

Episode #40 – COVID-19 Vaccines: Part 2 July 9, 2021

Evidence and knowledge related to SARS-CoV-2 and vaccines is rapidly evolving. The information contained in this Keynotes and Resources is current to July 9, 2021.

COVID-19 vaccines authorized in Canada[1]

Vaccine	Alternate name	Vaccine type	Authorization
Pfizer-BioNTech [1]	Tozinameran or BNT162b2	mRNA	December 9, 2020 (16 years and older), May 5, 2021 (12-15 years)
Moderna [2]	mRNA-1273	mRNA	December 23, 2020 (18 years and older)
AstraZeneca / COVISHIELD [3]	ChAdOx1-S	Adenovirus vector vaccine	Feb 26, 2021 (18 years and older)
Janssen (Johnson & Johnson) [4]	Ad26.COV2.S	Adenovirus vector vaccine	March 5, 2021 (18 years and older)

Recent vaccine updates

Health Canada updates Pfizer-BioNTech and Moderna COVID-19 vaccine labels to include information on myocarditis and pericarditis

On June 30, 2021, Health Canada updated the product monographs for the Pfizer-BioNTech and Moderna COVID-19 vaccines to describe very rare reports of myocarditis and pericarditis following vaccination.

Cases of myocarditis and/or pericarditis[2] following immunization with COVID-19 vaccines have been reported in a small number of people in Canada and internationally. These reports are very rare. Health Canada and other international regulators are continuing to investigate the potential relationship between COVID-19 vaccines and these rare events. Most reported cases to date have followed vaccination with an mRNA vaccine (Pfizer-BioNTech and Moderna) and, based on an analysis of international cases, have occurred more often after the second dose and in younger male adults and adolescents.

Myocarditis is an inflammation of the heart muscle, while pericarditis is an inflammation of the lining around the heart. Both conditions can result from an infection (including COVID-19), exposure to a toxic substance or radiation, or other health events. Symptoms can include chest pain, shortness of breath, or palpitations. In many cases,

[1] Refer to Episodes #15, #28 and #39 for more information on COVID-19 vaccines.
[2] Refer to Episode #39 for more information on myocarditis and pericarditis.

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these conditions are mild and require little to no treatment. However, more severe cases can lead to heart muscle damage.

Health Canada has updated the product labels for the Pfizer-BioNTech and Moderna COVID-19 vaccines to inform Canadians and healthcare professionals of these possible side effects and to provide information about the signs and symptoms and when to seek prompt medical attention following vaccination.

Health Canada reassures Canadians that COVID-19 vaccines continue to be safe and effective at protecting them against COVID-19. The benefits of COVID-19 vaccines continue to outweigh their potential risks, as scientific evidence shows they reduce deaths and hospitalizations due to COVID-19. [5]

Health Canada issues label change on AstraZeneca/COVISHIELD COVID-19 vaccines
On June 29, 2021, Health Canada updated the product monograph for the AstraZeneca and COVISHIELD COVID-19 vaccines to add capillary leak syndrome as a potential side effect, with a warning for patients with a history of capillary leak syndrome to not get the AstraZeneca or COVISHIELD COVID-19 vaccine. The label was also updated with information about very rare events of blood clots associated with low levels of platelets following immunization.

Capillary leak syndrome[3] is a very rare, serious condition that causes fluid leakage from small blood vessels (capillaries), resulting in limb swelling, low blood pressure, thickening of the blood, and low levels of albumin in the blood. Individuals should seek prompt medical attention if they experience any symptoms that could be capillary leak syndrome. Symptoms include rapid swelling of the arms and legs and sudden weight gain, which can be accompanied by feeling faint. [6] [7]

National Advisory Committee on Immunization (NACI)[4] Updates
On July 2, 2021, the document *An Advisory Committee Statement (ACS) National Advisory Committee on Immunization (NACI) Recommendations on the use of COVID-19 Vaccines* was updated to add additional information on myocarditis and pericarditis following vaccination with mRNA vaccines and a section was added on capillary leak syndrome following vaccination with AstraZeneca COVID-19 vaccine.

As a precautionary measure, NACI recommends the second dose in the mRNA COVID-19 vaccination series should be deferred in individuals who experience myocarditis or pericarditis following the first dose of an mRNA COVID-19 vaccine until more information is available. NACI will continue to monitor the evidence and update recommendations as needed. [8] [9] [10]

[3] Refer to Episode #39 for more information on capillary leak syndrome.
[4] 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. https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci.html

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Vaccine efficacy and effectiveness

Vaccine efficacy is the degree to which a vaccine prevents disease, and possibly also transmission, under ideal and controlled circumstances. For example, in a clinical trial comparing a vaccinated group with a placebo group.

Vaccine effectiveness refers to how well a vaccine performs in the real world (e.g., preventing illness in vaccinated people). Effectiveness of a vaccine is measured in observational studies because participants are not randomly assigned to a treatment versus a placebo group. For example, case-control studies assess effectiveness by comparing the vaccination status of individuals who develop the disease (cases) with a group of individuals without the disease (controls) who are also representative of the population from which the cases arise. If the vaccine is effective, cases of disease are more likely to be unvaccinated individuals.

Both vaccine efficacy and effectiveness are determined by calculating the risk of disease among vaccinated and unvaccinated individuals, and determining the percentage reduction in disease among vaccinated people relative to unvaccinated people.

Vaccines do not always need to have exceptionally high effectiveness to be beneficial. For example, studies show influenza vaccine is 40-60% effective yet it prevents millions of influenza-associated illnesses, and thousands of hospitalizations and deaths every year. [11] [12] [13]

COVID-19 vaccine efficacy

Pfizer-BioNTech COVID-19 vaccine

There was strong evidence from clinical trials that the Pfizer-BioNTech COVID-19 vaccine has a high level of efficacy. Clinical studies showed, beginning 1 week after the second dose, the vaccine had an efficacy of 95.0% in protecting trial participants aged 16 and older against symptomatic COVID-19, 94.7% in those 65 years and older, and a 100% efficacy in participants 12 to 15 years old. [14] [15] [16] [17] [18]

Moderna COVID-19 vaccine

Based on studies involving over 30,000 participants across the US, 18 years and older, the Moderna COVID-19 vaccine showed an efficacy of 94.1% in preventing COVID-19, including severe disease, beginning 2 weeks after the second dose. In participants 65 years of age and older, efficacy of the vaccine was 86.4%. [19] [20] [21]

