Today's Webinar

Wednesday, May 3rd, 2021 1:00-2:00pm EST

Hosted by The National Collaborating Centre for Infectious Diseases (NCCID), in partnership with the Public Health Agency of Canada (PHAC)

National Collaborating Centre for Infectious Diseases

Centre de collaboration nationale des maladies infectieuses

The Public Health Agency of Canada Webinar: National Advisory Committee of Immunization (NACI) Recommendations on Extended Dose Intervals for COVID-19 Vaccines

Speakers: Dr. Jesse Papenburg, Dr. Robyn Harrison, Dr. Bryna Warshawsky, Dr. Austin Nam, and Dr. Beate Sanders

Moderator: Dr. April Killikelly

Zoom

Please use the Q&A tab to pose questions to presenters at any time

Please send technical and troubleshooting questions to nccid@umanitoba.ca

Webinar recording and slides will be available after the webinar at nccid.ca

Recommendations of the National Advisory Committee on Immunization (NACI) on Extended Dose Intervals and Effectiveness of COVID-19 Vaccines

Declaration of interests

- Dr. Jesse Papenburg: *Grants from MedImmune and Sanofi Pasteur, and grants and personal fees from Seegene and AbbVie, all unrelated to COVID-19.*
- Dr. Bryna Warshawsky: Nothing to Declare
- Dr. Beate Sander: Nothing to Declare
- Dr. Austin Nam: Nothing to Declare
- Dr. Robyn Harrison: Nothing to Declare

Outline

- Overview of NACI
- Analysis of COVID-19 vaccine efficacy
- Modeling the impacts of COVID-19 vaccines
- NACI Recommendations

NACI Overview

Pandemic Context

- 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. Safe and effective COVID-19 vaccines could help achieve this goal.
- Canada has one of the **most robust, rigorous, dependable and highly proven vaccine approval systems** in the world.
- Provincial and territorial governments are responsible for decisions on who receives COVID-19 vaccines within their jurisdictions until there is sufficient supply to offer vaccination to everyone in Canada for whom authorized COVID-19 vaccines are recommended.
- The National Advisory Committee on Immunization (NACI) has updated its Guidance on the prioritization of initial doses of COVID-19 vaccine(s) to help inform provincial and territorial immunization program planning for the next stages of vaccine rollout, as vaccine supply increases in Canada.

canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/guidance-prioritization-initial-doses-covid-19-vaccines.html

Canadian Access to Vaccines

Health Canada

Authorizes health products for use in Canada, based on evidence of safety, efficacy and quality, and continues to regulate the products after authorization.

Public Health Agency

National Advisory Committee on Immunization (NACI) makes recommendations on use of authorized vaccines. based on safety and efficacy evidence, disease epidemiology, global effectiveness data and population need within Canada.

PHAC has a role in vaccine safety surveillance, working with the provinces and territories.

Provinces and Territories

Determine publicly funded vaccination program within their jurisdictions and responsible for vaccine funding, distribution and delivery.

Health Canada vs. NACI

	Regulator Review	NACI Vaccine Advice
Purpose	Authorize specific indications for use that are expected to be safe, immunogenic, efficacious, and of suitable quality for individuals	Recommend vaccination strategies to promote health, prevent and control infectious diseases, and prepare for or respond to public health emergencies
Focus	Individual use of product Risks and benefits of the vaccine for the individual.	Optimal use of product for public programs, and population health, and individuals. Benefits of the vaccine for public programs and the health needs within specific populations and for the individual.
Data reviewed	Pre-clinical and clinical trial data and manufacturing information submitted by manufacturers; post-marketing monitoring and published scientific evidence that informs benefit-risk analysis.	All relevant/available evidence for specific vaccines and similar vaccine formulations in the context of public health considerations, including existing vaccine programs and schedules, disease burden and distribution, and outbreak management.
Authority	Minister of Health / Federal Government	

- **NACI can make off-label vaccine recommendations when there is a clear need supported by vaccine characteristics, epidemiology, and a public health ethics analysis**

What is NACI?

- NACI is an external advisory body to the Public Health Agency of Canada that develops evidence-based advice on vaccines approved for use in Canada.

- NACI is comprised of experts in the fields of pediatrics, infectious diseases, immunology, pharmacy, nursing, epidemiology, pharmacoeconomics, social science, and public health.

- NACI's advice is published to the public in the form of NACI statements. All of NACI's statements are synthesized into the Canadian Immunization Guide (CIG).

- More information about NACI can be found at: www.canada.ca/naci

- To receive current information on NACI recommendations visit the Canadian Immunization Guide online at https://www.canada.ca/en/public-health/services/canadian-immunization-guide.html
- Additional subscriptions and RSS feeds are available: https://www.canada.ca/en/public-health/corporate/stay-informed-stay-connected/public-health-updates/subscribe.html

NACI Statement Development Timeline

December 2020

- **First COVID-19 vaccines approved**
- NACI begins providing evidence based guidelines on recommended interval between vaccine doses

January 2021

- **NACI provided initial advise on dosing intervals**
- Recommended extending intervals to 6 weeks

February 2021

- **NACI asked to address intervals in jurisdictions with supply and logistical challenges**
- Addressed what interval to balance individual & population impact. Impact on key populations.

March 2021

- **Rapid Response Statement**
- Provided updates on vaccine interval and rationale behind decisions

April 2021

- **Full Advisory Committee Statement**
- Explained the rationale for recommendations including updated evidence summaries and references.

Methodology to Reach a Decision

- After receiving a request from the Public Health Agency of Canada (PHAC) and the Chief Medical Officers of Health across the country seeking advice on dosing intervals for COVID-19 vaccines with limited supply, NACI reviewed all available evidence on extended intervals
- This was done using full Committee meetings that reviewed evidence from all available sources including; peer-reviewed studies, pre-prints, and cohort studies

Considerations regarding extended interval decisions

- Efficacy and effectiveness of the first dose
- Duration of protection following the first dose
- Impact of extending the interval between the priming and boosting doses on the immune response and vaccine efficacy
- Impact of more rapidly vaccinating a greater number of people
- Impact on variants of concern
- Impact on specific population groups
- Modelling information
- Ethics, equity, feasibility, and acceptability of extending the interval

Efficacy and effectiveness of COVID-19 vaccines and impact on transmission

Efficacy, effectiveness and immunogenicity

- **Efficacy:**
  - How well the vaccine works in a clinical trial
- **Effectiveness:**
  - How well the vaccine works in real-world observational studies
- **Immunogenicity:**
  - Measures the body's immune response to the vaccine
  - Humoral (B cells) and cellular (T cells)
  - No correlate of protection so can be challenging to interpret

Efficacy – based on clinical trials

Efficacy studies – two doses; symptomatic disease

Estimate	Description	Reference
95%	**Pfizer-BioNTech**	Polack et al. - published
94%	**Moderna**	Baden et al. - published
63%	**AstraZeneca** - UK, Brazil, South Africa	Voysey et al. - published
81%	**AstraZeneca** if delay interval between doses ≥12 weeks	
76%	**AstraZeneca** United States press release	AstraZeneca press release – March 25, 2021

