

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

Guidance on the use of COVID-19 vaccines starting fall
2026

PROTECTING AND EMPOWERING CANADIANS TO IMPROVE THEIR HEALTH



Public Health
Agency of Canada

Agence de la santé
publique du Canada

Canada

TO PROMOTE AND PROTECT THE HEALTH OF CANADIANS THROUGH
LEADERSHIP, PARTNERSHIP, INNOVATION AND ACTION IN PUBLIC HEALTH.

—Public Health Agency of Canada

Également disponible en français sous le titre :

Directives sur l'utilisation des vaccins contre la COVID-19 à partir l'automne 2026.

Information contained in this publication or product may be reproduced, in whole or in part, and by any means, for personal or public non-commercial purposes without charge or further permission, unless otherwise specified. Commercial reproduction and distribution are prohibited except with written permission from the Public Health Agency of Canada. To obtain permission to reproduce any content owned by the Government of Canada available for commercial purposes, please contact pubsadmin@hc-sc.gc.ca.

To obtain additional information, please contact:

Public Health Agency of Canada
130 Colonnade Rd
A.L 6501H
Ottawa, ON K1A 0K9
Toll free: 1-844-280-5020
Fax: 613-941-5366
TTY: 1-800-465-7735
E-mail: publications-publications@hc-sc.gc.ca

© His Majesty the King in Right of Canada, as represented by the Minister of Health,
2026.

Publication date: June 2026.

This publication may be reproduced for personal or internal use only without permission provided the source is fully acknowledged.

Cat.: HP40-376/2026E-PDF ISBN: 978-0-660-98782-8 Pub.: 250487

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.

Table of Contents

Preamble	3
Summary Of Guidance	5
I. Introduction	5
II. Methods	5
III. Epidemiology	6
IV. Vaccine	8
IV.1 Preparation(s) Authorized For Use In Canada	8
IV.2 Clinical Evidence On Covid-19 Vaccines	8
IV.3 Contraindications And Precautions	10
IV.4 Concurrent Administration With Other Vaccines	10
V. Ethics, Equity, Feasibility, And Acceptability Considerations	11
VI. Economics	12
VII. Recommendations	15
VIII. Knowledge Gaps And Research Needs	18
Abbreviations	20
Acknowledgments	21
References	22
Appendix	25

Summary of guidance

Note: While NACI statements are written for healthcare professionals and public health immunization program decision makers, the Public Health Agency of Canada (PHAC) issues summaries to inform the public on key details of the vaccine guidance included in NACI statements.

Please refer to the PHAC [Summary of NACI statement of Month XX, 20XX: Guidance on the use of COVID-19 vaccines starting fall 2026].

I. Introduction

The ongoing endemic circulation of SARS-CoV-2 has led Canadian public health programs to adopt a longer-term, more sustainable approach to COVID-19 disease management. Globally, SARS-CoV-2 vaccine strains are selected in advance of the fall/winter respiratory season. Surveillance activities including Canada's national [Respiratory Virus Detection Surveillance System](#) (RVDSS) have adapted to evolving information needs. However, uncertainty remains about the seasonal patterns of this virus, and immunization programs will need to adapt.

As with other publicly-funded immunization programs, provinces and territories are now responsible for the costs of purchasing COVID-19 vaccines. Previous NACI guidance provided recommendations on the use of COVID-19 vaccines through the summer of 2026.

The objective of this advisory committee statement is to summarize available evidence, identify what is known and not known, and provide guidance on COVID-19 vaccines starting fall 2026. Additionally, as Health Canada has authorized mNEXSPIKE, a new mRNA COVID-19 vaccine for individuals 18 years of age and older, updated NACI guidance now considers its use.

NACI will continue to monitor evolving COVID-19 epidemiology and vaccine information and is expected to provide updated guidance as per in the 2026-2028 NACI workplan.

II. Methods

In brief, the broad stages in the preparation of this NACI advisory committee statement are:

- Analysis of burden of disease of COVID-19 in Canada;
- Retrieval and summary of individual studies of the mNEXSPIKE COVID-19 vaccine and studies reporting on the effectiveness and duration of protection conferred by JN.1-lineage vaccines (JN.1 and KP.2; evidence synthesis is summarized in the Appendix);
- Use of a published, peer-reviewed framework and evidence-informed tools to ensure that issues related to ethics, equity, feasibility, and acceptability (EEFA) are systematically assessed and integrated into the guidance¹;
- Use of an environmental scan and model-based economic evaluation of COVID-19 vaccines for the prevention of COVID-19-related outcomes to generate economic evidence;
- Use of an environmental scan on vaccine guidance from international and domestic guidance issuing bodies;
- Consideration of vaccine principles when evidence is limited; and
- Translation of evidence into a recommendation.

A framework has been developed to facilitate systematic consideration of programmatic factors (now included in NACI's mandate, including: economics, ethics, equity, feasibility, acceptability) in developing clear, evidence-based recommendations for timely, transparent decision-making. This framework provides a clear outline with accompanying evidence informed tools to consider relevant aspects of each programmatic factor that may have an impact on the implementation of NACI recommendations. These tools have been completed by the NACI secretariat and incorporated into the analysis presented to the NACI COVID-19 Working Group (NACI COVID-19 WG) and NACI.

For details on the development and application of NACI's EEFA Framework and evidence-informed tools, please see [A framework for the systematic consideration of ethics, equity, feasibility, and acceptability in vaccine program recommendations](#)¹.

For details on when and how NACI incorporates economic evidence for vaccine recommendations, please refer to the [NACI process for incorporating economic evidence into federal vaccine recommendations](#).

For this advisory committee statement, NACI reviewed the key questions for the literature review as proposed by the NACI COVID-19 WG and considered available evidence on the burden of illness, safety, immunogenicity, efficacy, effectiveness of COVID-19 vaccine products, vaccine schedules, and other aspects of the overall COVID-19 immunization strategy. Knowledge synthesis was performed by the NACI Secretariat, and supervised by the WG. Following critical appraisal of individual studies, evidence was synthesized to inform recommendations for vaccine use.

The NACI COVID-19 WG chair and NACI Secretariat presented the evidence and proposed recommendations to NACI on June 18, 2025 and September 25, 2025. Following a review of the evidence, the committee deliberated and then voted on specific recommendations on September 25, 2025.

A note on language

NACI recognizes that not all people giving birth or breastfeeding will identify as women or mothers. The writing in this statement uses a gender additive approach where the term 'woman' is used alongside gender-neutral language. This is intended to demonstrate a commitment to redress the historic exclusion of trans and non-binary people, whilst avoiding the risk of marginalising or erasing the experience of women within the health care environment. However, in line with best practice, it is recognized that when discussing or caring for individuals in a one-on-one capacity language and documentation should reflect the gender identity of the individual.

Finally, NACI acknowledges the dynamic nature of language. It is likely that language deemed to be suitable or affirming in one context may not translate across others, and over the coming years will likely change and evolve with respect to appropriate representations.

