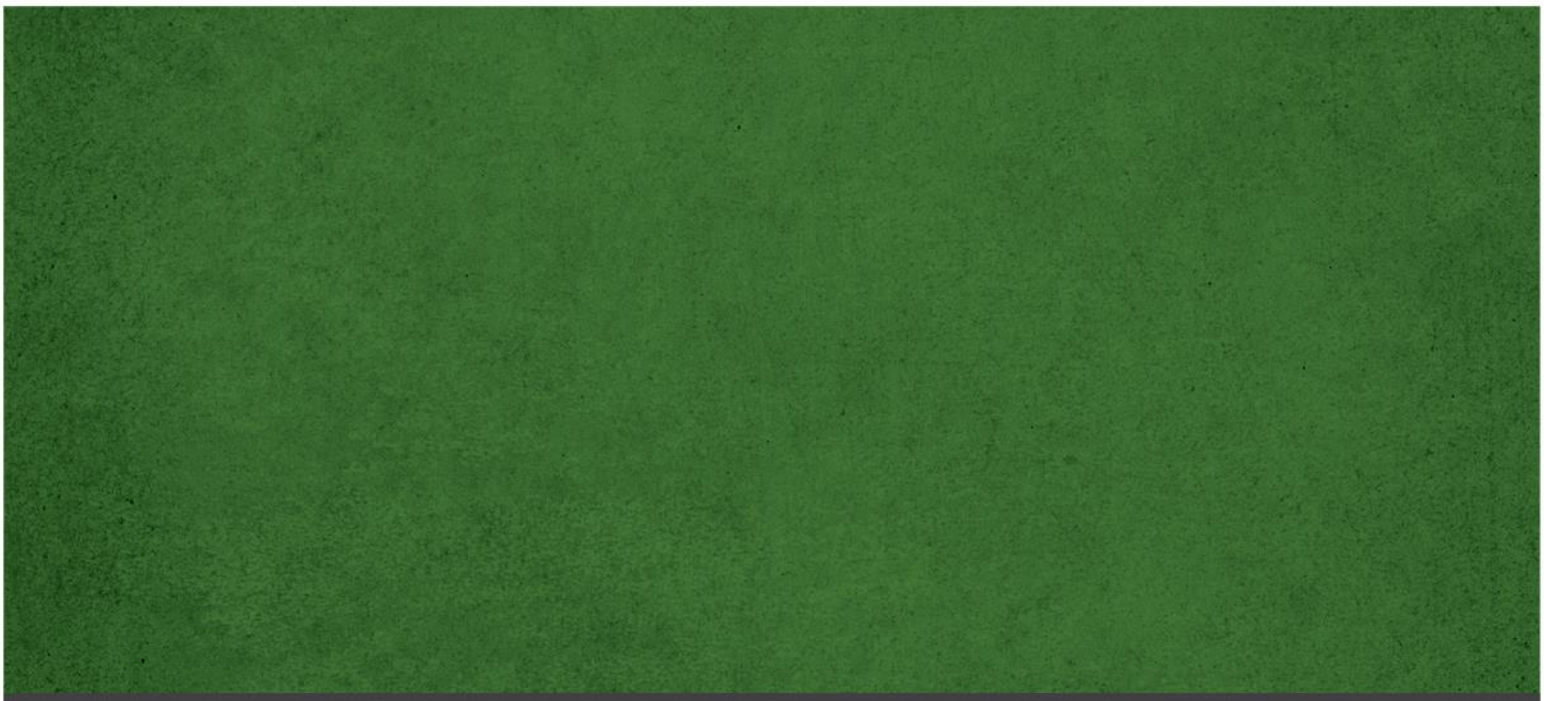
An Advisory Committee Statement (ACS) National Advisory Committee on Immunization (NACI)

Recommendation on the use of the Pfizer-BioNTech COVID-19 vaccine (10 mcg) in children 5-11 years of age

Published: November 19, 2021



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PREAMBLE

The National Advisory Committee on Immunization (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.

In addition to burden of disease and vaccine characteristics, PHAC has expanded the mandate of NACI to include the systematic consideration of programmatic factors in developing evidence-based recommendations to facilitate timely decision-making for publicly funded vaccine programs at provincial and territorial levels.

The additional factors to be systematically considered by NACI include: economics, ethics, equity, feasibility, and acceptability. Not all NACI Statements will require in-depth analyses of all programmatic factors. While systematic consideration of programmatic factors will be conducted using evidence-informed tools to identify distinct issues that could impact decision-making for recommendation development, only distinct issues identified as being specific to the vaccine or vaccine-preventable disease will be included.

This statement contains NACI's independent advice and recommendations, which are based upon the best current available scientific knowledge. This document is being disseminated for information purposes. People administering the vaccine should also be aware of the contents of the relevant product monograph. Recommendations for use and other information set out herein may differ from that set out in the product monographs of the Canadian manufacturers of the vaccines. Manufacturer(s) have sought approval of the vaccines and provided evidence as to its safety and efficacy only when it is used in accordance with the product monographs. NACI members and liaison members conduct themselves within the context of PHAC's Policy on Conflict of Interest, including yearly declaration of potential conflict of interest.

BACKGROUND

The Pfizer-BioNTech (Comirnaty) mRNA COVID-19 vaccine is the first COVID-19 vaccine authorized in Canada for use in pediatric populations under the age of 12 years. Pfizer-BioNTech [10 microgram (mcg) dose] was approved for children 5-11 years of age on November 19, 2021. The Pfizer-BioNTech (Comirnaty) COVID-19 vaccine has been previously authorized by Health Canada as follows:

- December 9, 2020 for individuals 16 years of age and over under an Interim Order using a 30 mcg dose
- May 18, 2021 for individuals 12 to 15 years of age under an Interim Order using a 30 mcg dose
- September 16, 2021 for individuals 12 years of age and over as a full authorization under the name Comirnaty using a 30 mcg dose

On May 18, 2021, following Health Canada authorization of the Pfizer-BioNTech vaccine (30 mcg dose) for individuals 12 to 15 years of age under the Interim Order, NACI recommended the use of the vaccine in adolescents (Strong NACI Recommendation) based on a review of available evidence including additional clinical trial results in the adolescent population. On August 27, 2021, Health Canada expanded the Interim Order authorization for the Moderna (SpikeVax) COVID-19 vaccine to also include adolescents 12 to 17 years of age. That same day, NACI issued updated guidance on the use of mRNA COVID-19 vaccines in adolescents, incorporating additional evidence including clinical data on the efficacy, safety, and immunogenicity of the Moderna COVID-19 vaccine in adolescents as well as post-market safety and effectiveness reports on both mRNA COVID-19 vaccines. Subsequently, Moderna received full authorization on September 16, 2021 for individuals 12 years of age and over under the name Spikevax.

For further information on the use of the Pfizer-BioNTech vaccine in individuals 12 years of age and older, please refer to NACI's Recommendations on the use of COVID-19 vaccines and NACI's Recommendation on the use of mRNA COVID-19 vaccines in adolescents 12 to 17 years of age.