Efficacy studies – one dose; symptomatic disease

Estimate	Description	Reference
92%	**Pfizer-BioNTech** clinical trial – recalculation, from 14 days after dose 1 until dose 2	Skowronski et al. - published
92%	**Moderna** clinical trial – FDA data – for those that only received one dose more than 14 days from that dose	FDA – December 17, 2020 - report
76%	**AstraZeneca** clinical trial – from 22 days to 90 days after dose 1	Voysey et al. - published
66%	**Janssen** clinical trial – ≥28 days after single dose	Sadoff et al. - published

Efficacy studies – asymptomatic

Estimate	Description	Reference
61%	**Moderna one dose –** calculated; based on swabs at first vaccination and second vaccination ~28 days later	Baden et al. - published
2.0 %	**AstraZeneca two doses** - United Kingdom; routine weekly swabbing May have higher efficacy for asymptomatic / unknown infection against non-B.1.1.7 strains	Voysey et al. - published Emary et al. - published
66%	**Janssen single dose** – Based on serology for nucleocapsid protein at day 71	Sadoff et al. - published

Efficacy against variants of concern

Pfizer-BioNTech (press release)

- 100% efficacy in study of 800 people in South Africa;
- 9 cases all in the placebo group, 6 were B.1.351

AstraZeneca (Madhi et al. – published)

- **10.4%** efficacy against B.1.351 in **South Africa**
- 1,010 placebo and 1,011 vaccine recipients, median age 30 years

Janssen (Sadoff et al. - published)

- **66% efficacy against moderate to severe disease** (28 days after single dose)
  - **72%** in the United States
  - **68%** in Brazil (69% of cases were the P.2)
  - **64%** in South Africa (95% of cases were the B.1.351 variant)

Effectiveness – based on observational studies

Effectiveness studies

- Studies are being released all the time
- Based on the programs that are being implemented
- **One-dose studies are either**
  - For the short period of time between the first and second dose (e.g., Israel, United States)
  - For a longer period if using an extended interval (e.g., United Kingdom, Quebec and British Columbia)
- **Study outcomes**
  - Symptomatic disease
  - Asymptomatic infection
  - PCR positive (symptomatic and asymptomatic combined)
  - Hospitalization
  - Death
  - Transmission

Efficacy study designs

- **Linked administrative data -** using laboratory test results, immunization registries, and sometimes patient's past medical records
  - Cohorts
  - Matched vaccinated and unvaccinated
- **Test negative design** – comparing immunization rates in those who underwent testing and were either negative or positive
- **Regularly screened cohorts**

Study populations

- Health care workers; some regularly screened
- Long term care residents; some during outbreaks
- Older adults
- General population
- Hospitalized patients

Summary of Effectiveness Data

AstraZeneca vaccine – one dose

- Symptomatic and asymptomatic - ~ **58% to 68%**
- Hospitalization **- ~80%**

AstraZeneca vaccine – two doses - Not available

Janssen vaccine – single dose – Not available

mRNA vaccines – one dose

- Symptomatic and asymptomatic - ~ **60 to 80%,** with some higher and some lower estimates
- Hospitalization **- ~80%**
- Death **- ~85%**

mRNA vaccines – two dose

- Symptomatic and asymptomatic - **~90 to 95%**
- Hospitalization - **~93 to 96%**
- Death - **~93 to 96%**

Comparing efficacy and effectiveness

Summary of protection

AstraZeneca

Description	Estimate
Two-dose efficacy Symptomatic	**63% to 76%** ≥ 15 days after vaccination
One-dose efficacy Symptomatic	**76%** 22 to 90 days after vaccination
One-dose effectiveness Symptomatic and asymptomatic	**~ 58% to 68%** At least 14 days after vaccination

Janssen

Description	Estimate
Single-dose efficacy Moderate, severe, critical symptomatic disease	**66%** ≥ 28 days after vaccination

Summary of protection

mRNA vaccines

Description	Estimate
Two-dose efficacy Symptomatic	**94 to 95%** ≥14 or ≥7 days after vaccination
Two-dose effectiveness Symptomatic and asymptomatic	**~90 to 95%** At least 14 days after vaccination
One-dose efficacy Symptomatic disease	**92%** For short period from 14 days to second dose
One-dose effectiveness Symptomatic and asymptomatic	**~ 60-80%,** with some higher and some lower estimates At least 14 days after vaccination

Why are effectiveness data lower than efficacy data?

- Observational studies include people not included in efficacy studies
- Often looking at symptomatic disease and asymptomatic infection combined, whereas clinical trials focused on symptomatic disease
- Vaccinated people may change their behaviour, increasing their risk of exposure
- B.1.1.7 more prominent in effectiveness data
- Other methodological consideration regarding effectiveness data:
  - Short time between first and second doses in some studies
  - Use of outcomes that occur later than symptom onset such as laboratory outcomes and hospitalizations
  - Declining rates in the community

Transmission

Factors that influence transmission

- Prevention of PCR-confirmed symptomatic disease
- Prevention of PCR-confirmed asymptomatic infection
- If not completely protective against PCR-confirmed disease or infection, may still be able to decrease transmission if:
  - Viral load and shedding is lower
  - Duration of viral shedding is shorter

Factors that impact transmission

Approximations based on efficacy and/or effectiveness data

	Symptomatic disease	Asymptomatic infection
mRNA – two doses	**95%**	**90%**
mRNA – one dose	**60 to 80%** with some higher and lower estimates	
AstraZeneca	**63 to 76%**	Some evidence (Shrotri et al.) but uncertain based on clinical trials; may be better for non-B.1.1.7 (Emary et al.)
Janssen	**66%**	**66%**

Viral load and shedding

- A few studies suggest that viral load may be lower / slightly lower (Ct values higher) in those who were vaccinated and infected compared to unvaccinated and infected
- Emary et al., Lumley et al., Shrotri et al., McEllistrem et al., Levin-Tiefenbrun et al.

Two studies assessed transmission

- Shah et al. – Pfizer-BioNTech and AstraZeneca in Scotland; one and two doses
  - Decreased transmission in households of vaccinated health care workers compared to unvaccinated health care workers
  - Not clear if because health care workers didn't get infected or health care workers became infected but doesn't transmit infection

- Harris et al. – Pfizer-BioNTech and AstraZeneca in the England; most only received one dose
  - Used record linkage to compare the rates of secondary case in households where a positive case was vaccinated compared to households were the positive case was unvaccinated
  - Based on a number of analyses:
    - "likelihood of household transmission is 40-50% lower for households in which the index cases are vaccinated 21 days or more prior to testing positive (compared to no vaccination)" with similar results for both vaccines

Considerations Regarding Interval Extension

Consideration regarding extended interval decisions

- Efficacy and effectiveness of the first dose
- Duration of protection following the first dose
- Impact of extending the interval between the priming and boosting doses on the immune response and vaccine efficacy
- Impact of more rapidly vaccinating a greater number of people
- Impact on variants of concern
- Impact on specific population groups
- Modelling information
- Ethics, equity, feasibility, and acceptability of extending the interval

Consideration regarding extended interval decisions (1/2)

