Canadian Paediatric Society / Société canadienne de pédiatrie

TECHNICAL REPORT
November 2023

COVID-19 vaccine for children and adolescents: Technical report

Dorothy L. Moore; Canadian Paediatric Society, Infectious Diseases and Immunization Committee

The most substantial effects of the coronavirus disease 2019 (COVID-19) pandemic on children and adolescents have related more to disruptions in educational, physical, and social activities than direct viral effects. Nonetheless, small numbers of cases of severe COVID-19 and SARS-CoV-2-associated multisystem inflammatory syndrome in children (MIS-C) have caused significant direct morbidity.

Over time, genetic mutations in the SARS-CoV-2 virus have resulted in variants that are more transmissible than the original strain, referred to as variants of concern (VOC). With the arrival of the Omicron variants, many more children and adolescents became infected. Consequently, the numbers of children and adolescents with severe disease, although still low, increased. These mutations also affect the level of protection offered by vaccines.

COVID-19 vaccines have been shown to be very effective at preventing severe disease, including hospitalization and death, due to COVID-19. Vaccination against COVID-19 is available in Canada for children and adolescents aged 6 months of age and over.

The Canadian Paediatric Society (CPS) advocates for the vaccination of children and adolescents. For recommendations see the CPS statement COVID-19 vaccine for children and adolescents updated September 25, 2023 [1].

The information below is, in general, extracted from the *Canadian Immunization Guide* (CIG) Part 4: COVID-19 vaccine, version dated October 20, 2023 [2]. Where other sources are used, references are provided.

SARS-CoV-2 impacts on children and adolescents

Direct impacts

The majority of children and adolescents with COVID-19 have mild or asymptomatic disease; however, a small number do get severe disease and require hospitalization [2].

Similar to other age groups, the emergence of the Omicron VOC led to significant increases in COVID-19 cases in all children as well as corresponding increases in the numbers of hospitalizations and intensive care unit (ICU) admissions. For children 6 months to 4 years of age the average monthly rate of hospitalization increased from 1.4 to 15.9 per 100,000, comparing data from March 1, 2020 to December 31, 2021 with that from January 1, 2022 to March 31, 2022. Children younger than 5 years of age have higher COVID-19-associated hospitalization and ICU admission rates compared to older paediatric age groups. Within this group, severe outcomes are more common among children younger than 6 months of age compared to children 6 months to 4 years of age, and more common among children 6 to 11 months of age compared to those 1 to 4 years of age [3][4].

Children who have SARS-CoV-2 infection are at risk of multisystem inflammatory syndrome in children (MIS-C), a rare but serious post-infection complication that generally requires hospitalization [2]. In Canada, 269 cases were reported to the Public Health Agency of Canada between March 11, 2020 and October 2, 2021. Hospitalization was required for 99% of cases and 36% required ICU admission. No deaths from MIS-C were

reported in Canada as of May 31, 2022, but deaths have been reported in the United States. Data suggest that the incidence and severity of MIS-C were reduced during the Omicron waves [3][4].

COVID-19 may also lead to post-COVID condition, also known as post-acute COVID syndrome (PCC), defined as symptoms persisting for more than 8 weeks and present 12 or more weeks following acute infection [2]. While limited, available evidence suggests that the incidence of PCC is lower in children younger than 5 years of age compared to older paediatric age groups, and lower in adolescents than in adults [4][5].

Children and adolescents with chronic medical conditions

Risk factors for severe COVID-19 disease in individuals 12 years of age or older include immunocompromise, cancer, chronic lung or cardiac disease, chronic kidney or liver disease, diabetes type 1 and 2, cerebrovascular disease, developmental disabilities, cerebral palsy, some mental health disorders, and obesity, being medically fragile, or having medically complex needs. Pregnancy is also a risk factor for more severe disease [6].

There is limited evidence on clinical risk factors for severe COVID-19 disease in children younger than 12 years of age, but being medically fragile, having medical complexities, or having more than one comorbidity have been suggested, as well as obesity, neurological disorders, and immunocompromising conditions [2].

Indirect impacts

The COVID-19 pandemic and the public health response to it have also had significant indirect adverse effects. Disruptions in family routines, school and other educational activities, play, and sports, as well as separation from friends, grandparents, and other close family members have affected the mental health and physical well-being of children and adolescents in Canada, with frequency of eating disorders, anxiety, depression, and problematic substance use on the rise [7]-[9]. The effect of the pandemic on the health care system has resulted in children missing out on routine vaccines [10][11].

Furthermore, both the pandemic and responses to it have exacerbated social inequities for racialized and Indigenous communities, refugees and other newcomers to Canada, persons living in low-income settings, and children or youth with disabilities [8][12].

COVID-19 vaccines for children and adolescents

To date, the COVID-19 vaccines used most extensively in children and adolescents in Canada are mRNA vaccines. mRNA vaccines target the spike proteins on the surface of the virus. SARS-CoV-2 messenger RNA directing production of these spike proteins is produced biochemically using recombinant technology, then enveloped in a protective lipid coat. When the mRNA vaccine is injected, it is taken up by macrophages and dendritic cells near the injection site. Inside these cells, the mRNA uses the host cell's ribosomes to produce the SARS-CoV-2 spike protein, which is then expressed on the surface of the cell, stimulating humoral and cellular immune responses. The SARS-CoV-2 mRNA itself does not replicate in the human cell, does not enter the cell nucleus or affect host DNA or RNA, and is rapidly broken down by cellular enzymes. mRNA vaccines are not live vaccines and cannot cause infection in the host [2][13].

The Pfizer-BioNTech COVID-19 vaccine Comirnaty™ was authorized for use in Canada for adults and adolescents aged 16 years and older in December 2020, and for adolescents aged 12 to 15 years old, children aged 5 to 11 years, and children aged 6 months to 4 years in May 2021, November 2021, and September 2022 respectively. The Moderna COVID-19 vaccine Spikevax™ was also authorized for adults 18 years and older in December 2020,

and for adolescents aged 12 to 17 years old, children aged 6 to 11 years, and children aged 6 months to 5 years in August 2021, March 2022, and July 2022 respectively [14].

The Novavax protein subunit vaccine, Nuvaxovid™, was authorized in Canada for adults in February 2022 and for adolescents aged 12 years and over in December 2022. Nuvaxovid consists of purified SARS-CoV-2 spike protein produced using recombinant technology and is adjuvanted [2][14].

Viral vector and virus-like particle COVID-19 vaccines were authorized for adults aged 18 and over in Canada but are not currently in use. For details see the CIG [2].

As of September 15, 2023, 77% of Canadian adolescents aged 12 to 17, 38% of children aged 5 to 11 years and 5.6% of children aged 4 years or less had received a primary series of COVID-19 vaccine, compared with 81% of the overall population [15].

Immunogenicity

All authorized COVID-19 vaccines induce humoral immune responses, including binding and neutralizing antibodies, as well as cellular immune responses. No immunological correlate of protection has been determined for SARS-CoV-2, and therefore the implications of differences in immune responses post-COVID-19 vaccination on protection against infection and severe disease, as well as on duration of protection, are uncertain [2].

Efficacy and effectiveness

Efficacy (protection observed in controlled clinical trials) and effectiveness (protection observed in "real world" vaccine use) of COVID-19 vaccines tend to be lowest against infection, somewhat higher against symptomatic disease, and highest against severe disease. Vaccine effectiveness may be affected by the vaccine product received, the interval between doses, time since last dose, and the age, health status, and prior SARS-CoV-2 infection history of the recipient.

Effectiveness varies by variant. Clinical trials for the original COVID-19 vaccines were mostly conducted when the original or early SARS-CoV-2 strains were circulating and before the emergence of Omicron variants. Compared with the original SARS-CoV-2 strain and earlier variants, the original COVID-19 vaccines have substantially lower effectiveness against infection or symptomatic disease with Omicron sub-lineages, and also somewhat lower effectiveness against severe disease.

Effectiveness against transmission has also been measured. To the extent that COVID-19 vaccines protect against infection, they also prevent transmission because individuals who are not infected cannot transmit. Even if infection is not prevented, vaccination may offer some protection against transmission by inducing shorter duration of illness.
Prevention of infection also prevents PCC. In addition, individuals who received two or more doses of original COVID-19 vaccines were less likely to develop PCC if they became infected than those who were unvaccinated [2].

Efficacy of the primary series against symptomatic COVID-19 disease

In clinical trials, the original mRNA COVID-19 vaccines had an efficacy of over 94% in the short term against confirmed symptomatic COVID-19 disease [16]. Efficacy was similar in children 5 to 11 years old, adolescents 12

to 17 years old, and adults. Clinical trials among children aged 6 months to 4 or 5 years took place during the time when the predominant circulating variant of SARS-CoV-2 was Omicron, but the vaccines studied contained the original virus strain. Short-term efficacy against confirmed symptomatic infection among participants without evidence of prior SARS-CoV-2 infection was 51% among those aged 6 to 23 months and 37% among those aged 2 to 5 years with the Moderna vaccine, and 76% for those 6 to 23 months of age and 72% for those aged 2 to 4 years with the Pfizer-BioNTech vaccine [2]-[4].

