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

Rapid response: Guidance on the use of booster COVID-19 vaccine doses in adolescents 12-17 years of age

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PROTECTING AND EMPOWERING CANADIANS TO IMPROVE THEIR HEALTH

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Canada

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

On December 3, 2021, NACI published updated guidance on booster COVID-19 vaccine doses in Canada for adults 18 years of age and older. These recommendations were reviewed and reaffirmed in the context of the Omicron (B.1.1.529) variant of concern (VOC) on December 14, 2021. Concurrently, NACI published updated recommendations on the use of COVID-19 vaccines in individuals aged 12 years and older in the context of myocarditis and pericarditis reported following administration of mRNA COVID-19 vaccines. Since these guidance documents:

- NACI released advice on vaccination with COVID-19 vaccines following myocarditis or pericarditis;
- Cases of COVID-19 have increased rapidly due to the widespread transmission of Omicron;
- A number of adolescents have approached, or will be approaching the 6 month interval being recommended between the primary series and a booster dose in adults 18 years of age and older;
- Data on vaccine protection from the primary series and booster dose against Omicron has emerged.

While the term "booster dose" is used in this guidance, NACI continues to monitor the emerging scientific data on whether this dose is indeed a booster dose (to stimulate the memory response once protection has truly waned), or should be considered part of the primary series (to establish strong immune response and memory). NACI will adjust the terminology as required.

NACI continues to recommend a primary COVID-19 vaccine series with an authorized mRNA vaccine in all authorized age groups, and continues to recommend that immunization in those who are eligible but who have not yet received their primary series should remain the top priority. NACI also acknowledges the urgency for vaccinating people around the world who have not yet received any COVID-19 vaccine or completed their primary series.

NACI's recommendations are aligned with the goals of the Canadian COVID-19 Immunization Program, updated in October 2021:

- 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
- Minimize serious illness and overall deaths while preserving health system capacity
- Reduce transmission to protect high risk populations.

COVID-19 VACCINES AUTHORIZED FOR USE IN ADOLESCENTS 12-17 YEARS OF AGE

The Pfizer-BioNTech Comirnaty COVID-19 vaccine has been authorized by Health Canada for individuals 12 years of age and older, using a 30 mcg dose (December 9, 2020, individuals 16 years of age and older; May 18th 2021, individuals 12 to 15 years of age). The Moderna Spikevax COVID-19 vaccine is authorized by Health Canada for individuals 12 years of age and older, using a 100 mcg dose (December 23, 2020, individuals 18 years of age and older; August 27th 2021, individuals 12 to 17 years of age).

Currently in Canada, booster doses of the Pfizer-BioNTech Comirnaty (30 mcg) and Moderna Spikevax (50 mcg) COVID-19 vaccines are authorized only for individuals 18 years of age and older). Therefore, recommendations made for the use of booster doses in adolescents are off-label.

For further information on NACI's recommendations on the use of COVID-19 vaccines, please refer to the COVID-19 vaccine chapter in the Canadian Immunization Guide (CIG).

METHODS

NACI's recommendations on booster doses have been based on the decision-making framework outlined in Interim guidance on booster COVID-19 vaccine doses in Canada, triggered by evidence of the need for (e.g., evidence of decreased vaccine effectiveness (VE) against severe illness and/or infection depending on the population) and benefit of (e.g., safety and effectiveness) a booster dose in the Canadian context.

On January 11 and 18, 2022, NACI reviewed the recent evidence on COVID-19 vaccines for adolescents 12-17 years of age, current disease epidemiology, and risk factors associated with severe outcomes from COVID-19 in this age group. Data on protection from the primary series and booster dose from other age groups were used as indirect evidence when data were not available for adolescents 12-17 years of age. The rapidity of spread of Omicron in Canada, potential forthcoming variant-specific vaccine formulations, the goals of the Canadian COVID-19 Immunization Program, and principles on the ethical implications of booster dose recommendations in various populations from the NACI consultations with the Public Health Ethics Consultative Group (PHECG) (September 2 and 21, 2021) were also considered in assessing the need for and benefit of a booster dose in this population. On January 24, 2022, NACI approved their recommendations on the use of booster doses of COVID-19 vaccines in adolescents 12 to 17 years of age who may be at higher risk of severe COVID-19 disease due to biological risk factors, social risk factors and/or experience systemic barriers to accessing health care.