AstraZeneca/COVISHIELD COVID-19 vaccine

The AstraZeneca/COVISHIELD COVID-19 vaccine showed an efficacy of 62.1% in preventing symptomatic COVID-19 beginning 15 days after the second dose based on analysis of data collected until November 4, 2020. [22]

Evidence demonstrated protection started from approximately 3 weeks after first dose of vaccine and persisted up to 12 weeks. It was recommended a second dose be given at a 4-to-12-week interval after the first dose considering evidence that efficacy increased with longer dosing intervals. [23]

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An updated analysis in an expanded population from data collected until December 7, 2020 demonstrated an efficacy of 59.5% when the second dose was administered 4 to 12 weeks after the first dose. In this data set, there were no hospitalizations or severe illness reported in participants who received two doses of the vaccine. [24] [25] [26] [27]

Janssen (Johnson & Johnson) COVID-19 vaccine
Based on studies in about 44,000 participants, the Janssen COVID-19 vaccine showed an efficacy of 66.9% in preventing moderate to severe/critical COVID-19 beginning 2 weeks after vaccination. [28] [29] [30]

Vaccine effectiveness research
Health Canada evaluates vaccines before they are authorized for use in Canada by reviewing detailed data about the vaccine's safety and efficacy from clinical trials. After Health Canada authorizes a vaccine for use, the vaccine continues to be studied to determine its effectiveness under real-world conditions. Health Canada monitors this real-world evidence while vaccines are on the market. [31]

Research in real-world conditions helps to determine if vaccines are performing as expected outside the controlled setting of clinical trials. As COVID-19 vaccine uptake increases globally, ongoing research will help to understand how well vaccines:

- Perform in specific subpopulations
- Reduce the risk of infection, including asymptomatic infection
- Protect against milder illness
- Prevent serious outcomes, including hospitalization
- Prevent transmission of the virus (e.g., transmission by those who are vaccinated)
- Provide long-term protection (i.e., assess duration of immunity)
- Protect against new variants
- Protect against COVID-19 when vaccines are administered using a single dose or when a second dose is extended, and if these dosing regimens are affective under real-world conditions

Several factors can affect real-world vaccine effectiveness, including:

- Population host factors (e.g., people not included in clinical trials who may respond differently to the vaccine, such as individuals who are pregnant or immunosuppressed)
- Virus factors (e.g., variants)
- Programmatic factors (e.g., adherence to dosing schedules or storage/handling of vaccines) [32]

COVID-19 vaccine effectiveness
Overall, vaccine effectiveness is estimated to be 60-80% for preventing SARS-CoV-2 infection 3-4 weeks after receiving a single dose of Pfizer-BioNTech, Moderna, or AstraZeneca COVID-19 vaccine, although this varies by population (e.g., general population, older adults, long-term care residents, healthcare workers). Vaccine effectiveness increases to greater than 85% after a second dose of a two-dose series. [33]

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A Pfizer-BioNTech vaccine study by Dagan et al. (2021) involving just under 1.2 million people 16 years and older in Israel supported findings from clinical trials. The study's results indicated two doses of the vaccine reduced symptomatic cases of COVID-19 by 94% across all age groups after 7 days of receiving the second dose. The vaccine also reduced severe illness by 92%. [34]

Pilishvili et al. (2021) in their vaccine effectiveness study among US healthcare personnel found a single dose of Pfizer-BioNTech or Moderna COVID-19 vaccine was 82% effective against symptomatic COVID-19 and 2 doses was 94% effective. The majority (75%) of the enrolled healthcare personnel worked at acute care hospitals (including emergency departments). Vaccine effectiveness of a single dose was measured 14 days after the first dose through 6 days after the second dose. Vaccine effectiveness of 2 doses was measured ≥7 days after the second dose. [35]

A study by Thompson et al. (2021) showed mRNA vaccines (Pfizer-BioNTech and Moderna) were 90% effective against SARS-CoV-2 infections after full immunization (≥14 days after second dose). Vaccine effectiveness from partial immunization (≥14 days after first dose but before second dose) was 80% among 3,950 healthcare personnel, first responders, and other essential and frontline workers. [36]

In general, vaccine effectiveness for preventing severe disease, hospitalizations, and intensive care unit admissions ranges from 70-90% for the Pfizer-BioNTech, Moderna, and AstraZeneca COVID-19 vaccines. Vaccine effectiveness estimates for mortality, largely from those receiving the Pfizer-BioNTech vaccines, is generally greater than 70% and as high as 96% in terms of reducing deaths attributable to COVID-19. [33]

Tenforde et al. (2021) found receipt of Pfizer-BioNTech or Moderna COVID-19 vaccine was 94% effective against COVID-19 hospitalization among fully vaccinated adults and 64% effective among partially vaccinated adults aged ≥65 years. A total of 417 participants (187 cases and 230 controls) were included in the analysis. [37]

A United Kingdom (UK) study by Lopez Bernal et al. (2021) of individuals over 70 years of age found a vaccine effectiveness of 60-75% for prevention of symptomatic disease after 28 days of receiving a first dose and 85-90% 14 days after the second dose of either the Pfizer-BioNTech or AstraZeneca COVID-19 vaccine. Additionally, vaccine effectiveness was 80% for preventing hospitalization and 85% for preventing death 28 days after receiving a first dose of either vaccine. The authors concluded that Pfizer-BioNTech and AstraZeneca COVID-19 vaccines offered similar levels of protection in adults aged 70 and older. [38]

Overall, emerging data assessing the impact of COVID-19 vaccines at the population level demonstrates vaccination is associated with reduced spread in individuals, populations, regions, or facilities with higher rates of vaccination or those that were vaccinated earlier than others. [39]

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Variants of concern (VOC)[5]
VOC identified globally and detected in Canada include:

- Alpha (B.1.1.7; first identified the UK)
- Beta (B.1.351; first identified in South Africa)
- Gamma (P.1; first identified in Brazil)
- Delta (B.1.617; first identified in India) [40] [41]

Prevalence of VOC in Ontario
From May 16 to June 12, 2021, there were 3,261 cases sequenced by the Ontario COVID-19 Genomics Network for representative surveillance. The majority were Alpha (66.9%), followed by Delta (21.7%), and Gamma (3.9%). The proportion that were Delta increased from 22.5% (May 30 to June 5) to 28.5% (June 6 to June 12). [42]

Vaccine effectiveness against VOC
As COVID-19 vaccinations increase globally, one of the major concerns has been whether the current vaccines are effective against VOC. Evidence to date for the Alpha variant suggests no significant impact on vaccine effectiveness. Other variants such as Beta, Gamma, and Delta may have a greater impact on vaccine effectiveness. [33]

Alpha, Beta, Gamma variants and COVID-19 vaccination
A study by Alter et al. (2021) led by D. Barouch examined the immune response to VOC in 20 volunteers after vaccination with Janssen COVID-19 vaccine versus a placebo vaccine. The researchers tested antibodies and immune cells against the original strain of SARS-Cov-2 as well as several variants, including Alpha, Beta, and Gamma variants.