III. Epidemiology

- COVID-19 is a respiratory infection caused by the SARS-CoV-2 virus and can cause mild to severe illness, including hospitalization and death. Certain populations, such as young infants, older adults, and those with chronic health conditions are at higher risk for serious illness.
- The evolutionary trajectory of SARS-CoV-2 is uncertain. The virus undergoes antigenic changes over time, leading to new variants and subvariants that may be less effectively neutralized by antibodies induced by vaccines targeting earlier strains. These antigenic changes have prompted regular reassessments of the strain(s) selected for global use in COVID-19 vaccines.
- SARS-CoV-2 seasonality has not yet been established; however laboratory surveillance data from [RVDSS](#) for the past three surveillance periods (2022-23 to 2024-25) have provided some general indications of COVID-19 epidemiology in Canada². In the past three surveillance periods, COVID-19 disease activity has started to increase in the late spring or late summer and has remained consistently higher from September to January (Figure 1).
- Canadian rates of hospitalization and ICU admissions associated with COVID-19 have consistently been the highest for adults 65 years of age and older. This was evident during the 2024-25 surveillance period where adults 65 years of age had a cumulative hospitalization rate with 506.5 hospitalizations per 100,000; the next highest rate was reported in children 0-4 years of age with 82.6 hospitalizations per 100,000 (Figure 2)².
- Overall, hospitalization rates associated with COVID-19 have decreased in recent years; the population-level rate of hospitalization for COVID-19 was approximately 2-fold lower in the 2024-2025 season compared to the 2023-2024 season³.

Figure 1. Percentage of SARS-CoV-2 tests positive by surveillance week and season in Canada (from 2022 week 35 to 2024 week 48, [RVDSS](#))

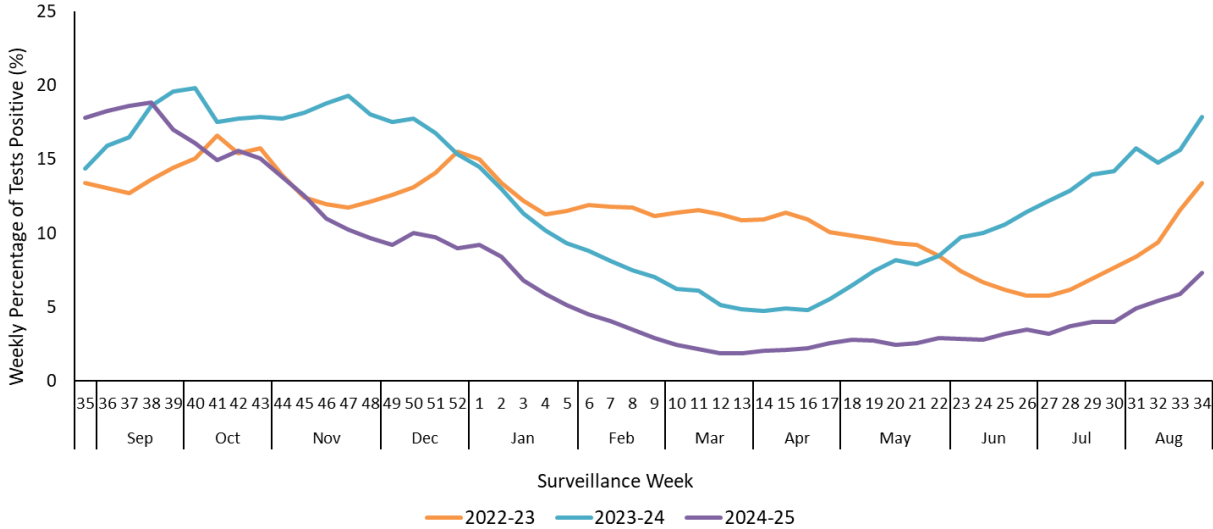
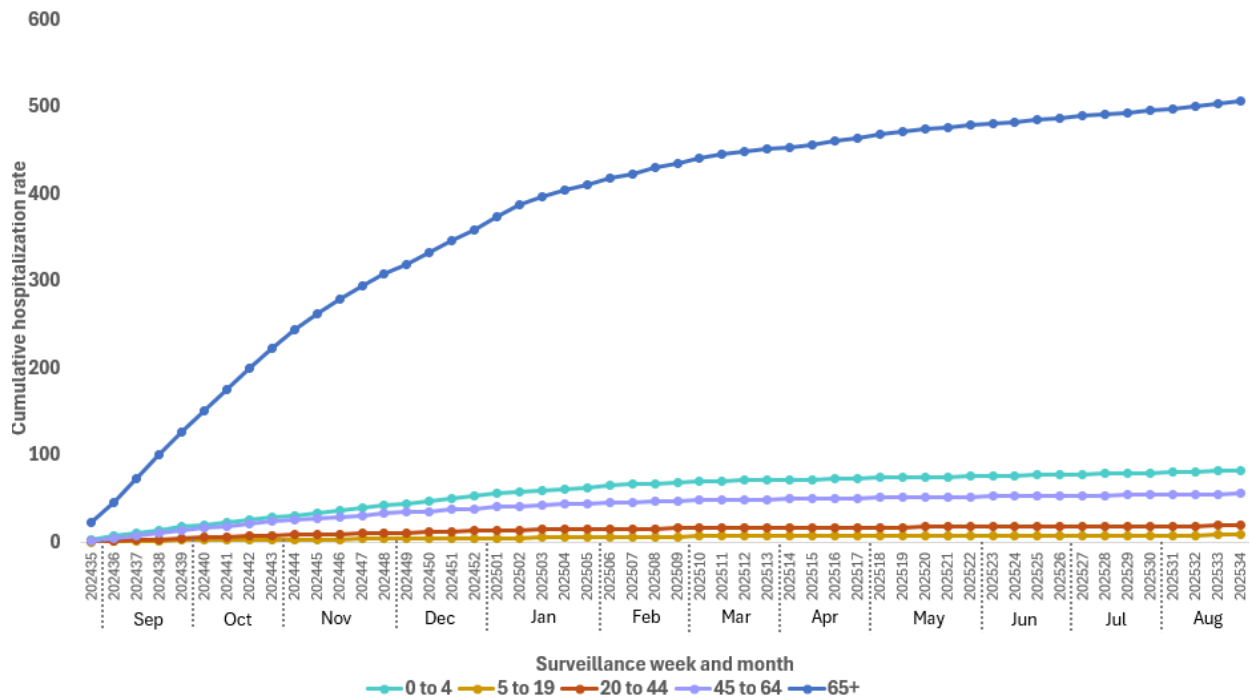


Figure 2. Crude cumulative rates of COVID-19 associated hospitalizations by age-group and surveillance week, 2024-25 surveillance period



IV. Vaccine

IV.1 Preparation(s) authorized for use in Canada

Characteristics of COVID-19 vaccines currently authorized for use can be found in the [Preparations Authorized for Use in Canada](#) section in the COVID-19 vaccines chapter of the Canadian Immunization Guide.

For complete prescribing information for COVID-19 vaccines, consult the product leaflet or information contained within Health Canada's authorized product monographs available through the [Drug Product Database](#).

IV.2 Clinical evidence on COVID-19 vaccines

Vaccine effectiveness and duration of protection

- COVID-19 vaccine effectiveness (VE) is influenced by several factors, including time since last dose, circulating virus strains and their relatedness to the vaccine strain, population characteristics (e.g., immunity from recent infection, age, presence of any immunocompromising conditions), and the specific outcomes measured (e.g., infection, symptomatic disease, hospitalization, ICU admission, death, or post-COVID-19 condition [PCC]). VE estimates also vary based on the comparison group used (e.g., an unvaccinated population, versus any population regardless of whether they have or have not been previously vaccinated, versus a population that was previously vaccinated against COVID-19 or recently infected with SARS-CoV-2).