For further information on NACI's recommendations on the use of COVID-19 vaccines, please refer to the COVID-19 vaccine chapter in the Canadian Immunization Guide (CIG).

Further information on NACI's process and procedures is available elsewhere.

Risk factors for severe outcomes from COVID-19

NACI reviewed existing guidance identifying biological or social risk factors for severe disease or exposure using the expertise of the committee to assess their applicability for adolescents 12-17 years of age in the context of Omicron VOC circulation. These guidance documents include:

Recommendation on the use of mRNA COVID-19 vaccines in adolescents 12 to 17 years of age

COVID-19 signs, symptoms and severity of disease: A clinician guide

Guidance on the prioritization of key populations for COVID-19 immunization

NACI acknowledges that evidence regarding risk factors for severe outcomes from COVID-19 continues to emerge, but also acknowledges that the absence of evidence does not equate to the absence of risk. Despite insufficient evidence on the full spectrum of biological and social risk factors, inequities resulting from the intersectionality between biological risk factors, social risk factors, and/or systemic barriers to accessing health care likely exist. Therefore, NACI also used its validated tools to inform guidance on a spectrum of health inequities.

SUMMARY OF EVIDENCE

COVID-19 Burden of Disease in the Adolescent Population

Recent COVID-19 epidemiological trends

Currently, Canada is facing a new wave of the COVID-19 pandemic, driven mainly by Omicron, which is partially evasive to previous immunity conferred by COVID-19 vaccine or a previous SARS-CoV-2 infection. Current data suggests that mRNA COVID-19 vaccines offer reduced protection against symptomatic infection with Omicron, with breakthrough cases in individuals of all age groups who have received 2 or 3 doses of mRNA and other COVID-19 vaccines [(1)].

Canadian adolescents 12 to 17 years of age are facing record-high incidence rates of COVID-19 during this new wave, driven in large part by Omicron [(1)]. Additional data are needed to fully determine the disease severity caused by infection with Omicron in specific populations including unvaccinated individuals, young children (<5 years of age), adolescents and older adults. However, emerging data suggest reduced frequencies of severe outcomes from COVID-19 associated with Omicron, when compared to disease severity seen with Delta (B.1.617).

Risk of severe outcomes

Consistent with pre-Omicron waves of the pandemic in Canada, adolescents remain at low risk of severe outcomes from Omicron (<1% of cases among adolescents 12 to 19 years of age are hospitalized). Additionally, intensive care unit (ICU) admissions among adolescents 12 to 19 years of age remain low (0.1% of cases are admitted to the ICU; data as of January 15, 2022) [(2)]. However, due to large increases in rates of infection, the number of severe cases ofCOVID-19 (including hospitalization) have been rising nationally across all groups, including in adolescents 12 to 17 years of age. In a recent study from the CDC conducted before the arrival of Omicron, among hospitalized adolescents 12 to 18 years of age, two doses of the Pfizer-BioNTech Comirnaty (30 mcg) COVID-19 vaccine were highly effective at preventing COVID-19–related hospitalization and ICU admission or the need for life support [(3)].

Risk factors associated with severe outcomes in adolescents

Current evidence is limited with respect to risk factors associated with severe outcomes specific to adolescents 12 to 17 years of age. A rapid review [(4)] of risk factors associated with severe outcomes of COVID-19 in any age group found a moderate certainty of evidence for a large increase (≥2-fold) in hospitalization among individuals 21 years of age and younger with 2 or more chronic conditions (compared to those with no chronic conditions). However, data included in this review pre-dates the emergence of the Omicron VOC.