As expected, no neutralizing immune responses were seen in the control group. Among those who received the vaccine, researchers found neutralizing antibodies against the variants. However, there was a reduction in antibodies that could neutralize the variants compared with the original virus. For example, there was a 3-fold reduction in antibodies that could recognize and bind to the Gamma variant and a 5-fold reduction in those targeting the Beta variant.

Importantly, other immune-system responses against the variants were similar to those against the original virus. These included the production of non-neutralizing antibodies, which can help immune cells recognize an invading pathogen. Different types of T cells, which help recognize and kill pathogens, responded similarly against the variants compared with the original virus.

The results indicated although the mechanistic correlates of protection for COVID-19 are not yet known, the vaccine's robust protective efficacy in these regions raises the possibility that non-neutralizing antibodies and/or T cell responses may also contribute to protection. Alternatively, it is possible low levels of neutralizing antibodies are sufficient for protection against the virus. [43]

[5] Refer to Episode #39 for more information on VOC.

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Impact of Delta variant

On May 11, 2021, the World Health Organization (WHO) designated Delta as a VOC due to evidence of increased transmissibility. At a June 25, 2021 press conference, WHO officials stated the Delta variant is the most transmissible of the variants identified so far and was spreading rapidly among unvaccinated populations. The officials emphasized the importance of becoming fully vaccinated and the need for everyone, including fully vaccinated people, to maintain measures to prevent transmission, such as mask wearing, hand hygiene, physical distancing, avoiding crowds, as the highly infectious Delta variant is becoming increasingly dominant and causing new COVID-19 surges around the world, including in highly vaccinated countries. [44]

As of June 29, 2021, 96 countries reported cases of the Delta variant, though this was likely underestimated as sequencing capacities needed to identify variants are limited. A number of these countries attributed surges in infections and hospitalizations to the Delta variant. The increase in the effective reproduction number (R_e)[6] compared with the Alpha variant was estimated to be 55%. Given the increase in transmissibility, the Delta variant is expected to rapidly outcompete other variants and globally become the dominant variant over the coming months. [45] [46]

Transmissibility of Delta variant

Evidence also indicates the Delta variant is at least 50% more transmissible than the Alpha variant. [47] In the UK, the Scientific Advisory Group for Emergencies (SAGE) reported on May 13, 2021 with high confidence that the Delta variant can be up to 50% more transmissible than the Alpha variant. This was based on the increasing number and proportion of COVID-19 cases in the UK. [48]

Allen et al. (2021) in a Public Health England study of 3,765 cases in household clusters, matched with 7,530 controls (i.e., single case in a household), to estimate the odds of household transmission of Delta compared with the Alpha variant. The study found the Delta was 64% more transmissible than the Alpha variant when it came to household transmission. The Alpha variant was already estimated to be at least 50% more transmissible than the wild-type virus (the strain with the original spike sequence). The findings support existing evidence the Delta variant has a substantially increased transmissibility advantage over the Alpha variant, which has contributed to the rapid increase in the number of Delta variant cases in the UK and may explain the rapid surge in cases seen in other countries where this variant has been observed. [49]

[6] Effective reproduction number (R_e), sometimes called R_t, is the number of people in a population who can be infected by an individual at a specific time. It changes as the population becomes increasingly immunized, either by infection-acquired or vaccine-acquired immunity. R_e is affected by the number of infected people and the number of susceptible individuals the infected people are in contact, as well as public health interventions (e.g., social distancing).
Basic reproduction number (R_0) is used to measure the transmission potential of a disease. It is the average number of secondary infections generated by one case in a population where everyone is susceptible (e.g., at the start of an epidemic, before widespread immunity starts to develop via infection or vaccination). For example, if one person develops the infection and passes it on to two others, the R_0 is 2.

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Increased virulence of Delta variant
The Delta variant may be more virulent increasing the risk of hospitalization. Sheik et al. (2021) conducted a study in Scotland where the Delta variant became the dominant strain in May 2021. The study showed that the Delta variant was detected mainly in younger groups. Risk of COVID-19 hospital admission approximately doubled in those with the Delta variant compared to the Alpha variant, with risk of admission particularly increased in those with five or more relevant comorbidities. [50]

A preliminary analysis by Public Health England (2021) of over 43,000 COVID-19 cases found an increased risk of hospitalization with the Delta variant compared with the Alpha variant. [51]

Delta variant and vaccine effectiveness
The Delta variant has the potential to reduce vaccine effectiveness. [52] In its June 2021 analysis, Public Health England reported a 10% absolute reduction in overall vaccine effectiveness after two doses against symptomatic disease with the Delta variant compared with the Alpha variant (79% vs 89%). Full vaccination offered similar protection against hospitalization for the Delta (96%) and Alpha (93%) variants. [51]

Wall et al. (2021) in a study conducted in London, UK, analyzed antibody titers produced by the Pfizer-BioNTech vaccine against five variants: Delta, Beta, Alpha, the original SARS-CoV-2 strain (the strain isolated during the first wave of infection in the UK), and the base wild-type strain (the strain with the original spike sequence). Neutralizing antibody levels were measured after one and two doses of vaccine.