NACI's recommendations are aligned with the following goals of the Canadian COVID-19 Immunization Program, updated in October, 2021: i) to enable as many Canadians as possible to be immunized as quickly as possible against COVID-19, while ensuring that high risk populations be prioritized; ii) minimize serious illness and overall deaths while preserving health system capacity; and iii) reduce transmission to protect high risk populations.

METHODS

On October 26, 2021 and November 2, 2021, NACI reviewed the available evidence on the use of the Pfizer-BioNTech COVID-19 vaccine (10 mcg dose) in children 5-11 years of age (including manufacturer's clinical data in the regulatory submission to Health Canada, modeling projections on the impact of a pediatric vaccine program, and post-market safety data for the 30 mcg dose in older age groups). Ethical considerations related to COVID-19 vaccination in pediatric populations were discussed with the Public Health Ethics Consultative Group (PHECG) on May 3, 2021, July 6, 2021 and September 21, 2021. The Canadian Immunization Committee (CIC) provided feedback on key policy questions to ensure alignment with program needs on October 21, 2021. NACI approved their recommendations on the use of mRNA COVID-19 vaccines in children 5-11 years of age on November 11, 2021.

Details of NACI's evidence-informed recommendation development process can be found elsewhere [1, 2].

SUMMARY OF EVIDENCE

COVID-19 burden of disease in children

Children 5-11 years of age generally present with mild or asymptomatic SARS-CoV-2 infection. Among the 12 jurisdictions currently reporting detailed age data to PHAC, severe outcomes from COVID-19 such as hospitalization and death are very infrequent in children, occurring in <0.3% and <0.002% of confirmed SARS-CoV-2 infections in children aged 5-11 years. As of November 09, 2021, children aged 5-11 years represent 7.5% of confirmed SARS-CoV-2 infections, 0.3% of COVID-19 associated hospitalizations, 0.3% of COVID-19 associated ICU admissions, and 0.007% of COVID-19 deaths in Canada [3]. Persons 12 years of age and older have been eligible to receive COVID-19 vaccines since at least May 2021, depending on age, and recently children 5-11 years of age have represented the population with the highest incidence of confirmed SARS-CoV-2 infection, although hospitalization rates in this age group have remained low during the fourth wave of the pandemic. While the exact prevalence of SARS-CoV-2 seropositivity among children aged 5-11 years is unknown, seroprevalence estimates in children from studies based in Quebec and British Columbia suggest case-level data is likely an underestimate of infection in this age group [4].

Children and adolescents are at risk of multisystem inflammatory syndrome in children (MIS-C) following infection with SARS-CoV-2 [5]. In these age groups, MIS-C is a serious, though uncommon, condition. MIS-C is more frequently reported in males and members of racialized groups or populations, with infrequent comorbidities reported aside from obesity [6, 7]. A large international cohort study on children with COVID-19 estimated MIS-C to affect between 0.5%-3.1% of all diagnosed pediatric COVID-19 patients and between 0.9%-7.6% of hospitalized

pediatric COVID-19 patients [8]. As of October 16, 2021, 272 cases of MIS-C in individuals 0-19 years of age have been reported in Canada [9]. Of these nationally reported cases, over half (59%) were in males, and 40% of cases occurred in children aged 5-11 years, with a median age of 6 years (range: 1 week to 18 years), and 40% of cases occurred in children aged 5 to 11 years. The majority of MIS-C cases in Canada have fully recovered with medical intervention, with no MIS-C associated deaths [9].

Myocarditis can also occur as a complication of SARS-CoV-2 infection, including [very rarely] in children [10].

While evidence is limited in pediatric populations, children may also be at risk of a post-COVID-19 condition (i.e., long COVID or post acute COVID-19 syndrome [11]). However, current evidence suggests the risk is lower in children compared to older age groups [12, 13].

Children are also at risk of collateral harms of the COVID-19 pandemic. Prolonged schooling disruptions, social isolation, and reduced access to academic and extra-curricular resources have had profound impact on the mental and physical well-being of children and their families. These harms can disproportionately affect some Canadian children and families as compared to others, and the impacts of these harms may further exacerbate social inequities among racialized and Indigenous communities, refugees and other newcomers to Canada, persons living in low-income settings, as well as children with disabilities [14-19].

Risk factors most frequently associated with severe disease in school-aged children

There is limited evidence on clinical risk factors for severe COVID-19 disease in children aged 5-11 years [20]. While not specific to pediatric populations, a rapid review of age-independent risk factors for severe COVID-19 conducted by the Alberta Research Centre for Health Evidence (ARCHE) [21] identified strong evidence (moderate or high certainty) for a ≥2-fold increase in mortality from COVID-19, for individuals with Down Syndrome, end-stage kidney disease, epilepsy, neurological disorders including motor neuron disease, multiple sclerosis, myasthenia gravis, and Huntington's disease, as well as type 1 and 2 diabetes. Obesity (BMI >40) was also identified as a risk factor for a ≥2-fold increase in mortality from COVID-19 (low certainty of evidence). Specifically for individuals 21 years of age and younger, having multiple (≥2) chronic comorbidities was identified as a risk factor for severe COVID-19 (moderate certainty of evidence) [21]. Several recent cohort studies in children and adolescents (≤18 years of age) hospitalized for COVID-19 identified the presence of multiple comorbidities [22, 23], obesity [22-24], neurological disorders [22, 24], feeding tube dependence [23], and congregate living settings [23] as independent risk factors for severe COVID-19. Although the relative risk for severe outcomes of COVID-19 may be substantial for children with the comorbidities specified above, the magnitude of the absolute excess risk remains small.

Implications of the SARS-CoV-2 Delta variant on COVID-19 in children

Due to its increased transmissibility compared to other variants of concern, the SARS-CoV-2 Delta variant may pose a higher risk of infection for children when in congregate settings, including in-person schooling, compared to other variants. The Delta variant has been the predominant circulating SARS-CoV-2 strain in Canada since June 2021. A recent rapid review conducted by the Public Health Agency of Canada estimates the Delta variant has increased transmissibility over the Alpha variant by 43-115% [25]. However, data from Canada [26] and the United States (US) [27] suggest that COVID-19 disease severity in children since June 2021 remains consistent with previous waves of the pandemic.

Clinical trial data on the Pfizer-BioNTech mRNA COVID-19 vaccine in children 5-11 years of age

Trial design: The Pfizer-BioNTech COVID-19 vaccine was evaluated in an ongoing, randomized, observer-blind, placebo-controlled Phase 1/2/3 clinical trial in healthy children from 6 months to 11 years of age (C4591007) [28]. In the Phase 1 dose finding trial, due to the frequency and severity of reactogenicity observed with a 30 mcg dose in the first 4 children 5-11 years of age that received two doses, 30 mcg each, the internal review committee (IRC) recommended that the 30 mcg dose be discontinued and the remaining participants who received 30 mcg as dose 1 received 10 mcg for dose 2 instead (n=12). Based on the reactogenicity and immunogenicity observed in the initial cohort of children 5-11 years of age in the Phase 1 trial, a dose of 10 mcg was selected for the Phase 2/3 trial for this age group. At time of regulatory submission, two cohorts totalling 4,647 participants (initial enrolment cohort: n=2,268; a further safety cohort: n=2,379) 5-11 years of age were randomized 2:1 to receive either two doses of the vaccine (10 mcg mRNA; n=3,109) or placebo (n=1,538), 21 days apart. Follow-up is planned for up to approximately 2 years following the second dose.

