

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

Interim guidance on booster COVID-19 vaccine
doses in Canada

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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

NACI's recommendations on booster doses will be based on the decision-making framework outlined in this document, triggered by evidence of the need for (e.g., evidence of decreased vaccine effectiveness 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.

The public health goal of Canada's pandemic response is to minimize serious illness and death while minimizing societal disruption as a result of the COVID-19 pandemic. COVID-19 vaccines have played a vital role in the response and have been shown to be very effective against symptomatic laboratory confirmed SARS-CoV-2 infection, severe disease, hospitalization, and death from COVID-19. Unfortunately, the COVID-19 pandemic is ongoing and continues to cause significant morbidity and mortality, as well as social and economic disruption in Canada and worldwide (including impacts on health system capacity). COVID-19 vaccination with a complete primary series is critical. Fully vaccinated individuals have much lower rates of SARS-CoV-2 hospitalizations, ICU admission and mortality compared to those who are unvaccinated. In addition, those who have been vaccinated are less likely to get infected, and therefore less likely to transmit SARS-CoV-2 infection to others. NACI continues to strongly recommend that all individuals in the authorized age groups should be immunized with a primary series of an authorized COVID-19 vaccine, and preferably with mRNA COVID-19 vaccines (Moderna Spikevax and Pfizer-BioNTech Comirnaty) ⁽¹⁾.

To date, COVID-19 vaccines have been shown to maintain high vaccine effectiveness (VE) against serious illness, hospitalization, and death from COVID-19 in most populations. However, evidence is emerging that VE against asymptomatic infection and mild COVID-19 disease may decrease with time, and that currently authorized COVID-19 vaccines may be less effective against the highly transmissible Delta variant (B.1.617.2), which could contribute to increased transmission of infection. Therefore, an additional or booster dose may be needed to obtain more durable protection in some populations.

Evidence from clinical trials suggests that booster doses of mRNA vaccines given six months after the primary series elicited a robust immune response against the wild type strain and variants of Concern (VoC), with titres often higher after the booster dose than after the primary series. Real-world data from Israel suggest that a booster dose provides good short-term effectiveness against SARS-CoV-2 infection and has a safety profile comparable to that observed after the second dose of the vaccine.

The intent of a booster dose is to restore protection that may have decreased over time to a level that is no longer deemed sufficient in individuals who initially responded adequately to a complete primary vaccine series. This is distinguished from the intent of an additional dose which might be added to the standard primary vaccine series with the aim of enhancing the immune response and establishing an adequate level of protection. For example, evidence suggests that compared to the general population, individuals who are moderately to severely immunocompromised have lower immune responses to COVID-19 vaccines. Therefore, NACI has recommended that

[moderately to severely immunocompromised individuals^a in the authorized age groups should be immunized with a primary series of three doses of an authorized mRNA vaccine.](#)

Historically in other vaccine programs, it can take years of post-market use to determine the optimal intervals and dose number needed for a complete primary series to sustain long-term protection. At present, there is scientific debate about whether a third dose for COVID-19 vaccines truly constitutes a booster dose in the traditional sense. NACI continues to monitor the emerging scientific data on how best to use these vaccines, and will study the important differences between a primary series (to establish strong immune memory), versus a booster (to stimulate the memory response once protection has truly waned). Over time, it may be learned that a short 2-dose primary series, with a booster at least 6 months after the second dose, can in fact be adjusted to achieve durable protection with a more streamlined primary series. For example, NACI has already highlighted benefit in terms of [longer-term protection when the second dose is provided at least 8 weeks after the first dose](#). In this guidance document, additional doses of COVID-19 vaccines after the authorized series are being described as booster doses but it should be acknowledged that over time, what defines an optimal primary series could also evolve and be refined.

NACI's recommendations on booster doses are occurring in the context of the World Health Organization's (WHO's) call for global vaccine equity, and take into consideration conclusions in its [Interim statement on booster doses for COVID-19 vaccination](#) including the call for evidence-based decisions: "Introducing booster doses should be firmly evidence-driven and targeted to the population groups in greatest need. The rationale for implementing booster doses should be guided by evidence on waning vaccine effectiveness, in particular a decline in protection against severe disease in the general population and in high-risk populations, or due to a circulating VoC. To date, the evidence remains limited and still inconclusive on any widespread need for booster doses following a primary vaccination series. The focus remains on urgently increasing global vaccination coverage with the primary series ⁽²⁾." NACI's recommendations on booster doses in those who have completed a primary series will be triggered by evidence on the need for a booster dose (in key populations at increased risk or in the general population), as well as the benefit of a booster dose.

Internationally, several countries, including the United States ⁽³⁾, the United Kingdom ⁽⁴⁾, France ⁽⁵⁾, and Germany ⁽⁶⁾, have recently recommended booster doses of COVID-19 vaccines at least 6 months following a primary vaccine series for certain high-risk groups, such as older adults, long-term care residents, and healthcare workers. Israel initially recommended a booster dose in adults 60 years of age and older and subsequently recommended a booster dose for the general

^a Moderately to severely immunosuppressed includes individuals with the following conditions:

- Active treatment for solid tumour or hematologic malignancies
- Receipt of solid-organ transplant and taking immunosuppressive therapy
- Receipt of chimeric antigen receptor (CAR)-T-cell therapy or hematopoietic stem cell transplant (within 2 years of transplantation or taking immunosuppression therapy)
- Moderate to severe primary immunodeficiency (e.g., DiGeorge syndrome, Wiskott-Aldrich syndrome)
- Stage 3 or advanced untreated HIV infection and those with acquired immunodeficiency syndrome
- Active treatment with the following categories of immunosuppressive therapies: anti-B cell therapies (monoclonal antibodies targeting CD19, CD20 and CD22), high-dose systemic corticosteroids (refer to the [CIG for suggested definition of high dose steroids](#)), alkylating agents, antimetabolites, or tumor-necrosis factor (TNF) inhibitors and other biologic agents that are significantly immunosuppressive.

population 12 years of age and over, at least 5 months following the primary series administered at the authorized dosage interval ⁽⁷⁾.

Countries that have rolled out primary series of COVID-19 vaccines using different vaccines and different intervals between doses of vaccines are experiencing different levels of protection over time, which is to be expected. NACI's recommendations for booster doses will differ from recommendations in other countries because of differences in a number of contextual factors including:

- the vaccine product(s) used to complete the primary series,
- the time that has elapsed since last dose in the primary series,
- the intervals between the first and second doses in the primary series,
- indirect protection from high vaccination coverage, and
- the use of other public health measures such as masking and physical distancing policies.