The key finding was that neutralizing antibody titers were comparably lower against both the Delta and Beta variants than either the Alpha or wild-type variant. The antibody levels were sufficient that people who had received two doses of the Pfizer-BioNTech vaccine would be consistently protected, while people who had received a single dose might not be, particularly against the Delta and Beta variants. The authors noted both increased age and time since the second dose of the vaccine was associated with decreased neutralizing antibodies against Delta and Beta variants emphasizing the importance of receiving the second dose as soon as it was available. [53]

Research by Public Health England conducted by Lopez Bernal et al. (2021) demonstrated two doses of COVID-19 vaccines were highly effective against the Delta variant. The study conducted from April-May 2021 found the Pfizer-BioNTech COVID-19 vaccine was 88% effective against symptomatic disease from the Delta variant 2 weeks after the second dose, compared to 93% effectiveness against the Alpha variant. Two doses of the AstraZeneca vaccine were 60% effective against symptomatic disease from the Delta variant compared to 66% effectiveness against the Alpha variant. Both vaccines were 33% effective against symptomatic disease from the Delta variant, 3 weeks after the first dose compared to approximately 50% effectiveness against the Alpha variant. The study is waiting peer-review. [54] [55]

Sheik et al. (2021) found both the AstraZeneca and Pfizer-BioNTech COVID-19 vaccines were effective in reducing the risk of SARS-CoV-2 infection (60% vs 79%) and

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COVID-19 hospitalization in people with the Delta variant, but these effects on infection appeared to be diminished when compared to those with the Alpha variant. [50]

Wall et al. (2021) conducted a study in the UK to compare the AstraZeneca to Pfizer-BioNTech vaccine in regard to neutralizing antibody titers against the Delta variant. The investigators used a high-throughput neutralization assay and found two doses of Pfizer-BioNTech vaccine produced a 2.5-fold better antibody response than two doses of AstraZeneca vaccine. Further, one dose of the AstraZeneca vaccine produced no detectable neutralizing antibodies to the Delta variant in most individuals. Responses to the AstraZeneca vaccine were better among individuals with a history of SARS-CoV-2 infection. [56]

On July 1, 2021, Johnson & Johnson announced data that demonstrated its single-shot Janssen COVID-19 vaccine generated strong, persistent activity against the Delta variant and other highly prevalent SARS-CoV-2 viral variants. In addition, the data showed that the durability of the immune response lasted through at least eight months, the length of time evaluated to date. [57]

Post-vaccination COVID-19 infection

Vaccines provide a high degree of protection from SARS-CoV-2 infection. However, protection does not occur immediately following vaccination as immunity develops over time. Also, since no vaccine is 100% effective, it is expected a small proportion of vaccinated individuals may become infected.

When COVID-19 cases occur following vaccination, there is evidence vaccines reduce symptomatic infection, the severity of illness, as well as transmission. As vaccination reduces severity of infection, asymptomatic post-vaccination cases are expected. Asymptomatically infected post-vaccination cases also may be less likely to transmit infection compared to symptomatic post-vaccination cases. Further, since the timing of infection (i.e., date of infection, approximated by symptom onset date) relative to vaccination (i.e., date of dose administration) is unclear for asymptomatic cases, it is possible that asymptomatic cases were infected prior to vaccination and may not be post-vaccination cases. [33]

Post-vaccination case terms

Public Health Ontario (PHO) uses the following definitions, based on proposed national case definitions, to describe COVID-19 infection following vaccination:

Case not yet protected from vaccination: Cases with a symptom onset date that was 0 to <14 days following the first dose of a COVID-19 vaccine. This time period from vaccination is not sufficient to develop immunity, therefore, these cases are not considered protected from vaccination.

Partially vaccinated case: Cases with a symptom onset date that was 14 or more days following the first dose of a two-dose series COVID-19 vaccine or 0 to <7 days after receiving the second dose. This time period from vaccination may be sufficient to develop some degree of immunity, but these cases are not considered fully protected as

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they have not yet received the second dose or have only recently received the second dose.

Breakthrough (i.e., fully vaccinated) case: Case with a symptom onset date that was 7 or more days following receipt of the second dose of a two-dose series COVID-19 vaccine or 14 or more days following the first dose of a one-dose series COVID-19 vaccine. These cases are considered fully protected from vaccination; however, as vaccine effectiveness is not 100%, it is expected a small number of cases will occur following complete vaccination. [33]

Post-vaccination COVID-19 cases

PHO (2021) analyzed confirmed cases of COVID-19 following COVID-19 vaccination in Ontario from December 14, 2020 to June 12, 2021. During that time period over 9.4 million individuals received at least one dose of vaccine. Amongst the vaccinated individuals, only 0.15% (14,293, asymptomatic and symptomatic cases) became infected when they were partially vaccinated and only 0.02% (1,648) were breakthrough cases. The majority (53.1%; 18,073) were cases not yet protected from vaccination. Hospital admissions, ICU admissions, and deaths were lower for both partially vaccinated and breakthrough cases than among unvaccinated COVID-19 cases. [33]

Birhane et al. (2021) analyzed breakthrough cases reported to the US Centers for Disease Control and Prevention (CDC) from January 1, 2021 to April 30, 2021. A total of 10,262 breakthrough cases were reported as of April 30, 2021. During that time period there were over 33 million cases and approximately 101 million persons had been fully vaccinated. Based on preliminary data of fully vaccinated people, 2,725 (27%) breakthrough cases were asymptomatic, 995 (10%) people were hospitalized, and 160 (2%) individuals died. Among the 995 hospitalized patients, 289 (29%) were asymptomatic or hospitalized for a reason unrelated to COVID-19. Of the 555 cases available for sequencing, 356 (64%) were identified as VOC. From those identified as VOC, the Alpha variant was responsible for more than half (56%; 199) of cases, 8% (28) were Gamma, 4% (13) were Beta, and 33% (116) were the variant of interest Epsilon, first noted in California.

Even though authorized vaccines are highly effective, breakthrough cases are expected, especially before population immunity reaches sufficient levels to further decrease transmission. Nonetheless, vaccine breakthrough infections occur in only a small fraction of all vaccinated persons and account for a small percentage of all COVID-19 cases. The number of COVID-19 cases, hospitalizations, and deaths that will be prevented among vaccinated persons will far exceed the number of vaccine breakthrough cases. [58] [59]

Thompson et al. (2021) conducted a prospective cohort study involving 3,975 healthcare personnel, first responders, and other essential and frontline workers (e.g., retail workers, teacher) to determine secondary benefits of mRNA vaccines (Moderna and Pfizer-BioNTech), including possible reductions in the severity of COVID-19, viral RNA load, and duration of viral RNA detection. The research indicated the adjusted vaccine effectiveness was 91% for fully vaccinated and 81% for partially vaccinated

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workers. Among participants with SARS-CoV-2 infection, the mean viral RNA load was 40% lower in partially or fully vaccinated participants than in unvaccinated participants. Moreover, risk of febrile illness (e.g., fever, feverishness, chills, or temperature higher than 38°C) in partially or fully vaccinated participants infected with the virus was 58% lower, and duration of the illness was shorter, with 2.3 days spent sick in bed compared to unvaccinated workers. [60]

Risk of SARS-CoV-2 transmission from vaccinated cases

As noted earlier, while vaccination has substantially reduced the risk of infection among vaccinated individuals, breakthrough cases do occur. Infections in vaccinated individuals are less severe and more likely to be asymptomatic, but the risk of onward transmission of infection from fully vaccinated individuals is unclear.