In clinical trials, the Novavax COVID-19 vaccine was over 90% efficacious in preventing confirmed symptomatic COVID-19 disease and severe disease caused by early SARS-CoV-2 variants [2].

Efficacy and effectiveness of the primary series against severe COVID-19 disease

In clinical trials, vaccine efficacy against severe COVID-19 disease (hospitalization or death) could not be assessed in children and adolescents because of the scarcity of severe events. Real world evidence suggests moderate to high effectiveness in preventing severe illness in persons aged 12 years and older. It has been estimated that the effectiveness of the Pfizer-BioNTech original vaccine against severe illness due to the Omicron variant in children 5 to 11 years of age was similar to that in older populations. Effectiveness against severe disease is unknown for the Moderna original vaccine in children 6 to 11 years of age due to limited use, or for either vaccine for younger children because severe disease is rare [2].

Real world evidence suggests that the Pfizer-BioNTech COVID-19 original vaccine was 91% effective in preventing hospitalization due to MIS-C among adolescents 12 to 18 years of age [17]. A systematic review indicated that vaccination was associated with lower risk of MIS-C among children 5 to 11 years of age [18].

Duration of protection

Vaccine efficacy as determined by clinical trials was generally assessed within a few months of vaccination. Subsequent studies have demonstrated waning effectiveness, particularly against infection and symptomatic disease, and to a lesser extent against severe disease. There is evidence that longer intervals between the first and second doses of COVID-19 vaccines resulted in more robust and potentially more durable immune responses and potentially higher vaccine effectiveness [2]. Evidence concerning the duration of protection provided by COVID-19 vaccines continues to be monitored [19].

Effectiveness of booster or additional doses

Booster or additional doses increase protection, particularly against severe disease, that has decreased over time. Booster doses of the original vaccines were highly effective against earlier strains of SARS-CoV-2 for both symptomatic and severe disease. Against Omicron, booster doses increased protection compared with pre-booster levels, although protection against infection or symptomatic disease was reduced. Boosters with bivalent vaccines containing the original strains and Omicron strains were more protective against symptomatic disease and severe disease caused by earlier Omicron strains [2][19]. Monovalent vaccines targeting the Omicron XBB.1.5 sub-lineage became available in fall of 2023 and are expected to provide enhanced protection against this strain of Omicron compared with earlier formulations [2][20].

A booster or additional doses are usually offered 6 months or longer after a previous vaccine dose or SARS-CoV-2 infection. Added protection from a booster dose may be affected by the interval between doses. A longer interval between doses is expected to result in a better response after any subsequent dose, because it allows

time for the immune response to mature in breadth and strength. A longer interval may, however, also increase the duration of waning protection while awaiting the next dose [2].
Previously, the National Advisory Committee on Immunization (NACI) recommended that children and adolescents 5 to 17 years of age who are at increased risk of severe illness from COVID-19 should receive booster doses, and that boosters may also be offered to other children and adolescents in this age group. In the fall of 2023, the COVID-19 XBB.1.5 mRNA vaccines were authorized for additional doses in children 6 months to 4 years of age. NACI now recommends that previously vaccinated children in this age group, especially those with risk factors for severe COVD-19, should receive additional doses [2]. Beginning in the fall of 2023, NACI recommends that all individuals previously vaccinated against COVID-19 with non-XBB.1.5 vaccines should receive a dose or doses of a COVID-19 XBB.1.5 vaccine [21]. See Table 2, below.

Safety and adverse events

Evidence regarding vaccine safety is available from COVID-19 clinical trials but the probability of detecting very rare adverse events in clinical trials is low, even in very large studies. Therefore, ongoing pharmacovigilance is essential. Intensive post-marketing surveillance for adverse effects is ongoing in Canada and internationally [2].

Very common and common adverse events

Very common and common adverse events are defined as those that occur in 10% or more or 1% to less than 10% of vaccine recipients respectively.

Local and systemic adverse events were usually mild or moderate and resolved within a few days of vaccination in all age groups. Pain at the injection site was very common. Redness and swelling were common or very common. Localized axillary or groin lymphadenopathy was very common after the Moderna original vaccine. Fatigue, headache, muscle pain, chills, and joint pain were all either common or very common after the administration of any authorized COVID-19 vaccine.

For children aged 6 months to 5 years, the Moderna and Pfizer-BioNTech vaccines were well tolerated. The most frequent reactions reported for children aged 6 months to 2 years were irritability or crying, sleepiness, and loss of appetite [2].

Uncommon, rare, and very rare adverse events

Uncommon adverse events occur in 0.1% to less than 1% of vaccine recipients. Rare and very rare adverse events occur in 0.01% to less than 0.1% and less than 0.01% of vaccine recipients, respectively [2].

Specific events

Lymphadenopathy: Although very common after the Moderna original vaccine, lymphadenopathy was uncommon after administration of the Pfizer-BioNTech original vaccine in clinical trials [2].

Myocarditis or pericarditis: Rare cases of myocarditis and/or pericarditis have been reported following vaccination with COVID-19 mRNA original vaccines. Cases are consistently reported to have occurred more often after the second dose, usually within a week after vaccination, more often in those 12 to 29 years of age and more often in males. Post-marketing studies indicate that extending the interval between doses in the primary series may have been associated with a reduced risk for myocarditis/pericarditis [2].

Analyses of primary series surveillance data in Canada and elsewhere suggest a higher rate of myocarditis/pericarditis cases after Moderna original vaccine (100 mcg mRNA) compared to Pfizer-BioNTech original vaccine, especially among 12- to 29-year-old males following a second dose of a primary series [2]. In Canada, as of November 12, 2021, the rates of myocarditis/pericarditis in the group at highest risk—males 18 to 29 years old after their second vaccine dose—were 15.9 per 100,000 doses for Moderna versus 2.6 per 100,000 for Pfizer-BioNTech vaccine [22].

Myocarditis unrelated to COVID-19 disease or COVID-19 vaccines is typically less common in children 5 to 11 years old than in older children. Surveillance data from the US suggest a lower risk of myocarditis or pericarditis in children aged 5 to 11 years following the Pfizer-BioNTech original vaccination compared to adolescents and young adults who receive this vaccine. The risk of myocarditis or pericarditis with the Moderna original vaccine in children 6 to 11 years of age is unknown, given its limited use in this age group [2]. Post-market vaccine safety data have not identified myocarditis among children aged 6 months to 5 years receiving the Moderna or Pfizer-BioNTech COVID-19 original vaccines after administration of about 1.5 million vaccine doses in this age group [2].

Post-market surveillance indicates that the risk of myocarditis following an original or bivalent booster dose is lower than that following the second dose in the primary series, with no difference in risk between Moderna and Pfizer-BioNTech vaccines. The Moderna vaccine booster doses contained half of the amount of mRNA used for the primary series [2]. Previously, the Pfizer-BioNTech vaccine had been preferred over the Moderna vaccine for the primary series among individuals 12 to 29 years of age. However, this product preference is no longer recommended by NACI. The risk of myocarditis is expected to be lower with the Moderna XBB.1.5 vaccine as it also contains half the amount of mRNA used for the original primary series. The risk of myocarditis and/or pericarditis with the COVID-19 XBB.1.5 mRNA vaccines is expected to be lower than with the original vaccines because primary vaccination for most individuals is only one dose [20].

Available data indicate that most individuals who had myocarditis/pericarditis after mRNA COVID-19 vaccination, though requiring hospitalization, responded well to conservative therapy and tended to recover quickly. Long-term follow-up is ongoing [2].

Cases of myocarditis have been reported rarely following the administration of Novavax Nuvaxovid COVID-19 vaccine [23] with rates of 2 to 4 per 100,000 doses [2]. Reports suggest a possible causal relationship [23]. In Canada, there have been no reported cases of myocarditis/pericarditis following Nuvaxovid as of March 26, 2023 [2].

The known risks of COVID-19 illness for Canadian children and adolescents (including hospitalization and complications such as MIS-C and myocarditis) outweigh the rare risk of myocarditis or pericarditis following vaccination. A US study found myocarditis rates with confirmed COVID-19 infection to be as high as 450 cases per million infections in young males aged 12 to 17 years [7][24]. Similar risk-benefit analysis has not been performed for children in Canada, but data from the US support vaccination for this age group [25].