- Recent NACI guidance on COVID-19 vaccines has considered studies on incremental VE, which measures the added protection provided by an updated vaccine dose compared to no recent vaccination, regardless of past vaccination or infection history.
- VE and duration of protection estimates for KP.2 vaccines are available from Canadian and US studies⁴⁻⁸. Overall, these studies demonstrate that a recent COVID-19 vaccine dose provides additional protection against medically attended COVID-19, clinic/emergency department visits and hospitalization, even in populations with immunity from high rates of past infections and/or vaccination, similar to findings from previous COVID-19 vaccine formulations.
 - A recent COVID-19 vaccine dose provided moderate protection against hospitalization in adults 60 years of age and older. Three studies assessed VE of KP.2 vaccines against hospitalization over time out to 6 months post-vaccination in the 2024-2025 respiratory virus season. Excluding the first 7 days after vaccination, overall VE was: 46% (95% CI: 32 to 58%) from the Ivy network in the United States (US) at a median of 92 days from vaccination⁷; 44% (95% CI: 38 to 50%) from the US VISION network at a median of 92 days from vaccination⁷; and 39% (95% CI: 32 to 45%) in a study from Quebec at a median of 79 days from vaccination⁹.
 - Data on protection from hospitalization over time is limited for the 2024-2025 season⁷. Based on trends from other seasons, VE against hospitalization has historically decreased 4 to 6 months following vaccination.
- The mechanism of increased protection from an updated COVID-19 vaccine is likely a combination of providing a recent vaccination that boosts the immune response and providing a vaccine that is more closely related to the circulating strain. The relative contribution of each of these factors is unknown.
- It is expected that updated COVID-19 vaccines will provide protection against a range of outcomes, with subsequent waning of protection over time.
- Hybrid immunity offers greater protection against infection and severe disease than prior infection or vaccination alone, particularly when hybrid immunity is in the context of a recent infection; however, this protection also wanes over time^{4,10-18}.

Vaccine safety

Evidence on vaccine safety is available from COVID-19 clinical trials and ongoing national and international COVID-19 vaccine safety monitoring. No new adverse events have been identified to date with the use of any updated COVID-19 vaccines.

For more information, please see the section on [Safety and adverse events](#) in the [COVID-19 Chapter](#) of the [Canadian Immunization Guide \(CIG\)](#).

Clinical evidence on new mRNA COVID-19 vaccine: mNEXSPIKE

mNEXSPIKE (mRNA-1283) is a next-generation version of Moderna SPIKEVAX (mRNA-1273). mRNA-1283 encodes for only part of the SARS-CoV-2 spike protein (the N-terminal domain and receptor-binding domain) instead of the whole spike protein as encoded in mRNA-1273¹⁹. In a Phase 3 randomized clinical trial (RCT), mRNA-1283 was compared to mRNA-1273 and demonstrated non-inferior efficacy against symptomatic COVID-19, non-inferior immune responses against the variants targeted by the vaccine, and a similar safety profile¹⁹.

mNEXSPIKE is currently authorized by Health Canada for use in previously vaccinated adults 18 years of age and older. Additional details are available in the Appendix.

For more information, please see the section on [Preparations authorized for use in Canada](#) in the [COVID-19 Chapter](#) of the [Canadian Immunization Guide \(CIG\)](#).

IV.3 Contraindications and precautions

For information on current COVID-19 vaccine contraindications and precautions, please see the section on [contraindications and precautions](#) in the [COVID-19 vaccines chapter](#) of the [Canadian Immunization Guide \(CIG\)](#).

IV.4 Concurrent administration with other vaccines

For individuals 6 months of age and older, COVID-19 vaccines may be given concurrently (i.e., same day), or at any time before or after non-COVID-19 vaccines (including live and non-live vaccines).

For more information, please see the section on [concurrent administration with other vaccines](#) in the [COVID-19 vaccines chapter](#) of the Canadian Immunization Guide (CIG).

IV.5 Vaccination of specific populations

No updates to NACI guidance on COVID-19 vaccines for specific populations have been made. For more information, please see the section on [vaccination of specific populations including individuals who are immunocompromised](#) in the [COVID-19 vaccines chapter](#) of the [Canadian Immunization Guide \(CIG\)](#).

IV.6 Additional considerations

Choice of COVID-19 vaccine

- The decision to include specific vaccines as part of provincial and territorial programs depends on several factors, including vaccine availability from the manufacturer, jurisdictional availability, vaccine characteristics, cost-effectiveness, and other programmatic and operational factors, such as implementation strategies.
- NACI has provided guidance on COVID-19 vaccine platforms, indicating that either an mRNA or a protein subunit COVID-19 vaccine platform can be used. At the time of this guidance development, it is unknown whether different strains will be used for different COVID-19 vaccine platforms in future years.
- Product preferences may continue to exist because of past products received, and considerable public awareness that developed during the pandemic around specific COVID-19 vaccine products. Public health programs should consider the impact of limiting access to only one COVID-19 vaccine platform on vaccine acceptance and uptake, especially for those who had a previous serious adverse reaction to one type of vaccine platform.

V. Ethics, equity, feasibility, and acceptability considerations

NACI evaluated the following core ethical principles for public health when making its recommendations: promoting well-being and minimizing risk of harm; maintaining trust; respect for people and fostering autonomy; and promoting justice and equity. In developing these recommendations, no significant ethical issues were identified by NACI other than the equity considerations discussed below.

- NACI aims to simplify COVID-19 recommendations where possible, balancing available scientific evidence, expert advice, and programmatic considerations. While broad recommendations support access to those who want to be vaccinated, risk-based recommendations highlight those for whom vaccination is particularly important and can facilitate more tailored communication of guidance to individuals at high risk. Complexity of vaccine recommendations may impact uptake by making it challenging for providers and the public to determine who is recommended to receive updated COVID-19 vaccines.
- COVID-19 vaccine uptake has declined over time. Vaccination continues to be highest in older adults (particularly those 75 years of age and older)²⁰.
- Individuals in or from First Nations, Inuit or Métis communities in Canada have a younger age distribution compared to the general Canadian population but also have increased risk for severe COVID-19 illness due to intersecting factors including social, environmental, and economic factors, rooted in historic and ongoing colonization and systemic racism (i.e., structural inequity). Therefore, these demographic and intersecting health determinants should be considered when making age-based recommendations for immunization programs to offer optimal protection to individuals in or from these communities. Autonomous decisions should be made by Indigenous Peoples with the support of culturally safe public health and healthcare partners in accordance with the United Nations Declaration on the Rights of Indigenous Peoples (UNDRIP)²¹.
- Social and structural inequities have contributed to increased risk of exposure to, and severe disease from, SARS-CoV-2. Throughout the pandemic, NACI has acknowledged that racialized, marginalized and other equity-denied populations in Canada were disproportionately affected by COVID-19. Systemic barriers to accessing necessary supportive care for COVID-19 included factors such as poverty, systemic racism, and being unhoused.
- Intersectionality must be considered in vaccine decision-making because multiple possible intersections such as place of residence, socioeconomic status or pre-existing conditions have the potential to worsen health outcomes, especially for equity-denied groups. This compounding risk is often overlooked when equity-related factors are assessed in isolation.

VI. Economics

An environmental scan and an economic evaluation using a previously described Canadian cost-utility model²²⁻²⁴ were used to generate economic evidence to inform COVID-19 vaccination program guidance. All costs are in 2024 Canadian dollars.

