# Weekend Rounds.msg

| | |
|---|---|
| **From:** | CCMOH SECRETARIAT / CMHC (PHAC/ASPC) <phac.ccmoh.secretariat-cmhc.aspc@canada.ca> |
| **To:** | CCMOH SECRETARIAT / CMHC (PHAC/ASPC), Tam, Dr Theresa (PHAC/ASPC), Njoo, Howard (PHAC/ASPC), Robinson, Kerry (PHAC/ASPC), Auger, Julie (PHAC/ASPC), Henry, Bonnie HLTH:EX, Shahab, Saqib (Ext.), XT:Hanley, Brendan HLTH:IN, Kandola, Kami (Ext.), Brent Roussin, Dr. Deena Hinshaw, Dr. David Williams, Dr. Barb Yaffe, Arruda, Horacio (Ext.), Sylvie Poirier, Russell, Jennifer (Ext.), Strang, Robert (Ext.), Morrison, Heather (Ext.), Dr. Janice Fitzgerald, Dr. Michael Patterson, Nadine Sicard, Strang, Robert, Davies, Stephanie (PHAC/ASPC) |
| **Cc:** | Levesque, Eric J. (DH/MS), Landsburg, Shelley (DH/MS), Dr. Heather Morrison |
| **Sent:** | December 16, 2020 7:03:14 AM PST |
| **Received:** | December 16, 2020 7:03:14 AM PST |
| **Visible Recipient Count:** | 26 |
| **Priority:** | Normal (5) |
| **Calendar Item Type:** | REQUEST |

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This discussion will take place from 11:00 am EST to 1:00 pm EST.
Dear SAC members,

In the interest of informing immunization programs and other interested parties across Canada, the Public Health Agency of Canada (PHAC) is providing you with an embargoed copy of the National Advisory Committee on Immunization's (NACI) "Recommendations on the Use of COVID-19 Vaccine(s)". Note that the French embargoed copy will be tomorrow.

Please note this electronic copy is for internal planning purposes only and is not for dissemination to outside organizations. This guidance is anticipated to be published on PHAC's website once HC authorizes the Moderna product. The French statement and message to follow.

Please find below the high level agenda for the weekend rounds:
· 11AM to noon: Discussion with NACI on Moderna recommendations and perspectives on intervals between doses
· Noon to 12:30: Discussion/Q&A with CSIS and RCMP representatives
· 12:30 to 13:00: In camera discussion amongst CMOHs
Thank you,
SAC Secretariat
Video Conference Meeting Information
Meeting link:
s.15; s.17

Meeting number/access code:
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# Weekend Rounds 1.msg

| | |
|---|---|
| **From:** | CCMOH SECRETARIAT / CMHC (PHAC/ASPC) <phac.ccmoh.secretariat-cmhc.aspc@canada.ca> |
| **To:** | CCMOH SECRETARIAT / CMHC (PHAC/ASPC), Njoo, Howard (PHAC/ASPC), Auger, Julie (PHAC/ASPC), Henry, Bonnie HLTH:EX, Shahab, Saqib (Ext.), XT:Hanley, Brendan HLTH:IN, Kandola, Kami (Ext.), Brent Roussin, Dr. Deena Hinshaw, Dr. David Williams, Dr. Barb Yaffe, Arruda, Horacio (Ext.), Sylvie Poirier, Yves Jalbert, Russell, Jennifer (Ext.), Strang, Robert (Ext.), Morrison, Heather (Ext.), Dr. Janice Fitzgerald, Dr. Michael Patterson, Dr. Denise Werker, Muecke, Cristin (Ext.), Gaynor.Watson-Creed@novascotia.ca, Tam, Dr Theresa (PHAC/ASPC), Jasmine Pawa, Catherine Elliott, Robinson, Kerry (PHAC/ASPC), Marcia Johnson, Denomie, Tami HE0, Fitzgerald, Janice, Dr. Heather Morrison, McGarr, Holly (PHAC/ASPC), Sharma, Supriya (HC/SC), Elmslie, Kim (PHAC/ASPC), Salvadori, Marina (PHAC/ASPC), Tunis, Matthew (PHAC/ASPC), Warshawsky, Bryna (PHAC/ASPC), Nam, Austin (PHAC/ASPC) |
| **Cc:** | Strang, Robert, Shelley Deeks |
| **Sent:** | December 31, 2020 9:32:33 AM PST |
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| **Visible Recipient Count:** | 39 |
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Meeting Information