Study population: All pediatric study participants for the Phase 2/3 trial were recruited from the US, Finland, Poland and Spain. Children with a history of prior SARS-CoV-2 infection or clinical symptoms/signs of COVID-19, children with known HIV, hepatitis B or hepatitis C, or stable pre-existing disease (defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment) were included. Children with an immunocompromising or immunodeficiency disorder, those with a history of MIS-C, or those receiving immunosuppressive therapy (including cytotoxic agents and systemic glucocorticoids) were excluded.

Cohort 1: 1,518 participants randomized to receive the Pfizer-BioNTech COVID-19 vaccine (10 mcg); 750 randomized to receive placebo, with a minimum duration of safety follow-up of 2-months post second dose (median duration of follow-up 3.3 months; data cut-off October 8, 2021). A preliminary descriptive efficacy analysis was also based on this cohort. A randomly selected subset of Cohort 1 was included in the immunogenicity analysis detailed below.

Cohort 2: 1,591 participants randomized to receive the Pfizer-BioNTech COVID-19 vaccine (10 mcg); 788 randomized to receive placebo, with a median duration of safety follow-up of 2.4 weeks post second dose (data cut-off October 8, 2021). Interim safety data from Cohort 2 were provided at the time of regulatory submission.

Immunogenicity comparator group: This was a randomly selected subset (n=300) of participants aged 16- 25 years from the earlier Phase 2/3 study C4591001 who received two doses of the Pfizer-BioNTech COVID-19 vaccine (30 mcg), 21 days apart.

Demographics: Demographic characteristics were similar in Cohort 1 and Cohort 2 study participants. Overall, 48.6% of participants were female, the median age at vaccination was 8.0 years (range: 5-11 years), 20% of participants had an underlying comorbidity, and the most commonly reported comorbidity was obesity (BMI ≥ 95th percentile; 11.4% of participants). 8.7% of participants in Cohort 1 and 10.3% of participants in Cohort 2 reported a positive baseline status for SARS-CoV-2 infection. No participants aged 5-11 years with known HIV were enrolled in the trial.

Safety: Overall, the Pfizer-BioNTech COVID-19 vaccine was well tolerated in children 5-11 years of age. The frequencies of reported solicited local and systemic events are provided in the Appendix. Local reactions were very common and mostly mild to moderate in severity. The median onset of solicited local reactions was 1-2 days after any dose and reactions resolved after a median of 1-2 days. Compared to Phase 3 participants ≥12 years of age in study C4591001 (who received a 30 mcg dose), children 5-11 years of age that received a 10 mcg dose had similar frequencies of pain at the injection site and higher frequencies of swelling and redness.

Systemic events were predominantly fatigue, headaches, muscle pain, chills, fever, and joint pain (in order of descending frequency) and occurred more frequently after the second dose. Fatigue after dose 1 occurred at similar rates in the vaccinated and placebo group, but was higher in the vaccinated group, compared to placebo, after dose 2. The median onset day for most solicited systemic events after either dose of vaccine was 1 to 4 days post-vaccination, with a median duration of 1 day. Most systemic events were mild or moderate in severity. In the vaccine group, the highest frequencies of systemic events graded as severe after dose 1 and dose 2 were for fatigue (0.3% and 0.7%); fever > 38.9°C after dose 1 and dose 2 was reported in 0.2% and 0.6% of participants. One vaccinated participant had a fever of 40.0°C that occurred 2 days after dose 2 and resolved within 1 day.

Compared to Phase 3 participants ≥ 12 years of age in study C4591001 (who received a 30 mcg dose), systemic reactogenicity in children 5-11 years of age receiving a 10 mcg dose was comparable and less frequent for some events (such as fever, chills, headache, and fatigue).

Serious adverse events and other adverse events of interest

In Cohort 1 participants 5-11 years of age (vaccine, n=1,518 and placebo n=750), vaccination-related lymphadenopathy (unsolicited adverse event [AE]) occurred in 0.7% of vaccine recipients. A 6-year-old female in the vaccine group, had an AE of Henoch-Schonlein purpura which was

diagnosed 21 days after dose 1 and was considered non-serious. A 5-year-old female in the vaccine group with transient neutropenia reported at baseline, had an AE of severe neutropenia (worsening from baseline) which was diagnosed 3 days after dose 1 and was considered non-serious and related to the intervention. The patient was withdrawn from the study and dose 2 was not administered. No allergic events or anaphylactoid reactions were reported after either dose. No serious adverse events (SAE) related to the vaccine, no cases of MIS-C, myocarditis/pericarditis or deaths were reported. Given the trial was limited to n=3,109 participants randomized to receive the Pfizer-BioNTech vaccine, it is unlikely that any AE occurring at a frequency less often than 1 in 1,000 would be detected.

Expanded safety data

The findings for Cohort 2 participants (vaccine, n= 1,591 and placebo, n= 778 for placebo) were limited to a median follow-up duration of 2.4 weeks after dose 2 at time of data cut-off.

Preliminary safety data available on Cohort 2 participants suggested a similar profile to the initial safety dataset [29]. No cases of myocarditis/pericarditis, MIS-C, anaphylaxis or anaphylactoid reactions or deaths were reported.

Concurrent administration with other vaccines

A small percentage (≤0.8%) of trial participants were administered a different non COVID-19 vaccine concurrently with the Pfizer-BioNTech vaccine or placebo. No analyses were performed to determine the impact of concurrent administration of other vaccines on safety or other outcomes.

Immunogenicity: The humoral immune response was evaluated based on SARS-CoV-2 50% neutralizing antibody titres (NT-50) assessed one month following the second dose. A 1.5-fold non-inferiority criterion was pre-established to compare immune responses in children 5-11 years of age to that in adolescents and young adults 16-25 years of age (point estimate of the geometric mean ratio [GMR] of titres ≥0.8 and lower bound of the 2-sided 95% confidence interval (CI) for the GMR of titres >0.67). The GMR of titres in children 5-11 years of age (n=264) relative to those in 16- 25 years of age (n=253) was 1.04 (95% CI: 0.93 to 1.18), meeting both criteria for non-inferiority. Immunogenicity data in children following dose 1 and prior to dose 2 were not assessed.

A smaller randomly selected subset of 38 participants aged 5-11 years were assessed for neutralization titres against both the Delta variant and wild-type strain using a non-validated plaque reduction neutralization assay. Of the 38 participants, 34 received the vaccine and 4 received placebo, and all were without evidence of prior SARS-CoV-2 infection. Neutralization of both the wild-type strain and the Delta variant were comparable by NT-50 assay in participants that received the vaccine, one month following dose 2 [GMT: 365.3 (95% CI: 279.0 to 478.4) for the wild-type strain, and 294.0 (95% CI: 214.6 to 405.3) for the Delta variant]. Participants that received the placebo had a GMT of 10 (95% CI: 10 to 10) for both the wild-type and the Delta variant.

Recent evidence suggesting that neutralizing antibodies may serve as a correlate of protection for vaccines against SARS-CoV-2 in humans is evolving [30]. However, since no correlate of protection has been established for COVID-19 at this time, it is unknown how reported immune responses are related to prevention of SARS-CoV-2 infection or disease or the ability to transmit infection to others.