NACI recommends that anyone receiving an mRNA COVID-19 vaccine should be informed of the risk of myocarditis or pericarditis and advised to seek medical attention if they develop acute chest pain, shortness of breath, or palpitations following vaccination [24]. Health care providers should consider the diagnoses of myocarditis and pericarditis in patients with any of these symptoms, and ask about prior COVID-19 vaccination when they are encountered. Initial investigations should include electrocardiogram (ECG), serum troponins, and echocardiogram, C-reactive protein, and erythrocyte sedimentation rate. If the ECG is abnormal or troponin levels are elevated, or if clinical suspicion of myocarditis or pericarditis is high, an echocardiogram and urgent

cardiology consultation should be obtained. Other potential causes of myocarditis or pericarditis, including acute COVID-19 infection (perform polymerase chain reaction [PCR] test), prior SARS-CoV-2 infection (perform serology), and other infectious or non-infectious etiologies should be investigated [2][7][26].

All cases of myocarditis and pericarditis post-COVID-19 vaccination should be reported promptly to local public health authorities [24].

Refer to the 'Contraindications and Precautions' section below for advice on re-vaccination of individuals who developed myocarditis or pericarditis after a COVID-19 vaccine.

Bell's palsy: Very rare cases of Bell's palsy have been reported following vaccination with COVID-19 mRNA vaccines among individuals aged 12 years and older. Investigations should exclude other potential causes of facial paralysis [2].

Multisystem inflammatory syndrome in children (MIS-C): Very rare cases of MIS-C have been reported following vaccination with COVID-19 mRNA vaccines in Canada and internationally among individuals aged 12 years and older. An assessment by the European Medicines Agency concluded that there is currently insufficient evidence to support a possible link between mRNA COVID-19 vaccinations and these very rare cases [2].

Severe immediate allergic reactions (anaphylaxis): Very rare cases of anaphylaxis have been reported following vaccination with mRNA COVID-19 vaccines [2]. The incidence is estimated to be between 2.0 to 7.9 cases per million doses of vaccine administered [24]. There have been reports of anaphylaxis following the Novavax COVID-19 vaccine [27].

Individuals tend to recover quickly with appropriate treatment and to date there have been no fatalities or long-term morbidity reported in Canada following severe immediate allergic reactions to mRNA COVID-19 vaccines. Most reported cases occurred within 30 minutes of vaccination [2].
Polyethylene glycol (PEG), a component of the mRNA vaccines, has rarely been associated with anaphylactic reactions. PEG is also present in medications including cough syrups, laxatives, prescription drugs and products used for bowel preparation for colonoscopy, ultrasound gel, and contact lens care solutions [2,24].

The mRNA vaccines also contain a buffer, tromethamine (also known as 'trometamol' or 'tris'), that has been used for many years in some other routine childhood vaccines (e.g., Act-Hib, Nimenrix) as well as in other injectable and oral medications, without safety concerns. Allergy to tromethamine has been reported but is extremely rare [24][28].

The Novavax vaccine contains polysorbate 80. Case reports of anaphylaxis to polysorbate 80 have been described. Polysorbate is used as a stabilizer in several other vaccines and in some intravenous and oral medications [24][28]. The vaccine vial stoppers do not contain natural rubber latex [27][29][30][31][32][33][34].

Studies have shown that individuals with a severe immediate allergic reaction after a previous dose of a mRNA COVID-19 vaccine may be revaccinated with the same or another mRNA COVID-19 vaccine following an appropriate medical assessment. Re-vaccination was safe and well tolerated with no or mild reactions when provided in a controlled environment. Available evidence also suggests that most of the reported severe immediate allergic reactions following mRNA COVID-19 vaccines are likely not immunoglobulin E-mediated, and therefore have a low risk of recurrence following future vaccine doses [2].

Refer to the 'Contraindications and Precautions' section below for advice on re-vaccination of individuals who have had an anaphylactic reaction after vaccination and regarding advice for those allergic to components of the COVID-19 vaccines.

Adverse events following Omicron-containing mRNA COVID-19 vaccines

Clinical trial data show that Moderna bivalent BA.1 and Pfizer-BioNTech bivalent BA.4/5 had similar reactogenicity profiles to those of the original versions of these vaccines when given as second booster dose [2]. Clinical trial data to date show that the Moderna XBB.1.5 vaccine has a reactogenicity profile similar to both the original and bivalent Moderna vaccines [33]. The safety of the Pfzer-BioNTech XBB.1.5 is inferred from results with the prior Pfzer-BioNTech original and bivalent vaccines, which are manufactured using the same process [34]. Surveillance for safety is ongoing [2].

Guidance on reporting adverse events following immunization (AEFIs)

Any serious (defined as resulting in hospitalization, permanent disability, or death) or unexpected adverse event that is temporally related to vaccination should be reported to local public health authorities [2]. Refer to 'Adverse Events Following Immunization' in Part 2 of the CIG for more information on vaccine safety, definitions of AEFIs, and for guidance on reporting AEFIs to public health [35].

Doses and administration

In the fall of 2023, there was an important change in approach to dosing of COVID-19 vaccines. With widespread circulation of XBB.1.5 sub-lineages of SARS-CoV-2 in Canada and globally, Canadian seroprevalence studies showing high levels of infection-acquired antibody, and the availability of COVID-19 vaccines targeting COVID-19 XBB.1.5, a single dose of a COVID-19 XBB.1.5 vaccine is considered sufficient for primary vaccination of individuals 5 years of age and over who are not moderately or severely immunocompromised. A primary series of multiple doses is still recommended for children 6 months to 4 years of age because seroprevalence is low in younger children. Doses after primary vaccination are now referred to as additional doses instead of boosters [20].

In the fall of 2023 NACI recommended that unvaccinated children 6 months to <5 years of age who are at high risk of severe illness due to COVID-19 should receive a primary series of a COVID-19 vaccine. High risk children includes those who are medically fragile, have medical complexities or more than one comorbidity, neurological disorders, chronic lung disease, Down syndrome, or other immunocompromising conditions. NACI continues to recommend that others in this age group may receive a primary series of a COVID-19 vaccine and that all individuals ≥5 years of age and previously unvaccinated for COVID-19 should be vaccinated. The latest formulations of mRNA COVID-19 vaccines should be used [20].

COVID-19 vaccine dosages by age and product*:* Non-XBB.1.5 products [2][19][29]

The vaccines in Table 1 are no longer available or of limited availability. COVID-19 XBB.1.5 vaccines are preferred. The information below is provided for assessment of primary vaccination status of previously vaccinated individuals.

Table 1. Primary series vaccine doses by age and product (non-XBB.1.5 vaccine products) *, †, ‡, §, ¶				
Vaccine product	**Age**			
	6 months to 4 years **	**5 years**	**6 to 11 years**	**12 years and older**
Pfizer-BioNTech Comirnaty Original	3 mcg in 0.2 mL (3 doses) ††	10 mcg in 0.2 mL	10 mcg in 0.2 mL	30 mcg in 0.3 mL
Moderna Spikevax Original	25 mcg in 0.25 mL	25 mcg in 0.25 mL	50 mcg in 0.25 mL	100 mcg in 0.5 mL
Novavax Nuvaxovid Original	Not applicable	Not applicable	Not applicable	5 mcg in 0.5 mL
Pfizer-BioNTech Comirnaty Bivalent BA.4/5	Not applicable	10 mcg in 0.2 mL	10 mcg in 0.2 mL	30 mcg in 0.3 mL
Moderna Spikevax Bivalent BA.1	25 mcg in 0.25 mL	25 mcg in 0.25 mL	25 mcg in 0.25 mL	50 mcg in 0.5 mL
Moderna Spikevax Bivalent BA.4/5	25 mcg in 0.25 mL	25 mcg in 0.25 mL	25 mcg in 0.25 mL	50 mcg in 0.5 mL

* By intramuscular injection into the deltoid muscle, or if this is not possible, the anterolateral thigh.
† mRNA vaccines preferred. Novavax vaccine may be offered to those who are not able or willing to receive an mRNA vaccine.
‡ Optimal interval between doses is 8 weeks. For minimal and authorized intervals see the Canadian Immunization Guide.
§ Moderately or severely immunocompromised individuals should receive an extra dose in the primary series (4 doses of the Pfizer-BioNTech vaccine for those 6 months to 4 years of age and 3 doses for all other vaccines and age groups). Recommended interval between doses is 4 to 8 weeks. The Moderna vaccine may be preferred, as the immune response may be better than with the Pfizer-BioNTech vaccine.
¶ If one product is used to start a primary series and another for a further dose, the previous dose is counted and the series continued (e.g., if a primary series is started with an original mRNA vaccine, a bivalent Omicron-containing vaccine can be used to complete the series).
** If a mixed schedule (e.g., at least one Moderna and one Pfizer-BioNTech dose), the 3-dose schedule should be used. Either product can be used for the third dose.
†† All other vaccines and age groups require 2 doses.

