pregnant or lactating women, although safety and efficacy data specific to pregnancy is not yet available.<sup>31, 32</sup> Following informed discussion, these vaccines could be considered as an alternative for pregnant and lactating women who cannot use the mRNA vaccine platform due to side effects or those who are opposed to using an mRNA vaccine platform.

### 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. COVID-19 vaccination has been shown to be efficacious in preventing infection in pregnant women.<sup>33</sup> Importantly, in Canadian CANCOVID-Preg dataset, none of the patients who had received at least 2 doses of a SARS-CoV-2 vaccine experienced any of the adverse maternal outcomes. Further, transplacental transmission of SARS-CoV-2 immunoglobulins from a vaccinated person to their infant has been documented and emerging data has suggested a potential reduction in infant SARS-CoV-2 hospitalization for infants <6 months whose mothers were vaccinated during pregnancy.<sup>34, 35</sup> 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. This recommendation extends to those who have previously been infected with SARS-CoV-2.<sup>36</sup>**

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.<sup>37</sup>

## 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.<sup>19</sup> 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**. Therefore, the decision around timing of vaccination should be optimized for maternal benefit.

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.<sup>38</sup> 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.<sup>25, 39</sup> There appears to be efficient antibody transfer via the placenta, similar to pertussis vaccination which does confer neonatal protection.<sup>25, 39, 40, 41</sup> Recent data from a case-control study conducted by the US-CDC demonstrates that receipt of a two-dose series of a mRNA COVID-19 vaccination during pregnancy is

associated with a reduction in COVID-associated infant hospitalizations <6 months.<sup>42</sup> In general maternal antibody transfer via the placenta is a more efficient way to confer neonatal protection than breastfeeding. Antibodies are also transferred to breast milk post vaccination,<sup>43, 44, 45, 46, 47, 48</sup> but there is yet no data on associated 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 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.<sup>49</sup>

## 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 Canadian registry to track pregnancy outcomes for individuals receiving any vaccine doses during pregnancy is currently open for registration. Pregnant individuals can get more information here: <https://covered.med.ubc.ca/>

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.

The bivalent Omicron-containing mRNA COVID-19 vaccine products are reformulations of previously-recommended mRNA vaccines and can be recommended based on previously published reassuring data on the safety of mRNA vaccines in pregnancy.<sup>50</sup> The bivalent Omicron-containing mRNA COVID-19 vaccines are currently the preferred booster products for its authorized age group.

**We recommend pregnant individuals (at any stage of pregnancy) and those who are breastfeeding should be offered a booster dose of COVID-19 when eligible, regardless of the number of previous booster doses or prior infection.**

## 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 individuals 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.<sup>51</sup>

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