Efficacy: Preliminary efficacy data were limited to the evaluable efficacy population from Cohort 1 (individuals who did not have evidence of SARS-CoV-2 infection prior to dose 2; 1,305 randomized to receive the vaccine; 663 randomized to receive placebo). As of October 8, 2021 (data cut-off date for analysis), a total of 19 confirmed, symptomatic cases of COVID-19 were identified at least 7 days after dose 2 of the Pfizer-BioNTech COVID-19 vaccine or placebo in study participants 5-11 years of age. The estimated efficacy of the vaccine against symptomatic COVID-19 from 7 days after dose 2 was 90.7% (95% CI: 67.7 to 98.3%; 3 cases identified in the vaccine group and 16 cases in the placebo group). An analysis of efficacy by various subgroups (sex, race, and ethnicity, presence of comorbidities, and country of recruitment) resulted in point estimates of vaccine efficacy (all above 85%) that were similar to the overall estimate. However, many of the subgroup efficacy estimates were based on a small number of cases, resulting in large confidence intervals around these point estimates.

The majority of confirmed cases in study participants were identified in August and September 2021, at a time when the Delta variant was the predominant circulating strain in the US and globally. However, no sequence analysis was reported on case isolates to determine whether they were caused by the Delta variant or another variant.

None of the identified cases met the pre-defined criteria for a severe case of COVID-19, therefore the data did not include estimates of vaccine efficacy against severe outcomes such as hospitalization, MIS-C or death [31].

Myocarditis and/or pericarditis and MIS-C/A following mRNA COVID-19 vaccination

Cases of myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of the lining around the heart) have been reported following vaccination with mRNA COVID-19 vaccines in Canada and internationally among individuals aged 12 years and older who received the 30 mcg formulation of the Pfizer-BioNTech COVID-19 vaccine or 100 mcg formulation of the Moderna COVID-19 vaccine; however, the risk is considered rare. Symptoms of myocarditis/pericarditis can include shortness of breath, chest pain, or the feeling of a rapid or abnormal heart rhythm. Symptoms can be accompanied by abnormal test results (e.g., electrocardiogram, serum troponins, echocardiogram) [32]. Available data indicate that most individuals affected have responded well to conservative therapy and have recovered quickly [33].

Cases of myocarditis/pericarditis following COVID-19 mRNA vaccination occur most commonly in adolescents and young adults (12 to 30 years of age), more often after the second dose, more

often in males than females, more often after Moderna than Pfizer-BioNTech, and usually within a week of vaccination. Emerging Canadian safety surveillance data suggest an extended interval between the first and second dose may reduce the risk of myocarditis/pericarditis associated with the second dose of an mRNA COVID-19 vaccine (note this data is currently under preparation for publication). Data from the US suggest the risk of myocarditis/pericarditis following mRNA COVID-19 vaccination may be higher in older adolescents aged 16-17 years compared to younger adolescents aged 12-15 years [33].

Myocarditis following mRNA COVID-19 vaccination tends to have a similar epidemiologic profile to classic myocarditis (unrelated to COVID-19), as it occurs more commonly in adolescents and young adult males. Classic myocarditis is less common in younger children 5-11 years of age. It is unknown whether myocarditis/pericarditis will occur after the lower doses of mRNA present within pediatric COVID-19 vaccines for children 5-11 years of age [33].

Very rare cases of MIS-C/A (multisystem inflammatory syndrome; in children and in adults, respectively) have been reported following vaccination with COVID-19 mRNA vaccines in Canada and internationally among individuals aged 12 years and older. However, on October 29, 2021, the European Medicines Agency (EMA) Pharmacovigilance Risk Assessment Committee (EMA-PRAC) issued a statement that there is currently insufficient evidence on a possible link between mRNA COVID-19 vaccines and very rare cases of MIS-C/A [34].

Adult/adolescent and pediatric formulations of the Pfizer-BioNTech vaccine

Table 1. Adult/adolescent and pediatric formulations of the Pfizer-BioNTech vaccine

	Adult/adolescent formulation	**Pediatric formulation[a]**
Age	12 years of age and over	5-11 years
Vial Cap Colour	**Purple**	**Orange**
Diluent (ONLY use 0.9% Sodium Chloride Injection, USP as the diluent)	**1.8 mL**	**1.3 mL**
Dose	**0.3 mL** (30 micrograms)	**0.2 mL** (10 micrograms)
Doses per vial	**6**	**10**
Potential allergens	Polyethylene glycol (PEG)	Polyethylene glycol (PEG) Tromethamine (Tris, Trometamol)[b]

Post-dilution time Can be at room temperature	6 hours	12 hours
Ancillary supplies	Low dead volume needle/syringe	Low dead volume needle/syringe

Storage[c,e]	• Ultra-frozen until expiry date printed on the label [g]
	• Frozen for up to 2 weeks [f, g]
	• Refrigerated [d] for up to 1 month
	• Room temperature [d] for:
	  ○ up to 2 hours prior to dilution;
	  ○ up to 6 hours after dilution (i.e., post first puncture)
		• Ultra-frozen up to 6 months from the date of manufacture printed on the vial and cartons [a]
		• Do not store frozen
		• Refrigerated [d] for up to 10 weeks
		• Room temperature [d] for:
		  ○ up to 12 hours prior to dilution;
		  ○ up to 12 hours after dilution (i.e., post first puncture)

Transport[c]	• Ultra-frozen full cartons containing vials [g] • Frozen vials up to 2 weeks (included in 2-week limit for frozen storage) [f, g] • Refrigerated [d] thawed vials up to 12 hours (included in 1-month limit for refrigerated storage)	• Ultra-frozen full cartons containing vials • Refrigerated [d] full cartons or individual undiluted vials

[a] Regardless of storage condition, vaccines should not be used after 6 months from the date of manufacture printed on the vial and cartons.

[b] Tromethamine (Tris or trometamol) is used as a buffer in vaccines and medications, including those for use in children, to improve stability and prevent pH fluctuations in the solution. No safety concerns have been identified with tromethamine [(35)]. While tromethamine has been identified as a potential allergen, a review of existing evidence did not identify any cases of allergic reactions to tromethamine in children [(36)].

[c] Ultra Frozen is -90°C to -60°C; Frozen is -25°C to -15°C; Refrigerated is +2°C to +8°C; Room temperature is up to + 25°C.

[d] Once vials are thawed, they should not be refrozen.

[e] During storage, minimize exposure to room light, and avoid exposure to direct sunlight and ultraviolet light.

[f] Frozen vials stored for up to 2 weeks at -25°C to -15°C may be returned one time to ultra-frozen storage. Total cumulative time the vials are stored at -25°C to -15°C should not exceed 2 weeks.

[g] Vials must be kept frozen and protected from light, in the original cartons, until ready to thaw.

For complete prescribing information for the pediatric and adult formulations of the Pfizer-BioNTech vaccine, consult the product leaflet or information contained within Health Canada's authorized product monographs available through the Drug Product Database.

Schedule

Refer to Table 2 for a summary of immunization schedules for authorized COVID-19 vaccines for children 5-11 years of age.