Table 2 shows COVID-19 XBB.1.5 vaccine doses and schedules for individuals who are not moderately or severely immunocompromised, and Table 3 shows the same information for individuals who are moderately or severely immunocompromised [2][20][36]

Table 2. COVID XBB.1.5 vaccine doses and recommended intervals by age group and product for immunocompetent individuals [*, †, ‡]				
Vaccine product to be administered	**COVID-19 vaccination history**	**Age**		
		6 months to 4 years	**5 to 11 years**	**12 years and older**
Moderna Spikevax XBB.1.5		Dose 25 mcg in 0.25 mL	Dose 25 mcg in 0.25 mL	Dose 50 mcg in 0.5 mL
	Unvaccinated	2 doses 8 weeks apart	1 dose	1 dose
	1 or more doses of non-XBB vaccine, all of which were Moderna	1 dose 8 weeks from previous dose if 1 previous dose, 6 months[§] from last dose if >1 previous dose		
	If 6 months to 4 years of age: 1 or more doses of non-XBB vaccine, of which 1 or more were Pfizer-BioNTech	1 or 2 doses One previous dose: 2 doses 8 weeks from last dose and 8 weeks apart Two previous doses: 1 dose 8 weeks from last dose Three or more previous doses: 1 dose 6 months[¶] from last dose	1 dose One previous dose: 1 dose 8 weeks from last dose Two or more previous doses: 1 dose 6 months[¶] from last dose	
Pfizer-BioNTech Comirnaty XBB.1.5		Dose 3 mcg in 0.2 mL	Dose 10 mcg in 0.3 mL	Dose 30 mcg in 0.3 mL
	Unvaccinated	3 doses, 8 weeks between doses	1 dose	1 dose
	If 6 months to 4 years of age: 1 or more doses of non-XBB vaccine of which 1 or more were Pfizer-BioNTech	1 or 2 doses One previous dose: 2 doses 8 weeks from last dose and 8 weeks apart Two previous doses: 1 dose 8 weeks from last dose Three or more previous doses: 1 dose 6 months[¶] from last dose	1 dose One previous dose: 1 dose 8 weeks from last dose Two or more previous doses: 1 dose 6 months[¶] from last dose	
Novavax Nuvaxovid XBB.1.5 **		Not available	Not available	Dose 5 mcg in 0.5 mL
	Unvaccinated			2 doses 3 to 8 weeks apart
	1 or more doses of non-XBB vaccine			1 dose 8 weeks after last dose

* With the XBB.1.5 vaccines there is no longer a preference for Pfizer-BioNTech vaccine over Moderna vaccine for individuals 12 years of age and older. See *Specific events: Myocarditis or pericarditis* section.
† By intramuscular injection into the deltoid muscle, or if this is not possible, the anterolateral thigh.
‡ mRNA vaccines preferred. Novavax vaccine (if available) may be offered to those who are not able or willing to receive an mRNA vaccine.
§ If both Pfizer-BioNTech and Moderna vaccines are used in a primary series for an individual 6 months to 4 years of age, the total number of doses in the series should follow the Pfizer-BioNTech schedule.
¶ Shorter intervals (3 months to less than 6 months) have not been shown to pose a safety risk, but antibody response is higher with longer intervals [2]. **A submission for Novavax Nuvaxovid XBB.1.5 vaccine is currently being reviewed by Health Canada. Pending authorization in Canada, information presented in this table is from the US Advisory Committee on Immunization Practices.

Table 3. COVID XBB.1.5 vaccine. Recommended intervals for moderately to severely immunocompromised individuals [*, †, ‡]				
Vaccine product to be administered	**COVID-19 vaccination history**	**Age**		
		6 months to 4 years	**5 to 11 years**	**12 years and older**
Moderna Spikevax XBB.1.5	Unvaccinated	3 doses with 4 to 8 weeks between doses	2 doses 4 to 8 weeks apart	
	1 or more doses of non-XBB vaccine, all of which were Moderna	1 or 2 doses One previous dose: 2 doses 4 to 8 weeks from last dose and 4 to 8 weeks apart Two previous doses: 1 dose 4 to 8 weeks from last dose Three or more previous doses: 1 dose 6 months[§] from last dose		
	If 6 months to 4 years of age: 1 or more doses of non-XBB vaccine of which 1 or more were Pfizer-BioNTech	1 to 3 doses One previous dose: 3 doses 4 to 8 weeks from last dose and 4 to 8 weeks between doses Two previous doses: 2 doses 4 to 8 weeks from last dose and 4 to 8 weeks apart Three or more previous doses: 1 dose 6 months[§] from last dose	1 or 2 doses [¶] One previous dose: 2 doses 4 to 8 weeks from last dose and 4 to 8 weeks apart Two previous doses: 1 dose 4 to 8 weeks from last dose Three or more previous doses: 1 dose 6 months[§] from last dose	
Pfizer-BioNTech Comirnaty XBB.1.5	Unvaccinated	4 doses with 4 to 8 weeks between doses	2 doses 4 to 8 weeks apart	
	If 6 months to 4 years of age: 1 or more doses of non-XBB vaccine of which 1 or more were Pfizer-BioNTech	1 to 3 doses One previous dose: 3 doses 4 to 8 weeks from last dose and 4 to 8 weeks between doses Two previous doses: 2 doses 4 to 8 weeks from last dose and 4 to 8 weeks apart Three or more previous doses: 1 dose 6 months[§] from last dose	1 or 2 doses [¶] One previous dose: 2 doses 4 to 8 weeks from last dose and 4 to 8 weeks apart Two previous doses: 1 dose 4 to 8 weeks from last dose Three or more previous doses: 1 dose 6 months[§] from last dose	

* For doses, see Table 2.

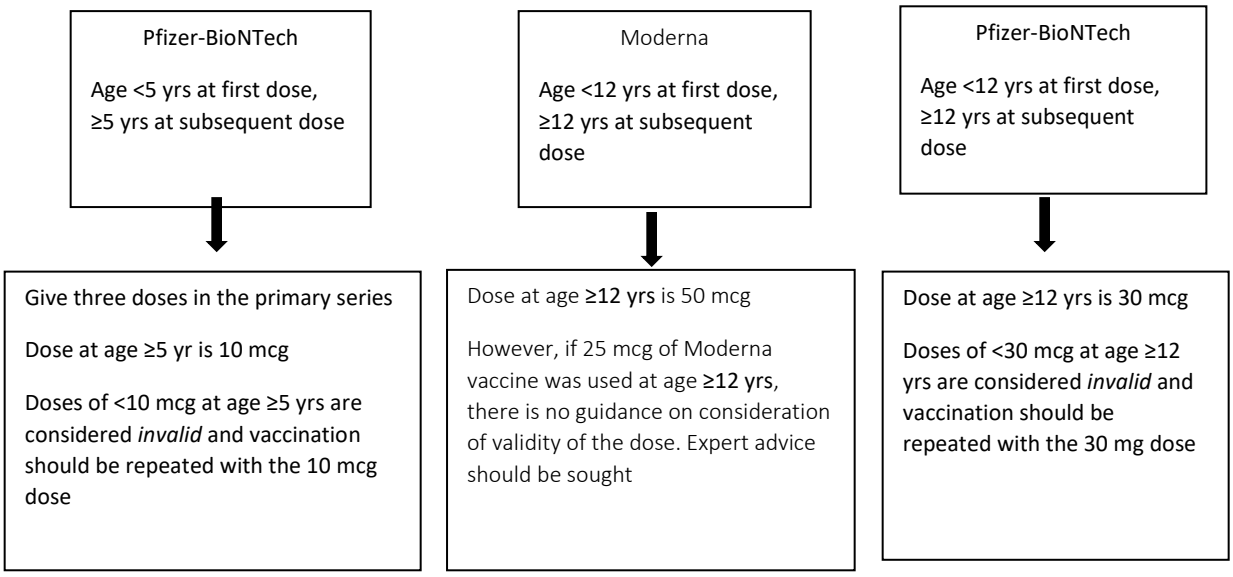
† With the XBB.1.5 vaccines there is no longer a preference for Pfizer-BioNTech vaccine over Moderna vaccine for individuals 12 years of age and older. See *Specific events: Myocarditis or pericarditis* section.

‡ For those 6 months to <5 years of age who are moderately to severely immunocompromised, the Moderna vaccine is preferred because it requires only 3 doses, while the Pfizer-BioNTech vaccine requires 4 doses.

§ Shorter intervals (3 to 6 months) have not been shown to pose a safety risk and may be considered if necessary.