This review also provides indirect evidence of risk factors for severe outcomes from COVID-19 from the adult population. From indirect data in the adult population, adolescents at increased risk for severe outcomes may include (but is not limited to) those: who are obese; who are medically fragile/have medical complexities (i.e., having complex chronic conditions, functional limitations, high health care utilization and/or a high need for caregiving [5]); with more than one comorbidity; with neurological disorders; with Down Syndrome; and with immune dysregulation associated with immunocompromising conditions.

Data are currently limited for the broad range of biological and/or social risk factors that may intersect in individuals at high risk for severe outcomes due to SARS-CoV-2 infection. It is also unclear how these factors may differ between illness due to the Omicron and Delta VOCs. However, a spectrum of health inequities has been identified in validated tools that can be applied to adolescents 12-17 years of age.

For more information on risk factors in adolescents 12 to 17 years of age, please refer to Recommendation on the use of mRNA COVID-19 vaccines in adolescents 12 to 17 years of age.

Multisystem inflammatory syndrome in children, post-COVID condition and myocarditis following COVID-19

Children and adolescents infected with SARS-CoV-2 are at risk of multisystem inflammatory syndrome in children (MIS-C), a rare but serious condition that can occur in the weeks following infection [6]. MIS-C has also been reported following vaccination, but at much lower rates. Preliminary data from a recent large pharmacovigilance study in adolescents 12 to 17 years of age in France [7] reported a rate of 1.1 (95% CI: 0.5-2.1) MIS-C cases per 1,000,000 doses administered, compared to 113 (95% CI: 95-135) cases per 1,000,000 SARS-CoV-2 infections in this age group. Data from pediatric patients 12-18 years of age diagnosed with MIS-C in France between September 1, 2021 and October 31, 2021 found the hazard ratio for MIS-C was 0.09 (95% CI: 0.04-0.21; $P < .001$) after the first vaccine dose compared with unvaccinated adolescents [8]. Recent surveillance data from the US have reported high VE for the Pfizer-BioNTech Comirnaty (30 mcg) COVID-19 vaccine (2 dose series) in adolescents 12 to 18 years of age against MIS-C (VE 91%; 95% CI: 78-97%) [9].

While evidence is limited in adolescents 12 to 17 years of age, SARS-CoV-2 infection may lead to post-COVID condition/post-acute COVID syndrome (i.e., long COVID) [10]. However, current evidence suggests the risk is lower in children and adolescents compared to older age groups [11, 12].

Myocarditis can also occur as a complication of SARS-CoV-2 infection, including, very rarely, in adolescents [13]. For more information, please refer to the summary of evidence in NACI rapid response on updated recommendations 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.

Collateral harms to adolescents during the COVID-19 pandemic

Adolescents 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 adolescents and their families.

These harms can disproportionately affect some Canadian adolescents 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].

For the most up to date information on the epidemiology of COVID-19 in Canada, please refer to the COVID-19 daily epidemiology update.

For further information, please refer to the chapter on COVID-19 vaccine in the Canadian Immunization Guide.

COVID-19 Vaccine Protection in Adolescents 12-17 Years of Age

Vaccine effectiveness of the primary series

There are three recent studies that have provided estimates of the effectiveness of a primary two-dose series of the Pfizer-BioNTech Comirnaty (30 mcg) COVID-19 vaccine against various outcomes in adolescents, and two studies that have examined the trends in Pfizer-BioNTech Comirnaty (30 mcg) VE in adolescents and adults over time since receipt of the primary vaccination series. All of these studies were conducted prior to the emergence of the Omicron VOC.

A prospective cohort study in the US [20] found the Pfizer-BioNTech Comirnaty (30 mcg) COVID-19 vaccine was 92% effective in preventing SARS-CoV-2 infection in adolescents 12–17 years of age. The study was conducted between July and December 2021, at a time when Delta was the predominantly circulating strain. A test-negative case-control study conducted in the US [21] between June and September 2021 when Delta was the predominantly circulating strain found two doses of the Pfizer-BioNTech Comirnaty (30 mcg) COVID-19 vaccine was 93% protective against COVID-19 related hospitalization in adolescents 12–18 years of age (12–15 years of age: VE= 91%; 16–18 years of age, VE= 94%). Of the 179 identified cases in this study, 173 (97%) were unvaccinated. All of the cases admitted to the ICU (n=77) were unvaccinated, including 29 individuals who were critically ill and required life support, two of whom died.