PHO (2021) conducted a literature review of selected public health guidance documents up to May 26, 2021. Results indicated there is emerging evidence that the risk of secondary transmission from breakthrough cases is likely reduced compared to unvaccinated cases, as a result of potential lower viral load and shortened period of virus detection. Most of the evidence was found for jurisdictions where Alpha was a dominant variant, although there was limited evidence for other VOC. Most jurisdictions have maintained public health isolation requirements for vaccinated cases, likely due to the uncertainty around the vaccine effectiveness in sub-populations (e.g., elderly, immune suppressed) and against the emerging VOC with immune escape potential. [61]

Immune response from SARS-CoV-2 infection

Previous infection with SARS-CoV-2 may offer some natural immunity, but current evidence suggests that reinfection is possible and experts do not know for sure how long protection from natural immunity might last. Research is ongoing to determine the length and type of immunity from previous SARS-CoV-2 infection.

Dan et al. (2021) analyzed cross-sectional data of SARS-CoV-2-specific immune memory (e.g., antigen-specific antibodies, memory B cells, $CD8^+$ T cells, $CD4^+$ T cells) from 188 participants across a range of severity of COVID-19 for more than 6 months after infection. The researchers found durable immune responses in the majority of people studied. Antibodies against the spike protein of SARS-CoV-2, which the virus uses to get inside cells, were found in 98% of participants 1 month after symptom onset. As seen in previous studies, the number of antibodies ranged widely between individuals. These levels remained fairly stable over time, declining only modestly at 6 to 8 months after infection. Similar to the antibodies, the numbers of different immune cell types varied substantially between individuals. Neither gender nor differences in disease severity could account for this variability. About 95% of participants retained immune memory at approximately 6 months after infection. [62]

Hansen et al. (2021) estimated the amount of protection towards repeat SARS-CoV-2 infection in a population-level observational study. The researchers found that previous infection with SARS-CoV-2 resulted in future protection that lasted at least 3 months and appeared not to decline over 6 months. They estimated protective immunity to be

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approximately 80-83% in people <65 years. Among those aged 65 years and older, immunity was estimated to be approximately 47%. However, the observed low natural immunity in people aged 65 years and older underscored the need to vaccinate previously infected individuals, in particular this age group. [63]

Furthermore, not all individuals recovering from SARS-CoV-2 infection develop SARS-CoV-2-specific antibodies. Studies have shown seroconversion rates are surprisingly variable. For example, Oved et al. (2020) conducted a multicenter study in Israel and found 5% of participants remained seronegative despite a positive nasal swab test and being symptomatic. [64] Similarly, Pathela et al. (2021) in a seroprevalence study from New York found 20% of persons with a positive RT-PCR test result did not seroconvert. [65]

A study by Wellinghausen et al. (2020) in Germany reported 85% of asymptomatic PCR-positive contact persons of COVID-19 cases failed to develop antibodies. [66] Liu et al. (2021) examined the reasons why some people do not seroconvert after SARS-CoV-2 infection. The researchers found non-seroconversion was associated with younger age and lower SARS-CoV-2 viral loads in the nasopharynx. [67]

Post-COVID-19 infection and vaccination

COVID-19 vaccination confers benefit for people who have already been infected from COVID-19. For example, research by Greaney et al. (2021) found the immunity acquired from Moderna COVID-19 vaccination seemed to be more adept at creating antibodies to a wider range of SARS-CoV-2 variants compared to antibodies acquired post-COVID-19 infection. These results suggest individuals who have recovered from COVID-19 have differing levels of antibody protection and would benefit from vaccination. [68]

A study by Ebinger et al. (2021) analyzed blood samples donated by hospital healthcare workers before vaccination and then after each dose of the 2-dose series Pfizer-BioNTech vaccine. Overall, those previously infected with SARS-CoV-2 had higher levels of antibodies at all three time points. The levels of antibodies taken before vaccination in people who were previously infected by the virus were similar to those seen in uninfected people after their first dose. Antibody levels in previously infected people after their first dose were as high as those from uninfected people after their second dose. [69]

Krammer et al. (2021) saw similar results in their study. Participants with SARS-CoV-2 antibodies before the first mRNA vaccine injection (Pfizer-BioNTech or Moderna) rapidly developed uniform, high antibody titers within days after the first dose and second dose, as compared to seronegative participants after first and second dose. [70]

On March 30, 2021, NACI reaffirmed its recommendation that those previously infected with SARS-CoV-2 be offered a complete series with a COVID-19 vaccine. Also, in the absence of one-dose vaccine effectiveness data in previously infected individuals (particularly as it relates to the variants of concern), limited second-dose safety data (i.e., impact of disease severity and the interval since previous infection on

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reactogenicity), individuals with previous SARS-CoV-2 infection should continue to receive a complete vaccine series at the recommended intervals, regardless of the severity of their previous infection. [10]

Vaccine reactogenicity[7] and post-COVID-19 infection
Occurrence of solicited and unsolicited systemic adverse events in individuals with prior SARS-CoV-2 infection was slightly higher compared to the population without prior infection, primarily in younger adults. However, there was no observed increase in the frequency of more severe adverse events in this population. [10]

Post-COVID syndrome and vaccination
Observational studies by Raw et al. (2021), published in the *Journal of Infection*, and Arnold et al. (2021), not yet peer-reviewed, assessed adverse events after COVID-19 vaccination in individuals with post-COVID syndrome or long COVID[8]. Their results indicated receipt of COVID-19 vaccination with either an mRNA or viral vector vaccine was not associated with a worsening of post-COVID syndrome symptoms or increased reactogenicity following immunization. The authors recommended individuals with prolonged COVID-19 symptoms should still receive vaccinations as suggested by national guidance. [71] [72]