¶ Children who started their primary series with 2 or 3 doses of a non-XBB.1.5 Pfizer-BioNTech product when they were younger than 5 years old and are completing their primary series at 5 years of age or older should receive a total of 4 doses of COVID-19 vaccine in their primary series (i.e., an additional dose of XBB.1.5-containing vaccine above what is listed here) at 4 to 8 weeks from the previous dose.Note: Novavax Nuvaxovid XBB.1.5 vaccine is not yet authorized for use in Canada. For general information on use of this vaccine in immunocompromised individuals 12 years of age and older see the US Advisory Committee on Immunization Practices recommendations.

Figure 1. Children who change age group between doses in their primary series (XXB.1.5 vaccines)



Information drawn from reference 2

Special circumstances

Previous SARS-CoV-2 infection

Children and adolescents who have had a confirmed SARS-CoV-2 infection should receive COVID-19 vaccine because re-infections occur. Immunity resulting from a prior SARS-2-CoV-2 infection can vary due to factors such as the severity of infection, age, presence of comorbidities, the SARS-CoV-2 variant involved, time since the infection, and vaccination history. People who have had both SARS-CoV-2 infection and COVID-19 vaccination have "hybrid immunity", which confers higher vaccine effectiveness than either infection or vaccination alone. A longer interval between infection and vaccination may result in a better immune response because this allows time for the immune response to mature. COVID-19 mRNA vaccination in individuals previously infected with SARS-CoV-2 has a good safety profile and is well tolerated.

COVID-19 primary series and booster or additional doses should be offered to individuals with previous SARS-CoV-2 infection in accordance with recommendations for their age and other risk factors.

Testing for previous SARS-CoV-2 infection is not needed before administering COVID-19 vaccines.

The efficacy and safety of the Novavax COVID-19 vaccine has not yet been established in individuals previously infected with SARS-CoV-2 [2].

Refer to Table 4 for suggested intervals between previous SARS-CoV-2 infection and COVID-19 vaccination [2][20].

Table 4. Suggested intervals between previous SARS-CoV-2 infection* and COVID-19 vaccination		
SARS-CoV-2 infection timing relative to COVID-19 vaccination	**Population**	**Suggested interval between SARS-CoV-2 infection and vaccination†**
Infection prior to completion or initiation‡ of primary vaccination series	Individuals 6 months of age and older who are not considered moderately to severely immunocompromised and with no history of MIS-C	Receive vaccine dose 8 weeks after symptom onset or positive test, if asymptomatic
	Individuals 6 months of age and older who are moderately to severely immunocompromised and with no history of MIS-C	Receive vaccine dose 4 to 8 weeks after symptom onset or positive test, if asymptomatic
	Individuals 6 months of age and older with a history of MIS-C (regardless of immunocompromise status)	Receive vaccine dose when clinical recovery has been achieved or ≥90 days since diagnosis of MIS-C, whichever is longer
Infection after primary series but before a booster or any additional dose	Individuals 6 months of age and older	6 months after symptom onset or positive test, if asymptomatic

***** Previous infection may be defined as confirmed by a polymerase chain reaction or Health Canada-approved antigen detection test (including rapid antigen tests performed at home) OR symptomatic disease compatible with COVID-19 AND household exposure to a confirmed COVID-19 case.

† These intervals are a guide and clinical discretion is advised. The intervals suggested here are based on immunological principles and expert opinion and may change as evidence emerges. When considering the intervals suggested here, biological and social risk factors for exposure (e.g., local epidemiology, circulating variants of concern, living settings) and risks for severe disease should be taken into account. Note that administering an additional dose after shorter intervals (i.e., 3 months to less than 6 months since a previous vaccination or infection) has not been shown to pose a safety risk. Evidence does show that the antibody response is higher with longer intervals between infection and vaccination and with longer intervals between vaccination doses.

‡ Individuals who have not had any previous doses of COVID-19 vaccine may receive their first dose after acute symptoms of COVID-19 have resolved and they are no longer considered infectious, or in accordance with the intervals suggested in this table. Individual benefit and risk assessment and clinical discretion are advised. Waiting until the infected person is no longer infectious is intended to minimize the risk of transmission of SARS-CoV-2 at an immunization venue and to enable monitoring for COVID-19 vaccine adverse events without confounding from symptoms of COVID-19.

Immunocompromise

Immunocompromised individuals are at increased risk for prolonged infection and serious complications from SARS-CoV-2 infection. Studies in adolescent and adults have shown that immunogenicity of mRNA COVID-19 vaccine is substantially decreased in some immunocompromised individuals when compared to healthy vaccine recipients. Observational studies have also shown lower vaccine effectiveness against COVID-19 disease in immunocompromised adults when compared to the general population. Therefore, a primary series that includes an additional dose is recommended [2].

The frequency and severity of adverse events with an mRNA COVID-19 vaccine in immunocompromised populations are comparable to those of non-immunosuppressed individuals. Worsening of underlying disease after immunization has not been reported [2].

For children 6 months to 4 years of age who are moderately to severely immunocompromised a primary series of three doses of the Moderna vaccine is recommended as this product requires one fewer dose than the Pfizer-

BioNTech vaccine and may therefore be more acceptable and feasible for this age group. If the Moderna vaccine is not readily available, the Pfizer-BioNTech vaccine may be offered with a primary series of four doses [2][20]. See Table 3 .

For individuals 5 years of age and older who are moderately to severely immunocompromised, a primary series of three doses of a pre-XBB.1.5 mRNA COVID-19 vaccine was recommended. With the mRNA COVID-19 XBB.1.5 vaccines, two doses are recommended. The Moderna vaccine may result in higher vaccine effectiveness compared to the Pfizer-BioNTech vaccine [2][20]. See Table 3.

mRNA COVID-19 vaccines are preferred for moderately to severely immunocompromised individuals.
Based on clinical discretion, the Novavax XBB.1.5 protein subunit vaccine, if available, may be offered to those who are unable or unwilling to receive an mRNA COVID-19 vaccine. The efficacy and safety of the Novavax XBB.1.5 vaccine has not yet been established in immunocompromised individuals [2].

The recommended interval between doses is 4 to 8 weeks. An interval longer than 4 weeks is likely to result in a better immune response and longer duration of protection, but also lengthens the period of time that an immunocompromised individual may be susceptible to infection. When the longer interval is being considered, risk factors for exposure to SARS-CoV-2 during this interval, including local transmission of SARS-CoV-2, types of circulating VOC, and the individual's risk for severe disease should be taken into account [2].

Individuals with the following conditions are considered moderately to severely immunocompromised: [2]

- Immunocompromised due to solid tumour or hematologic malignancies or undergoing immunosuppressive therapy for these conditions
- Solid-organ transplant and taking immunosuppressive therapy
- Hematopoietic stem cell transplant (within 2 years of transplantation or taking immunosuppression therapy)
- Immunocompromise due to chimeric antigen receptor (CAR) T-cell therapy targeting lymphocytes
- Moderate to severe primary immunodeficiency with associated humoral and/or cell-mediated immunodeficiency or immune dysregulation
- HIV with AIDS-defining illness or TB diagnosis in the last 12 months before starting vaccine series OR severe immune compromise with CD4 <200 cells/uL <500 cells/uL or <750 cells/uL if age 6 years or older, 1 to 5 years old, or <1 year old respectively, OR without HIV viral suppression [2][37].
- Recent treatment with the following categories of immunosuppressive therapies: anti-B-cell therapies (monoclonal antibodies targeting CD19, CD20, and CD22), high-dose systemic corticosteroids (prednisone equivalent of ≥ 2mg/kg/day if weight 10 kg or less, or 20 mg/day if weight >10 kg, for ≥14 days), alkylating agents, antimetabolites, or tumor necrosis factor (TNF) inhibitors and other biologic agents that are significantly immunosuppressive.
- Chronic kidney disease on dialysis.

Refer to 'Immunization of Immunocompromised Persons' in CIG Part 3 for a definition of high-dose steroids, and for guidance on COVID-19 vaccination pre- and post-hematopoietic stem cell transplantation and for chimeric antigen receptor T-cell therapy recipients [38].

In general, immunocompromised individuals should be immunized when maximum immune response can be anticipated [38]. Specific considerations include:

- Completing the primary series at least 2 weeks before any planned immunosuppression, if possible;

- Delaying immunization if the deficiency is transient and if exposure to SARS-CoV-2 is unlikely during this delay; and
- Stopping or reducing immunosuppression to permit better vaccine response, if medically appropriate

Refer to 'Immunization of Immunocompromised Persons' in CIG Part 3 for detailed information on conditions and therapies associated with immunodeficiency and the timing of vaccination in relation to immunosuppressive therapy [38].

Pregnancy and breastfeeding

Pregnant individuals are at risk for more severe COVID-19, with higher rates of hospitalization and ICU admission compared with non-pregnant individuals. COVID-19 in pregnancy is also associated with an increased risk of preterm birth, low birth weight, and admission to a neonatal intensive care unit (NICU) [2].