Environmental scan

An updated environmental scan was conducted to identify recent economic evaluations considered by other National Immunization Technical Advisory Groups (NITAGs) and new Canadian studies relevant to COVID-19 program guidance. The cutoff date for included publications was June 9, 2025.

- No new economic evaluations reviewed by other NITAGs were identified beyond those previously summarized, which generally found COVID-19 vaccination most cost-effective when focused on older adults, with lower cost-effectiveness for programs including younger groups and biannual dosing²².
- One new Canadian economic evaluation, funded by industry, assessed a strategy of annual vaccination with mNEXSPIKE (mRNA-1283) for all adults aged 65 years and older and individuals aged 12 to 64 years at high risk of severe COVID-19 outcomes, with a biannual dose for adults aged 80 years and older, among other strategies²⁵. This analysis assumed that mNEXSPIKE had higher vaccine effectiveness than other currently authorized mRNA vaccines, based on point estimates of relative vaccine efficacy from the phase 3 RCT NextCOVE¹⁹ and an indirect treatment comparison; of note, the RCT showed non-inferior VE for mNEXSPIKE compared to SPIKEVAX (mRNA-1273). Compared to the PHAC-led analysis described below, this analysis also assumed slower waning of vaccine protection and included non-medically attended cases.
 - Using a static decision-analytic model, the healthcare payer perspective, and a one-year time horizon, the analysis estimated that the program would be cost-effective at a vaccine price below \$297 per dose, using a \$50,000 per quality-adjusted life year (QALY) cost-effectiveness threshold.
 - Expanding biannual vaccination to all adults aged 65 years and older reduced the maximum cost-effective vaccine price to \$258 per dose.

Cost-utility analysis

A previously described²²⁻²⁴ Canadian cost-utility model was updated to assess:

1. The cost-effectiveness of a vaccination program with features similar to NACI recommendations included in the 2025/2026 statement at the time of the analysis.
 2. The cost-effectiveness of including biannual vaccination for different groups, compared to a program offering only annual vaccination.
- The modelled current vaccination program reflected recommendations included in the 2025/2026 NACI statement and features included biannual vaccination for all adults aged 80 years and older, and annual vaccination for all adults aged 65 to 79 years and people aged less than 65 years with one or more chronic medical conditions (CMCs).

- Additional analyses explored expanding biannual vaccination for: adults aged 65 to 79 years with CMCs; all adults aged 65 to 79 years; or all individuals aged less than 80 years with CMCs.
- Model updates included: revising the model age groups and associated parameters to reflect NACI recommendations at the time of the analysis; updating costs to 2024 Canadian dollars; incorporating more recent sociodemographic data; applying the monthly distribution of cases from July 2024 to June 2025 surveillance data²⁶ for the base case analysis; and using updated vaccine coverage estimates by age and risk. Other inputs and assumptions were unchanged, including an assumed vaccine price of \$43 per dose. Results are presented for the health system perspective.
- Compared to a strategy of not vaccinating, a vaccination program with features of NACI strong recommendations for COVID-19 vaccine at the time of the analysis contained in the 2025/2026 statement (as described above) was cost-effective, using a cost-effectiveness threshold of \$50,000 per QALY.
 - These findings held as long as the vaccine price was less than \$60 per dose in the base case.
 - If the epidemiology shifted such that incidence of medically-attended COVID-19 was reduced by 25% from the base case values, the incremental cost-effectiveness ratio (ICER) was \$56,000 per QALY and required a vaccine price of less than \$40 per dose to be considered cost-effective at a \$50,000 per QALY threshold.
 - Conclusions about cost-effectiveness did not change when other base case assumptions were changed, including: increased vaccine wastage; increased vaccine effectiveness for people with CMCs; increased risk of PCC following infection; alternate distributions of cases throughout the year; or alternate program timing to better align with periods of increased case occurrence.
- In the base case analysis of biannual vaccination program options, adding currently recommended biannual vaccination for adults aged 80 years and older had an ICER of \$3,000 per QALY compared to annual-only vaccination for all adults aged 65 years and older and people aged less than 65 years with one or more CMCs (groups currently included in current NACI strong recommendations for annual vaccination). Expanding the biannual program to include adults aged 65 to 79 years with CMCs resulted in an ICER of \$30,000 per QALY (compared to biannual vaccination for all adults aged 80 years and older), while including all individuals with CMCs aged less than 65 years resulted in an ICER of \$214,000 (compared to biannual vaccination for adults aged 65 to 79 years with CMCs and all adults aged 80 years and older). A program offering biannual vaccination for all adults 65 years of age and older was excluded by extended dominance.
 - The optimal biannual vaccination strategy varied by vaccine price: below \$65 per dose, biannual vaccination for those aged 65 to 79 years with CMCs and all aged 80 years and older was optimal; at \$65 to \$110 per dose, limiting biannual vaccination to adults aged 80 years and older was optimal.
 - Scenario and sensitivity analyses showed that the optimal biannual vaccination strategy depended on program timing and COVID-19 incidence.
 - When annual vaccination was assumed to start in July instead of October to better match observed COVID-19 trends in recent years, the cost-effectiveness of adding a

- biannual dose for adults aged 80 and older was reduced (i.e., higher ICERS). Under this assumption, the ICER for biannual vaccination increased to \$48,000 per QALY compared to annual-only vaccination starting in July (from \$3,000 per QALY in the base case). This reflects the enhanced impact of a well-timed annual dose and the correspondingly reduced additional impact of an additional dose. Shortening the interval between doses from six to four months for a program beginning in July such that the second dose would be administered starting in November improved the cost-effectiveness for this group, with an ICER of \$29,000 per QALY for including a biannual dose for adults aged 80 years and older compared to an annual-only program starting in July. However, even with a shorter dose interval, adding biannual vaccination for adults aged 65 to 79 years with CMCs exceeded a \$50,000 per QALY threshold, with an ICER of \$55,000 per QALY for a program with an earlier start.
- Varying the epidemiological assumptions to have a condensed season with a larger concentration of COVID-19 cases in the winter months favoured no biannual dose, reflecting limited additional benefit of the second dose given low COVID-19 case incidence during the period following the second dose (i.e., April/May in the model).
 - An assumed lower overall COVID-19 incidence (a reduction of medically-attended COVID-19 by 25% from base case values) also supported the currently recommended biannual dose for those aged 80 years and older.
 - Conclusions about the optimal strategy for a biannual program were most sensitive to uncertainty about vaccine price for scenarios assuming a larger winter wave, lower COVID-19 incidence, or an earlier program start.
- Limitations of this analysis include:
 - Modelled population groups did not fully align with program recommendations and excluded some recommended populations such as: individuals in or from First Nations, Inuit and Métis communities; members of racialized and other equity-denied populations; pregnant women and pregnant individuals; and residents of long-term care homes and other congregate living settings.
 - Estimates of COVID-19 disease burden for the no-vaccination scenario were based on data through April 2024. As COVID-19 hospitalization rates appear to have declined in recent years, cost-effectiveness may be lower than estimated. This was explored in sensitivity analyses assuming reduced burden.
 - Optimal COVID-19 vaccination timing remains uncertain given lack of established seasonal patterns, and the analysis did not assess how shifting program timing might affect efficiencies gained by aligning with influenza vaccination programs.
 - The analysis may underestimate cost-effectiveness and disease burden by not modelling indirect effects on transmission and the assumption that PCC occurs only in individuals with medically attended initial COVID-19 infections, with impacts limited to a maximum of one year.