Duration of vaccine protection of the primary series

Data regarding the protection against SARS-CoV-2 infection in adolescents is starting to emerge, indicating waning similar to that seen in adults. In a test-negative case control assessment study assessing VE for a 2-dose primary series with the Pfizer-BioNTech Comirnaty vaccine against symptomatic infection in the US during the Delta wave, VE was highest among 12-15 year olds, then 16-19 year olds, compared to those 20 years of age and older. Across all age groups, VE waned over time [22].

A non-peer reviewed matched case-control study conducted in Israel [23], during a time when Delta was the predominant circulating strain, examined Pfizer-BioNTech Comirnaty (30 mcg) VE against documented SARS-CoV-2 infection (regardless of symptoms) and against symptomatic COVID-19, by time since primary vaccination in adolescents 12–16 years of age. The study found peak VE against documented SARS-CoV-2 infection (85%) and symptomatic COVID-19 (90%) at 14–89 days after receipt of the second dose, decreasing to 75% and 78% respectively after 90–149 days, and 58% and 65% respectively after 150–180 days after receipt of the second dose.

A large retrospective cohort study conducted in the US [24], during a time of emergence of Delta, examined Pfizer-BioNTech Comirnaty (30 mcg) VE against SARS-CoV-2 infection and against COVID-related hospitalizations in individuals 12 years of age and older. The study estimated VE against these outcomes by time since primary vaccination. As adolescents 12–15 years of age were only eligible to receive COVID-19 vaccination beginning in May 2021, there was limited follow-up available in this age group. The point estimates of effectiveness against SARS-CoV-2 infection of two doses of Pfizer-BioNTech Comirnaty (30 mcg) COVID-19 vaccine in adolescents 12–15 years of age remained relatively stable 3 to less than 4 months after the second dose, but the confidence interval around the latter estimate is wide and includes zero: 7 to 36 days: 91% (95% CI: 86-94%), 37 to 66 days: 92% (95% CI: 88-94%); 67 to 96 days: 88% (95% CI: 68-96%); 97 to 126 days: 84% (95% CI: -14-98%). As there was only one individual between the ages of 12 to 15 years that was hospitalized during the study period, the data was insufficient to derive precise estimates of VE against COVID-related hospitalization.

Although evidence continues to emerge on the duration of protection in adolescents against severe outcomes, such as hospitalization and deaths, it is expected to be more durable than protection against infection, as observed in the adult population.

For more information on the duration of protection in the adult population, please refer to the NACI Interim guidance on booster COVID-19 vaccine doses in Canada.

It is important to note that these studies were conducted prior to the emergence of Omicron and both countries recommended the manufacturer authorized interval between doses in the primary series. A summary of the data on Omicron is presented elsewhere in the statement.

Safety of COVID-19 vaccine booster doses in adolescents 12-17 years of age

Based on preliminary post-market safety data [25-31], no safety concerns have been noted following the booster doses beyond those recognized after the primary series. The frequency of adverse events (AEs) in adults following mRNA booster doses is comparable or lower than those reported after dose 2 of the primary series. In the US where both mRNA vaccines were used, reactogenicity was higher for the Moderna Spikevax (50 mcg) COVID-19 vaccine than for the Pfizer-BioNTech Comirnaty (30 mcg) vaccine [25]. While the safety data specific to adolescents 12-17 years of age are currently limited, a similar trend is expected in that age group.