NACI reviewed available evidence on the factors presented in Table 1 in the context of the current Canadian epidemiology, vaccine programs, and vaccine schedules. Over 80% of Canadians aged 12 years and older have completed a primary COVID-19 vaccine series. Most are at a lower risk of declining protection due to receipt of mRNA vaccines (following NACI's [preferential recommendation for mRNA vaccines](#) ⁽¹⁾) or a combination of vaccine products in some instances (following NACI's recommendation on the interchangeability of authorized COVID-19 vaccines ⁽⁸⁾), and at intervals longer than the manufacturer authorized intervals (following NACI's recommendation for extended intervals ⁽⁹⁾). Furthermore, the Moderna Spikevax vaccine, authorized for use in Canada, appears to offer more durable protection against severe disease and asymptomatic infection ⁽¹⁰⁾. There is no evidence of decreasing protection over time against severe disease in the general Canadian population who have been vaccinated against COVID-19 disease. To date, Health Canada has not authorized booster doses of COVID-19 vaccines. NACI will continue to closely monitor the evidence and encourages a coordinated evidence-informed national approach.

On September 28, 2021, NACI recommended that [a booster dose of an authorized mRNA vaccine should be offered to all long-term care residents and seniors living in other congregate settings who have received a primary COVID-19 vaccine series \(with the primary series being a homologous or heterologous schedule using mRNA and/or viral vector vaccines\) at an interval of at least 6 months after the primary series has been completed](#) ⁽¹¹⁾. This population was also initially prioritized as a key population to receive initial doses of a primary series of COVID-19 vaccines based on evidence of an increased risk of severe illness and death and increased risk of exposure to SARS-CoV-2. The recommendation for a booster dose was triggered by increases in COVID-19 cases and outbreaks in long-term care homes with signs emerging that protection from vaccination might not persist as long in this population compared to other populations in Canada. In addition, long-term care residents are at high risk of exposure to SARS-CoV-2 due to their congregate living environment and at high risk of severe outcomes due to age and underlying health status. Longer time since last dose and shorter intervals between doses in the primary series, as well as older age/immunosenescence, also contribute to waning vaccine protection against infection and severe outcomes in this population. Assessment of the need for and benefit of a booster dose in other populations based on the criteria in Table 1 in the Canadian context and NACI's decision-making framework inform and guide NACI's recommendations herein subsequent to the [Rapid response: Booster doses in long-term care residents and seniors living in other congregate care settings](#).

Guidance objective

The objective of this advisory committee statement is to provide evidence-informed guidance on the equitable, ethical, and effective use of additional doses of authorized COVID-19 vaccines in the Canadian context based on the need for, and benefit of, booster doses to minimize serious illness and deaths while minimizing societal disruption as a result of COVID-19.

Methods

The evidence pertaining to COVID-19 and COVID-19 vaccines is rapidly evolving. NACI reviewed the decision-making framework and evidence on the need for and benefit of additional doses of COVID-19 vaccines in various populations on September 7, 14, 27, October 12 and 15, 2021. NACI consulted with the Public Health Ethics Consultative Group (PHECG) on the ethical implications of booster dose recommendations in various populations on September 2 and 21, 2021. Following a comprehensive review of available evidence and consultations with the provinces and territories through the Canadian Immunization Committee (CIC) and the Chief Medical Officers of Health (CMOH), NACI made and approved these recommendations on October 22, 2021.

NACI's decision-making framework on booster doses was modified from NACI's original prioritization framework of key populations for COVID-19 vaccination. The evidence supporting the development of the original framework is summarized in NACI's previously published guidance:

1. [Preliminary guidance on key populations for early COVID-19 immunization](#) (November 2020)
2. [Guidance on the prioritization of initial doses of COVID-19 vaccines](#) (December 2020)
3. [Guidance on the prioritization of key populations for COVID-19 immunization](#) (February 2021)

To guide ethical decisions that are based on evidence and on clear, transparent criteria, NACI developed a decision-making framework for booster doses modified from its [original evidence-informed prioritization framework for COVID-19 vaccination](#) ⁽¹²⁾. NACI's recommendations on booster doses will be based on this decision-making framework, triggered by evidence of the need for, and benefit of, a booster dose in the Canadian context (Table 1).

Key populations prioritized for a primary series of COVID-19 vaccination in NACI's original framework were based on evidence of increased risk of severe illness and death from COVID-19 and increased risk of exposure to SARS-CoV-2, summarized in NACI's 2020 guidance ⁽¹²⁻¹⁷⁾. NACI's decision-making framework on booster doses also considered populations with emerging evidence suggesting decreased protection from the primary series (e.g., vaccination with only viral vector vaccines, a longer time since completion of the primary series, shorter interval between doses of the primary series). NACI's recommendations are also guided by ethics and rooted in the foundational elements of equity, feasibility and acceptability.

Table 1. Underlying factors for consideration based on evolving evidence to determine the need for and benefit of a booster dose of COVID-19 vaccine in various populations

Underlying factors for consideration	Evidence reviewed to determine the need for and benefit of a booster dose of COVID-19 vaccine
Risk benefit analysis	<ul style="list-style-type: none"> • Risk of severe illness and death • Risk of exposure (including ability to physically distance and access to infection prevention and control measures and healthcare) • Risk of transmission to vulnerable populations • Risk of societal disruption
Vaccine characteristics in different groups against wild-type and VoC	<ul style="list-style-type: none"> • Duration of protection • Immunogenicity • Efficacy/effectiveness • Safety and reactogenicity of boosters • Effect of vaccine in preventing transmission
Vaccine supply/types/intervals	<ul style="list-style-type: none"> • Number and type of available vaccines • Initial vaccination series (type, interval between doses, time since initial series)
COVID-19 epidemic conditions	<ul style="list-style-type: none"> • Circulation of SARS-CoV-2 wild-type and VoC • Breakthrough cases, outbreaks • Case rates and implications for health system capacity

NACI recommendations on the use of COVID-19 vaccines are available [here](#).

Data on COVID-19 vaccination coverage and doses administered in various key populations in jurisdictions across Canada is available [here](#).

Further information on [NACI's process and procedures](#) is available elsewhere ^(18, 19).

Summary of evidence

Vaccine principles for booster doses

The immune responses to a vaccine are determined by a number of factors including vaccine type, interval between doses in the primary series, time since completion of the primary series, and underlying health status and age.

Higher antibody titres occur with the Moderna vaccine compared to the Pfizer-BioNTech vaccine and both have a higher titre than the viral vector vaccines ⁽²⁰⁾. A longer interval between the first and second doses also results in higher titres ^(21, 22). Although correlates of protection against SARS-CoV-2 have not yet been clearly defined, a higher antibody titre appears to be associated with longer duration of protection against symptomatic infection, including against VoC.