- **Efficacy and effectiveness of the first dose**
  - Effectiveness is about 60 to 80%, with some lower and some higher estimates
  - 80% effective against hospitalizations
- **Duration of protection following the first dose**
  - Canadian data with follow-up of some individuals to 12 weeks
  - Efficacy modeled out to 90 days for AstraZeneca
  - Protection from one dose of other vaccines last for 6 months or more
  - Will need to continue to monitor
- **Impact of extending the interval between the priming and boosting doses on the immune response and vaccine efficacy**
  - Longer interval results in maturing of the B memory cells with higher and more durable response
  - AstraZeneca had higher efficacy with an interval of ≥ 12 weeks

Consideration regarding extended interval decisions (2/2)

- **Impact of more rapidly vaccinating a greater number of people**
  - Allows all eligible individuals to be offered a vaccine by early to mid-June and then go back and offer second dose
  - Faster direct and indirect protection as well as possibility of having a faster herd effect
- **Impact on variants of concern**
  - Unknown, but decreased transmission by wide scale vaccination may decrease emergence of variants (Cobey et al.)
- **Impact on specific population groups**
  - Immunogenicity data for older adults and some underlying medical conditions assessed
  - No correlate of protection
- **Modelling information**
- **Ethics, equity, feasibility, and acceptability of extending the interval**

Modeling the impact of extended intervals

Impact of Extended Vaccine Intervals

- Extending the interval is a temporary measure to decrease the burden of disease as quickly as possible
  - With extension, expected supplies of mRNA vaccines would allow 90% of people 50+ and 75% of those 16-49 years to be vaccinated with one dose by mid June
- Extending intervals also reflect a need to balance individual protection with population health

Modeling the impact of extended intervals

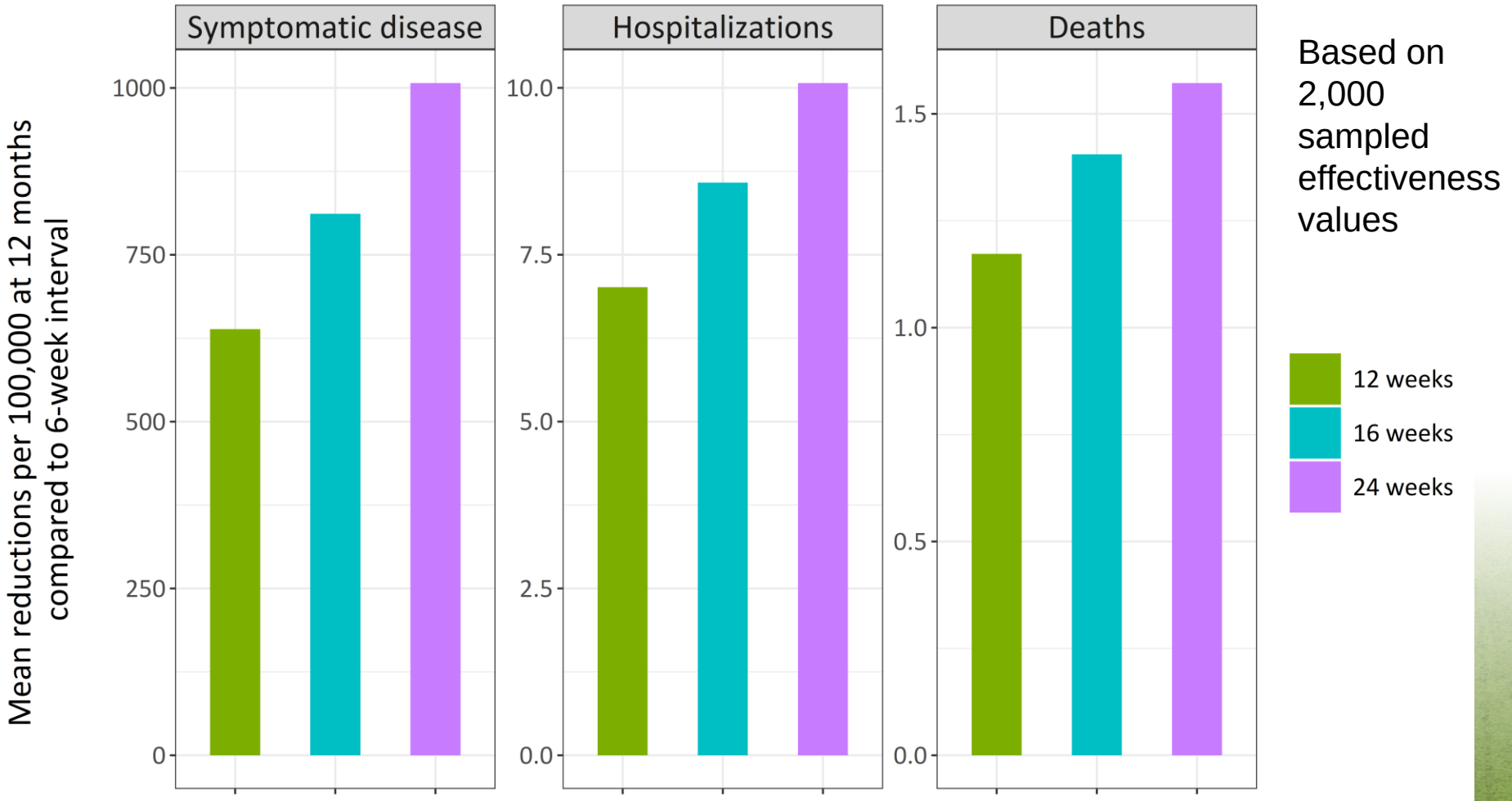
- PHAC model examines impact of accelerating vaccine coverage with dose intervals of 12, 16, and 24 weeks (Excluding long-term care residents)
- Vaccine effectiveness values sampled from range of likely values based on real-world effectiveness estimates
- Sensitivity analysis tested
  - Wide range of first-dose effectiveness against hospitalizations and deaths
  - Shorter duration of protection of 3 to 6 months to examine waning protection
- Key assumptions:
  - Vaccines prioritized by age in descending order until age 55 years; then offered in no particular order to those 20 to 54 years of age
  - Coverage: 65% (20-64 years); 80% (65+ years)
  - Daily vaccination capacity: 150,000 doses in Q1, increased to 350,000 (April), 450,000 (May), and 525,000 (June-onward)
  - A 3rd wave was simulated beginning on April 1, 2021

medRxiv preprint: Modelling the impact of extending dose intervals for COVID-19 vaccines in Canada (DOI: https://doi.org/10.1101/2021.04.07.21255094)