Reasons for delaying COVID-19 vaccination
The benefits of COVID-19 vaccination have been established. However, there are reasons why individuals should delay COVID-19 vaccination, such as:

- They have received another vaccine (not a COVID-19 vaccine) in the previous 14 days.
- They are experiencing symptoms of an acute illness (e.g., runny nose, sore throat, cough, fever, chills, diarrhea, nausea, vomiting). These individuals should wait until symptoms have completely resolved in order to avoid attributing any complications resulting from the illness to vaccine-related side effects.
- They are experiencing symptoms of COVID-19 (e.g., anosmia, ageusia, dyspnea, etc.) to minimize the risk of COVID-19 transmission.
- They have been advised to self-isolate due to suspected or confirmed SARS-CoV-2 infection or due to close contact with a COVID-19 case. These individuals should wait until their isolation period is over to minimize risk of virus transmission. [73]

COVID-19 vaccination and special populations
Pregnancy
Most pregnant individuals who become infected with SARS-CoV-2 will have mild-to-moderate symptoms and many can be asymptomatic. However, both Canadian and international data from large studies spanning multiple jurisdictions demonstrate approximately 7-11% of pregnant individuals will require hospitalization for COVID-19-related morbidity and between 1-4% of pregnant individuals require admission to an

[7] Reactogenicity denotes the physical manifestation of the inflammatory response to vaccination, e.g., injection-site pain, redness, swelling, or induration at the injection site, and systemic symptoms, e.g., fever, myalgia, rash, or headache. https://www.nature.com/articles/s41541-019-0132-6
[8] Refer to Episode #38 for more information on Post-COVID Syndrome (Long COVID)

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intensive care unit (ICU). Compared to non-pregnant individuals with COVID-19, pregnant individuals are at increased risk of admission to hospital, critical care, and invasive ventilation compared to age-matched peers.

The risk of severe morbidity from COVID-19 in pregnant individuals appears to be associated with risk factors including age ≥ 35 years old, asthma, obesity, preexisting diabetes, preexisting hypertension, and heart disease. Additionally, both Canadian and US data demonstrate an increased risk of preterm birth associated with SARS-CoV-2 infection in pregnancy which will cause consequent morbidity to the infant related to prematurity. [74]

For example, a systematic review and meta-analysis by Wei et al. (2021) found COVID-19 in pregnant individuals was associated with preeclampsia, stillbirth, and preterm birth compared with no SARS-CoV-2 infection in pregnancy. Symptomatic COVID-19 was associated with an increased risk of Caesarean delivery and preterm birth compared with asymptomatic infection. Compared with mild COVID-19, severe COVID-19 was strongly associated with preeclampsia, gestational diabetes, preterm birth, and low birth weight. [75]

All pregnant individuals in the authorized age group are recommended to be vaccinated as soon as possible, at any stage in pregnancy, as COVID-19 infection during pregnancy can be severe, and the benefits of vaccination outweigh the risks. [76] [10]

NACI preferentially recommends that a complete vaccine series with an mRNA COVID-19 vaccine should be offered to individuals in the authorized age group who are pregnant. NACI recommends that a viral vector COVID-19 vaccine may be offered to individuals in the authorized age group who are pregnant to initiate a series when other authorized COVID-19 vaccines are contraindicated or inaccessible. [10]

The Society of Obstetricians and Gynaecologists of Canada (SOGC) recommends that pregnant individuals should be offered vaccination at any point during pregnancy or while breastfeeding if no contraindications exist. Also, all available COVID-19 vaccines approved in Canada can be used during pregnancy and breastfeeding, but SOGC recommends following provincial and territorial guidelines on type of vaccine to prioritize for pregnant and breastfeeding individuals. [74]

Breastfeeding

COVID-19 vaccines can be safely given to breastfeeding individuals and recent data shows that mRNA from vaccines do not transfer into breastmilk. Anti-COVID-19 antibodies produced by the breastfeeding person have been shown to transfer through the breastmilk and provide protection to the infant. The vaccines are safe for the breastfeeding person, and should be offered to those eligible for vaccination. [76]

NACI preferentially recommends that a complete vaccine series with an mRNA COVID-19 vaccine should be offered to individuals in the authorized age group who are breastfeeding. NACI recommends that a viral vector COVID-19 vaccine may be offered

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to individuals in the authorized age group who are breastfeeding to initiate a series when other authorized COVID-19 vaccines are contraindicated or inaccessible. [10]

Gray et al. (2021) assessed vaccine-induced immunity in vaccinated pregnant, lactating, and nonpregnant individuals. The researchers found mRNA vaccines (Pfizer-BioNTech and Moderna) generated robust humoral immunity in pregnant and lactating individuals, with immunogenicity and reactogenicity similar to that observed in nonpregnant people. Vaccine-induced immune responses were statistically significantly greater than the response to natural infection. Immune transfer to neonates occurred via placenta and breastmilk. [77]

Autoimmune conditions and immunosuppression due to disease or treatment
Health Canada authorized COVID-19 vaccines are considered safe in these groups because they are not live vaccines. However, there is limited data on efficacy. Individuals in the authorized age group with autoimmune conditions, immunodeficiency conditions or those immunosuppressed due to disease or treatment that are receiving stem cell therapy, CAR-T therapy, chemotherapy, immune checkpoint inhibitors, monoclonal antibodies (e.g., rituximab) and other targeted agents (e.g., CD4/6 inhibitors, PARP inhibitors etc.) should be offered the vaccine.

These individuals are strongly encouraged to speak with their treating healthcare provider regarding the timing of vaccination in relation to therapy for their underlying health condition and/or treatment modification in view of possible decreased vaccine effectiveness with the use of immunosuppressive therapy.

All other individuals in the authorized age group with autoimmune conditions, immunodeficiency conditions, or those immunosuppressed due to disease or treatment may choose to receive the vaccine. These individuals may choose to consult with their health care provider prior to vaccination (e.g., to discuss immunosuppressive medication management and timing in relation to their vaccination). [76]

NACI preferentially recommends that a complete vaccine series with an mRNA COVID-19 vaccine should be offered to individuals in the authorized age group with an autoimmune condition or who are immunosuppressed due to disease or treatment. NACI recommends that a viral vector COVID-19 vaccine may be offered to individuals in the authorized age group with an autoimmune condition or who are immunosuppressed due to disease or treatment to initiate a series when other authorized COVID-19 vaccines are contraindicated or inaccessible. [10]

Children and adolescents[9]
The Pfizer-BioNTech vaccine is licensed by Health Canada for adolescents aged 12 years and older. It has been proven to be safe in clinical trials and provided excellent efficacy in adolescents. Side effects reported in adolescents were similar to those observed in adults, and were more frequent after the second dose. [76]

[9] Refer to Episode #33 and #34 for more information on COVID-19 and the pediatric population.