For the 2-dose primary series, adolescents 12-17 years of age are among the age groups at highest risk for the rare event of myocarditis/pericarditis following mRNA vaccine. Cases of myocarditis have also been reported following mRNA COVID-19 booster doses. In Israel [31] and the United States [25, 26], the rates of myocarditis following a booster dose in adults are generally falling between the rates post-dose 1 and post-dose 2. As of early January 2022, 2 cases of myocarditis have been reported in Israel among 41,610 third doses of Pfizer-BioNTech Comirnaty (30 mcg) COVID-19 vaccine administered to adolescents aged 12 to 15 years [30]. However, preliminary data from the United Kingdom (UK) compared the risk of myocarditis post COVID-19 vaccines to the baseline risk and observed that among males aged 13 to 39 years, the estimated association between myocarditis and Pfizer-BioNTech Comirnaty (30 mcg) COVID vaccine was higher post vaccine dose 3 (Incidence rate ratio [IRR]: 7.60 [1.92 – 30.15]) compared to post vaccine dose 2 (IRR: 3.41 [2.44 – 4.78]).

Safety data on COVID-19 booster doses are still emerging, especially in adolescents. Data on the risk of myocarditis and/or pericarditis following COVID-19 boosters and on the safety of the

Moderna Spikevax (50 mcg) booster dose in any age group are currently limited. There are no data on the use of Moderna Spikevax (50 mcg) booster dose in adolescents 12-17 years of age at this time. NACI continues to assess the evidence as it emerges and will update its recommendations as needed.

Effectiveness of COVID-19 vaccine booster doses in adolescents 12-17 years of age

Emerging real-world data from Israel's booster dose program with Pfizer-BioNTech Comirnaty (30 mcg) COVID-19 vaccine are available for adolescents 12-17 years of age, which show a significant reduction in the confirmed rate of infection in adolescents 12-15 years of age following the booster dose compared to those who were vaccinated with a primary series 5-6 months earlier [30]. Among those 16-29 years of age, the rate ratio for infection (pre-Omicron) in those who did not receive a booster compared to those who did was 17.2 (15.4-19.2) [32].

There are currently no data on the effectiveness of booster doses against severe outcomes in adolescents 12-17 years of age, although current evidence suggests VE against severe outcomes remains high in this age group following completion of the primary series. In adults, an mRNA booster dose has been shown to improve protection against severe outcomes. Data from the UK during the time period when Delta was the predominately circulating VOC estimated that VE against hospitalisation or death of a Pfizer-BioNTech Comirnaty (30 mcg) booster dose range from 97% to 99% in all age groups irrespective of the primary series, with no evidence of waning up to 10 weeks [33]. Data from Israel showed similar results, (during the period of time where Delta was the predominately circulating VOC) with a VE against hospitalization of 93% (95% CI: 88-97%) at least 7 days after a booster dose [34]. A separate study from Israel estimated a reduction in severe outcomes by a factor of 19.5 (95% CI: 12.9-29.5) at least 12 days after a booster dose compared to those who had only received 2 doses [32].

Protection of COVID-19 vaccine (primary series and booster dose) against Omicron

Emerging evidence suggests VE against infection and symptomatic disease due to Omicron after an mRNA primary vaccine series is lower compared to effectiveness against previous VOCs [35-40]. Currently, there is no available evidence on the effectiveness of an mRNA booster dose against Omicron in adolescents 12 to 17 years of age. However, in adult populations, a booster dose with an mRNA COVID-19 vaccine improves protection against severe outcomes from Omicron [36, 41]. Protection is also increased against symptomatic disease and infection [36, 37, 39, 40, 42], although this increase is substantially less than was observed against Delta. Preliminary, non-peer reviewed Canadian data, using a test-negative study design from Ontario, estimated VE against symptomatic Omicron infection 7 or more days after a third dose with any mRNA vaccine was 61%, compared to unvaccinated individuals [43]. VE against severe outcomes caused by Omicron remained high (~82-86%) in individuals with 2 doses, but increased to 95% after a third dose. Comparatively, VE against symptomatic Delta infection after a third dose was 97% overall, and 99% against severe outcomes caused by Delta. Preliminary evidence from the UK estimated VE against hospitalization was 94% (95% CI: 89-97%) at 2 to 9 weeks after the booster dose and 89% (95% CI: 80-95%) at 10 or more weeks after the booster dose. Additional surveillance data from the UK estimated VE against hospitalization to be 88% (95% CI: 78-93%) at least 2 weeks after a booster dose [41]. Data from these studies were obtained during the period of time where Omicron was the predominately circulating VOC.