Evidence suggests that COVID-19 mRNA vaccination during pregnancy leads to antibody levels similar to those in non-pregnant individuals. Maternal antibody crosses the placenta to the fetus, leading to potentially protective antibody titres in the neonatal bloodstream and a lower risk of hospitalization with COVID-19 in the first 4 to 6 months of life compared with infants born to individuals who were unvaccinated [39].

Both anti-spike IgG and IgA are present in breast milk for at least 6 weeks after maternal vaccination with mRNA vaccines [2].

Primary vaccination with an mRNA COVID-19 vaccine should be offered to all individuals who are pregnant or breastfeeding. Booster or additional doses are also recommended for persons who are pregnant. All recommended doses may be given during the course of a pregnancy, regardless of the trimester [2].

An mRNA vaccine is preferred due to reassuring published data on the safety of these vaccines in pregnancy. Rates of adverse events are the same as for non-pregnant persons. Vaccination during pregnancy does not increase risk for miscarriage, stillbirth, low birth weight, preterm birth, NICU admission, or other adverse pregnancy or birth outcomes [2].

People who are breastfeeding experience the same rates of side effects as those who are not. Studies have not found any impact of mRNA COVID-19 vaccination on the child being fed the breast milk, or on milk production [2].

The Novavax COVID-19 vaccine may be offered to pregnant individuals who are not able or willing to receive an mRNA COVID-19 vaccine. Safety and efficacy data with this vaccine in pregnant or breastfeeding individuals are not available. Informed consent should include discussing the limited evidence for the use of the Novavax vaccine in pregnancy or while breastfeeding [2].

Individuals who have received a COVID-19 vaccine during pregnancy are encouraged to enroll in a COVID-19 vaccine pregnancy registry. For further information see the CIG [2].

Contraindications and precautions

Hypersensitivity and allergies

Previous severe immediate allergic reaction (anaphylaxis) to a COVID-19 vaccine: In individuals with a history of a severe, immediate allergic reaction (anaphylaxis) after receiving an mRNA COVID-19 vaccine, consultation

with an allergist or other appropriate physician or special immunization clinic [40] should be sought before re-vaccination.

If a risk assessment deems that the benefits of vaccination outweigh potential risks for the individual, and if informed consent is provided, re-vaccination may be offered with the same or another mRNA vaccine. Vaccine administration should be in a controlled setting, with expertise and equipment present to manage anaphylaxis. Individuals should be observed for at least 30 minutes after re-vaccination. A longer period of observation is warranted for individuals exhibiting any symptom suggestive of an evolving immediate reaction at the end of the 30-minute observation period [2].

If advice from an allergist or other appropriate physician precludes further vaccination with an mRNA vaccine, re-vaccination with the Novavax Nuvaxovid XBB.1.5 vaccine, if available, should be offered provided there are no contraindications, followed by an observation period of at least 30 minutes [2].

Previous confirmed severe immediate allergic reaction to a component of a COVID-19 vaccine: Ingredients of COVID-19 vaccines that have been associated with allergic reactions in other products are PEG and tromethamine (in the mRNA vaccines) and polysorbate 80 (in the Novavax vaccine). There is a potential for cross-reactive hypersensitivity between PEG and polysorbate.

In individuals with a history of confirmed anaphylaxis to a component of a specific COVID-19 vaccine, consultation with an allergist or special immunization clinic is recommended before administering the vaccine. For individuals with a serious PEG allergy in whom mRNA vaccination is precluded based on consultation, vaccination with the Novavax vaccine, if available, may be considered.

Other, less serious reactions may mimic allergic reactions (e.g., vasovagal syncope), and vaccination is not contraindicated in such cases [2].

Mild to moderate immediate allergic reactions to a COVID-19 vaccine or a vaccine component: In individuals with mild to moderate immediate allergic reactions to a previous dose of a COVID-19 vaccine or any of its components, re-vaccination may be offered with the same vaccine or a different mRNA vaccine. Assessment by a physician or nurse with expertise in immunization may be warranted before re-immunization. Most instances of anaphylaxis to a vaccine begin within 30 minutes of administration. Therefore, if re-vaccination is chosen, an observation period of at least 30 minutes post-vaccination should be provided [2].

Allergy to other products: Individuals with a proven severe allergic reaction to injectable therapy unrelated to a component of the COVID-19 vaccines (e.g., other intramuscular, intravenous, or subcutaneous vaccines or therapies) and those with a suspected but unproven allergy to a vaccine component may be routinely vaccinated with COVID-19 vaccines followed by an observation period of 30 minutes.

People with a history of allergy unrelated to a component of the COVID-19 vaccines or other injectable therapy (e.g., foods, oral drugs, insect venom, or environmental allergens) may be vaccinated with the usual observation period of 15 minutes, as recommended for those without allergies [2].

Myocarditis and/or pericarditis

For individuals who have had confirmed myocarditis and/or pericarditis within 6 weeks following a dose of mRNA COVID-19 vaccine, a further dose should be deferred until more information about the risk of recurrent myocarditis becomes available. This precaution also applies to anyone with pericarditis who has had an

abnormal cardiac investigation (ECG, elevated troponins, echocardiogram, or cardiac magnetic resonance imaging). Individuals whose history is compatible with pericarditis but who either did not have a cardiac workup or whose cardiac investigations were normal, can be re-vaccinated when they are symptom-free and at least 90 days have passed since vaccination [2].

Some individuals with confirmed myocarditis or pericarditis may choose to receive another dose of vaccine after discussing risks and benefits with their health care provider. Informed consent should include discussion regarding the unknown risk for recurrence of myocarditis or pericarditis following re-vaccination, and the need to seek immediate medical assessment if symptoms occur [2].

Individuals who have a history of myocarditis unrelated to COVID-19 vaccination should consult their physicians for advice about receiving an mRNA COVID-19 vaccine. If the myocarditis diagnosis is remote and they are no longer followed clinically for cardiac issues, they should receive the vaccine [2].

Guillain-Barré syndrome and Bell's palsy

Individuals with past history of Guillain-Barré syndrome (GBS) unrelated to COVID-19 vaccination should receive an mRNA COVID-19 vaccine.

Individuals who developed GBS or Bell's palsy after a previous dose of a COVID-19 vaccine may receive an mRNA COVID-19 vaccine, after consultation with their health care provider, if it is determined that benefits outweigh risk, and informed consent is provided. When mRNA COVID-19 vaccines are contraindicated, the Novavax XBB.1.5 vaccine, if available, could be considered [2].

Previous MIS-C

It is not yet known whether individuals who have had MIS-C are at risk for recurrence following vaccination or following reinfection with SARS-CoV-2. These theoretical concerns should be weighed against the known risks of reinfection, taking into account risk factors for exposure and for having severe COVID-19 if reinfection occurs. For children with a previous history of MIS-C, vaccination should be postponed until clinical recovery is complete or ≥90 days post-diagnosis, whichever is longer [2].

Acute illness

Vaccination should be deferred in individuals with confirmed or suspected SARS-CoV-2 infection, or with symptoms of a viral respiratory infection, to minimize the risk of COVID-19 transmission at an immunization venue. NACI recommends that if individuals are identified with symptoms on arrival at the venue, they should not be immunized and should be instructed to seek medical and public health advice as appropriate and follow current local public health measures [2]. They should not attend an immunization clinic while isolation or quarantine is recommended [24].

Concurrent administration of other vaccines

COVID-19 vaccines may be given concurrently with, or at any time before or after, any other vaccines, live or non-live, including influenza vaccines. Preferably they should be administered in different limbs. If the same limb must be used, the injection sites should be separated by at least 2.5 cm. Concurrent administration will reduce barriers to the provision of routine childhood immunizations and seasonal influenza immunization. No specific

safety concerns have been identified to date. Studies and surveillance activities to assess the safety and immunogenicity of concurrent administration of COVID-19 vaccines with other vaccines are ongoing [2].

Medications

Prophylactic oral analgesics or antipyretics, such as acetaminophen or ibuprofen, should not be *routinely* used before or at the time of vaccination, due to a theoretical concern regarding their interference with immune response. However, use of these medications before or during vaccination is *not* a contraindication to receiving the vaccine. Oral analgesics or antipyretics may be used to manage pain or fever after vaccination [2].

Tests for tuberculosis reactivity

There is a theoretical risk that mRNA vaccines could temporarily affect cell-mediated immunity, resulting in false-negative tuberculin skin test (TST) or interferon gamma release assay (IGRA) test results. In the absence of data and acknowledging the importance of timely TB testing and of immunization, vaccination with COVID-19 vaccines may take place at any time before, after, or at the same visit as the TST or IGRA test. For individuals for whom there is high suspicion of latent TB infection whose TST or IGRA results are negative, repeat testing at least 4 weeks post-COVID-19 immunization may be considered [2].