VII. Recommendations

Following the review of available evidence summarized above, NACI makes the following recommendations for public health and to support individual level decision-making.

For reference:

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 considered for some populations/individuals in some circumstances. Alternative approaches may be reasonable.

See the [Appendix](#) for a more detailed explanation of strength of NACI recommendations.

NACI will continue to carefully monitor the scientific developments related to COVID-19 and will update recommendations as evidence evolves.

Recommendations for public health program decision-making

These recommendations are intended to support Provinces and Territories when making decisions for publicly funded immunization programs.

The following recommendations apply COVID-19 immunization programs starting fall 2026. **Recommendation 1A. NACI continues to strongly recommend COVID-19 immunization for individuals at increased risk of SARS-CoV-2 exposure or severe COVID-19 disease as listed in [List 1](#).**

(Strong NACI recommendation)

Recommendation 1B. NACI recommends that programs may also offer immunization to all individuals 6 months of age and older not listed in [List 1](#).

(Discretionary NACI recommendation)

Recommendation 2A. NACI recommends the following individuals should receive a second dose of COVID-19 vaccine per year, at a minimum interval of 3 months from the previous dose:

- **Adults 80 years of age or older**
- **Residents of long-term care homes, as well as residents of other congregate living settings for seniors**
- **Individuals 6 months of age and older who are moderately to severely immunocompromised (due to an underlying condition or treatment)**

- **NEW: Adults 65 to 79 years of age with [underlying medical conditions](#) that place them at higher risk of severe COVID-19**

(Strong NACI recommendation)

Recommendation 2B. NACI recommends the following individuals may receive a second dose of COVID-19 vaccine per year, at a minimum interval of 3 months from the previous dose:

- **All other adults 65 to 79 years of age (i.e., not on the list above in Recommendation 2A)**

(Discretionary NACI recommendation)

Recommendations to support individual decision-making

This recommendation is intended to support individuals and healthcare providers when considering COVID-19 immunizations. COVID-19 vaccines are particularly important for individuals listed in [List 1](#).

Recommendation 3. NACI recommends that individuals 6 months of age and older, not listed in [List 1](#), may also receive the COVID-19 vaccine. Risks of acquiring COVID-19 are higher in some settings and risks from SARS-CoV-2 infection are higher in some individuals. Individuals may choose to receive the vaccine based on individual COVID-19 risk assessment or preference.

(Discretionary NACI recommendation)

List 1. Individuals at increased risk of SARS-CoV-2 exposure or severe COVID-19 disease

- All adults 65 years of age or older
- Those 6 months of age and older who are:
 - Residents of long-term care homes and other congregate living settings
 - Individuals with [underlying medical conditions](#) that put them at higher risk of severe COVID-19, including children^a with complex health needs
 - Pregnant women and pregnant individuals
 - Individuals in or from First Nations, Inuit and Métis communities^b
 - Healthcare workers and other care providers in facilities and community settings^c
 - Members of racialized and other equity-denied communities^d

^a There is limited evidence on clinical risk factors for severe COVID-19 disease in pediatric populations. Children at increased risk for severe outcomes may include children who are medically fragile/have medical complexities, children with more than one comorbidity, children with neurological disorders, children with chronic lung disease, and children with Down syndrome (Trisomy 21), and other immunocompromising conditions.

^b Autonomous decisions should be made by Indigenous Peoples with the support of culturally safe public health and healthcare partners in accordance with UNDRIP.

^c For the purposes of this statement, “healthcare workers (HCWs) and other care providers in facilities and community settings” refers to HCWs, care providers, emergency response workers (i.e., first responders including fire, police, and ambulance), those who work in continuing care or long-term care facilities or residences, those who provide home care for people at high risk, and students/trainees of related healthcare services. HCWs include any person, paid or unpaid, who provides services, works, volunteers, or trains in a hospital, clinic, or other healthcare facility.

^d Social and structural inequities have contributed to increased risk of exposure to, and severe disease from, SARS-CoV-2. Throughout the pandemic, NACI has acknowledged that racialized, marginalized and other equity-denied populations in Canada were disproportionately affected by COVID-19. Systemic barriers to accessing necessary supportive care for COVID-19 included factors such as poverty, systemic racism and being unhoused. To recognize the health inequities these individuals may continue to face in the post-pandemic context, these groups should remain priority populations recommended for vaccination.

Additional considerations:

- Based on age and vaccine availability, either an mRNA (for those 6 months of age and older) or protein subunit COVID-19 vaccine (for those 12 years of age and older) can be used in individuals who do not have contraindications to the vaccine.
- It is expected that COVID-19 vaccines will continue to be updated annually to align with circulating variants. When possible, the manufacturers’ most recently updated COVID-19 vaccine should be used as it is expected to provide the best immune response against circulating SARS-CoV-2 strains. However, if COVID-19 vaccination is indicated, it should not be delayed while waiting for an updated vaccine.
- A recent vaccination can be expected to provide some cross-protection against strains not targeted by the vaccine, based on evidence to date.
- Consistent with previous guidance, COVID-19 vaccines may be given concurrently or at any time before or after non-COVID-19 vaccines (including live and non-live vaccines).

Summary of evidence and rationale:

- COVID-19 vaccination programs are most likely to be cost-effective when focused on groups at higher risk of severe disease.
- Individuals at increased risk of severe COVID-19 disease likely benefit from two doses of COVID-19 vaccine per year, given the current year-round circulation of SARS-CoV-2 and the anticipated duration of vaccine protection.
- Adults aged 65 and older are at highest risk of COVID-19 hospitalization, with those aged 80 and above most vulnerable to severe illness. Under the assumptions used in the economic modelling, biannual vaccination is likely cost-effective for adults aged 65–79 with [underlying medical conditions](#) as well as all adults aged 80 and older.
- As the risk of severe illness from COVID-19 follows an age-related gradient of risk in older adults, it may continue to be beneficial for adults 65 to 79 years of age without chronic medical conditions to be biannually vaccinated against COVID-19.
- It is important to note that both age and living setting remain proxies for frailty in older adults due to their ease of measurement.

Additional considerations on duration of protection and program timing

- COVID-19 vaccines provide the greatest protection against severe outcomes of COVID-19.

