# NACI rapid response: Extended dose intervals for COVID-19 vaccines to optimize early vaccine rollout and population protection in Canada

## On this page



## 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(s). Recommendations for use and other information set out herein may differ from that set out in the product monograph(s) of the Canadian manufacturer(s) 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.

# Summary


- NACI has considered evidence from recent scientific studies on efficacy and effectiveness of COVID-19 vaccines in preventing various health outcomes such as infection, symptomatic disease, hospitalizations and death from COVID-19.
- While studies have not yet collected four months of data on vaccine effectiveness after the first dose, the first two months of real world effectiveness are showing sustained high levels of protection.
- Short term sustained protection is consistent with immunological principles and vaccine science where it is not expected to see rapid waning of a highly effective vaccine in adults over a relatively short period of time. Extending the interval between doses was shown to be a good strategy through modelling, even in scenarios considering a six month interval and in theoretical scenarios where waning protection was considered.
- NACI recommends that in the context of limited COVID-19 vaccine supply, jurisdictions should maximize the number of individuals benefiting from the first dose of vaccine by extending the interval for the second dose of vaccine to four months.
- Extending the dose interval to four months allows NACI to create opportunities for protection of the entire adult population within a short timeframe. This will not only achieve protection of the adult population, but will also contribute to health equity,
- NACI will continue to monitor the evidence on effectiveness of extended dose intervals and will adjust recommendations as needed.


# Introduction

Since COVID-19 vaccines were first authorised in Canada in December 2020, the National Advisory Committee on Immunization (NACI) has been providing evidence-informed guidance on the recommended interval between vaccine doses. In the most recent update, January 12, 2021, NACI provided advice on extending intervals for mRNA vaccines to six weeks. In February 2021 the Public Health Agency of Canada (PHAC) asked NACI to address the following context and question: Due to limited vaccine supply and logistical challenges, jurisdictions need to implement COVID-19 mRNA vaccine intervals beyond six weeks. Given emerging evidence as mRNA vaccines are rolled out to populations in Canada and elsewhere in the world, what extended interval would be recommended in order to balance individual protection and population impact? Are extended intervals a particular concern for any key populations?

### Guidance objective

The objective of this bulletin is to provide guidance for the equitable, ethical, and efficient allocation of authorized COVID-19 vaccines in the context of staggered arrival of vaccine supply. This guidance builds on the foundational framework of NACI's Recommendations on the use of COVID-19 vaccines. The 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.

# Methods

NACI reviewed available evidence in full Committee meetings (February 8, 2021; February 24-25, 2021) and Working Group meetings (February 19, 2021) on extended intervals for COVID-19 vaccines. This included evidence available from published peer-review studies, pre-prints, and data available from population-based assessments from within and outside of Canada. On March 1, 2021, NACI voted on and approved the revised recommendations by majority. Due to the urgency for provinces and territories to consider implementing extended dose intervals, NACI is providing an abridged rationale in this document. The complete analysis, including more detailed evidence summaries and references, will be provided in coming weeks as the NACI evergreen guideline is updated online in the Recommendations on the use of COVID-19 vaccines.

# Recommendations

Based on emerging evidence of the protection provided by the first dose of a two dose series for COVID-19 vaccines currently authorized in Canada, NACI recommends that in the context of limited COVID-19 vaccine supply jurisdictions should maximize the number of individuals benefiting from the first dose of vaccine by extending the second dose of COVID-19 vaccine up to four months after the first. NACI will continue to monitor the evidence on effectiveness of an extended dose interval and will adjust recommendations as needed. **(Strong NACI Recommendation)**

- In addition to emerging population-based data, this recommendation is based on expert opinion and the public health principles of equity, ethics, accessibility, feasibility, immunological vaccine principles, and the perspective that, within a global pandemic setting, reducing the risk of severe disease outcomes at the population-level will have the greatest impact. Current evidence suggests high vaccine effectiveness against symptomatic disease and hospitalization for several weeks after the first dose, including among older populations.
- This recommendation applies to all COVID-19 vaccines currently authorized for use in Canada.
- In situations where informed consent included assumptions about second dose timing, jurisdictions may consider offering second doses at shorter intervals for those who provided consent for the vaccine series prior to this recommendation.
- The vaccine effectiveness of the first dose will be monitored closely and the decision to delay the second dose will be continuously assessed based on surveillance and effectiveness data and post-implementation study designs. Effectiveness against variants of concern will also be monitored closely, and recommendations may need to be revised.

Please note:

- A **strong recommendation** applies to most populations/individuals and should be followed unless a clear and compelling rationale for an alternative approach is present.
- A **discretionary recommendation** may be offered for some populations/individuals in some circumstances. Alternative approaches may be reasonable.

# Summary of rationale

Due to the urgency for provinces and territories to consider implementing extended dose intervals, NACI is providing an abridged rationale in this document. The complete analysis, including more detailed evidence summaries

and references, will be provided in coming weeks as the NACI evergreen guideline is updated online in the Recommendations on the use of COVID-19 vaccines.