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As of July 2, 2021, children ≤19 years contributed 19.2% (272,257) of the total COVID-19 cases (1,414,929) in Canada. In the pediatric population, COVID-19 is usually mild and often asymptomatic. However, in rare cases, children can become seriously ill and need hospitalization and intensive care. For example, as of July 2, 2021, 1,258 (1.8%) of children 0-19 years were hospitalized, 163 (1.2%) were admitted to ICU, and 14 (0.1%) died in Canada. [78]

One of the possible adverse outcomes for children is multisystem inflammatory syndrome in children (MIS-C).[10] Children with MIS-C have fever and become severely inflamed, developing multisystem disorders involving the heart, lungs, kidneys, brain, skin, eyes, and gastrointestinal tract. The overall mortality of MIS-C is approximately 1-2%. [79] Evidence has shown an association between COVID-19 and MIS-C occurrence. These adverse outcomes of COVID-19 in children justified the necessity to vaccinate children against COVID-19, as the Pfizer-BioNTech COVID-19 vaccine has shown 100% efficacy in children aged 12-15 years.

Herd immunity against COVID-19 is the prerequisite to end this pandemic, either through vaccinations or natural infection. Most estimates placed the threshold for herd immunity at 70% to 90% of the population gaining immunity, mainly by vaccination. [80] Moreover, from an epidemiological perspective, if children are left unvaccinated when adults achieve immune protection, the possibility that unvaccinated children become the virus shelter cannot be excluded, given that most COVID-19 cases in children are mild and asymptomatic. [81]

NACI recommends that a complete series with a Pfizer-BioNTech COVID-19 vaccine should be offered to individuals 12 to 15 years of age without contraindications to the vaccine. [10]

Moderna has filed for authorization with Health Canada for its COVID-19 vaccine in adolescents (12 to less than 18 years). Results are pending. [82]

Clinical trials of the Moderna COVID-19 vaccine, and Janssen COVID-19 vaccine are currently in progress in pediatric populations. The Moderna, Janssen, and AstraZeneca COVID-19 vaccines are not indicated for use for those under the age of 18 years. For children less than 12 years of age, vaccination is not recommended at this time. [76]

Timing of COVID-19 vaccination with other vaccines

There are many routine vaccinations that are important for children and adults to receive to provide protection against vaccine-preventable diseases, such as measles, polio, influenza, HPV-related cancer, tetanus, and chicken pox. [83] [84]

As a precautionary approach, NACI recommends that COVID-19 vaccines and non-COVID-19 vaccines should not be routinely given at the same time. Currently, no data on the simultaneous administration of COVID-19 vaccine with other vaccines are available, although a number of studies are in progress.

[10] Refer to Episode #33 for more information on MIS-C.

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If possible, COVID-19 vaccines should be given at least 14 days after or 28 days before other vaccines, with some exceptions. This will help to avoid possible overlapping side effects and potential, but unknown, interference with the immune response between vaccines.

However, there may be circumstances when a COVID-19 vaccine and a non-COVID-19 vaccine need to be administered at the same time or when a non-COVID-19 vaccine needs to be administered within 28 days after a COVID-19 vaccine. Examples include when a non-COVID-19 vaccine is required for post-exposure prophylaxis or when an individual is about to start treatment that causes immunosuppression. A healthcare professional can help to make this assessment and can discuss the benefits and possible risks with the individual. [85] [10]

COVID-19 vaccine booster doses and re-immunization
Currently, there is no evidence on the need for booster doses of COVID-19 vaccine after a vaccine series is complete. Given the emergence of VOC against, which vaccine effectiveness may be decreased, additional vaccine doses may be necessary. NACI will continue to monitor the evidence and update recommendations as needed. [10]

In the UK, vaccine advisers have recommended a two-stage approach to COVID-19 booster vaccine doses**.** The Joint Committee on Vaccination and Immunisation (JCVI) advised that any potential booster program should begin in September 2021, in order to maximize protection in those who are most vulnerable to serious COVID-19 ahead of the winter months alongside flu vaccination.

For stage one, the JCVI recommended a third dose COVID-19 booster vaccine and the annual influenza vaccine should begin with those most at risk form serious disease, including:

- Adults aged 16 years and older who are immunosuppressed
- Those living in residential care homes for older adults
- All adults aged 70 years or older
- Adults aged 16 years and older who are considered clinically extremely vulnerable
- Frontline health and social care workers [86]

Vaccine hesitancy[11]
COVID-19 vaccines are one of the many important tools that will help put an end to the COVID-19 pandemic in Canada and globally. However, the success of Canada's COVID-19 vaccination program depends on Canadians' acceptance and uptake of these vaccines.

Vaccine hesitancy represents a key barrier to vaccination success. When vaccine uptake is low or decreases, it undermines the strength and public health impact of vaccination programs that exist to keep individuals and communities safe from vaccine-

[11] Refer to Episode #15 for more information on vaccine myths and hesitancy and fostering vaccine acceptance.

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preventable diseases. The World Health Organization defines vaccine hesitancy as “the reluctance or refusal to vaccinate despite the availability of vaccines”. [87]

Most Canadians indicate they intend to get vaccinated against COVID-19 when a vaccine is available to them. Additionally, many studies indicate public confidence in COVID-19 vaccines has increased since COVID-19 vaccines were first authorized, and vaccination of priority groups began in December 2020.

However, research from the initial months of COVID-19 vaccine availability in Canada demonstrates many Canadians express some level of hesitancy in the vaccines. Surveys conducted during this time by the Government of Canada and various polling firms suggest that while a small portion of Canadians do not intend to get a COVID-19 vaccine, others intend to either wait before getting vaccinated or have not yet made up their minds about vaccination.

Vaccine hesitancy is not restricted to the general population as some healthcare providers report apprehension about COVID-19 vaccines. A survey of healthcare providers conducted by the Public Health Agency of Canada in December 2020 identified that 15% of respondents indicated they would not get a COVID-19 vaccine when one became available or were unsure.