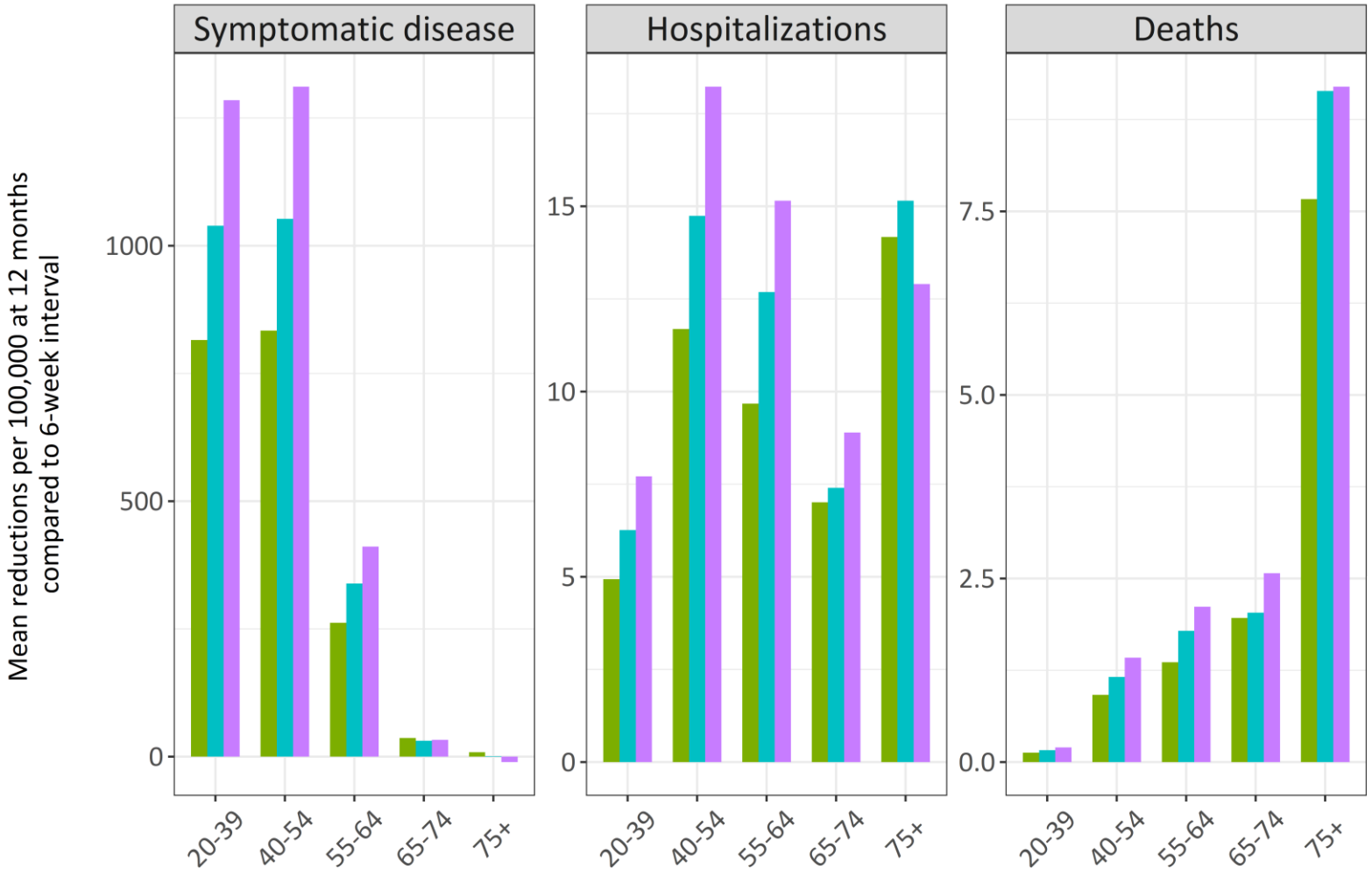
Vaccine effectiveness assumptions

Characteristic	Likely value	Range
VE Infection	90% x VE disease 50% x VE disease (conservative)	80-95% x VE disease 40-60% x VE disease
VE Symptomatic Disease, Dose 1	67% (<65 years) 58% (65+ years)	48-79% (<65 years) 36-71% (65+ years)
VE Symptomatic Disease, Dose 2	94% (20+ years)	87-98% (20+ years)
VE Hospitalization, Dose 1	80% (20+ years)	70-85% (20+ years)
VE Hospitalization, Dose 2	96% (20+ years)	95-97% (20+ years)
VE Deaths, Dose 1	85% (20+ years)	75-92% (20+ years)
VE Deaths, Dose 2	96% (20+ years)	95-97% (20+ years)

Extended intervals: Greater reductions in symptomatic disease, hospitalizations, and deaths at 12 months, relative to a 6-week interval



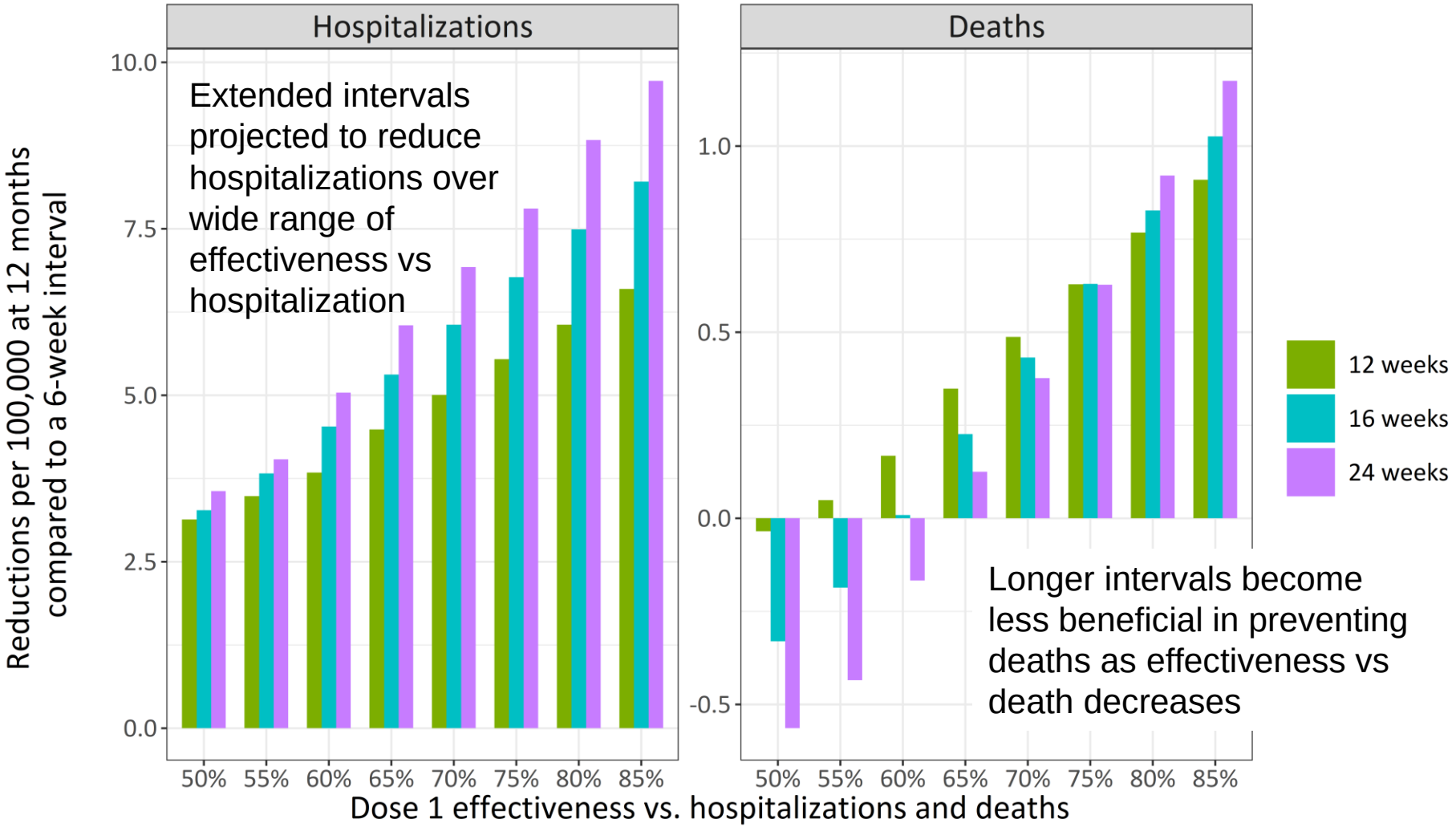
Extended intervals: Greater reductions in symptomatic disease,* hospitalizations and deaths across most age groups at 12 months, relative to 6-week interval