NACI will continue to evaluate evidence of booster dose protection against Omicron in adolescents 12 to 17 years of age.

Additional Information and Considerations

NACI continues to endeavour to make ethical, equitable and evidence-informed recommendations. Health Canada has not authorized the use of boosters in individuals less than 18 years of age, therefore the use of booster doses in adolescents 12-17 years of age would be off-label in Canada. There must be a strong ethical rationale to justify offering booster doses to this population in the broader context of the objectives of the vaccination program, changing epidemiological and pandemic conditions, and emerging evidence. It is expected at this time that a booster dose is unlikely to have a significant impact on mitigating Omicron transmission due to its high immune escape potential and transmissibility. The booster rollout alone has been predicted to be less impactful than the use of public health measures alone due to the slower roll out of boosters and the time to mount protection compared to the speed of Omicron transmission [(1)].

The relative risks and benefits of a third dose of the Pfizer-BioNTech Comirnaty (30 mcg) COVID-19 vaccine in adolescents, including duration and breadth of protection compared to infection from Omicron are largely unknown at this time. Although being highly transmissible, Omicron appears to be less severe than earlier VOCs, and adolescents 12-17 years of age who have received a primary series continue to be at low risk for severe outcomes due to SARS-CoV-2 infection.

In order to mitigate the emergence and impact of new VOCs, the World Health Organization's Technical Advisory Group on COVID-19 Vaccine Composition (TAG-CO-VAC) urges broader global access to current COVID-19 vaccines with an immediate priority for vaccination of groups at greater risk of developing severe disease. A vaccination strategy based on repeated booster doses with the original vaccine composition without consideration of the evolution of the virus and vaccine coverage in the global context is unlikely to be effective [(44)]. In addition, variant-specific vaccines are in development and may be available in the coming months. The relative benefit of the new vaccine formulations as booster doses will be assessed when more information is available.

The need for and benefit of a booster dose in the general adolescent population is unclear [(45)]; however, NACI acknowledges that some populations are at increased risk of exposure to the SARS-CoV-2 virus (e.g., due to living settings), and some populations are at increased risk of severe COVID-19 disease (e.g., hospitalization and death) due to various biological (e.g., pre-existing medical conditions) and social (e.g., low socioeconomic status) factors that may intersect. Factors for risk of severe disease and risk of exposure may overlap, further increasing risk. Any combination of these factors, as well as varying access to health care services, has the potential for disproportionate consequences for specific populations characterized by increased rates of infection and disease, severe illness, hospitalizations, and deaths. NACI continues to recommend elements as outlined in its original prioritization guidance to guide ethical decision-making [(46)].

Program planning should ensure equitable access to vaccination information and services and minimize differences in vaccine acceptance and uptake based on socioeconomic status.

RECOMMENDATIONS

Please see Table 1 for an explanation of strong versus discretionary NACI recommendations.

NACI strongly reiterates previous evidence-informed recommendations for the primary series of COVID-19 vaccines:

1. **NACI recommends that a complete primary series with an mRNA COVID-19 vaccine should be offered to individuals 12 to 17 years of age without contraindications to the vaccine. (Strong NACI Recommendation)**

For adolescents 12 to 17 years of age receiving an mRNA COVID-19 vaccine primary series:

- The use of Pfizer-BioNTech Comirnaty (30 mcg dose) is preferred to Moderna Spikevax (100 mcg dose) to start or continue the mRNA primary vaccine series.
- The second dose of mRNA vaccine should be provided 8 weeks after the first dose as a longer interval between doses is associated with higher VE and potentially lower risk of myocarditis/pericarditis.

2. **For moderately to severely immunocompromised adolescents 12 to 17 years of age who have not yet been immunized, it is recommended that a primary series of 3 doses of an mRNA vaccine should be offered. For these individuals who have previously received a 2-dose COVID-19 vaccine series (with a homologous or heterologous schedule using mRNA vaccines), it is recommended that an additional dose of an mRNA COVID-19 vaccine should be offered (Strong NACI recommendation).**

NACI recommendations for booster doses of COVID-19 vaccines in adolescents 12 to 17 years of age who may be at higher risk of severe outcomes from COVID-19 infection:

These individuals experience biological and/or social risk factors that may intersect, and may experience systemic barriers to accessing health care.