While there are various studies showing decreasing levels of circulating neutralizing antibodies as well as binding antibodies over time, studies also show that the mRNA vaccines elicit a memory

B and T cell response ^(23, 24). Even if circulating antibodies decrease, future exposure to SARS-CoV-2 is expected to drive a ‘recall’ response and long-lived memory T and B cells will help produce new antibodies. Therefore, even if a vaccinated individual is infected with SARS-CoV-2, vaccine-induced immunity through immune memory is expected to help to prevent progression to severe disease in most individuals, although the duration of immune memory is not known at this time.

For more information on vaccine principles, please consult the chapter on [basic immunology and vaccinology in the Canadian Immunization Guide](#).

Recent COVID-19 epidemiological trends

There is currently a resurgence of COVID-19 cases in regions of Canada fuelled by the highly transmissible Delta variant. Outbreaks continue to occur in multiple settings, including long-term care homes and retirement residences, industrial settings, school and daycare settings, as well as other settings that are enclosed and crowded, and can be a significant source of spread of SARS-CoV-2 infection. School and daycare settings have experienced an increasing number of outbreaks since mid-August ⁽²⁵⁾ due in part to a large proportion of ineligible and unvaccinated population (children under 12). In early August, the rate of active cases started rising in First Nations communities for the first time since mid-January 2021, and was 4.2 times higher than the rate in the general population as of October 12 ⁽²⁶⁾. As such, this NACI guidance is provided in the midst of the fourth COVID-19 pandemic wave driven by the Delta variant.

Canadian surveillance data up to October 2, 2021 shows that rates of new SARS-CoV-2 infection are highest among persons who are unvaccinated and lowest in persons who are fully vaccinated. Unvaccinated persons have also had much higher rates of hospitalizations, ICU admission and deaths compared to those fully vaccinated. Compared to those who are fully vaccinated, the rate of SARS-CoV-2 infection in unvaccinated persons was 8 times higher and the rate of COVID-19 related hospitalization in unvaccinated persons was 25 times higher, on average, for each week during the period of September 5 to October 2, 2021. While the incidence rate of infection is much lower in fully vaccinated people, it increased slightly across all age groups since mid-July, but has declined as of the week of September 26 - October 2, 2021 for all age groups.

Compared to fully vaccinated younger age groups, fully vaccinated cases 80 years of age and over have the highest rates of hospitalizations and deaths, followed by those aged 70 to 79 years. Among the fully vaccinated, these older age groups have the highest proportion of cases who are hospitalized and who have died from COVID-19. The weekly proportions of fully vaccinated cases who are hospitalized or who died has remained relatively low and stable since mid-July and the case fatality has decreased more recently in the older age groups, indicating that fully vaccinated people who become infected do not appear to be getting more severely ill over time.

Duration of COVID-19 vaccine protection against infection

Emerging evidence suggests a decrease in COVID-19 vaccine protection against SARS-CoV-2 infection over time following completion of the primary series. However, it can be challenging to distinguish potential signals of waning from increasing case numbers driven by community spread during the fourth wave of the pandemic and the rise of the Delta variant. Evidence on increasing incidence of infection in vaccinated individuals coincides with periods when the Delta variant predominated, and estimates of lower VE may be a reflection of decreased effectiveness against

the Delta variant rather than waning in COVID-19 vaccine protection. Further, increasing incidence in vaccinated individuals may also be observed in areas with lower vaccine coverage as a result of overall higher community rates driven by SARS-CoV-2 infection in the unvaccinated population. Continued research evaluating VE is needed to accurately determine trends in protection over time, as well as to learn more about the effects on transmission and the magnitude, if any, of potential decrease in protection. Immunogenicity data alone is insufficient to assess waning of protection against disease, and may not be indicative of protection against severe outcomes. To date, protection against severe COVID-19 outcomes, such as hospitalization and death, consistently appear to be more durable than protection against infection. There are some data that suggest decreases in protection may be greater in older age groups and in individuals with clinical risk factors for more severe outcomes ^(27, 28).

A recent rapid review ⁽²⁹⁾ on vaccine efficacy/effectiveness over time in COVID-19 vaccinated individuals identified seven studies that examined vaccine efficacy/effectiveness longitudinally over a period of 4 months or longer and provided both baseline and follow-up data. Studies that reported on confirmed infection ⁽³⁰⁻³²⁾ as an outcome generally indicated a decrease in VE against SARS-CoV-2 infection at 4 and 6 months after primary series completion compared to 7 to 14 days after primary series completion. Trends were similar for studies reporting on symptomatic infection ^(27, 30, 33, 34). In contrast, the studies that reported on COVID-19 related hospitalization ^(27, 31, 32, 35) and deaths ^(27, 30, 32) indicated that VE against severe COVID-19 outcomes remained stable over time thus far. These patterns were generally similar across vaccine products and in individuals over 60 years old. However, evidence was limited by the small number of heterogeneous studies, which were observational in design.

Studies on duration of protection have typically examined protection after a manufacturer-recommended dosing interval of 3 or 4 weeks between first and second doses for mRNA vaccines. It is currently uncertain how a longer interval between first and second vaccine doses in a primary series might affect the duration of protection. Provincial data from British Columbia and Quebec found that shorter intervals between doses in a primary series result in lower VE against SARS-CoV-2 infection and COVID-19 related hospitalizations compared to extended intervals. Further, emerging evidence suggests that shorter intervals between doses may be associated with lower VE against infection over time ^(27, 28). Evidence to date suggests that delaying the second dose by several weeks leads to higher antibody titres and greater VE of the series ^(22, 36, 37) which is likely to result in a more durable immune response and longer protection over time.

It is currently unclear to what extent the duration of protection may vary by vaccine product. In general, VE against symptomatic SARS-CoV-2 infection and severe COVID-19 outcomes has consistently been somewhat lower with viral vector vaccines compared to mRNA vaccines ⁽³⁸⁾. Emerging data on effectiveness suggests that vaccine protection against infection and symptomatic disease decreases more quickly with viral vector vaccines in comparison to mRNA vaccines, whereas the difference is less pronounced for severe disease ^(27, 28). Limited real-world data from Canada and the United States suggests that protection from Moderna Spikevax may be more durable compared to Pfizer-BioNTech Comirnaty ^(28, 39), but more research is required.

There is limited evidence on duration of protection following a mixed COVID-19 vaccination schedule. Data from two studies indicate that VE for those who received a mixed schedule of AstraZeneca Vaxzevria/COVISHIELD followed by an mRNA vaccine is similar compared to those who received a complete series of mRNA vaccines ^(28, 40).