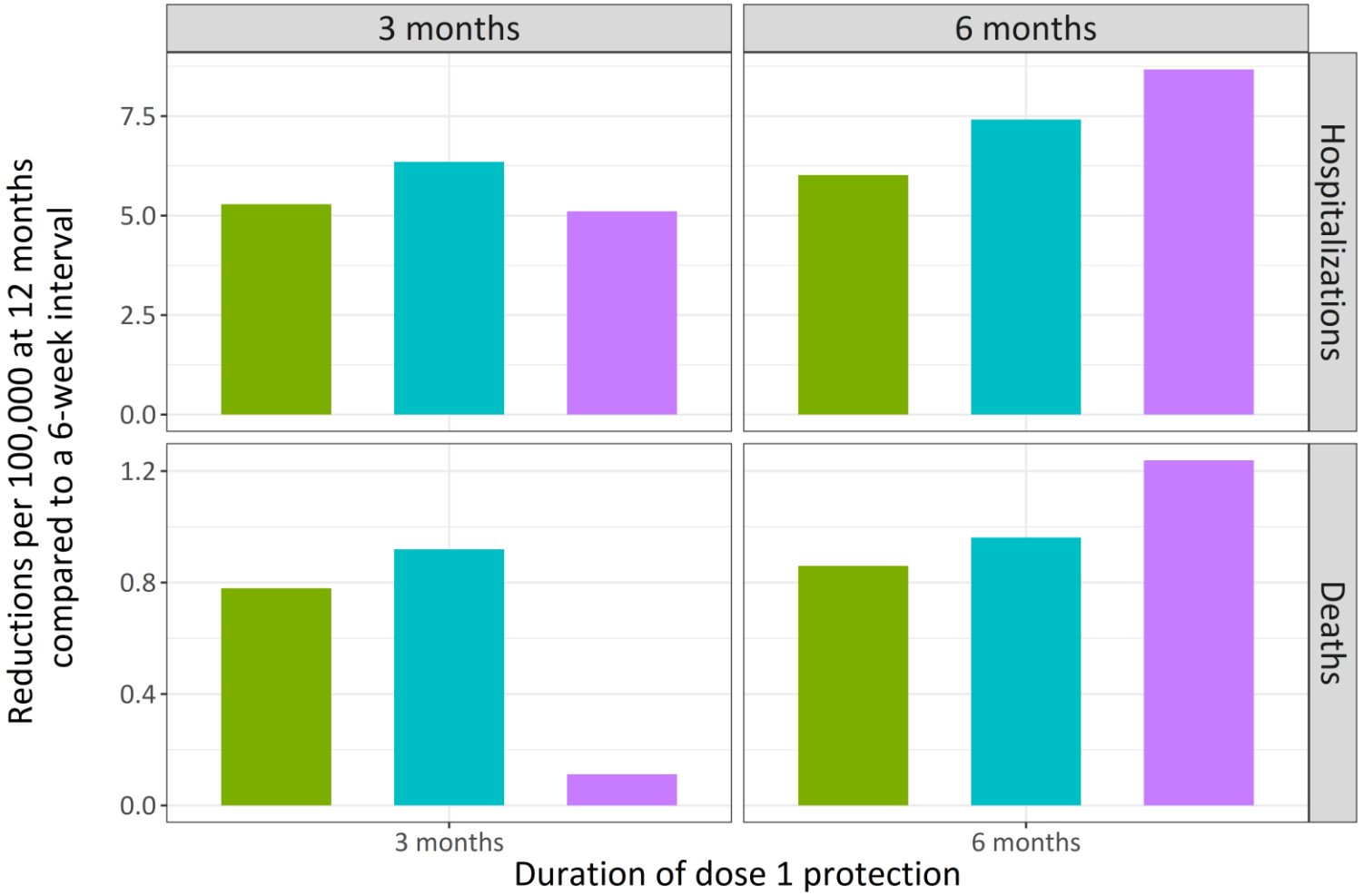
Largest reductions in hospitalizations projected with 16 week interval in 75+ years

* Intervals ≥16 weeks projected to increase symptomatic disease (mild/moderate) in 75+ years

Extended intervals: Reduction in deaths when effectiveness vs death ≥65% at 12 months, relative to 6-week interval



Extended Intervals: Benefits were generally robust to shorter duration of protection of 3 and 6 months



Large decrease in the benefit of a 24-week interval (vs deaths) when the average dose 1 duration of protection was 3 months

- 12 weeks
- 16 weeks
- 24 weeks

Limitations and Caveats

- The model represents population-level effects and does not account for subgroups who may have lower protection from the first dose
- The simulated 3rd wave does not include additional public health responses (over those already in place) and represents a type of worst-case epidemic (but best case for vaccination benefit)
  - Milder 3rd wave scenario also projected reductions in symptomatic disease, hospitalizations and deaths
- Variants of concern (VOCs) were not explicitly modelled
  - The 3rd wave scenario could be used as a proxy for a severe resurgence under VOCs and sensitivity analyses could be used to consider how potentially reduced effectiveness under VOCs may affect the extended interval strategy
- Transmission in health care settings (e.g. hospitals, long-term care) were not modelled
- Hospital capacity was not considered in the model

Summary

- At current effectiveness estimates, extended dose intervals are projected to reduce overall symptomatic disease, hospitalizations, and deaths where vaccine supply is constrained
- Sensitivity analysis indicated that:
  - first dose effectiveness against death is an important outcome to monitor
  - waning protection needs to be rapid for extended intervals to become a poor strategy
- Longer intervals were generally associated with fewer hospitalizations and deaths by the end of 12 months
  - Rate of reduction in hospitalizations and deaths diminishes as interval length increases with prioritization of older individuals and assumed vaccination (throughput) capacity
- Benefits are primarily due to accelerating partial protection in adults aged 20-74 years
- Extended intervals provide a strategy for reducing overall incidence of serious outcomes when there is an expectation of increasing risk of infection and serious outcomes in the near-term while vaccine supply is constrained
- The optimal interval to obtain a fair balance between short-term and long-term protection is unknown