1. **NACI recommends that a booster dose of an mRNA COVID-19 vaccine* may be offered ≥6 months after completion of a primary COVID-19 vaccine series to adolescents 12 to 17 years of age:**
    a. **with an underlying medical condition at high risk of severe illness due to COVID-19**** (including those who are immunocompromised and who received a three-dose primary series);
    b. **who are residents of congregate living settings (e.g., shelters, group homes, quarters for migrant workers, correctional facilities);**
    c. **who belong to racialized and/or marginalized communities disproportionately affected by COVID-19.**

(Discretionary NACI recommendation)

Note: No recommendations for booster doses for the general adolescent population 12 to 17 years of age are being made at this time.

*The use of Pfizer-BioNTech Comirnaty (30 mcg dose) booster dose is preferred to Moderna Spikevax (50 mcg dose) booster dose as there are currently no data on the use of Moderna Spikevax (50 mcg dose) booster dose in adolescents 12-17 years of age.

** Adolescents 12-17 years of age who may be at high risk of severe illness due to COVID-19 include those with one or more of the following underlying medical conditions (based on expert opinion and evolving evidence):

- Cancer – active treatment
- Chronic kidney disease
- Chronic lung diseases, including uncontrolled asthma
- Cystic fibrosis
- Neurodevelopmental and other chronic neurological conditions including epilepsy and cerebrovascular disease
- Diabetes (type 1 & 2)
- Down syndrome
- Congenital heart disease or other chronic heart diseases, including pulmonary hypertension
- Chronic liver disease
- Obesity (BMI ≥30)
- Pregnancy
- Sickle cell disease or thalassemia
- Substance use disorders
- Immunocompromised state, including primary immune deficiency, solid organ or haematopoietic stem cell transplant, HIV infection, or immunosuppressive therapy
- Medically fragile/having medically complex needs.

SUMMARY OF EVIDENCE AND RATIONALE

- In considering the burden of COVID-19 illness in the general adolescent population, the rapidity of spread of the Omicron VOC in Canada, the goals of the Canadian COVID-19 Immunization Program, the impact of the booster dose on disease transmission, the rare risk of myocarditis or pericarditis following mRNA vaccination, and potential forthcoming vaccine formulations, the overall benefit of a booster dose in the general adolescent population remains unclear at this time.
- Due to high transmissibility and partial immune evasion in vaccinated individuals, adolescents 12 to 17 years of age and older populations alike are at high risk of infection with Omicron regardless of vaccination status. It is anticipated that many adolescents will be infected with SARS-CoV-2 during the Omicron wave of the pandemic.
- While adolescents 12 to 17 years of age are currently experiencing record-high incidence rates of confirmed SARS-CoV-2 infection, they remain at low risk of severe outcomes from Omicron, including hospitalization, ICU admission and death from COVID-19. There is, however, a small risk of MIS-C and post-COVID condition/post-acute COVID-19 syndrome associated with SARS-CoV-2 infection, although the risk of post-COVID condition following Omicron is not known.
- While VE against SARS-CoV-2 infection following the completion of a primary series was originally demonstrated to be high (>90%) in adolescents 12 to 17 years of age, emerging

evidence is indicative of waning protection over time. Protection against severe outcomes, such as hospitalization and deaths, is expected to be more durable than protection against infection as seen in adults. Omicron-specific information on VE against infection, symptomatic illness, and hospitalization in adolescents is not currently available.