- Available evidence, which is largely limited to previous COVID-19 vaccine products and data prior to the 2024-2025 respiratory virus season, suggests protection conferred from COVID-19 vaccination wanes after approximately four to six months.
- In jurisdictions where vaccines are available throughout the year, individuals may choose to receive their COVID-19 vaccine at a particular time in the year based on anticipated exposure risk, including travel, or anticipated immunocompromised status (e.g., planned immunosuppressive therapy). Individuals who have not previously been vaccinated against COVID-19 can be offered a COVID-19 vaccine dose at any time in the year. For additional guidance, please see the [COVID-19 Chapter of the CIG for vaccine schedules for unvaccinated individuals](#).
- Many Canadian jurisdictions may continue to offer a combined fall immunization program for seasonal influenza and COVID-19. This approach is efficient in terms of logistics and resource allocation. However, several key assumptions and current gaps in available evidence should be considered:
 - Concurrent administration of influenza and COVID-19 vaccines offers the greatest clinical benefit only if the peak circulation periods of seasonal influenza viruses and SARS-CoV-2 closely align (which is currently not the case), and if the COVID-19 vaccine provides protection that lasts through the expected peak of SARS-CoV-2 activity.
 - Current evidence, including limited data from the 2024–2025 COVID-19 season, indicates that vaccine-induced protection against COVID-19 wanes after approximately four months following administration.
 - In 2023 and 2024, peak disease incidence between influenza and COVID-19 were different. Data from this limited time period suggests influenza virus typically peaks later than SARS-CoV-2, suggesting a potential mismatch in timing when considering concurrent administration and vaccine duration of protection. However, seasonal patterns for COVID-19 have varied from year to year, and there is uncertainty about optimal timing for COVID-19 immunization programs.
- The timing of vaccination impacts cost-effectiveness, particularly for individuals receiving two doses annually²³. Aligning vaccination with periods of increasing transmission enhances public health benefit.
- NACI will continue to monitor SARS-CoV-2 seasonality and vaccine durability and will also engage with provinces and territories to assess feasibility, acceptability, and resource considerations when updating recommendations on COVID-19 vaccine timing.

VIII. Knowledge gaps and research needs

After review of the existing evidence, NACI has identified the need for further research to address current knowledge gaps where data are absent or limited. NACI recognizes that there are studies already in progress that may address some of these gaps, but the findings of these studies were not available at the time of review. Knowledge gaps and priority areas for research are listed below. Research to address the following outstanding questions is encouraged:

Vaccine efficacy/effectiveness

- Monitoring VE in special populations at high risk of severe outcomes, including further evaluation of the optimal vaccine schedule for individuals who are moderately to severely immunocompromised to provide optimal vaccine effectiveness and duration of protection.
- Evaluating vaccine efficacy/effectiveness against a range of outcomes, including asymptomatic infection, transmission, symptomatic disease, severe disease, severe outcomes from secondary nosocomial infections, the potential long-term consequences of SARS-CoV-2 infection (such as PCC and persistent functional decline), as well as the duration of protection due to vaccination. The research should also consider the clinical implications of previous SARS-CoV-2 infection and repeated immunization. The relative efficacy/effectiveness of the most recently updated vaccine compared to a previous vaccine (regardless of strain) should be assessed.
- Monitoring of VE and cost effectiveness based on timing of program implementation.

Immunogenicity and immunological mechanisms

- Short- and long-term immune responses, as well as long-term immune and health implications when the first immunological exposure is infection vs. vaccination.

Vaccine safety

- Monitoring of vaccine safety, including new safety signals and those related to adverse events of special interest.

Epidemiology and Surveillance

- Continuous monitoring of the epidemiology of COVID-19, including SARS-CoV-2 variants/sub-lineages and seasonal trends, to inform future programs and the optimal timing for vaccination programs.
- Additional analyses to determine the burden of COVID-19 disease in infants under 6 months of age.

Ethics, equity, feasibility and acceptability

- Continuous monitoring of COVID-19 vaccine acceptance and coverage in Canada, including consideration of measures that may reduce the risk of disparities in vaccine confidence and uptake across different sub-populations (including individuals in racialized and other equity-denied communities who may be disproportionately affected due to intersecting equity-related factors).

Abbreviations

ACS	Advisory committee statement
ACIP	Advisory Committee on Immunization Practices (United States)
CI	Confidence interval
CIG	Canadian Immunization Guide
CMC	Chronic medical condition
EEFA	Equity, ethics, feasibility, and acceptability
HCW	Healthcare worker
ICER	Incremental cost-effectiveness ratio
ICU	Intensive care unit
JCVI	Joint Committee on Immunisation (United Kingdom)
NACI	National Advisory Committee on Immunization
NITAG	National Immunization Technical Advisory Group
PCC	Post-COVID-19 condition
PHAC	Public Health Agency of Canada
QALY	Quality-adjusted life year
RCT	Randomized controlled trial
RVDSS	Respiratory virus detection surveillance system
UNDRIP	United Nations Declaration on the Rights of Indigenous Peoples
US	United States
VE	Vaccine effectiveness
WG	Working Group

Acknowledgments

This statement was prepared by: N Forbes, M Salvadori, A Tuite, R Krishnan, B Warshawsky, K Young, M Tunis, and M Andrew, on behalf of NACI.

NACI gratefully acknowledges the contribution of: J Daniel, E Wong, N Nguyen, RM Tazinya, M Lan, A Howarth, and the NACI Secretariat.

NACI COVID-19 Vaccine Working Group

Members: M Andrew (Chair), A Buchan, H Decaluwe, P De Wals, D Moore, B Sander, S Wilson, Y-G Bui, M Miller, D Singh, L Roper, L Panagiotakopoulos, and M Willcott.

NACI

NACI Members: R Harrison (Chair), V Dubey (Vice-Chair), M Andrew, N Brousseau, A Buchan, H Decaluwe, E Dubé, K Hildebrand, K Klein, M O'Driscoll, J Papenburg, A Pham-Huy, E Rafferty, T Ramsey, K Top, and S Wilson.

Former NACI Members: J Bettinger, P De Wals, and B Sander

Liaison Representatives: L Bill/ M Nowgesic (Canadian Indigenous Nurses Association), S Buchan (Canadian Association for Immunization Research, Evaluation and Education) E Castillo (Society of Obstetricians and Gynaecologists of Canada), J Comeau (Association of Medical Microbiology and Infectious Disease Control), M Lavoie (Council of Chief Medical Officers of Health), J MacNeil (Center for Disease control and Prevention), M McIntyre (Canadian Nurses Association), D Moore (Canadian Paediatric Society), M Osmack (Indigenous Physicians Association of Canada), J Potter (College of Family Physicians of Canada), A Pucci (Canadian Public Health Association), D Singh (Canadian Immunization Committee), and E Zannis (Canadian Pharmacists Association).

Ex-Officio Representatives: K Barnes (National Defence and the Canadian Armed Forces), P Fandja (Marketed Health Products Directorate, Health Canada), K Franklin (Centre for Emerging and Respiratory Infections and Pandemic Preparedness (CERIPP), PHAC), E Henry (Centre for Immunization Surveillance and Programs (CISP), PHAC), M Lacroix (Public Health Ethics Consultative Group, PHAC), T Stothart (Vaccine Safety Surveillance, Centre for Immunization Surveillance and Programs (CISP), PHAC), J Kosche (Centre for Vaccines and Therapeutics Readiness (CVTR), PHAC), C Pham (Biologic and Radiopharmaceutical Drugs Directorate, Health Canada), M Routledge (National Microbiology Laboratory, PHAC), and T Wong (First Nations and Inuit Health Branch, Indigenous Services Canada).