Despite some evidence of increasing risk of breakthrough infection over time, those vaccinated against COVID-19 with a two-dose series continue to demonstrate significantly lower odds of SARS-CoV-2 infection compared to unvaccinated individuals and, when infections occur, symptoms tend to be milder in vaccinated cases ⁽⁴¹⁾. VE against severe COVID-19 outcomes with all vaccine types remains high, even in the context of the Delta variant. Breakthrough infections in vaccinated persons could contribute to ongoing transmission of SARS-CoV-2. Early evidence from when the Alpha variant predominated suggested that vaccinated individuals who became infected were less infectious ⁽⁴²⁾. The evidence on transmission with the Delta variant is less clear, with some studies suggesting the differences in viral load between vaccinated and unvaccinated persons who become infected may be less compared to when the Alpha variant was predominant ⁽⁴²⁻⁴⁶⁾.

Immunogenicity, Safety, and Effectiveness of COVID-19 vaccine booster doses

Ongoing manufacturer-sponsored trials on mRNA vaccines have reported higher titres following the third doses compared to those after the initial series ^(47, 48) of two doses (administered at manufacturer authorized intervals), suggesting that the higher titres produced by a booster dose may lead to longer lasting protection than the primary series administered at manufacturer authorized intervals. Early results also show a favourable reactogenicity profile for booster mRNA vaccine doses, similar to that of the second dose in the primary series ^(47, 48). Evidence from these trial data is limited by small sample size (less than 350 participants in each published manufacturer-sponsored trial ^(49, 50)) and short duration of follow-up of study populations. Pfizer-BioNTech Comirnaty and Moderna Spikevax have filed submissions for booster doses ≥ 6 months after the primary series to Health Canada for regulatory approval as of October 1 and 5, 2021 respectively. The regulatory submission for a Moderna Spikevax booster dose is for half the current dosage of Moderna Spikevax primary series dose (i.e., a 50 mcg booster dose vs. 100 mcg full dose). The regulatory submission for a Pfizer-BioNTech Comirnaty booster dose is the same as the current dosage of the primary series dose for this vaccine (i.e., a 30 mcg booster dose).

Emerging real-world data from Israel's booster dose program with Pfizer-BioNTech Comirnaty indicates that a third dose (after a primary series using the manufacturer authorized interval of 21 days between doses) resulted in improved short-term vaccine effectiveness against infection and severe illness ⁽⁵¹⁾. In one Israeli study of individuals ≥ 60 years of age, a booster dose of Pfizer-BioNTech Comirnaty at least 5 months after the primary series decreased the relative risk of confirmed SARS-CoV-2 infection by 11.3-fold and of severe illness by 19.5-fold at 12 or more days from the booster dose, compared to those with two doses ⁽⁵²⁾. An extension of this analysis ⁽⁵³⁾ found that, compared to a two-dose series, a booster dose resulted in about a 10-fold reduction in confirmed infection rates in persons ≥ 16 years of age. In another Israeli study of persons ≥ 40 years of age, those who received a third dose had a 70 to 84% reduction in the odds of testing positive for SARS-CoV-2 infection 14 to 20 days after receiving the booster compared to people who received two doses of Pfizer-BioNTech Comirnaty ⁽⁵⁴⁾. There are no data currently on the long-term effectiveness of booster doses so it remains unknown at this time how long benefit might last. The effect of booster doses on transmission is unknown.

Studies evaluating boosters following different primary series vaccine schedules are ongoing ^(55, 56). Unpublished data from the Cov-Boost trial presented to the United Kingdom's Joint Committee on Vaccination and Immunisation (JCVI) suggest that mRNA booster doses are generally well

tolerated and provide a strong booster effect regardless of the vaccine used in the primary series ⁽⁴⁾. Similarly, recent data from the US National Institutes of Health “Mix and Match” trial indicates that heterologous booster doses given at least 12 weeks following completion of the primary series of mRNA vaccines or Janssen COVID-19 vaccine were well-tolerated and immunogenic. Additionally, those who received an mRNA booster following a dose of Janssen COVID-19 vaccine had higher antibody titres compared to those who received a second dose of Janssen as a booster ⁽⁵⁷⁾.

The safety and effectiveness of a third dose in persons who had a previous SARS-CoV-2 infection is currently unknown.

Rare cases of myocarditis and pericarditis following vaccination with COVID-19 mRNA vaccines have been reported, more frequently after the second dose compared to the first dose, and more commonly in younger males and adolescents. Canadian data also suggest that myocarditis/pericarditis occur more frequently after Moderna Spikevax compared to Pfizer Comirnaty COVID-19 vaccines. The rate of myocarditis and pericarditis following a booster dose of a COVID-19 mRNA vaccine is currently unknown. Initial surveillance data from Israel up to October 10, 2021 has reported 17 cases of myocarditis or peri-myocarditis out of approximately 3.7 million booster doses of Pfizer-BioNTech Comirnaty administered ⁽⁵¹⁾. In Israel, this rate is lower than observed after the second dose, but higher than observed after the first dose. Data collection is ongoing. NACI will continue to monitor the evidence and update recommendations as needed.

Optimal primary series to booster dose interval

There are currently limited data to determine the optimal interval between the completion of the primary series and administration of the booster dose. Most studies on mRNA COVID-19 vaccine booster doses have used an interval of 6 months or more following the completion of the primary series, although some have used an interval as short as 3 months ^(55, 56). Submissions filed with regulatory authorities in the US, EU and Canada are for 6 months or more following the second dose, which was the interval used in booster doses trials for Pfizer-BioNTech Comirnaty and Moderna Spikevax ^(49, 50). However, it is currently unknown at what interval a maximum boosting effect is achieved. For older adults who may have a decrease in protection over time, delaying the booster dose will increase the period during which individuals may have reduced protection against SARS-CoV-2 infection, although to date protection against severe outcomes has been shown to be more durable than protection against infection.

Summary of primary COVID-19 vaccine series that have been used in Canada to date

Vaccine types received in the primary series in Canada

As of October 9, 2021, 82% of eligible Canadians have been fully vaccinated with a COVID-19 vaccine, while 87% have received at least one dose. Of those fully vaccinated, the majority received a complete two-dose series of mRNA vaccines. A small percentage received a complete series with a viral vector vaccine. At least 469,371 Canadians have received a viral vector vaccine primary series and 1,395,324 Canadians have received a heterologous primary series containing both a viral vector vaccine and an mRNA vaccine. Almost all viral vector primary series were with AstraZeneca Vaxzevria/COVISHIELD vaccines. Data on vaccination coverage by vaccine product was missing for two provinces.