Additional evidence from the literature

- A total of 5 different modeling studies were identified in publications or pre-prints as of February 14, 2021
- These investigations were completed considering mRNA vaccines and examined various delay intervals, single dose strategies
- Results indicated that vaccine interval extension of 9-12 weeks can reduce infections, hospitalizations, and deaths compared to no delays in limited vaccine supply conditions
- The population benefits are due to greater vaccine coverage to more people, even when the level of protection from a single dose is lower than the protection offered by two doses
- Single dose effectiveness critical: under high first dose effectiveness against disease (72-80%) an extended interval was preferred over no delay in all tested scenarios
  - These modelling studies were completed before effectiveness estimates against hospitalizations and deaths became available

Internal and external studies suggest benefit from extended intervals for reducing symptomatic disease, hospitalizations, and deaths from COVID-19

Ethics, Equity, Feasibility, and Acceptability (EEFA)

Ethics, Equity, Feasibility, and Acceptability (EEFA)

- NACI applies a rigourous EEFA framework for decisions and recommendations, considering the following:
- **Ethics**
  - Risk/benefit balance favors extending the interval between doses, especially in the context of high disease burden of disease.
  - Consider offering second dose at shorter interval if already consented.
- **Equity**
  - Allows many more eligible people to be vaccinated earlier. Enhances equity compared to leaving large groups at risk for longer periods.
  - Some people will become infected with one dose when they might not have if they received the second dose, although illness may be milder.
- **Feasibility**
  - The same number of doses need to be administered with an extended compared to a standard interval.
- **Acceptability**
  - To maximize any adverse impact on public trust due to off-label use of COVID-19 vaccines and evolving recommendations, transparent and clear communication is important.

NACI Recommendations

Strong NACI Recommendation

- 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 and ongoing pandemic disease, 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**.
- **Second doses should be offered as soon as possible after all eligible populations have been offered first doses**, with priority given to those at highest risk of severe illness and death from COVID-19 disease.
- **Vaccinated people (with one or two doses) should continue to follow recommended public health measures.**
- NACI will **continue to monitor the evidence on effectiveness** of an extended dose interval and will adjust recommendations as needed.

Key Messages

- NACI released its full statement on April 7
  - Providing detailed **evidence summaries and analysis** that support the recommendation to extend the time between the first and second dose of COVID-19 vaccines up to four months.

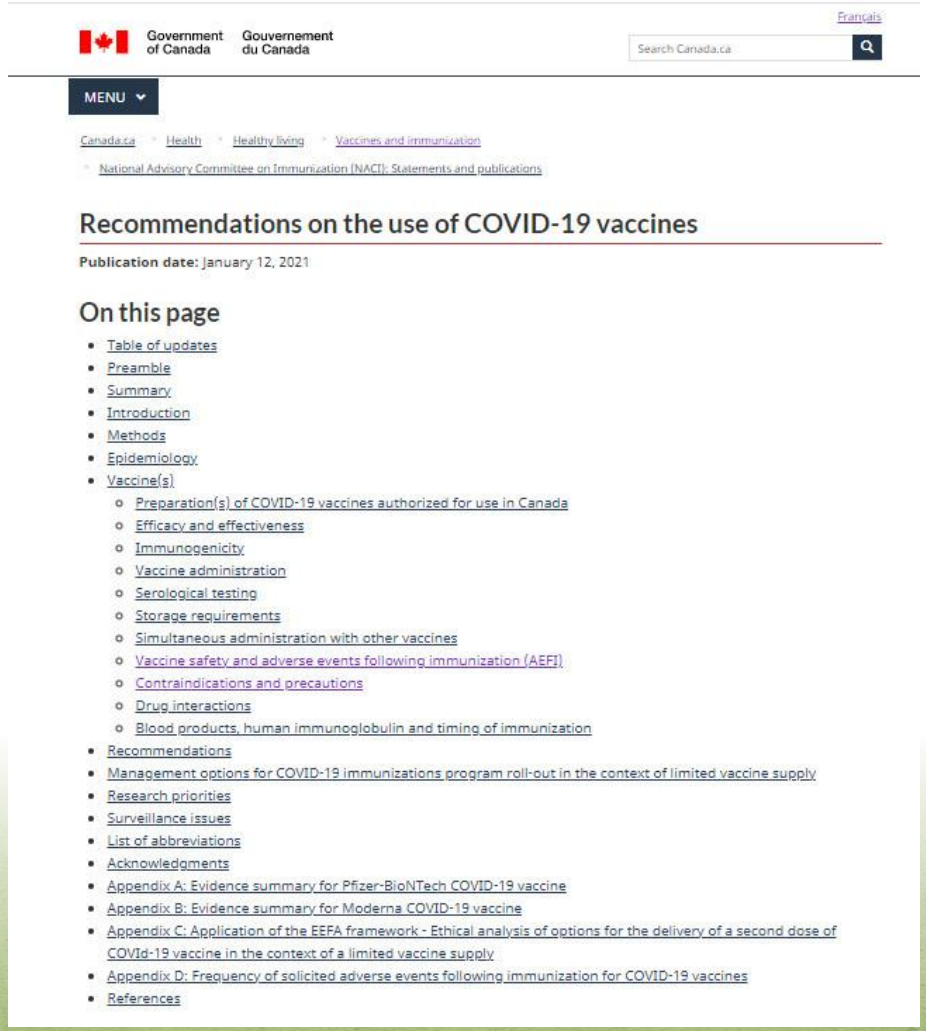
- Extending COVID-19 vaccine dose intervals will optimize early vaccine rollout for population protection.
  - By allowing many more people to gain protection through their 1st dose against severe COVID-19 outcomes.

- Jurisdictions may choose to **shorten the interval** between the first and second dose in specific populations based on local epidemiology, local vaccine supply, public health considerations and emerging data.

- Vaccine effectiveness against **variants of concern (VOC)** will also be monitored closely, especially as the prevalence of variants increases in Canada.

NACI Statement on COVID-19 Vaccines

- Refer to NACI recommendations on the use of COVID-19 vaccines for guidance on COVID-19 vaccines.



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> National Advisory Committee on Immunization (NACI): Statements and publications