While most Canadians are confident in and accepting of COVID-19 vaccines, COVID-19 vaccine hesitancy - among healthcare providers and the general public alike - remains prevalent. [88]

Building confidence in COVID-19 vaccines

Health care providers play a critical role in influencing their clients' decisions around vaccination. Many Canadians have questions about COVID-19 vaccines and may be hesitant to get vaccinated when they have the opportunity. The information and advice healthcare providers share with clients about vaccines, and how they share it, can be a determining factor in clients' decision to get vaccinated against SARS-CoV-2.

Healthcare providers' advice and encouragement can make the largest positive impact on vaccine uptake with clients who are taking a "wait and see" approach to COVID-19 vaccination, or are undecided about vaccination. [88]

The use of a presumptive approach has been shown to be an effective strategy at increasing vaccine acceptance when discussing vaccines (e.g., asking when a client will get their COVID-19 vaccine rather than asking how they feel about getting the vaccine). In addition, motivational interviewing may be useful when discussing concerns about vaccination. There is strong evidence supporting its use when speaking to parents who are hesitant about vaccinating their children. [89]

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Key principles for engaging in conversations about vaccines* [89]

Principle	Talking Tip
Start from a place of empathy and understanding	*There are no wrong questions, my goal is to support you and make sure you have all the information you need to make a decision.* *Can you tell me a bit more about your concerns? I hear your concerns about COVID-19 vaccine. They are all important.*
Assume patients will want to be vaccinated but be prepared for questions.	*Do you have any particular questions you want me to address? When are you planning on booking your COVID-19 vaccine appointment?*
Give your strong recommendation.	*I have already received my COVID-19 vaccine, I am happy I am protecting myself and my community.*
Address misinformation by sharing key facts. Do not repeat the myth (this may reinforce it).	*The vaccine technology is new; however, it has been built upon years of research which is why development was able to occur so quickly.*
Listen to and respond to client questions, and use a tailored approach.	*I understand why you may be concerned about receiving the vaccine while pregnant. I'm happy to share the information I have with you.*
Include information on risks and benefits of vaccination, as most people are looking for balanced information. Frame immunization in terms of positive gains.	*I hear your specific concerns; these are the risks of the vaccine and these are the risks of getting COVID-19.* *I understand you may want to wait for XXX vaccine; however, I recommend you take the first available vaccine to you. Here are the reasons why…*
Proactively explain side effects.	*Most people say that they feel fine after receiving the vaccine, the most common side effect is a sore arm.*

*The key principles may be useful for healthcare providers when engaging in conversations about vaccines with clients. For marginalized community members, messages building trust and confidence should also focus on transparency, supporting autonomy, and validating past and ongoing lived experiences of discrimination.

Take home messages

As more people receive vaccines, cases, hospitalizations, and deaths related to COVID-19 have decreased. The data and studies on people who are becoming infected make it clear that vaccination works. Nonetheless, cases are still occurring, mostly in the unvaccinated populations. Unvaccinated people are more vulnerable to contracting the virus, including the more transmissible variants of concern (VOC). VOC can cause more severe symptoms, illness, and hospitalization among unvaccinated people. The more unvaccinated people there are, the more opportunities for the virus to multiply and mutate creating more VOC and prolonging the pandemic. The virus will probably be with us for the long-term becoming endemic, circulating in pockets of the global population for years to come. [90] However, its social and economic impact will lessen as more people acquire immunity. Therefore, it is vital for everyone who is eligible for vaccination to do so to achieve herd immunity to end the pandemic and get the virus under control.

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Client resources

'My COVID-19 Visit Risk Calculator' can assist individuals in determining their individualized risks based on factors such as personal and family health, vaccination status, and setting safety. https://covidvisitrisk.com/index.html

How to protect yourself from COVID-19, Ministry of Health, June 15, 2021
https://www.publichealthontario.ca/-/media/documents/ncov/factsheet/2021/06/lp/fact-sheet-covid-19-preventive-layers.pdf

Vaccinated against COVID-19? What does it mean to me? Government of Canada, June 25, 2021. This fact sheet outlines prevention measures individuals can use to reduce the spread of SARS-CoV-2.
https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/awareness-resources/vaccinated-against-covid-19-public-health-measures.html

Vaccination in pregnancy & breastfeeding patient decision-making tool, Version 2.0, Ministry of Health, June 22, 2021. This guidance document can be used by individuals to help them make an informed decision about the COVID-19 vaccination during pregnancy and breastfeeding.
https://www.health.gov.on.ca/en/pro/programs/publichealth/coronavirus/docs/vaccine/COVID-19_vaccination_pregnancy_decision_making_support_tool.pdf

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Sick Kids COVID-19 learning hub. Developed by SickKids experts, the learning hub includes parent and caregiver resources on COVID-19, how to support children's mental health and general wellbeing, and information on COVID-19 vaccines. The webpages are available in multiple languages.
https://www.aboutkidshealth.ca/COVID-19

COVID-19 Vaccines for Ontario Youth. The website was created by the Children's COVID-19 Vaccine Table and contains COVID-19 vaccine information for youth, parents, and health and social service providers in a variety of languages.
https://kidshealthfirst.ca/

Vaccines for children: Deciding to vaccinate, Government of Canada, May 18, 2021
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Preparing children for school vaccinations: A parent's guide
https://www.health.gov.on.ca/en/pro/programs/publichealth/coronavirus/docs/vaccine/CARD_parent_pamphlet.pdf

The CARD System. Fact sheet on strategies for youth to aid with vaccination.
https://www.health.gov.on.ca/en/pro/programs/publichealth/coronavirus/docs/vaccine/School_Vaccine_Student_Poster.pdf

19 to zero is a 500+ member coalition of multi-disciplinary experts working to build confidence in vaccines. The website contains information and factsheets for healthcare providers and the public.
https://www.19tozero.ca/

Immunize Canada provides information on COVID-19
- COVID-19 information for the public https://immunize.ca/covid-19-info
- COVID-19 information for healthcare providers https://immunize.ca/covid-19

How to talk about vaccines, World Health Organization, May 19, 2021
https://www.who.int/news-room/feature-stories/detail/how-to-talk-about-vaccines

How to talk to your patients about COVID-19 vaccination, CDC, June 28, 2021
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Additional Resources

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COVID-19 real-world vaccine effectiveness – What we know so far, Public Health Ontario, June 3, 2021, p 1-33
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