- Current evidence is limited with respect to biological and/or social risk factors associated with severe outcomes from COVID-19 in adolescents 12 to 17 years of age. Some populations are at increased risk of exposure to the SARS-CoV-2 virus (e.g., due to living settings), and some populations are at increased risk of severe COVID-19 disease (e.g., hospitalization and death) due to various biological (e.g., pre-existing medical conditions) and social (e.g., low socioeconomic status) factors that may intersect. It is important to note that much of the existing data pre-dates the emergence of the Omicron VOC. Given some noted differences in disease presentation observed with Omicron, it is essential that NACI continues to monitor evidence as it emerges.
- Currently, data on the effectiveness of a booster dose in adolescents are limited. Pre-Omicron preliminary data from Israel showed a significant reduction in the confirmed rate of infection in adolescents 12-15 years of age following the booster dose. Data in adults have demonstrated improvements in protection from severe outcomes from COVID-19, and less so from SARS-CoV-2 infection. Data are still emerging with respect to the effectiveness of a booster dose against Omicron. In addition, the duration of protection from the booster dose remains uncertain.
- For the 2-dose primary series, adolescents 12 to 17 years of age are among the age groups at highest risk for the rare event of myocarditis/pericarditis following mRNA vaccine. While there have been rare reports of myocarditis following an mRNA booster dose, preliminary data from the US and Israel suggest the rate of myocarditis following a Pfizer-BioNTech Comirnaty (30 mcg) booster dose may fall between the rates observed after dose 1 and the rates observed after dose 2. However, preliminary data from the UK estimated association between myocarditis and a Pfizer-BioNTech Comirnaty (30 mcg) COVID vaccine was higher post-vaccine dose 3 compared to post-vaccine dose 2. Data are still emerging at this time and NACI will continue to assess the evidence and update recommendations as needed. Based on preliminary post-market safety data, no additional safety concerns have been noted following the booster doses beyond those recognized after the primary series.
- NACI is continuing to monitor the evidence related to waning immunity in various populations and the evidence on immunogenicity, safety and effectiveness of booster doses (including those who have been previously infected with SARS-CoV-2 and have received a complete primary vaccine series with authorized COVID-19 vaccines). NACI will update guidance as required.

Refer to NACI's Recommendations on the use of COVID-19 vaccines for further information on COVID-19 vaccines.

Refer to NACI's Guidance on the prioritization of key populations for COVID-19 immunization for further information on NACI's initial framework and foundational elements guiding ethical decision-making.

Research priorities

- NACI recommends continuous monitoring of long-term consequences of infection in adolescents 12-17 years of age.
- NACI recommends continuous monitoring of data on the safety, immunogenicity, efficacy, and effectiveness of the COVID-19 vaccines, including booster doses, 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 adolescent populations.
- NACI recommends continuous monitoring of vaccine uptake, particularly according to the socioeconomic status of families with adolescents 12-17 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 adolescent populations following COVID-19 vaccination. In addition, efforts should be made to facilitate investigation of previous SARS-CoV-2 infection in cases of suspected adverse events following immunization. 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 specific adolescent populations.
- NACI recommends that further evaluations of the optimal interval between previous infection and vaccination be undertaken (for both COVID-19 vaccine primary series and additional doses) to ensure vaccine safety and maximize effectiveness, duration, and breadth of protection.
- NACI recommends further evaluation of risk factors for severe outcomes from COVID-19 in adolescent populations, to ensure current disease pathophysiology is accurately reflected and to ensure those at highest risk of severe outcomes from COVID-19 can be adequately informed.

Table 1. Strength of NACI Recommendations

Strength of NACI Recommendation *based on factors not isolated to strength of evidence* (e.g., public health need)	**STRONG**	**DISCRETIONARY**
Wording	"*should/should not be* offered"	"*may/may not be* offered"
Rationale	Known/anticipated advantages outweigh known/anticipated disadvantages ("should"), OR Known/Anticipated disadvantages outweigh known/anticipated advantages ("should not")	Known/anticipated advantages are closely balanced with known/anticipated disadvantages, OR uncertainty in the evidence of advantages and disadvantages exists
Implication	A strong recommendation applies to most populations/individuals and should be followed unless a clear and compelling rationale for an alternative approach is present.	A discretionary recommendation may be offered for some populations/individuals in some circumstances. Alternative approaches may be reasonable.

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