Refer to [COVID-19 vaccination in Canada](#) for the most current information on vaccination coverage.

Intervals between doses in the primary series of COVID-19 vaccines in Canada

Shorter intervals between doses results in lower antibody titres which may wane to below protective levels over time. While individuals who received their second dose in the primary COVID-19 vaccine series at a shorter interval from the first dose were well protected in the short-term, they may have produced lower antibody levels, which may decrease over time compared with those who had a longer interval between doses.

Intervals between the first and second doses of a two-dose primary series of COVID-19 vaccines varied across Canada as vaccine supply and evidence evolved. Groups [prioritized for vaccination early in the vaccine roll-out](#) ⁽¹²⁾ often received their vaccines using the manufacturers' recommended interval of 21 days for Pfizer-BioNTech Comirnaty and 28 days (or as short as 21 days) for Moderna Spikevax. Subsequently, [intervals between doses were extended up to 16 weeks](#) to optimize early vaccine rollout and population protection in Canada in the context of limited vaccine supply ⁽⁹⁾. As vaccine supply was no longer limited, and in the context of the increasing prevalence of the Delta variant, jurisdictions accelerated second doses with shorter intervals. Aggregated vaccination coverage data obtained from provincial and territorial vaccination registries up to August 14, 2021, showed that an interval of 7-11 weeks between first and second doses was the most common dosing interval across all vaccine products. Dosing intervals varied widely by jurisdiction and age group. Most notably, 66% of vaccinated adults aged 80 years old and older had an interval of 12 weeks or more between first and second dose, while 9% had an interval of 28 days or less. Data on vaccination coverage by dosing interval was missing for one province.

There is evidence that the Moderna Spikevax vaccine remains efficacious against severe disease and asymptomatic infection at more than 5 months when given at the authorized interval of 28 days between doses ⁽¹⁰⁾. There is evidence that while the Pfizer-BioNTech Comirnaty vaccine prevents COVID-19 for up to 6 months, there is a gradual decline in efficacy when given at the authorized interval of 21 days between doses ⁽³⁴⁾. Though limited data suggests that protection from Moderna Spikevax may be more durable compared to Pfizer-BioNTech Comirnaty ^(28, 39), more research is required.

Time since completion of primary COVID-19 vaccine series in Canada

As noted above, protection against infection may decrease with time since completion of the second dose of vaccine. [Key populations at highest risk of severe illness due to COVID-19 and/or highest risk of exposure to SARS-CoV-2](#) (e.g., residents and staff of congregate living settings that provide care for seniors, older adults, frontline healthcare workers, adults in or from Indigenous communities) were prioritized to receive COVID-19 vaccines earlier than others when initial vaccine supply was limited ⁽¹²⁾. Therefore, many in these populations would have completed their primary series longer than 6-8 months ago. A number of these key populations received their second doses between January and April 2021. The vast majority of Canadians who are fully vaccinated completed their primary series in June or July 2021 (84%). Only 4% received their second doses between January and April 2021. Data on vaccination coverage by time since last dose was missing for one province.

Ethics, Equity, Feasibility and Acceptability Considerations

Ethics

Advice provided to NACI by the PHAC Public Health Ethics Consultative Group (PHECG) on the ethical implications of booster dose recommendations included the following ^(58, 59):

- Decisions about extending boosters ought to be evidence-informed and fair, and clearly communicate why and when groups will become eligible for boosters. It is necessary to be clear about the rationale for offering an additional dose, including how the criteria fit within, and are consistent with, a broader booster framework, if and when such a recommendation is made.
- Besides a general duty to protect the public's health, Canada also has a duty to protect the most vulnerable. The precautionary principle supports offering a booster dose of a COVID-19 vaccine to those who are at greatest risk of serious harms due to COVID-19, prior to a significant degree of waning VE against severe outcomes being observed.

Equity

Global equity:

- On September 8, 2021 the WHO called for a global moratorium on booster doses until at least the end of 2021, to enable every country to vaccinate at least 40 percent of its population ⁽⁶⁰⁾. NACI acknowledges the importance of global equity in this pandemic, although global vaccine supply considerations are outside the purview of NACI's mandate. As advised by the PHECG, global vaccine equity requires that need (e.g., risk of severe illness and death and risk of exposure) be taken into account when allocating vaccines. This includes prioritizing high-risk groups globally who have not yet received first or second doses over individuals who are at lower risk due to having completed a primary vaccine series ⁽⁵⁸⁾.

Domestic equity:

- Inter-jurisdictional equity is also a relevant consideration both for reasons of promoting fairness and fostering trust. As advised by the PHECG, consistency and transparency in public health messaging and programs contribute to public trust in public health advice. Equity may not necessarily require a uniform response across all jurisdictions, since there are a variety of ethically-relevant factors that could justify triggering a recommendation for one jurisdiction but not in another. For example, in order to offer equitable protection against risk of COVID-19-related harms, disparate recommendations across jurisdictions may be justified when the populations in these jurisdictions face disparate levels of risk ⁽⁵⁸⁾. This includes the continued allocation of resources to encourage high acceptance and uptake of the primary series, which offers the most benefit against severe outcomes and deaths due to COVID-19, for those who have not yet received the vaccine. However, where possible, alignment across jurisdictions is expected to positively impact inter-jurisdictional equity and public trust in public health advice.

Feasibility

- COVID-19 vaccine supply in Canada has increased and mechanisms for distributing and administering vaccines have been established. However, if boosters are administered all at once for the general population, there may be operational challenges with implementation. Consideration should also be given to minimizing wastage of product reaching its expiry date and open vials that need to be used within a specified period of time.

Acceptability

- According to survey data from August 2021, there is generally high acceptability for COVID-19 booster doses amongst Canadians. Approximately 80% of individuals, regardless of vaccination status, are willing to get an annual booster or booster doses now or within the next year; and those aged 65 or older are the most likely to be willing to take a booster shot (92%)^(61, 62).
- Of those who are already fully vaccinated, around 80-93% are willing to get a booster dose^(61, 63). Of those who received a mixed schedule with AstraZeneca and an mRNA COVID-19 vaccine, 58% agreed to get a third dose if studies show that a third dose is required⁽⁶⁴⁾.
- Most Canadians (74%) agree that the priority for vaccines should be first doses for those who want them before making booster shots available⁽⁶³⁾.

Refer to [NACI's previous guidance](#) for a comprehensive overview of the ethical, equity, feasibility and acceptability considerations for prioritizing key populations for COVID-19 vaccination^(12, 13, 16, 17).