SARS-CoV-2 monoclonal antibodies or other blood products

COVID-19 vaccines should not be given concurrently with anti-SARS-CoV-2 monoclonal antibodies. Anti-SARS-CoV-2 monoclonal antibodies have high affinity for the spike protein which could prevent the stimulation of antibody production by the vaccine, or binding of vaccine antigen to the monoclonal antibody may neutralize the antibody. To minimize interference, it is recommended that anti-SARS-CoV-2 monoclonal antibodies should be administered at least 2 weeks following COVID-19 vaccination. If the monoclonal antibody is given first, there is no evidence on which to base a specific minimum interval before COVID-19 vaccination. Expert clinical opinion should be sought on a case-by-case basis, also assessing whether vaccination should be repeated if a dose of monoclonal antibodies has been given too close to the time of vaccination [2].

There is no evidence on which to base recommendations for COVID-19 vaccination and administration of other blood products, including immunoglobulin. Expert clinical opinion should be sought on a case-by-case basis.

Pre-vaccination counselling

Before providing a COVID-19 vaccine, obtaining informed consent should include discussion about frequently occurring minor adverse events and the risks and symptoms of potential but rare severe adverse events (myocarditis/pericarditis, anaphylaxis, Bell's palsy). Parents should be advised to seek medical attention if signs or symptoms suggestive of these conditions occur [2].

Refer to 'Vaccine Administration Practices' in CIG Part 1 for more information on pre-and post-vaccination counselling [41].

Immunization stress-related responses

Immunization can be stressful for children and adolescents and may trigger immunization stress-related responses such as fainting, tachycardia, difficulty breathing, hyperventilation, functional neurological symptoms,

fatigue, and nausea. Symptoms may resemble anaphylaxis. Evidence-based strategies to mitigate pain and stress, such as the CARD (Comfort, Ask, Relax, Distract) system, may be helpful in controlling stress [42][43].

Vaccine hesitancy

COVID-19 vaccine hesitancy has been highly publicized, with most concern focused on the speed with which vaccines have been developed. However, a survey conducted in March 2021 revealed that 77% of Canadians were willing to receive a COVID-19 vaccine [44] and a survey of Canadian parents from December 2020 found that 63% intended to vaccinate their children [45]. Hundreds of millions of doses of mRNA COVID-19 vaccines administered worldwide to date have demonstrated a favourable safety profile. Parents, adolescents, and children should be reassured that despite the rapid development of COVID-19 vaccines, clinical trials and regulatory review have met accepted standards for these processes, and extensive post-marketing surveillance for adverse events is ongoing.

CANADIAN PAEDIATRIC SOCIETY INFECTIOUS DISEASES AND IMMUNIZATION COMMITTEE (August 2023)
Members: Michelle Barton-Forbes MD (Chair); Ari Bitnun MD; Sergio Fanella MD; Justin Penner MD; Jeannette Comeau MD, MSC, FRCPC, FAAP; Laura Sauve MD (Past chair); Raphael Sharon MD (Board representative)
Liaisons: Ari Bitnun MD, Canadian Pediatric and Perinatal HIV/AIDS Research Group; Cora Constantinescu MD, AMMI Canada; Dorothy L. Moore MD, National Advisory Committee on Immunization (NACI); Sean O'Leary MD, Committee on Infectious Diseases, American Academy of Pediatrics; Rupeena Purewal MD, IMPACT (Immunization Monitoring Program, ACTive); Marina Salvadori MD, Public Health Agency of Canada; Isabelle Viel-Thériault MD, Committee to Advise on Tropical Medicine and Travel (CATMAT), Public Health Agency of Canada. **Principal author:** Dorothy L. Moore MD

References

1. Dorothy L. Moore; Canadian Paediatric Society, Infectious Diseases and Immunization Committee. COVID-19 vaccine for children and adolescents. September 25, 2023.
2. Public Health Agency of Canada. Canadian Immunization Guide. Part 4. Immunizing Agents. COVID-19 Vaccines. October 20, 2023. https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/page-26-covid-19-vaccine.html (Accessed November 17, 2023).
3. Public Health Agency of Canada. National Advisory Committee on Immunization (NACI). Archived 42: Recommendations on the use of Moderna Spikevax COVID-19 vaccine in children 6 months to 5 years of age [2022-07-14]. https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/recommendations-use-moderna-spikevax-covid-19-vaccine-children-6-months-5-years.html (Accessed November 17, 2023).
4. Public Health Agency of Canada. National Advisory Committee on Immunization (NACI). Archived 46: Recommendations on the use of Pfizer-BioNTech Comirnaty (3 mcg) COVID-19 vaccine in children 6 months to 4 years of age [2022-10-21]. https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/recommendations-use-pfizer-biontech-comirnaty-3-mcg-covid-19-vaccine-children-6-months-4-years.html (Accessed November 17, 2023).
5. National Advisory Committee on Immunization (NACI). Rapid response: Guidance on the use of booster COVID-19 vaccine doses in adolescents 12 to 17 years of age [2022-01-28]. https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/rapid-response-guidance-use-booster-covid-19-vaccine-doses-adolescents-12-17-years-age.html (Accessed November 17, 2023).
6. Public Health Agency of Canada. COVID-19 signs, symptoms and severity of disease: A clinician guide. June 1, 2022. https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/guidance-documents/signs-symptoms-severity.html#a3 (Accessed November 23, 2023).
7. Public Health Agency of Canada. National Advisory Committee on Immunization (NACI). Archive 18: Recommendation on the use of mRNA COVID-19 vaccines in adolescents 12 to 17 years of age [2021-08-27].

https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/recommendations-use-covid-19-vaccines/mrna-adolescents.html#b1 (Accessed November 17, 2023).
8. Public Health Agency of Canada. National Advisory Committee on Immunization (NACI). Archived 24: National Advisory Committee on Immunization (NACI) statement: Recommendation on the use of the Pfizer-BioNTech COVID-19 vaccine (10 mcg) in children 5 to 11 years of age [2021-11-19]. https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/recommendations-use-covid-19-vaccines/pfizer-biontech-10-mcg-children-5-11-years-age.html (Accessed November 17, 2023).
9. Canadian Paediatric Society. Advocacy Statement, September 2020. Keeping schools open must be a priority for all governments.
10. Sell H, Assi A, Driedger SM, et al. Continuity of routine immunization programs in Canada during the COVID-19 pandemic. Vaccine 2021;39(39):5532-37. doi: 10.1016/j.vaccine.2021.08.044.
11. Piché-Renaud PP, Ji C, Farrar DS, et al. Impact of the COVID-19 pandemic on the provision of routine childhood immunizations in Ontario, Canada. Vaccine 2021;39(31):4373-82. doi: 10.1016/j.vaccine.2021.05.094.
12. Suleman S, Ratnani Y, Loock C, et al; Canadian Paediatric Society, Social Paediatrics Section. What paediatricians can do to support children and youth during the COVID-19 pandemic. May 5, 2020.
13. Pardi N, Hogan MJ, Porter FW, Weissman D. mRNA vaccines – A new era in vaccinology. Nat Rev Drug Discov 2018;17(4):261-79. doi: 10.1038/nrd.2017.243.
14. Health Canada. Drug and vaccine authorizations for COVID-19: List of authorized drugs, vaccines and expanded indications. 2023-10-10. https://www.canada.ca/en/health-canada/services/drugs-health-products/covid19-industry/drugs-vaccines-treatments/authorization/list-drugs.html (Accessed November 17, 2023).
15. Public Health Agency of Canada. COVID-19 vaccination: Vaccine coverage. Last updated 2023-10-30. https://health-infobase.canada.ca/covid-19/vaccination-coverage/ (accessed November 17, 2023).
16. Public Health Agency of Canada. National Advisory Committee on Immunization (NACI). Archived 3: Recommendations on the use of COVID-19 vaccines [2021-01-12]. https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/recommendations-use-covid-19-vaccines/january-12-2021.html (Accessed November 17, 2023).
17. Zambrano LD, Newhams MM, Olson SM, et al. Effectiveness of BNT162b2 (Pfizer-BioNTech) mRNA vaccination against multisystem inflammatory syndrome in children among persons aged 12–18 years — United States, July-December 2021. MMWR Morb Mortal Wkly Rep 2022;71(2):52-58. doi: 10.15585/mmwr.mm7102e1.
18. Piechotta V, Siemens W, Thielemann I, Toews M, Koch J, Vygen-Bonnet S, Kothari K, Grummich K, Braun C, Kapp P, Labonté V, Wichmann O, Meerpohl JJ, Harder T. Safety and effectiveness of vaccines against COVID-19 in children aged 5-11 years: A systematic review and meta-analysis. Lancet Child Adolesc Health 2023;7(6):379-91. doi: 10.1016/S2352-4642(23)00078-0.
19. National Advisory Committee on Immunization (NACI). Interim guidance on the use of bivalent Omicron-containing COVID-19 vaccines for primary series. June 9, 2023. https://www.canada.ca/en/public-health/services/publications/vaccines-immunization/national-advisory-committee-immunization-interim-guidance-use-bivalent-omicron-containing-covid-19-vaccines-primary-series.html (Accessed November 17, 2023).
20. Public Health Agency of Canada. An Advisory Committee Statement (ACS) National Advisory Committee on Immunization (NACI). Updated guidance on the use of COVID-19 vaccines in individuals who have not previously been vaccinated against COVID-19. Published: October 27, 2023. https://www.canada.ca/content/dam/phac-aspc/documents/services/publications/vaccines-immunization/national-advisory-committee-immunization-updated-guidance-covid-19-vaccines-individuals-not-previously-vaccinated/naci-statement-2023-10-27.pdf (Accessed November 17, 2023).
21. Public Health Agency of Canada. National Advisory Committee on Immunization. An Advisory Committee Statement (ACS) National Advisory Committee on Immunization (NACI). Addendum to the guidance on the use of COVID-19 vaccines in the fall of 2023. September 12, 2023. https://www.canada.ca/content/dam/phac-aspc/documents/services/publications/vaccines-immunization/national-advisory-committee-immunization-addendum-guidance-use-covid-19-vaccines-fall-2023/statement.pdf (Accessed November 17, 2023).
22. Public Health Agency of Canada. National Advisory Committee on Immunization. Archived 25: NACI rapid response: Updated recommendation on the use of authorized COVID-19 vaccines in individuals aged 12 years and older in the context of myocarditis and pericarditis reported following mRNA COVID-19 vaccines [2021-12-03]. https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-