References

1. Ismail S, Hardy K, Tunis M, et al. A framework for the systematic consideration of ethics, equity, feasibility, and acceptability in vaccine program recommendations. *Vaccine*. 2020 Aug 10;38(36):5861-5876. <http://doi.org/10.1016/j.vaccine.2020.05.051>.
2. Public Health Agency of Canada. Canadian Respiratory Virus Surveillance Report [Internet]. Ottawa (ON). Public Health Agency of Canada; 2025 [cited 2025 Aug 28]. Available from: <https://health-infobase.canada.ca/respiratory-virus-surveillance/archive/>.
3. Canadian Institute for Health Information. Discharge Abstract Database (DAD) Metadata. Data cut off: Week 35, 2022 to Week 48, 2024 [Internet]. Canadian Institute for Health Information; 2025 [cited 2025 Nov 21]. Available from: <https://www.cihi.ca/en/discharge-abstract-database-dad-metadata>.
4. Link-Gelles R, Chickery S, Webber A, et al. Interim Estimates of 2024–2025 COVID-19 Vaccine Effectiveness Among Adults Aged ≥18 Years — VISION and IVY Networks, September 2024–January 2025. 2025 May 16. https://www.cdc.gov/mmwr/volumes/74/wr/mm7406a1.htm?s_cid=mm7406a1_w. <http://dx.doi.org/10.15585/mmwr.mm7406a1>.
5. Appaneal HJ, Lopes VV, Puzniak L, et al. Early effectiveness of the BNT162b2 KP.2 vaccine against COVID-19 in the US Veterans Affairs Healthcare System. *Nature Communications*. 16 <http://doi.org/10.1038/s41467-025-59344-7>. <https://www.nature.com/articles/s41467-025-59344-7>.
6. Wilson A, Bogdanov A, Zheng Z, et al. Evaluating the Effectiveness of 2024-2025 Seasonal mRNA-1273 Vaccination Against COVID-19-Associated Hospitalizations and Medically Attended COVID-19 among adults aged ≥ 18 years in the United States. Data cut-off 2025 Mar 28.
7. Centers for Disease Control & Prevention. Updates to COVID-19 Vaccine Effectiveness Centers for Disease Control & Prevention; 25 June 2025 [cited 13 Aug 2025]. Available from: <https://www.cdc.gov/acip/downloads/slides-2025-06-25-26/03-MacNeil-COVID-508.pdf>.
8. Separovic L, Sabaiduc S, Zhan Y, et al. Effectiveness of 2024/25 KP.2 vaccine against outpatient COVID-19 in Canada. 2025.
9. WHO Technical Advisory Group on COVID-19 Vaccine Composition. Annex: Statement on the antigen composition of COVID-19 vaccines 15 May 2025 [cited 13 Aug 2025]. Available from: https://cdn.who.int/media/docs/default-source/documents/epp/tag-co-vac/tag-co-vac-annex_15052025.pdf?sfvrsn=17bae565_5.
10. Altarawneh HN, Chemaitelly H, Ayoub HH, et al. Effects of previous infection and vaccination on symptomatic Omicron infections. *N Engl J Med*. Jul 7;387(1):21-34. <http://doi.org/10.1056/NEJMoa2203965>. <https://www.ncbi.nlm.nih.gov/pubmed/35704396>.
11. Bobrovitz N, Ware H, Ma X, et al. Protective effectiveness of previous SARS-CoV-2 infection and hybrid immunity against the omicron variant and severe disease: a systematic review and meta-regression. *Lancet Infect Dis*. May;23(5):556-567.

[http://doi.org/10.1016/S1473-3099\(22\)00801-5](http://doi.org/10.1016/S1473-3099(22)00801-5).
<https://www.ncbi.nlm.nih.gov/pubmed/36681084>.

12. Carazo S, Skowronski DM, Brisson M, et al. Protection against omicron (B.1.1.529) BA.2 reinfection conferred by primary omicron BA.1 or pre-omicron SARS-CoV-2 infection among health-care workers with and without mRNA vaccination: a test-negative case-control study. *Lancet Infect Dis*. Jan;23(1):45-55. [http://doi.org/10.1016/S1473-3099\(22\)00578-3](http://doi.org/10.1016/S1473-3099(22)00578-3).
<https://www.ncbi.nlm.nih.gov/pubmed/36152671>.

13. Carazo S, Skowronski DM, Brisson M, et al. Prior infection- and/or vaccine-induced protection against Omicron BA.1, BA.2 and BA.4/BA.5-related hospitalisations in older adults: a test-negative case-control study in Quebec, Canada. *medRxiv*.
<http://doi.org/10.1101/2022.12.21.22283740>.

14. Cerqueira-Silva T, de Araujo Oliveira V, Paixao ES, et al. Vaccination plus previous infection: protection during the omicron wave in Brazil. *Lancet Infect Dis*. 22(7):945-946.
[http://doi.org/10.1016/S1473-3099\(22\)00288-2](http://doi.org/10.1016/S1473-3099(22)00288-2).
<https://www.ncbi.nlm.nih.gov/pubmed/35588753>.

15. Chin ET, Leidner D, Lamson L, et al. Protection against Omicron from vaccination and previous infection in a prison system. *N Engl J Med*. 2022 Nov 10;387(19):1770-1782.
<http://doi.org/10.1056/NEJMoa2207082>. <https://www.ncbi.nlm.nih.gov/pubmed/36286260>.

16. Spreco A, Dahlstrom O, Joud A, et al. Effectiveness of the BNT162b2 mRNA Vaccine Compared with Hybrid Immunity in Populations Prioritized and Non-Prioritized for COVID-19 Vaccination in 2021-2022: A Naturalistic Case-Control Study in Sweden. *Vaccines (Basel)*. 2022 Aug 7;10(8)<http://doi.org/10.3390/vaccines10081273>.
<https://www.ncbi.nlm.nih.gov/pubmed/36016162>.

17. Vicentini M, Venturelli F, Mancuso P, et al. Risk of SARS-CoV-2 reinfection by vaccination status, predominant variant and time from prior infection: a cohort study, Reggio Emilia province, Italy, February 2020 to February 2022. *Euro surveillance*. 28(13)<http://doi.org/10.2807/1560-7917.ES.2023.28.13.2200494>.
<https://pubmed.ncbi.nlm.nih.gov/36995374/>.

18. Lind ML, Robertson AJ, Silva J, et al. Effectiveness of primary and booster COVID-19 mRNA vaccination against Omicron variant SARS-CoV-2 infection in people with a prior SARS-CoV-2 infection. *medRxiv*. <http://doi.org/10.1101/2022.04.19.22274056>.

19. Chalkias S, Dennis P, Petersen D, et al. Efficacy, immunogenicity, and safety of a next-generation mRNA-1283 COVID-19 vaccine compared with the mRNA-1273 vaccine (NextCOVE): results from a phase 3, randomised, observer-blind, active-controlled trial. *The Lancet Infectious Diseases*. [http://doi.org/10.1016/S1473-3099\(25\)00236-1](http://doi.org/10.1016/S1473-3099(25)00236-1).
<https://www.sciencedirect.com/science/article/pii/S1473309925002361>.

20. Public Health Agency of Canada (PHAC). Surveillance and Epidemiology Division, Centre for Immunization Surveillance and Programs, Infectious Diseases and Vaccination Programs Branch. Reference date: December 31, 2024. Ottawa (ON): 13 Aug 2025.

21. Office of the High Commissioner for Human Rights. UN Declaration on the Rights of Indigenous Peoples [Internet]. United Nations; 2007 Sep 13 [cited 2025 November 21].

Available from: <https://www.ohchr.org/en/indigenous-peoples/un-declaration-rights-indigenous-peoples>.