Recommendations

Please see Table 2 for an explanation of strong vs discretionary NACI recommendations.

NACI strongly reiterates its previous evidence-informed recommendations for the primary series of COVID-19 vaccines in all authorized age groups:

1. NACI preferentially recommends ⁽¹⁾ that a complete series with an mRNA COVID-19 vaccine should be offered to individuals in the authorized age group without contraindications to the vaccine. *(Strong NACI Recommendation)*

Additional details are available in the [NACI statement on Recommendations on the use of COVID-19 vaccines](#).

2. NACI recommends ⁽⁶⁵⁾ that moderately to severely immunocompromised individuals^b in the authorized age groups should be immunized with a primary series of three doses of an authorized mRNA vaccine. For those who have previously received a 1- or 2-dose complete primary COVID-19 vaccine series (with a homologous or heterologous schedule using mRNA or viral vector vaccines), NACI recommends that an additional dose of an authorized mRNA COVID-19 vaccine should be offered. *(Strong NACI Recommendation)*

Additional details are available in the [NACI rapid response: Additional dose of COVID-19 vaccine in immunocompromised individuals following 1- or 2- dose primary series](#).

NACI's evidence-informed recommendations for booster doses of COVID-19 vaccines:

NACI recognizes that epidemiological and logistical/operational contexts, as well as impacts on health system capacity, vary between provinces and territories across Canada. NACI encourages jurisdictions to align with these recommendations as much as possible to ensure the equitable, ethical and effective use of booster doses of COVID-19 vaccines in Canada, maintaining vaccine acceptance and confidence, while considering their local contexts.

NACI also acknowledges that the epidemiology of COVID-19 (including the impact of SARS-CoV-2 variants of concern) and the evidence on booster doses of COVID-19 vaccines are rapidly evolving, and will continue to monitor the evidence in the Canadian context and provide additional recommendations and updates subsequent to this interim statement as data emerge.

Following an evaluation of the need for, and benefit of, additional doses of COVID-19 vaccines based on evolving evidence on the criteria outlined in Table 1, as well as the systematic

^b Moderately to severely immunosuppressed includes individuals with the following conditions:

- Active treatment for solid tumour or hematologic malignancies
- Receipt of solid-organ transplant and taking immunosuppressive therapy
- Receipt of chimeric antigen receptor (CAR)-T-cell therapy or hematopoietic stem cell transplant (within 2 years of transplantation or taking immunosuppression therapy)
- Moderate to severe primary immunodeficiency (e.g., DiGeorge syndrome, Wiskott-Aldrich syndrome)
- Stage 3 or advanced untreated HIV infection and those with acquired immunodeficiency syndrome
- Active treatment with the following categories of immunosuppressive therapies: anti-B cell therapies (monoclonal antibodies targeting CD19, CD20 and CD22), high-dose systemic corticosteroids (refer to the [CIG for suggested definition of high dose steroids](#)), alkylating agents, antimetabolites, or tumor-necrosis factor (TNF) inhibitors and other biologic agents that are significantly immunosuppressive.

assessment of ethics, equity, feasibility and acceptability considerations with the EEFA framework⁽¹⁹⁾, NACI makes the following evidence-informed recommendations on booster doses of authorized COVID-19 vaccines in the context of ongoing risk of severe illness from COVID-19 and exposure to SARS-CoV-2 and VoCs in Canada:

For key populations at highest risk of severe illness from COVID-19 and highest risk of waning protection:

3. NACI recommends that a booster dose of an authorized mRNA COVID-19 vaccine* *should be offered* ≥6 months after completion of a primary COVID-19 vaccine series (where the primary series consisted of a homologous or heterologous schedule using mRNA or viral vector vaccines) to individuals in the following key populations:
 - Adults living in long-term care homes for seniors or other congregate living settings that provide care for seniors (as [previously recommended by NACI](#))
 - Adults ≥80 years of age

(Strong NACI Recommendation)

For key populations at increased risk of severe illness from COVID-19 and increased risk of waning and/or lower protection:

4. NACI recommends that a booster dose of an authorized mRNA COVID-19 vaccine* *may be offered* ≥6 months after completion of a primary COVID-19 vaccine series to individuals in the following key populations:
 - Adults 70-79 years of age (whose primary series consisted of a homologous or heterologous schedule using mRNA or viral vector vaccines)
 - Recipients of a viral vector vaccine series completed with only viral vector vaccines (AstraZeneca/COVISHIELD or Janssen COVID-19 vaccine), regardless of age based on local epidemiology and any evidence of diminished protection, and with consideration of individual risks and potential benefits.

(Discretionary NACI Recommendation)

For key populations who may be at increased risk of severe illness from COVID-19 (due to intersecting social and health risk factors⁽¹³⁾) and waning protection (due to increased time since completion of the primary COVID-19 vaccine series after a shorter interval between doses) where infection can have disproportionate consequences⁽¹²⁾:

5. NACI recommends that a booster dose of an authorized mRNA COVID-19 vaccine* *may be offered* ≥6 months after completion of a primary COVID-19 vaccine series (where the primary series consisted of a homologous or heterologous schedule using mRNA or viral vector vaccines) to individuals in the following key population:
 - Adults in or from First Nations, Inuit and Métis communities based on local epidemiology, vaccine coverage, any evidence of waning protection and with consideration of individual risks and potential benefits. Whether or not booster dose vaccine programs are needed in distinct Indigenous communities should be determined by Indigenous leaders and communities, considering these same factors, and with the support of public health partners.

(Discretionary NACI Recommendation)

For key populations who are essential for maintaining health system capacity and who may be at increased risk of waning protection (due to increased time since completion of the primary COVID-19 vaccine series after a shorter interval between doses) and who could pose increased risk of transmission to vulnerable populations:

6. NACI recommends that a booster dose of an authorized mRNA COVID-19 vaccine* may be offered ≥ 6 months after completion of a primary COVID-19 vaccine series (where the primary series consisted of a homologous or heterologous schedule using mRNA or viral vector vaccines) to individuals in the following key population:
 - Adults who are frontline healthcare workers (having direct close physical contact with patients) and who were vaccinated with a very short minimum interval (less than 28 days) between the first and second doses of an mRNA COVID-19 primary vaccine series, based on local epidemiology, any evidence of waning protection, and impacts on health system capacity, and with consideration of individual risks and potential benefits.