Table 2. Immunization schedule for primary series, by COVID-19 vaccine

Vaccine Product	Dose	Immunization Schedule	Minimum Interval	Authorized Interval	NACI - Recommended Interval[1]
Pfizer-BioNTech (Comirnaty; 10 mcg)	0.2mL	2-dose schedule	19 days	21 days	At least 8 weeks

[1]There is emerging evidence that longer intervals between the first and second doses of COVID-19 vaccines result in more robust and durable immune response and higher vaccine effectiveness. See Evidence to inform an optimum dosing interval for the primary series of an mRNA COVID-19 vaccine section below. NACI will continue to monitor the evidence and update this interval as needed.

Evidence to inform an optimum dosing interval for the primary series of an mRNA COVID-19 vaccine

Shorter intervals between doses of COVID-19 mRNA vaccines result in lower antibody titres, which may wane to below protective levels more quickly over time. Currently, there is no direct evidence to establish an optimal interval between doses in pediatric populations. However, evidence on COVID-19 mRNA vaccines in adult populations indicates that a longer dose interval such as 8 weeks, compared with the authorized 21-day interval, improves the immune response and is associated with greater vaccine effectiveness that may last longer, which is consistent with general principles of vaccinology [37-40]. In addition, emerging Canadian safety surveillance data suggest an extended interval between the first and second dose may reduce the risk of myocarditis/pericarditis following the second dose of an mRNA COVID-19 vaccine (note this data is currently under preparation for publication).

Ethics considerations on the use of the Pfizer-BioNTech COVID-19 vaccine in children 5-11 years of age

The guiding consideration for COVID-19 pediatric vaccine recommendations should be whether vaccination is in children's best interests. Decisions regarding pediatric COVID-19 vaccination programs should not only evaluate the direct and indirect benefits and risks of vaccination in this age group, but also consider principles such as the precautionary principle, equity, trust, and proportionality. There are multiple and intersecting uncertainties at play, including those related to the impact of COVID-19 on children's health; the long-term effectiveness of vaccination in this age group; potential safety concerns (e.g., uncertainty around the risk of myocarditis and pericarditis); and the future progression of the pandemic, including the emergence of variants of

concern. While it is not justified to vaccinate children only to benefit others, the indirect, population-level benefits of vaccination can also benefit children.

The overall safety and effectiveness data are limited for children. While it is justifiable to make recommendations based on available data for children 5-11 years of age, including following the dosing intervals associated with the clinical trial data, the precautionary principle also justifies taking action under conditions of scientific uncertainty to mitigate vaccine-related risks, including through active post-market surveillance. This includes using data available from other age groups and applying vaccination principles.

Generally, a vaccination program is justified if its anticipated benefits outweigh its potential risks. Children aged 5-11 years are unlikely to be deemed capable of consenting to vaccination, and decisions related to their vaccination will likely be made by parents or guardians. Given the short-term uncertainties surrounding pediatric vaccination at this time, children and their parents or guardians should be supported and respected in their decisions regarding COVID-19 vaccinations for the child, whatever decisions they make, and should not be stigmatised for accepting, or not accepting, the vaccination offer.

RECOMMENDATIONS

NACI recommends that a complete series with the Pfizer-BioNTech COVID-19 vaccine (10 mcg) may be offered to children 5-11 years of age who do not have contraindications to the vaccine, with a dosing interval of at least 8 weeks between first and second dose. (Discretionary NACI Recommendation)

- The Phase 2/3 clinical trial had 1,518 children who received the Pfizer-BioNTech COVID-19 vaccine (10 mcg), and 750 who received the placebo; both groups were followed a minimum of 2 months. A further safety cohort of 1,591 received the vaccine and were followed for a median of 2.4 weeks. Interim findings did not indicate any safety concerns and preliminary efficacy against symptomatic COVID-19 was 90.7%. No cases of myocarditis/pericarditis or any other SAE were reported. Any uncommon, rare, or very rare AE that occurs at the frequency less often than 1 in 1,000 would not be detected with this trial size. NACI will closely review emerging evidence and will update their recommendation, as well as its strength, as the evidence base evolves.

- **Children aged 5-11 years with a history of previous SARS-CoV-2 infection (confirmed by PCR or antigen testing from a respiratory specimen) should no longer be considered infectious based on current criteria, and symptoms of an acute illness should be completely resolved prior to vaccination.** Consistent with current recommendations for adolescents and adults with previous infection, two doses of a COVID-19 vaccine may be offered to children with a previous history of SARS-CoV-2 infection. NACI will closely review emerging evidence and will update their recommendation as the evidence base evolves.

- **For children with a previous history of MIS-C, vaccination should be postponed until clinical recovery has been achieved or until it has been ≥ 90 days since diagnosis, whichever is longer.**

- Unlike adolescent and adult populations with defined risk estimates for rare and very rare AEs following COVID-19 vaccination, thorough post-market safety surveillance will be required to inform risk estimates of any AEs that may occur in children 5-11 years of age. Therefore, considering the risk of erroneous attribution of an AEFI to a given vaccine, it may be preferential during early program rollout to refrain from offering concomitant administration of COVID-19 vaccines and other vaccines for children 5-11 years of age. However, feasibility may be challenging for both healthcare providers and parents if multiple visits to healthcare providers are required to administer all recommended immunizations. Concomitant administration or a shortened interval between COVID-19 vaccines and other vaccines may be warranted on an individual basis in some circumstances at the clinical discretion of the healthcare provider. Given these considerations, in the early program rollout:
    - **COVID-19 vaccines for children 5-11 years old should not routinely be given concomitantly (i.e., same day) with other vaccines (live or non-live).** In the absence of evidence, it would be prudent to wait for a period of at least 14 days BEFORE or AFTER the administration of another vaccine before administrating a COVID-19 vaccine to prevent erroneous attribution of an AEFI to one particular vaccine or the other. This suggested minimum waiting period between vaccines is **precautionary** at this time.

- Children who receive the 10 mcg Pfizer-BioNTech COVID-19 vaccine for their first dose and who have turned 12 years of age by the time the second dose is due may receive the 30 mcg Pfizer-BioNTech COVID-19 vaccine that is authorized for individuals aged 12 years and older to complete their primary series. If the second dose of 10 mcg is given, the dose should still be considered valid and the series complete.

- Risk of severe outcomes of COVID-19 may be an important element of individual decision-making, and the literature is evolving and emerging to clarify areas of heightened risk with infection. Children at increased risk for severe outcomes may include children who are obese, children who are medically fragile/ have medical complexities, children with more than one comorbidity, children with neurological disorders, and children with immune dysregulation associated with Down Syndrome and other immunocompromising conditions.

Additional Considerations, Summary of Evidence, and Rationale

- The Pfizer-BioNTech COVID-19 vaccine (10 mcg dose) met non-inferiority criteria for generating a humoral immune response to the vaccine in children aged 5-11 years compared to young adults and adolescents aged 16 to 25 years (who received a 30 mcg dose). Interim phase 2/3 findings in children 5-11 years of age suggest the vaccine is efficacious at preventing symptomatic COVID-19, with a similar estimate of vaccine efficacy against symptomatic COVID-19 to that observed in individuals aged 12 years and over. The systemic reactogenicity profile in children ages 5-11 years (10 mcg dose) was lower than that observed for adolescents and young adults (who received a 30 mcg dose).