Recommendations on the use of COVID-19 vaccines

Publication date: January 12, 2021

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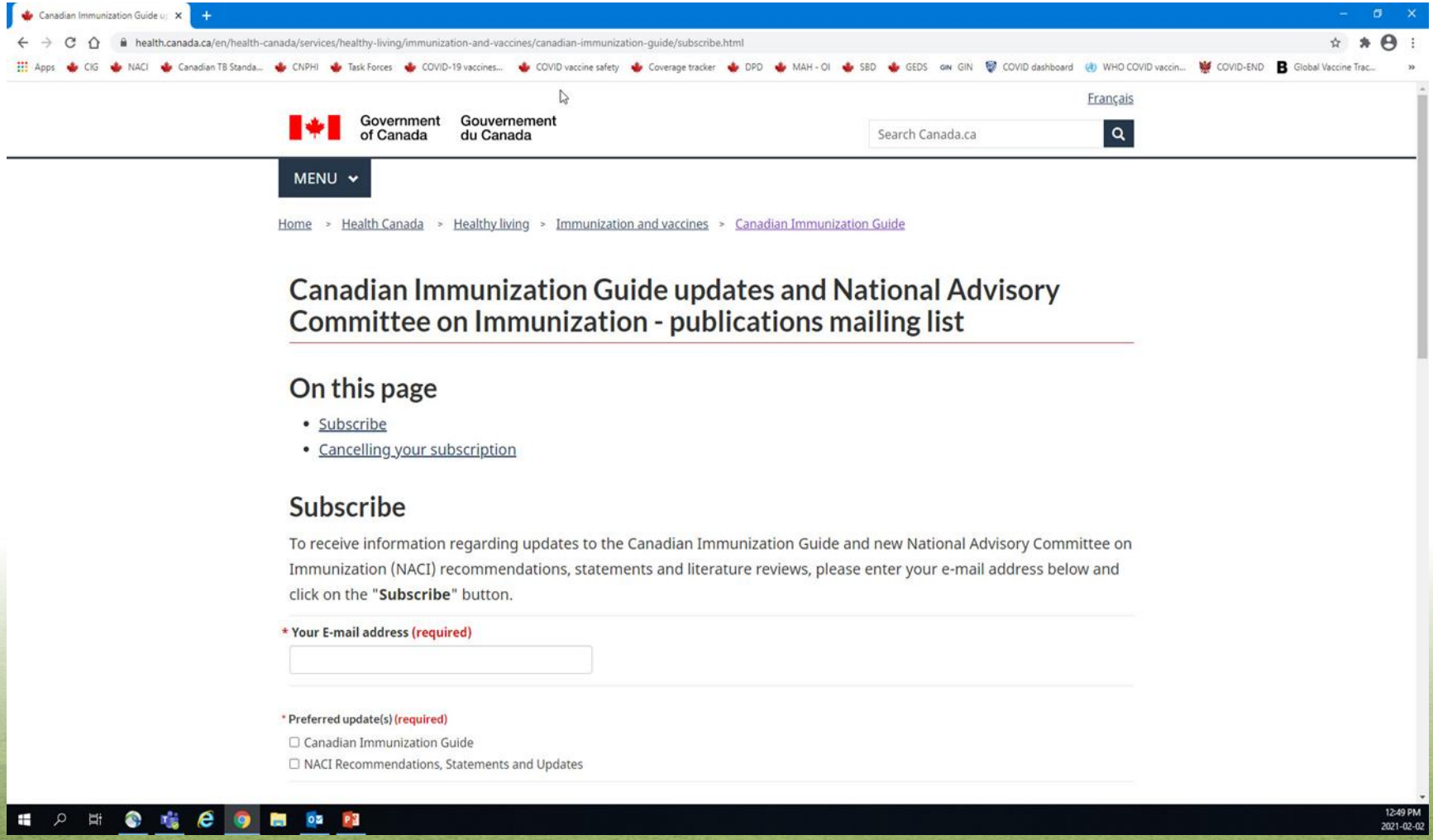


Thank you

Supplemental Slides

Duration of Protection

- Modeling in the AstraZeneca study demonstrated that protection from a single dose was maintained up to 90 days post vaccination
- Observational cohort studies from Canada and the UK show efficacy up to 8 weeks post vaccination
- Similar multi-dose vaccinations, such as hepatitis A and human papilloma virus, demonstrate that protection could last six months or longer in both adolescents and adults
- Investigations with longer-term follow-up in ongoing clinical trial participants and results from public vaccination campaigns will assist in determining vaccine effectiveness intervals for both one and two doses

National Immunization Technical Advisory Groups (NITAGs)

- NITAGs are multidisciplinary groups of national experts responsible for providing independent, evidence-informed advice to policy makers and programme managers on policy issues related to immunization and vaccines.

- NITAGs now established in 134 countries and are recommended by the WHO.

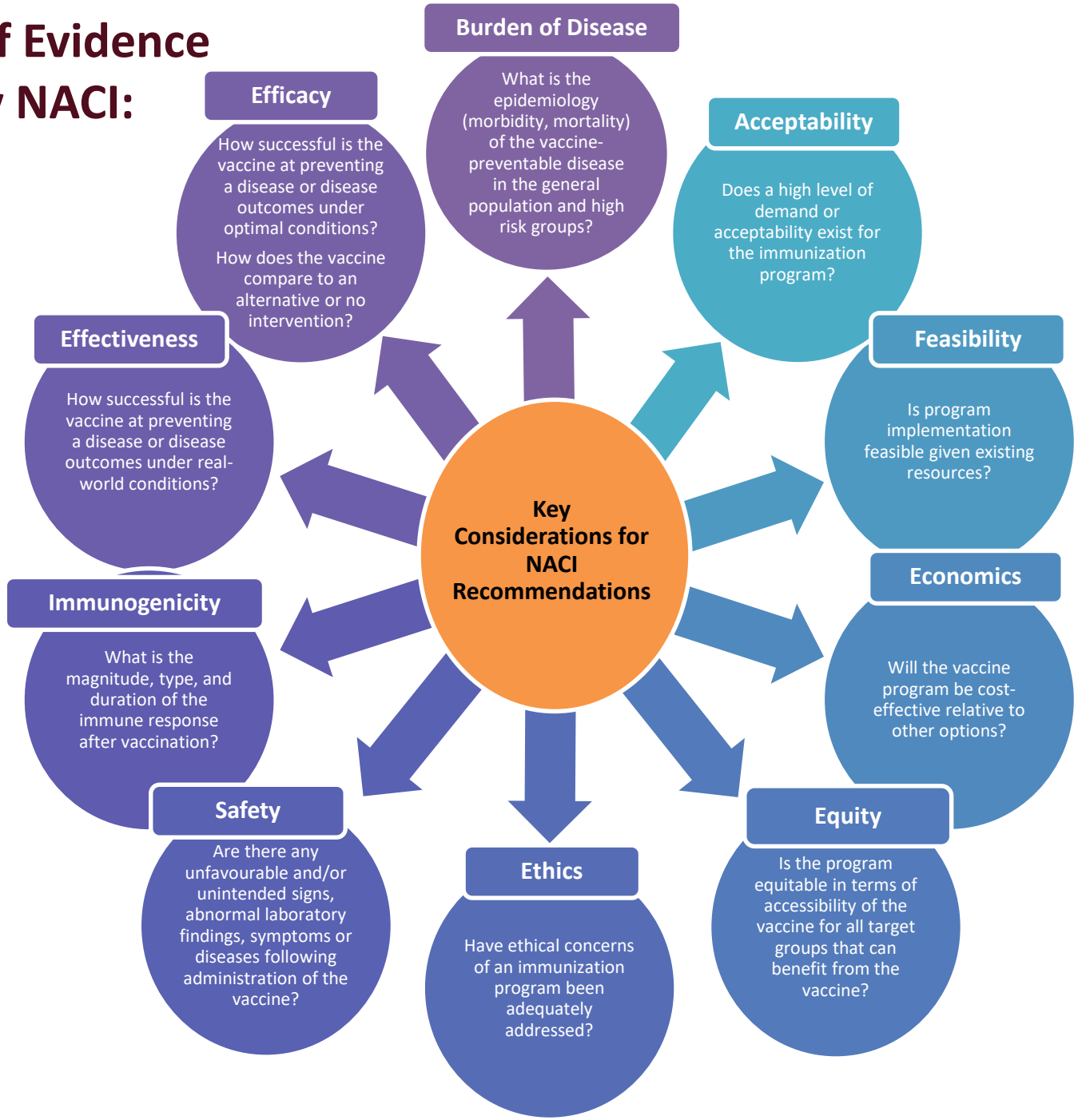
- The National Advisory Committee on Immunization (NACI) is Canada's national NITAG and is one of the longest standing (over 50 years)

- NACI makes recommendations for the use of vaccines currently or newly approved for use in humans in Canada, including the identification of groups at risk for vaccine-preventable diseases for whom vaccination should be targeted.