(Discretionary NACI Recommendation)

For other populations not included in the above recommendations for a booster dose, NACI will continue to closely monitor the evidence and will make additional recommendations if there is evidence of the need for, and benefit of, a booster dose. This includes monitoring the specific evidence for:

- Individuals who have had previously PCR-confirmed SARS-CoV-2 infection and have completed a primary series of COVID-19 vaccines.
- Moderately to severely immunocompromised individuals who have completed a 3-dose primary series of COVID-19 vaccines. Populations with underlying medical conditions that may be at higher risk of severe disease after breakthrough infection

*Either Moderna Spikevax or Pfizer-BioNTech Comirnaty vaccines may be used as a booster dose (regardless of which COVID-19 vaccine was used in the primary series). As previously recommended, adults living in long-term care homes for seniors or other congregate living settings that provide care for seniors are recommended to receive the full dose (100 mcg) if being offered Moderna Spikevax. For other adults recommended to receive a booster dose, the full dose (100 mcg) is recommended for adults 70 years of age or older, if offering Moderna Spikevax, while a half dose (50 mcg) is recommended for those less than 70 years of age. If offering Pfizer-BioNTech Comirnaty, the full dose (30 mcg) is recommended

Individuals who had a severe immediate allergic reaction (e.g., anaphylaxis) to a previous mRNA vaccine or who have a severe immediate allergic reaction (e.g., anaphylaxis) to a component of the mRNA vaccine should consult with an allergist or other appropriate physician as vaccination with an mRNA has been safely performed in these populations. Additional guidance for individuals with myocarditis/pericarditis after a previous dose of an mRNA vaccine is under consideration and will be forthcoming.

Summary of evidence and rationale

- To date, almost 2 in 10 eligible Canadians have not been fully vaccinated. Efforts should be made to encourage vaccination of those unvaccinated with a primary COVID-19 vaccine series.
- Unvaccinated individuals are at highest risk of SARS-CoV-2 infection and severe outcomes from COVID-19. There is no evidence to date of waning of protection against severe disease in the general Canadian population who have been vaccinated against COVID-19 disease.
- NACI continues to strongly recommend that all individuals in the authorized age groups should be immunized with a primary series of an authorized COVID-19 vaccine, and preferably with mRNA COVID-19 vaccines (Moderna Spikevax and Pfizer-BioNTech Comirnaty) ⁽¹⁾.
- Fully vaccinated individuals are less likely to get infected, and therefore are less likely to transmit infection to others.
- Emerging evidence suggests a waning in COVID-19 vaccine immunogenicity and effectiveness against SARS-CoV-2 infection over time following completion of the primary series, although protection against severe COVID-19 outcomes appears to be more durable than protection against infection.
- Increased incidence of breakthrough infections amongst those fully vaccinated is expected in the context of high community rates of SARS-CoV-2 (especially where vaccination coverage rates for the primary COVID-19 vaccine series are low) and the predominance of the Delta variant in Canada, given the somewhat lower vaccine effectiveness against infection with this VoC.
- Decreased protection against infection could contribute to more transmission which can have significant impacts especially on some populations and on health system capacity. Vaccinated individuals infected with the Delta variant are less likely to develop severe disease. However, vaccinated individuals infected with this highly transmissible variant may be more infectious to others, potentially facilitating transmission if infected ⁽⁶⁶⁾.
- Decreased protection against infection over time has been noted to potentially occur more quickly with the viral vector vaccines than the mRNA vaccines, while protection with Moderna Spikevax may be more durable than with Pfizer-BioNTech Comirnaty. Shorter intervals between the first and second dose for 2-dose COVID-19 vaccine series result in lower initial titres that may result in protection that decreases sooner.
- Studies suggest that booster doses of mRNA vaccines elicit a robust immune response, have a favourable safety profile (comparable to that of the second dose of the primary series) and provide good short-term effectiveness against SARS-CoV-2 infection and severe disease. Health Canada is reviewing the evidence submitted by Moderna and Pfizer BioNTech for regulatory approval of a booster dose, but neither vaccine is currently authorized for use as a booster dose in Canada. Post-market safety surveillance on mRNA COVID-19 vaccines found an increased frequency of myocarditis and pericarditis following a second dose of a COVID-19 mRNA vaccine in younger males and adolescents. Higher unadjusted rates of cases of myocarditis and/or pericarditis have been reported after the Moderna vaccine compared to Pfizer-BioNTech vaccine in some jurisdictions ^(67, 68). Additional analyses are ongoing. The majority of cases reported while hospitalized were relatively mild and individuals tended to recover quickly. The rate of myocarditis and pericarditis following a booster dose of a COVID-19 mRNA vaccine is currently unknown,

although initial data from Israel to date has shown lower rates of myocarditis/pericarditis after the booster dose than after the second dose, but higher than after the first dose; data collection is ongoing. Informed consent for vaccination with a booster dose should include that a primary series of COVID-19 vaccines remains effective against severe COVID-19, and that a booster dose is intended to restore protection against infection that may have decreased over time. However, the effectiveness against transmission of infection, long-term effectiveness against infection and severe disease, and rate of myocarditis and pericarditis after a booster dose are currently unknown. In addition, recommendations for a booster dose of COVID-19 vaccines are currently off-label in Canada.

Key Populations included in this initial guidance on booster doses of COVID-19 vaccine:

- The [key populations identified by NACI for early COVID-19 immunization](#) were prioritized due to an increased risk of severe illness and exposure. The evidence and rationale for prioritizing these groups is summarized in [Table 2 of NACI's previous guidance](#). Those prioritized in the earliest stages may now be at an increased risk of waning of protection because for some of them, more time has elapsed since their second dose and a number of them were vaccinated with a very short interval between doses to optimize protection as quickly as possible.
- The combined factors of high risk of severe outcomes, high risk of exposure, increased time since completion of primary series, shorter interval between doses in the primary series (in some cases), and immunosenescence in older age can contribute to decreased protection and increase the risk for infection and possibly severe outcomes in the key populations for whom NACI recommends a booster dose of COVID-19 vaccine.
- An individual's risk benefit analysis for a booster dose recommended in key populations should include an assessment of:
 - Risk of severe illness from COVID-19 (e.g., older age, underlying medical condition)
 - Risk of increased waning of protection (e.g., shorter interval between doses, longer time since completion of primary series, vaccination with only viral vector COVID-19 vaccines)
 - Local epidemiology (e.g., circulation of VoC, evidence of waning protection)
 - Vaccine coverage of primary series in the community (e.g., the risk of breakthrough infection in fully vaccinated individuals is higher in the context of high community rates of SARS-CoV-2 especially where vaccination coverage rates for the primary COVID-19 vaccine series are low)
 - Health system capacity

Long-term care residents and seniors living in other congregate settings

- Refer to NACI's [Rapid response: Booster dose in long-term care residents and seniors living in other congregate settings](#) for a summary of the evidence and rationale for booster doses in this population.