- The Pfizer-BioNTech vaccine for children 5-11 years of age is authorized as a primary series of two 10 mcg doses given 21 days apart. In adults, emerging evidence suggests that longer intervals between the first and second doses of a primary series result in a stronger immune response and higher vaccine effectiveness that is expected to last longer, compared to shorter intervals. Data from older age groups also suggests an extended interval may also be associated with a reduced risk of myocarditis/pericarditis following a second dose of an mRNA COVID-19 vaccine.
- Rare cases of myocarditis and/or pericarditis have been reported following administration of the Pfizer-BioNTech vaccine (30 mcg dose) in adolescents and young adults 12 years of age and older, most commonly after dose 2 and in males.
- Currently, the risk of myocarditis/pericarditis in children following immunization with the 10 mcg dose of the Pfizer-BioNTech vaccine is unknown. Safety surveillance data from individuals aged 12 and older does not suggest the risk of myocarditis/pericarditis following mRNA COVID-19 vaccination would be greater in children aged 5-11 years compared to older populations. Additionally, the impact of a reduced vaccine dose (10 mcg vs 30 mcg) is also unknown. Real-world evidence in large pediatric populations is required to provide risk estimates of myocarditis/pericarditis and any other AE that may occur in children aged 5-11 years at a frequency less often than 1 in 1,000.
- As a precautionary measure, and consistent with current recommendations for adolescents and adults, **the second dose in the mRNA COVID-19 vaccination series should be deferred in children who experience myocarditis or pericarditis following the first dose of the Pfizer-BioNTech COVID-19 vaccine until more information is available**. **Children who have a history of myocarditis unrelated to mRNA COVID-19 vaccination should consult their clinical team for individual considerations and recommendations.** If they are no longer followed clinically for cardiac issues, they may receive the vaccine. NACI will continue to monitor the evidence and update recommendations as needed. Caregivers are advised to seek medical attention for children if they develop symptoms including chest pain, shortness of breath, or palpitations following receipt of the Pfizer-BioNTech vaccine.
- The exact prevalence of SARS-CoV-2 seropositivity among children aged 5-11 years is unknown and likely underestimated when inferred by case-level data due to the frequency of mild/asymptomatic infections that may not be captured.
- While most children with COVID-19 have mild or no symptoms, some do become ill and require hospitalization.
- Children with SARS-CoV-2 infection are at risk of MIS-C, a rare but serious syndrome that can occur several weeks following SARS-CoV-2 infection.
- Program planning should ensure equitable access to vaccination information and services and minimize inequities in vaccine acceptance and uptake based on socioeconomic status.
- It is essential that children aged 5-11 years and their parents are supported and respected in their decisions regarding COVID-19 vaccinations for their children, whatever decisions they make, and are not stigmatised for accepting, or not accepting, the vaccination offer.
- Adults, including caregivers and youth who interact with children, should be vaccinated to ensure protection for themselves and to offer additional protection to children.

- In addition to vaccination, public health measures are very important for preventing transmission in children. It is important that everyone, regardless of vaccination status, continue to follow recommended public health measures.
- The Pfizer-BioNTech COVID-19 vaccine is not authorized for use in children under 5 years of age at this time.

RESEARCH PRIORITIES

- NACI recommends continuous monitoring of data on the safety, immunogenicity, efficacy, and effectiveness of the Pfizer-BioNTech COVID-19 vaccine in children through clinical trials and studies in real-world settings, including clinical implications of previous SARS-CoV-2 infection, MIS-C, or myocarditis or pericarditis on the safety, efficacy, and effectiveness of COVID-19 vaccines in pediatric populations and in children considered moderately to severely immunocompromised.
- NACI recommends continuous monitoring of vaccine uptake, particularly according to the socioeconomic status of families with children aged 5-11 years, and for decision makers to consider measures to reduce the risk of socioeconomic disparities in vaccine confidence and uptake.
- NACI recommends vigilant reporting across Canadian jurisdictions for timely assessment of myocarditis and pericarditis cases as well as other potential rare or very rare AEs in pediatric populations following COVID-19 vaccination. In addition, efforts should be made to facilitate investigation of previous SARS-CoV-2 infection in cases of suspected AEFI. Global collaboration should be prioritized to enable data sharing so decision makers around the world can weigh benefits and risks of COVID-19 vaccination for their own specific pediatric populations.
- NACI recommends that further evaluations of dosage intervals and the impact of the interval on effectiveness and safety in children aged 5-11 years should be undertaken.

REFERENCES

1. Ismail SJ, Hardy K, Tunis MC, Young K, Sicard N, Quach C. A framework for the systematic consideration of ethics, equity, feasibility, and acceptability in vaccine program recommendations. Vaccine. 2020 Aug 10;38(36):5861,5876. doi: 10.1016/j.vaccine.2020.05.051.

2. Ismail SJ, Langley JM, Harris TM, Warshawsky BF, Desai S, FarhangMehr M. Canada's National Advisory Committee on Immunization (NACI): Evidence-based decision-making on vaccines and immunization. Vaccine. 2010;28:A58,63. doi: 10.1016/j.vaccine.2010.02.035.

3. Surveillance and Epidemiology Division, Centre for Immunization and Respiratory Infectious Diseases, Infectious Disease Prevention and Control Branch. Data cut-off November 9, 2021. Ottawa (ON): Public Health Agency of Canada; 2021 Nov.

4. COVID-19 Immunity Task Force; CanCOVID. Risks and impacts of the COVID-19 pandemic on Canada's kids, their parents, and teachers: Latest research results and policy implications. Seminar series [presentation slides] [Internet]. CanCOVID; 2021 Sep 29 [cited 2021 Nov 12]. Available from: https://www.covid19immunitytaskforce.ca/wp-content/uploads/2021/09/CITF_CanCOVID_Seminar1_FINAL_EN.pdf.

5. World Health Organization (WHO). Multisystem inflammatory syndrome in children and adolescents temporally related to COVID-19. Scientific brief. [Internet]. Geneva: WHO; 2021 May 15 [cited 2021 Nov 12]. Available from: https://www.who.int/news-room/commentaries/detail/multisystem-inflammatory-syndrome-in-children-and-adolescents-with-covid-19.

6. Hoste L, Van Paemel R, Haerynck F. Multisystem inflammatory syndrome in children related to COVID-19: a systematic review. Eur J Pediatr. 2021 Jul;180(7):2019,2034. doi: 10.1007/s00431-021-03993-5.

7. Merckx J, Cooke S, Tal TE, Laxer RM, Bitnun A, Morris SK, et al. Multicenter cohort study of multisystem inflammatory syndrome in children (MIS-C). medRxiv. 2021 May 19. doi: 10.1101/2021.05.14.21257058.

8. Duarte-Salles T, Vizcaya D, Pistillo A, Casajust P, Sena AG, Lai LYH, et al. Thirty-day outcomes of children and adolescents with COVID-19: An international experience. Pediatrics. 2021 Sep;148(3):e2020042929. doi: 10.1542/peds.2020-042929.