## Protecting individuals

- By implementing an extended four month interval strategy, Canada will be able to provide access to first doses of highly efficacious vaccines to more individuals earlier which is expected to increase health equity faster. Canada has secured enough vaccines to ensure that a second dose will be available to every adult.
- As a general vaccination principle, interruption of a vaccine series resulting in an extended interval between doses does not require restarting the vaccine series. Principles of immunology, vaccine science, and historical examples demonstrate that delays between doses do not result in a reduction in final antibody concentrations nor a reduction in durability of memory response for most multi-dose products.
- **Assessment of available data on efficacy and effectiveness** of a single dose of mRNA vaccine was a critical factor in assessing the impact of a delayed second dose at this time. The two available clinical trials for mRNA vaccines (Pfizer-BioNTech and Moderna) provide evidence that indicates that efficacy against symptomatic disease begins as early as 12 to 14 days after the first dose of the mRNA vaccine. Excluding the first 14 days before vaccines are expected to offer protection, both vaccines showed an efficacy of 92% up until the second dose (most second doses were administered at 19-42 days in the trials). Recently, real world vaccine effectiveness data presented to or reviewed by NACI assessing PCR-positive COVID-19 disease and/or infection from Quebec, British Columbia, Israel, the United Kingdom and the United States support good effectiveness (generally 70-80%, depending on the methodology used and outcomes assessed) from a single dose of mRNA vaccines (for up to two months in some studies). While studies have not yet collected four months of data on effectiveness of the first dose, the first two months of population-based effectiveness data are showing sustained and high levels of protection. These data include studies in health care workers, long term care residents, elderly populations and the general public. While this is somewhat lower than the efficacy demonstrated after one dose in clinical trials, it is important to note that vaccine effectiveness in a general population setting is typically lower than efficacy from the controlled setting of a clinical trial, and this is expected to be the case after series completion as well.
- Published data from the AstraZeneca clinical trial indicated that delaying the second dose to ≥ 12 weeks resulted in a better efficacy against symptomatic

disease compared to shorter intervals between doses.
- **The duration of protection** from one or two doses of COVID-19 vaccines is currently unknown. Experience with other multi-dose vaccines after a single dose suggests persistent protection could last for six months or longer in adolescents and adults. Longer-term follow-up of clinical trial participants and those receiving vaccination in public programs will assist in determining the duration of protection following both one and two doses of vaccination. NACI will continue to monitor the evidence on effectiveness of an extended interval, which is currently being collected weekly in some Canadian jurisdictions, and will adjust recommendations as needed if concerns emerge about waning protection.

## Protecting populations

- Although effectiveness after two-doses will be somewhat higher than with one dose, many more people will benefit from immunization when extending the interval between doses in times of vaccine shortage; offering more individuals direct benefit and also the possibility of indirect benefit from increasing population immunity to COVID-19 disease. Everyone is expected to obtain the full benefit of two doses when the second dose is offered after 4 months.
- **Internal PHAC modelling** reviewed by NACI based on Canadian supply projections suggested that accelerating vaccine coverage by extending dose intervals of mRNA vaccines could have short-term public health benefits in preventing symptomatic disease, hospitalizations, and deaths while vaccine supply is constrained. Even a theoretical scenario analysis in which intervals were extended up to six months and protection was lost at a rate of 4% per week after the first dose also showed that extending the mRNA vaccine dose intervals would still have public health benefits. External modelling results have also suggested that extending dose intervals can avert infections, hospitalizations and deaths.
- **The impact on variants of concern** by extending the interval between doses is unknown, but there is currently no evidence that an extended interval between doses will either increase or decrease the emergence of variants of concern. COVID-19 mRNA vaccines and AstraZeneca vaccine have shown promising early results against variant B.1.1.7. As effectiveness of the first dose against other variants of concern is emerging, ongoing monitoring will be required.
- **Vaccine distribution** will be optimized through this strategy, and current vaccine supply projections will work well with an extended dose strategy that aims to immunize as many Canadians as efficiently as possible. Extending

the dose intervals for mRNA vaccines up to four months has the potential to result in rapid immunization and protection of a large proportion of the Canadian population. Based on the expected supply of mRNA vaccines (six million doses in the first quarter of the year, some of which was used to provide two doses, and 23 million doses in the second quarter of the year), approximately 80% of the eligible population (16 years of age and over) could be offered a dose of mRNA vaccine by the end of June 2021 if a four month interval is implemented in March 2021. Second doses would begin in July 2021 when the additional supply of mRNA vaccines is expected in the third quarter of the year (55 million doses are expected at that time).

# Acknowledgments

**This statement was prepared by**: Dr. M Tunis, Dr. B Warshawsky, Dr. M Salvadori, Dr. R Harrison, Dr. S Deeks on behalf of NACI.

NACI gratefully acknowledges the contribution of: Ms. K Young, Ms. YE Chung, Ms. K Farrah, Dr. A Nam, Ms. MW Yeung, Dr. R Ximenes, G De Serres, D Skowronski, N Andrews, and the NACI Secretariat.

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