Older age

- There are some signs that decreasing protection may be greater in older age groups and in individuals with clinical risk factors for more severe outcomes ^(27, 28). Among the fully vaccinated, older age groups (80 years of age and over, followed by those 70 to 79 years of age) have the highest hospitalization and mortality rates from COVID-19 compared to younger age groups who are fully vaccinated.
- There was a large independent association of severe COVID-19 with increasing age and moderate certainty of evidence for a very large association of hospitalization and mortality particularly in those over 70 years of age in OECD countries before vaccination ⁽⁶⁹⁾.
- The proportion of individuals with at least one underlying medical condition associated with an increased risk of severe COVID-19 increases with increasing age ⁽⁷⁰⁾.
- It is important to acknowledge that the regulatory submission for a Moderna booster dose is for half the current dosage of Moderna Spikevax (i.e., a 50 mcg booster dose vs. 100 mcg full dose). However, as older adults have dampened immune function, and may need to receive a higher dose formulation of a vaccine or an immunostimulatory adjuvant to increase the potency of their response to vaccines, this population may benefit from a full dose (100 mcg) of Moderna Spikevax as a booster dose ⁽¹¹⁾.

Recipients of only viral vector vaccines

- Individuals who received a complete series with only a viral vector vaccine have somewhat lower initial VE and may experience waning protection. Emerging data suggests vaccine protection against infection and symptomatic infection decreases more quickly with viral vector vaccines in comparison to mRNA vaccines.
- NACI preferentially recommended COVID-19 vaccination with mRNA vaccines ⁽¹⁾ due to their high efficacy and safety and the availability of mRNA vaccine supply in Canada. Only a small percentage of fully vaccinated Canadians to date (<1%) have been vaccinated with only viral vector vaccines.

Adults in or from First Nations, Inuit and Métis communities

- The rate of active COVID-19 cases started rising in First Nations communities in August 2021 and was 4.2 times higher than the rate in the general population as of October.
- Racialized and marginalized populations such as Indigenous Peoples have been disproportionately affected by COVID-19 due to a number of intersecting equity factors.
- The proportion of Canadians who identify as Indigenous and have at least one underlying medical condition associated with severe COVID-19 is higher compared to other Canadians for every age category above 20 years of age. This increases the risk of severe outcomes for COVID-19 in this population.
- Remote or isolated communities may not have ready access to sufficient healthcare infrastructure. Therefore, their risk for severe outcomes, including death, and societal disruption is proportionally greater than in other communities.
- The risk of transmission is higher in settings where physical distancing and other infection prevention and control measures are challenging and individuals may not be able to exercise sufficient precautions to adequately protect themselves from infection.

- Immunization of individuals in this population has the potential to reduce or prevent the exacerbation of intersecting health and social inequities.
- Adults in or from Indigenous communities were included in the earliest stages of initial COVID-19 immunization and may be at increased risk of waning of protection because for some of them, more time has elapsed since their second dose and a number of them were vaccinated with a very short interval between doses to optimize protection as quickly as possible.
- Autonomous decisions should be made by Indigenous Peoples with the support of healthcare and public health partners in accordance with the [United Nations Declaration on the Rights of Indigenous Peoples](#) ⁽⁷¹⁾.

Frontline healthcare workers

- Maintaining health system capacity is crucial to minimize serious illness and overall deaths while minimizing societal disruption as a result of the COVID-19 pandemic.
- Frontline healthcare workers can be at risk for occupational exposure and can potentially transmit infection to vulnerable populations. Healthcare workers are essential to the provision of healthcare, and their absence due to illness could compromise health system capacity. At present, the health system continues to be strained due to the hospitalization of people with COVID-19, especially where infection rates have been high during the fourth (Delta) wave in Canada. Optimizing the protection of healthcare workers can help to balance any disproportionate burden of those taking on additional risks to protect the public, thereby upholding the ethical principle of reciprocity.
- The risk of waning of protection is associated with shorter intervals between doses in the primary vaccine series. Therefore, while frontline healthcare workers who received their second dose at very short minimum intervals (less than 28 days) from the first dose were well protected in the short-term, the durability of that protection may wane more quickly than those who had a longer interval between doses.
- There is evidence that the Moderna Spikevax vaccine remains efficacious against severe disease and asymptomatic infection at more than 5 months when given at the authorized interval of 28 days between doses ⁽¹⁰⁾. There is evidence that while the Pfizer-BioNTech Comirnaty vaccine prevents COVID-19 effectively for up to 6 months, there is a gradual decline in efficacy when given at the authorized interval of 21 days between doses ⁽³⁴⁾. Emerging data also suggest that protection from Moderna Spikevax may be more durable compared to Pfizer-BioNTech Comirnaty ^(28, 39); more research is required.

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.

Table 2. Strength of NACI Recommendations

Strength of NACI Recommendation <i>based on factors not isolated to strength of evidence</i> (e.g., public health need)	STRONG	DISCRETIONARY
Wording	<i>“should/should not be offered”</i>	<i>“may/may not be offered”</i>
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/may not be offered for some populations/individuals in some circumstances. Alternative approaches may be reasonable.

Research Priorities

1. What is the efficacy, effectiveness, immunogenicity and safety of booster dose COVID-19 vaccine individuals who have had a previous laboratory-confirmed SARS-CoV-2 infection?
2. What is the effect of booster doses of COVID-19 vaccines on transmission of infection at a population level? How long do any beneficial effects on transmission last?
3. Is a booster dose required after a 3-dose primary series of COVID-19 vaccines in those who are moderately to severely immunocompromised?
4. What is the optimal product (including the booster vaccine in relation to the product(s) received for the primary series), booster vaccine dose, interval between doses in the primary series, interval between the primary series and additional/booster dose, and potential need for (and frequency of) future booster doses in groups at high risk for severe COVID-19 outcomes and in the general population to ensure protection against SARS-CoV-2?
5. What is the optimal timing and trigger for booster doses? What are the risks associated with providing a booster dose earlier than necessary?
6. Will special adverse events that have been associated with the primary series (e.g., myocarditis/pericarditis) also be associated with additional/booster doses? Will any new or previously unrecognized adverse event occur with booster doses?

7. What is the efficacy, effectiveness, immunogenicity, and safety of booster doses of COVID-19 vaccine following a complete series across diverse population groups (e.g., adults of advanced age, those with high-risk medical conditions including autoimmune conditions and transplant recipients, individuals with social or occupational vulnerabilities, individuals who are pregnant or breastfeeding, adolescents, frailty)?

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