9. Laverty M, Salvadori M, Squires SG, Ahmed M, Eisenbeis L, Lee S, et al. Canadian children with multisystem inflammatory syndrome. Can Commun Dis Rep. 2021;47(11):461,465. https://doi.org/10.14745/ccdr.v47i11a03.

10. Boehmer TK, Kompaniyets L, Lavery AM, Hsu J, Ko JY, Yusuf H, et al. Association between COVID-19 and myocarditis using hospital-based administrative data - United States, March 2020-January 2021. MMWR Morb Mortal Wkly Rep. 2021 Sep 3;70(35):1228,1232. doi: 10.15585/mmwr.mm7035e5.

11. Nalbandian A, Sehgal K, Gupta A, Madhavan MV, McGroder C, Stevens JS, et al. Post-acute COVID-19 syndrome. Nat Med. 2021 Apr;27(4):601,615. doi: 10.1038/s41591-021-01283-z.

12. Molteni E, Sudre CH, Canas LS, Bhopal SS, Hughes RC, Antonelli M, et al. Illness duration and symptom profile in symptomatic UK school-aged children tested for SARS-CoV-2. Lancet Child Adolesc Health. 2021 Oct;5(10):708,718. doi: 10.1016/S2352-4642(21)00198-X.

13. Radtke T, Ulyte A, Puhan MA, Kriemler S. Long-term symptoms after SARS-CoV-2 infection in children and adolescents. JAMA. 2021 Jul 15;326(9):869,871. doi: 10.1001/jama.2021.11880.

14. Gallagher-Mackay K, Srivastava P, Underwood K, Dhuey E, McCready L, Born KB, et al. COVID-19 and education disruption in Ontario: Emerging evidence on impacts. Science Briefs of the Ontario COVID-19 Science Advisory Table. 2021;2(34):doi: 10.47326/ocsat.2021.02.34.1.0.

15. Van Lancker W, Parolin Z. COVID-19, school closures, and child poverty: a social crisis in the making. Lancet Public Health. 2020 May;5(5):e243,e244. doi: 10.1016/S2468-2667(20)30084-0.

16. Panchal U, Salazar de Pablo G, Franco M, Moreno C, Parellada M, Arango C, et al. The impact of COVID-19 lockdown on child and adolescent mental health: systematic review. Eur Child Adolesc Psychiatry. 2021 Aug 18:1,27. doi: 10.1007/s00787-021-01856-w.

17. Ma L, Mazidi M, Li K, Li Y, Chen S, Kirwan R, et al. Prevalence of mental health problems among children and adolescents during the COVID-19 pandemic: A systematic review and meta-analysis. J Affect Disord. 2021 Oct 1;293:78,89. doi: 10.1016/j.jad.2021.06.021.

18. Leeb RT, Bitsko RH, Radhakrishnan L, Martinez P, Njai R, Holland KM. Mental health-related emergency department visits among children aged <18 years during the COVID-19 pandemic - United States, January 1-October 17, 2020. MMWR Morb Mortal Wkly Rep. 2020 Nov 13;69(45):1675,1680. doi: 10.15585/mmwr.mm6945a3.

19. Cost KT, Crosbie J, Anagnostou E, Birken CS, Charach A, Monga S, et al. Mostly worse, occasionally better: impact of COVID-19 pandemic on the mental health of Canadian children and adolescents. Eur Child Adolesc Psychiatry. 2021 Feb 26:1,14. doi: 10.1007/s00787-021-01744-3.

20. National Collaborating Centre for Methods and Tools (NCCMT). Rapid Review: What are the risk factors associated with severe COVID-19 outcomes in children 12 years and under? [Internet]. Hamilton (ON): NCCMT, McMaster University; 2021 Oct 25 [cited 2021 Nov 12]. Available from: https://www.nccmt.ca/pdfs/res/risk-factors-children.

21. Gates M, Pillay J, Wingert A, Guitard S, Rahman S, Zakher B, et al. Risk factors associated with severe outcomes of COVID-19: An updated rapid review to inform national guidance on vaccine prioritization in Canada. medRxiv. 2021 May 22. doi: 10.1101/2021.04.23.21256014v2.

22. Schober T, Caya C, Barton M, Bayliss A, Bitnun A, Bowes J, et al. Risk factors for severe PCR-positive SARS-CoV-2 infection in hospitalized children: a multicenter cohort study. medRxiv. 2021 Nov 8. doi: 10.1101/2021.10.28.21265616.

23. Woodruff RC, Campbell AP, Taylor CA, Chai SJ, Kawasaki B, Meek J, et al. Risk factors for severe COVID-19 in children. Pediatrics. 2021 Oct 22. doi: 10.1542/peds.2021-053418.

24. Drouin O, Hepburn CM, Farrar DS, Baerg K, Chan K, Cyr C, et al. Characteristics of children admitted to hospital with acute SARS-CoV-2 infection in Canada in 2020. CMAJ. 2021 Sep 27;193(38):E1483,E1493. doi: 10.1503/cmaj.210053.

25. Young K, Waddell L. Living summary of SARS-CoV-2 variants of concern: The Delta variant (B.1.617.2) profile, Highlights up to September 15, 2021. Ottawa (ON): Public Health Agency of Canada, Emerging Science Group; 2021 Sep.

26. Surveillance and Epidemiology Division, Centre for Immunization and Respiratory Infectious Diseases, Infectious Disease Prevention and Control Branch. Data cut-off October 12, 2021. Ottawa (ON): Public Health Agency of Canada; 2021 Oct.

27. Delahoy MJ, Ujamaa D, Whitaker M, O'Halloran A, Anglin O, Burns E, et al. Hospitalizations associated with COVID-19 among children and adolescents - COVID-NET, 14 States, March 1, 2020-August 14, 2021. MMWR Morb Mortal Wkly Rep. 2021 Sep 10;70(36):1255,1260. doi: 10.15585/mmwr.mm7036e2.

28. Walter EB, Talaat KR, Sabharwal C, Gurtman A, Lockhart S, Paulsen GC, et al. Evaluation of the BNT162b2 Covid-19 vaccine in children 5 to 11 years of age. N Engl J Med. 2021 Nov 9. doi: 10.1056/NEJMoa2116298.

29. Vaccines and Related Biological Products Advisory Committee Meeting (VRBPAC). October 26, 2021. FDA Briefing Document [Internet]. Silver Spring (MD): United States Food and Drug Administration; 2021 Oct [cited 2021 Nov 12]. Available from: https://www.fda.gov/media/153447/download.

30. Khoury DS, Cromer D, Reynaldi A, Schlub TE, Wheatley AK, Juno JA, et al. Neutralizing antibody levels are highly predictive of immune protection from symptomatic SARS-CoV-2 infection. Nat Med. 2021 Jul;27(7):1205,1211. doi: 10.1038/s41591-021-01377-8.

31. Olson SM, Newhams MM, Halasa NB, Price AM, Boom JA, Sahni LC, et al. Effectiveness of Pfizer-BioNTech mRNA vaccination against COVID-19 hospitalization among persons aged 12-18 years - United States, June-September 2021. MMWR Morb Mortal Wkly Rep. 2021 Oct 22;70(42):1483,1488. doi: 10.15585/mmwr.mm7042e1.