22. National Advisory Committee on Immunization. Guidance on the use of COVID-19 vaccines for 2025 to summer 2026. [Internet]. Ottawa (ON). Public Health Agency of Canada; 2025 Jan 10 [cited 2025 Jul 15]. Available from: <https://www.canada.ca/en/public-health/services/publications/vaccines-immunization/national-advisory-committee-immunization-statement-guidance-covid-19-vaccines-2025-summer-2026.html#a6>.
23. Miranda R, Simmons A, Li M, et al. Cost-Utility Analysis of COVID-19 Vaccination Strategies for Endemic SARS-CoV-2. *JAMA network open*. 8(6)<http://doi.org/10.1001/jamanetworkopen.2025.15534>.
<https://pubmed.ncbi.nlm.nih.gov/40512495/>.
24. Simmons AE, Miranda RN, Li MWZ, et al. Cost-utility analysis of current COVID-19 vaccination program recommendations in Canada. *Vaccine: X*. 24<http://doi.org/10.1016/j.jvacx.2025.100660>.
<https://www.sciencedirect.com/science/article/pii/S2590136225000543>.
25. Fust K, Kohli M, Cartier S, et al. The potential impact of the next-generation COVID-19 mRNA-1283 vaccine in Canada. *Journal of Medical Economics*.
<http://doi.org/10.1080/13696998.2025.2549630>.
<https://www.tandfonline.com/doi/full/10.1080/13696998.2025.2549630>.
26. Public Health Agency of Canada. Respiratory virus detections in Canada. [Internet]. Ottawa (ON). Public Health Agency of Canada; 2025 [cited 2025 Jul 15]. Available from: <https://www.canada.ca/en/public-health/services/surveillance/respiratory-virus-detections-canada.html>.

Appendix

Table 1. Strength of NACI recommendations

Strength of NACI recommendation <i>based on factors not isolated to strength of evidence (e.g., public health need)</i>	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 be considered for some populations/individuals in some circumstances. Alternative approaches may be reasonable.

Clinical data on the efficacy, immunogenicity and safety of mNEXSPIKE® (mRNA-1283)

Trial design and objectives

mNEXSPIKE (mRNA-1283) was evaluated in a multi-centre (US, UK and Canada), randomized, observer-blind, active-controlled Phase 3 clinical trial, which compared the relative vaccine efficacy (rVE), safety, reactogenicity, and immunogenicity of a single dose of mRNA-1283 to mRNA-1273 in previously vaccinated individuals 12 years of age and older¹⁹. The primary objectives were to demonstrate non-inferiority of mRNA-1283 compared to mRNA-1273 for the prevention of symptomatic COVID-19 starting 14 days after vaccination with a 10% non-inferiority margin (lower bound of rVE 99.4% CI to be above -10%), to demonstrate non-inferior neutralizing antibody responses compared to mRNA-1273 (lower bound of 95% CI of geometric mean ratios [GMR] to be above 0.667 and lower bound 95% CI of difference in seroresponse rates [SRR] to be above -10%), and to evaluate the safety and reactogenicity of mRNA-1283. Both vaccines used in the study were bivalent, targeting the original strain of SARS-CoV-2 and the Omicron BA.4/5 variant.

Study population and period

A total of 11,417 participants age 12 years and older were enrolled in the study. Of the total cohort, 992 (8.7%) participants were aged 12–17 years, 7151 (62.6%) were aged 18–64 years, and 3274 (28.7%) were 65 years of age and older; in addition, 6857 participants (60.1%) were 50 years and older. Participants were randomised 1:1 to receive mRNA-1283 10 µg (n=5706) or mRNA-1273 50 µg (n=5711). Participants were enrolled from March 2023 to August 2023. The median follow up time was 8.0 months (IQR: 6.7, 8.8) for rVE analyses and 8.8 months (IQR: 7.7, 9.5 months) for safety and immunogenicity (data cut-off February 23, 2024).

Efficacy

The rVE of mRNA-1283 compared to mRNA-1273 against symptomatic COVID-19 infection was 9.3% (99.4% CI -6.6, 22.8; data cut-off January 31, 2024), meeting the pre-specified non-inferiority criterion for rVE. Stratifying by age, rVE was highest in individuals 65 years and older (13.5%; CI: -7.7, 30.6) compared to individuals 18 to <65 years old (9.66%; CI: -3.8, 21.3) and individuals 12 to <18 years old (-29.17%; CI: -123.3, 25.3). Enrollment was lowest for 12 to <18 year-olds, which may have contributed to wide confidence intervals/imprecision.

In a post-hoc analysis, rVE against severe COVID-19 was estimated to be 35.9% (95% CI: -8.2, 62.1) for mRNA-1283 compared to mRNA-1273.

Immunogenicity

mRNA-1283 met pre-specified non-inferiority criteria for GMRs of neutralizing antibody responses and SRR differences, comparing mRNA-1283 to mRNA-1273. GMRs were 1.335 (95% CI 1.194, 1.492) and 1.240 (95% CI 1.1328, 1.362) for BA.4/5 and original SARS-CoV-2, respectively. SRR differences between mRNA-1283 and mRNA-1273 were 14.4% (95% CI 9.3, 19.4) for BA.4/5 and 10.7% (95% CI 6.0, 15.4) for original SARS-CoV-2. At Day 181 post-vaccination a similar trend for higher neutralizing antibody responses for mRNA-1283 vs. mRNA-1273 was observed, with GMRs of 1.71 (95% CI 1.31, 2.23) for BA.4/5 and 1.23 (95% CI 1.10, 1.38) for original SARS-CoV-2.

In age-based sub-group analyses, GMRs at Day 29 for both strains were highest for adults 65 years of age and older (1.76 [95% CI 1.40, 2.22] for BA.4/5 and 1.53 [95%CI 1.26, 1.87 for original SARS-CoV-2), followed by adults 18 to 64 years of age (1.29 [95% CI 1.10, 1.48] for BA.4/5 and 1.18 [95%CI 1.04, 1.34 for original SARS-CoV-2) and adolescents 12 to 17 years of age (1.05 [95% CI 0.84, 1.31] for BA.4/5 and 1.10 [95%CI 0.92, 1.31] for original SARS-CoV-2).

Safety

Overall, the safety profile of mRNA-1283 was similar to that of mRNA-1273. Solicited reactogenicity reported within seven days of vaccination was similar for both vaccines. Injections site pain and axillary swelling or tenderness were very common (frequency $\geq 10\%$), local reactions for both vaccines; however injection site pain was lower with mRNA-1283 (68.5%) compared with mRNA-1273 (77.5%). Erythema and swelling at the injection site were common (frequency 1% to $<10\%$) for both mRNA-1283 and mRNA-1273. Among solicited systemic reactions, headache, fatigue, myalgia, arthralgia, nausea/vomiting and chills were very commonly reported, with headache, fatigue and myalgia being the most frequently reported systemic reactions. Fever was common for both vaccines, reported by 5.6% of mRNA-1283 recipients and 4.5% of mRNA-1273 recipients. The majority of reactions (72.2% for mRNA-1283 and 76.9% for mRNA-1273) were Grade 1 or 2 severity. There was one Grade 4 reaction of fever $>40^{\circ}\text{C}$ that occurred on Day 2 with mRNA-1273 and resolved on the same day. The median day of onset for solicited reactions was Day 2 post-vaccination for mRNA-1273 and Day 1 post-vaccination for mRNA-1283, with a median duration of 3 days for both vaccines. The rates of adverse events of special interest (AESI) and serious adverse events (SAE) were similar between both groups. There were no cases of myocarditis and/or pericarditis deemed to be related to vaccination. Given the size of the study, it is unlikely that rare (frequency 0.01% to $<0.1\%$) or very rare (less than 0.01%) adverse events would be detected.