naci/rapid-response-recommendation-use-covid-19-vaccines-individuals-aged-12-years-older-myocarditis-pericarditis-reported-following-mrna-vaccines.ht (Accessed November 17, 2023).
23. Twentyman E, Wallace M, Roper LE, et al. Interim recommendation of the Advisory Committee on Immunization Practices for use of the Novavax COVID-19 vaccine in persons aged ≥18 years — United States, July 2022. MMWR Morb Mortal Wkly Rep 2022;71(31):988-92. doi: 10.15585/mmwr.mm7131a2.
24. Public Health Agency of Canada. National Advisory Committee on Immunization (NACI). Archive 22: Recommendations on the use of COVID-19 vaccines [2021-10-22]. https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/recommendations-use-covid-19-vaccines.html (Accessed November 17, 2023).
25. Block JP, Boehmer TK, Forrest CB, et al. Cardiac complications after SARS-CoV-2 infection and mRNA COVID-19 vaccination — PCORnet, United States, January 2021–January 2022. MMWR Morb Mortal Wkly Rep 2022;71(14):517-23. doi: http://dx.doi.org/10.15585/mmwr.mm7114e1.
26. Wong PD, McCrindle BW, Wong K, Khoury M, Chan K, Salvadori M; Canadian Paediatric Society, Acute Care Committee, Community Paediatrics Committee. September 1, 2021. Clinical guidance for youth with myocarditis and pericarditis following mRNA COVID-19 vaccination.
27. Novavax, Inc. Product monograph including patient medication information NUVAXOVID ™ COVID-19 vaccine. Date of revision: July 18, 2023. https://covid-vaccine.canada.ca/info/pdf/nuvaxovid-pm-en.pdf (Accessed November 17, 2023).
28. Public Health Agency of Canada. Canadian Immunization Guide Part 1 − Key Immunization Information. Contents of immunizing agents authorized for use in Canada. https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-1-key-immunization-information/page-15-contents-immunizing-agents-available-use-canada.html (Accessed November 17 2023).
29. 29. Pfizer Canada ULC. Product monograph including patient medication information COMIRNATY®. Date of revision: March 21, 2023 https://covid-vaccine.canada.ca/info/pdf/pfizer-biontech-covid-19-vaccine-pm1-en.pdf (Accessed November 17, 2023).
30. 30.Pfizer Canada ULC. Product monograph including patient medication information COMIRNATY® Original & Omicron BA.4/BA.5. COVID-19 mRNA vaccine, Bivalent. Date of revision: September 13, 2023. https://covid-vaccine.canada.ca/info/pdf/comirnaty-original-omicron-ba4ba5-pm-en.pdf (Accessed November 17, 2023).
31. 31. ModernaTX, Inc. Product monograph including patient medication information SPIKEVAX™. Date of revision: October 4, 2023. https://covid-vaccine.canada.ca/info/pdf/covid-19-vaccine-moderna-pm-en.pdf (Accessed November 17, 2023).
32. 32. ModernaTX, Inc. Product monograph including patient medication information SPIKEVAX™ Bivalent (Original/Omicron). Date of revision: October 4, 2023. https://covid-vaccine.canada.ca/info/pdf/spikevax-bivalent-en.pdf (Accessed November 17, 2023).
33. Moderna Biopharma Canada Corp. Product monograph including patient medication information SPIKEVAX™ XBB.1.5. Date of initial authorization: September 12, 2023. https://pdf.hres.ca/dpd_pm/00072370.PDF (Accessed November 17, 2023).
34. Pfizer Canada ULC. Product monograph including patient medication information COMIRNATY®Omicron XBB.1.5 COVID-19 mRNA vaccine, September 28, 2023. https://covid-vaccine.canada.ca/info/pdf/comirnaty-omicron-xbb-1-5-pm-en.pdf.
35. Public Health Agency of Canada Canadian Immunization Guide: Part 2 - Vaccine Safety. Adverse events following immunization. https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-2-vaccine-safety/adverse-events-following.html (Accessed November 17, 2023).
36. Regan JJ, Moulia DL, Link-Gelles R, et al. Use of updated COVID-19 vaccines 2023–2024 formula for perso ns aged ≥6 months: Recommendations of the Advisory Committee on Immunization Practices —United States, September 2023. MMWR Morb Mortal Wkly Rep 2023;72(42):1140–46. doi: 10.15585/mmwr.mm7242e1.
37. U.S. Department of Health and Human Services. Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection. Appendix C: CDC Pediatric HIV CD4 Cell Count/Percentage and HIV-Related Diseases Categorization. April 11, 2022. https://clinicalinfo.hiv.gov/en/guidelines/pediatric-arv/appendix-c-cdc-pediatric-hiv-cd4-cell?view=full (Accessed November 17, 2023).
38. Public Health Agency of Canada. Canadian Immunization Guide: Part 3 − Vaccination of Specific Populations. Immunization of immunocompromised persons. https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-3-vaccination-specific-populations.html (Accessed November 17, 2023).

39. Public Health Agency of Canada. National Advisory Committee on Immunization (NACI). Archived 44: Updated guidance on COVID-19 vaccines for individuals who are pregnant or breastfeeding [2022-09-09]. https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/guidance-covid-19-vaccines-individuals-pregnant-breastfeeding.html (Accessed November 17, 2023).
40. The Canadian Immunization Research Network (CIRN). Special Immunization Clinic (SIC) Network. https://cirnetwork.ca/network/special-immunization/ (Accessed November 17, 2023).
41. Public Health Agency of Canada. Canadian Immunization Guide Part 1 − Key Immunization Information. Vaccine administration practices. https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-1-key-immunization-information/page-8-vaccine-administration-practices.html (Accessed November 17, 2023).
42. Taddio A, Gudzak V, Jantzi M, et al. Impact of the CARD (Comfort Ask Relax Distract) system on school-based vaccinations: A cluster randomized trial. Vaccine 2022;40(19):2802-09. doi: 10.1016/j.vaccine.2022.02.069.
43. Immunize Canada. CARD for Parents: Preparing children for school vaccinations; A parent's guide. https://immunize.ca/sites/default/files/Resource%20and%20Product%20Uploads%20(PDFs)/Products%20and%20Resources/Pain%20Management/Parents/CARD_general_parentPamphlet_June%2013%202019.pdf (Accessed November 17, 2023).
44. Statistics Canada. Archived: COVID-19 vaccine willingness among Canadian population groups. August 20, 2021. https://www150.statcan.gc.ca/n1/pub/45-28-0001/2021001/article/00011-eng.htm (Accessed November 17, 2023).
45. Humble RM, Sell H, Dubé E, et al. Canadian parents' perceptions of COVID-19 vaccination and intention to vaccinate their children: Results from a cross-sectional national survey. Vaccine 2021;39(52):7669-76. doi: 10.1016/j.vaccine.2021.10.002.

Last updated: November 2023