32. Brighton Collaboration. Myocarditis/pericarditis case definition [Internet]. Decatur (GA): The Task Force for Global Health; 2021 Jul 16 [cited 2021 Nov 12]. Available from: https://brightoncollaboration.us/myocarditis-case-definition-update/.

33. Oster, M. mRNA COVID-19 vaccine-associated myocarditis [slides presented at Advisory Committee on Immunization Practices (ACIP) meeting [Internet]. Atlanta (GA): Centers for Disease Control and Prevention (CDC); 2021 Nov 2 [cited 2021 Nov 10]. Available from:

https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-11-2-3/04-COVID-Oster-508.pdf.

34. European Medicines Agency (EMA). Meeting highlights from the Pharmacovigilance Risk Assessment Committee (PRAC) 25-28 October 2021 [Internet]. Amsterdam: EMA; 2021 Oct 29 [cited 2021 Nov 12]. Available from: https://www.ema.europa.eu/en/news/meeting-highlights-pharmacovigilance-risk-assessment-committee-prac-25-28-october-2021.

35. FDA authorizes Pfizer-BioNTech COVID-19 vaccine for emergency use in children 5 through 11 years of age [Internet]. Silver Spring (MD): United States Food and Drug Administration; 2021 Oct 29 [cited 2021 Nov 12]. Available from: https://www.fda.gov/news-events/press-announcements/fda-authorizes-pfizer-biontech-covid-19-vaccine-emergency-use-children-5-through-11-years-age.

36. Nilsson L, Csuth Á, Storsaeter J, Garvey LH, Jenmalm MC. Vaccine allergy: evidence to consider for COVID-19 vaccines. Curr Opin Allergy Clin Immunol. 2021 Aug 1;21(4):401,409. doi: 10.1097/ACI.0000000000000762.

37. De Serres G, Febriani Y, Ouakki M, Talbot D, Deceuninck G, Brousseau N, et al. Efficacité de deux doses de vaccin contre la COVID-19 chez les adultes québécois vivant dans la communauté [Internet]. Montréal: Institut national de santé publique du Québec (INSPQ); 2021 Nov 3 [cited 2021 Nov 12]. Available from: https://www.inspq.qc.ca/covid-19/vaccination/efficacite-2-doses.

38. BC Centre for Disease Control (BCCDC). Two doses prevent about 95 per cent of COVID-19 hospitalizations: B.C. COVID-19 vaccine effectiveness results [Internet]. Vancouver: Provincial Health Services Authority; 2021 Sep 29 [cited 2021 Oct 15]. Available from: http://www.bccdc.ca/about/news-stories/stories/2021/covid-19-vaccine-effectiveness-results.

39. Payne R, Longet S, Austin J, Skelly D, Dejnirattisai W, Adele S, et al. Immunogenicity of standard and extended dosing intervals of BNT162b2 mRNA vaccine. Cell. 2021 Oct 16. doi: 10.1016/j.cell.2021.10.011.

40. Tauzin A, Gong SY, Beaudoin-Bussières G, Vézina D, Gasser R, Nault L, et al. Strong humoral immune responses against SARS-CoV-2 Spike after BNT162b2 mRNA vaccination with a sixteen-week interval between doses. medRxiv. 2021 Sep 21. doi: 10.1101/2021.09.17.21263532.

ACKNOWLEDGMENTS

This statement was prepared by: N Forbes, M Salvadori, J Zafack, J Montroy, R Stirling, R Krishnan, B Warshawsky, E Wong, E Abrams, S Ismail, K Young, M Tunis, R Harrison and S Deeks on behalf of NACI.

NACI gratefully acknowledges the contribution of: K Farrah, K Ramotar, N St-Pierre, L Coward, C Jensen, A Nam, R Ximenes, MW Yeung, A Tuite, SH Lim, and the NACI Secretariat.

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ABBREVIATIONS

Abbreviation	***Term***
AE	Adverse event
AEFI	Adverse event following immunization
ARCHE	Alberta Research Center for Health Evidence
CI	Confidence Interval
CIC	Canadian Immunization Committee
COVID-19	Coronavirus disease 2019
GMR	Geometric mean ratio
GMT	Geometric mean titre
ICU	Intensive Care Unit
MCG	microgram
MIS-C	Multisystem Inflammatory Syndrome in Children
mL	Millilitre
mRNA	Messenger Ribonucleic Acid
NACI	National Advisory Committee on Immunization
NT-50	SARS-CoV-2 50% neutralizing titres
PHAC	Public Health Agency of Canada
PHECG	Public Health Ethics Consultative Group
PCR	Polymerase Chain Reaction
SAE	Serious adverse event
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
US	United States
VE	Vaccine efficacy

APPENDIX A: FREQUENCY OF SOLICITED ADVERSE EVENTS FOLLOWING IMMUNIZATION FOR COVID-19 IN CLINICAL TRIALS

Table 1. Frequency of solicited local AEs in 5 to 11 year olds for the Pfizer-BioNTech COVID-19 vaccine (Comirnaty™)[a,b]

AEFI	Vaccine		Placebo control	
	Dose 1 N=1,511	Dose 2 N=1,501	Dose 1 N=749	Dose 2 N=741
Pain at injection site	74.1%	71.0%	31.3%	29.5%
Redness/erythema	14.7%	18.5%	5.7%	5.4%
Swelling	10.5%	15.3%	2.7%	2.7%

Abbreviations: AEFI: adverse event following immunization vaccine; NS: not solicited

[a] Very common = occur in 10% or more of vaccine recipients, common = occur in 1 to less than 10% of vaccine recipients, uncommon= occur in 0.1% to less than 1% of vaccine recipients

[b] AEFIs were solicited within 7 days after each dose in a Phase 2/3 clinical trial. The information in this table is up to date as of November 19, 2021. For updated information, please consult the Comirnaty product monograph.

Table 2. Frequency of solicited systemic AEs in 5 to 11 year olds for the Pfizer-BioNTech COVID-19 vaccine (Comirnaty™)[a,c]

AEFI	Vaccine		Placebo control	
	Dose 1 N=1,511	Dose 2 N=1,501	Dose 1 N=749	Dose 2 N=741
Fatigue	33.6%	39.4%	31.3%	24.3%
Headache	22.4%	28.0%	24.1%	18.6%
Muscle Pain	9.1%	11.7%	6.8%	7.4%
Chills	4.6%	9.8%	4.7%	4.3%
Joint Pain	3.3%	5.2%	5.5%	3.6%
Fever[b]	2.5%	6.5%	1.3%	1.2%
Diarrhea	5.9%	5.3%	4.1%	4.7%
Vomiting	2.2%	1.9%	1.5%	0.8%

Abbreviations: AEFI: adverse event following immunization vaccine; NS: not solicited

[a] Very common = occur in 10% or more of vaccine recipients, common = occur in 1 to less than 10% of vaccine recipients, uncommon= occur in 0.1% to less than 1% of vaccine recipients

[b] Fever was objectively reported as having a temperature ≥38°C/100.4°F.

[c] AEFIs were solicited within 7 days after each dose in a Phase 2/3 clinical trial. The information in this table is up to date as of November 19, 2021. For updated information, please consult the Comirnaty product monograph.