- In Canada, most jurisdictions also have formal provincial/territorial immunization technical advisory groups (PITAGs)

- In 2019, NACI expanded its mandate to include consideration of ethics, equity, feasibility, acceptability and economics

Types of Evidence Used by NACI:



NACI Membership

- PHAC appoints voting members, Chair and Vice Chair
  - Members: 4-year term with option of one renewal
  - Chair / Vice Chair: 2-year term two 1-year optional extensions (total 4 years)

- Voting members (Chair + 15) members appointed based on their expertise
  - Canadian experts in pediatric ID (2), adult ID (2), allergy/immunology (1), pharmacy (1), public health nursing (1), pharmacoeconomics (2), public health and preventive medicine (4), epidemiology (1), social sciences (1)

- 9 non-voting liaison representatives with an interest/role in immunization
  - E.g. Canadian Public Health Association, The Council of Chief Medical Officers of Health (CCMOH), Canadian Pediatric Society, College of Family Physicians of Canada

- 6 non-voting ex-officio federal representatives
  - PHAC, Health Canada, Indigenous Services Canada, National Defence and Canadian Armed Forces

NACI approach to conflicts of interest

- Members declare relevant interests at the beginning of each NACI meeting, and each WG meeting.
- Members declare any new relevant interests to NACI Secretariat when they emerge.
- Members complete annual Declaration of Interest Statements
- Member declarations are assessed for potential conflicts by NACI Executive Committee using an established PHAC tool.
- If COIs are identified, management strategies are applied (e.g. may not lead certain Working Groups, may not vote on some topics).

Efficacy against variants of concern

Pfizer-BioNTech (press release)

- 100% efficacy in study of 800 people in South Africa; 9 cases all in the placebo group, 6 were B.1.351

AstraZeneca (Madhi et al. – published)

- **10.4%** efficacy against B.1.351 in **South Africa**
- 1,010 placebo and 1,011 vaccine recipients, median age 30 years

Janssen (FDA – February 26, 2021)

- **66% efficacy against moderate to severe disease** (one month after single dose)
  - **72%** in the United States
  - **61%** in Latin America (68% of cases were the P.2)
  - **64%** in South Africa (95% of cases were the B.1.351 variant)

Novavax (press release)

- **89.3% efficacy in the United Kingdom** (7 days post second dose against mild, moderate and severe disease)
  - 95.6% efficacy against the original strain
  - 85.6% efficacy against the UK variant
- **49.5% efficacy in South Africa** (mild, moderate and severe) (92.6% of cases had the South African escape variant)
  - 60% efficacy against the SARS-CoV-2 among HIV negative individuals

Effectiveness study methodologies

- **Studies from:**
  - United Kingdom, Canada, Israel, United States, Denmark
- **For one dose, depends on the schedule used in the country:**
  - United Kingdom, Canada – based on first dose
  - Israel, United States, Denmark – based on short period to the second dose
- **Variants of concern:**
  - B.1.1.7 circulating in United Kingdom and Israel
- **Study designs:**
  - Linked administrative data using laboratory test results, immunization registries, and sometimes patient's past medical records
  - Healthcare workers; in some studies they were regularly screened
  - Long term care residents; one study during an outbreak
  - Test negative design – comparing immunization rates in those who underwent testing and were either negative or positive
- **Study outcomes:**
  - Two doses and one dose
  - Symptomatic infection, asymptomatic infection, PCR-positive (combined symptomatic disease and asymptomatic infection), hospitalization and death

Impact of Extended Vaccine Intervals

- It is widely accepted that the interruption of a vaccine series resulting in an extended timeframe between doses does not require restarting the series regardless of the period between doses
- Extended timeframes between primary and boosting doses allow memory B cells to mature resulting in a higher and more durable response
- In support of this, the AstraZeneca clinical study determines that the maximum efficacy occurred when the doses were ≥12 weeks apart (81.3%, 95% CI: 60.3 to 91.2%)

Impact on Variants of Concern

- This is unknown
- Existing studies have not investigated increased or reduced efficacy in any Variant of Concern (VOC)
- It is believed that reducing infection and transmission rates by covering more people with an initial dose will result in reductions in VOCs
- The Pfizer and the AstraZeneca vaccines have shown promising efficacy against the B.1.1.7 variant in studies from the UK and Israel
- The Pfizer vaccine has also shown efficacy against the B.1.351 variant after two doses
- Ongoing investigation will be required in order to determine vaccine effectiveness against VOCs

Impact on Population Subgroups

VE in Older Adults

Country of Study	Age Group	Vaccine	Interval (days post dose 1)	Vaccine Effectiveness (%)				
				Symptomatic	Asymptomatic	Hospitalization	Deaths	SARS-CoV-2
England	≥70	Pfizer/AZ	28 / 35	58				
	≥80	Pfizer/AZ				80		
	≥80	Pfizer					85	
UK	frail elderly	Pfizer	≥14 to 80			71-79		
		AZ	≥14 to 53			80		
Canada	LTC residents	Pfizer/Moderna	21 to 62					80-90
Denmark	LTC residents	Pfizer	~24 days	21	21			
				60*	60*			
USA	LTC residents	Pfizer	>14 to 7 days after 2nd dose					63
UK	LTC residents	Pfizer	35-48 days	65				
		AZ		68				

* - first 14 days after vaccination removed

For LTC residents the extent to which indirect protection from vaccinating HCP and visitors in contributing to effectiveness is unknown

Impact on Population Subgroups

VE in People with Underlying Medical Conditions

- VE following a complete series of COVID-19 vaccines in this population is unknown as in most cases these patients were excluded from clinical trials
- Three immunogenicity studies are available (Note: there limitations in the interpretation of immunogenicity studies as a result of unknowns regarding immune mechanisms for protection against COVID-19 and no available correlate of protection)
  - Study of 436 organ transplant patients, only 17% (95% CI: 14-21%) had antibody response a median of 20 days post dose 1 for Pfizer and Moderna vaccines. Patients were more likely to have detectable titre with Moderna if they were not receiving anti-metabolite maintenance or if they were younger
  - Study of 151 cancer patients, average age 73 years were compared to 54 healthier controls (40.5 years mostly HCP). Demonstrated low antibody response 3-5 weeks post dose one of Pfizer vaccine for people with solid tumors and even lower antibody response inn those with hematological malignancies. T cell responses were better in both types of cancer. Up to day 21 6 patients were positive (2 deaths) no positive results after day 21
  - Study of 241 kidney transplant patients; 10% had antibody response 28 days post dose one form Moderna vaccine. Those who had seroconverted had longer time after transplant, were receiving less immunosuppressive therapy and had better kidney function

Thank you!

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