Material:
Extended Dose Interval

Meeting link:
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Meeting number:
s.15; s.17

Password:
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## 5. CCMOH Statement_Vaccine dose interval FINAL Jan. 13 - EN.docx

**Statement from the Council of Chief Medical Officers of Health: Implementing COVID-19 Vaccination in Canada — Vaccine Dose Interval**

Jan 2, 2021

# Considerations for Extended Dose Interval

## Current Science:

The manufacturers of Pfizer-BioNTech and Moderna vaccines recommended a two-dose immunization schedule based on neutralizing antibody levels that were achieved after the second dose of vaccine, with the second dose given 21 and 28 days after the first for Pfizer-BioNTech and Moderna, respectively. However efficacy data from the two recently published phase 3 clinical trials demonstrate that high efficacy is achieved beginning 14-days after the first dose of vaccine.

The recently published data from Pfizer-BioNTech and Moderna show efficacy against symptomatic COVID-19 disease after two doses of vaccine as follows:

- **Pfizer-BioNTech: 95%** (95% confidence interval (CI): 90.3 to 97.6%) at least 7 days after the second dose
- **Moderna: 94.1%** (95% CI: 89.3 to 96.8%) at least 14 days after the second dose

However, both studies provide evidence that suggest that efficacy begins as early as 14 days after the first dose, and either provide or allow the calculation of the estimates of efficacy with only one dose starting 14 days after the first dose. In assessing efficacy after one dose is important to exclude the first 14 days as it takes a few days for vaccination to begin to generate an immune response and the virus may already be incubating in the first 14 days after vaccination. The following estimates are available for **one dose efficacy** against symptomatic COVID-19 disease beginning 14 days after the first dose:

- **Pfizer-BioNtech:**
  - **92.3% (**95% CI: 69 to 98%) from 14 days after dose 1 until dose 2 based on data from FDA – December 10, 2020 as quoted by the Institut national de santé publique du Québec
- **Moderna:**
  - **92.1% (**95% CI: 68.8 to 99.1%) based on those who received only one dose and were more than 14 days after that dose (FDA data – December 17, 2020)
  - **94.3%** calculated efficacy based on published data indicating 2 cases in the vaccine group and 35 cases in the placebo group from 14 days after dose 1 until dose 2 (New England Journal of Medicine – December 30, 2020).

However, the duration of the protection and how quickly it will decrease with only one dose is unknown as the vast majority of the participants in the trials received a second approximately dose 21 (Pfizer-BioNTech) or 28 (Moderna) days after the first dose.

### Data regarding a delayed second dose

No data is provided in the Moderna or Pfizer studies regarding a delayed second dose. However, a different vaccine, the AstraZeneca viral-vector COVID-19 vaccine, showed generally similar efficacy when the second dose was delayed by more than 6-8 weeks from the first dose. It is unknown whether this is applicable to the mRNA vaccines.

**Data regarding protection from asymptomatic infection (as opposed to symptomatic COVID-19 disease) and transmission after one dose**

It is unknown if mRNA COVID-19 vaccines prevent asymptomatic infection and subsequent person to person transmission of virus and how this would be impacted by the number of doses of vaccine. However, some information was provided from the Moderna trial that suggests that asymptomatic infection may be decreased by a single dose of vaccine. By taking nasal swabs for SARS-CoV-2 from participants before their first and second doses of vaccine or placebo, they found that:

- Among those who had no initial evidence of infection at the first dose, 15 people have asymptomatic infection in the group that received one dose of Moderna vaccine, compared to 39 people in the placebo group.

Again here it is important to note that this estimate includes the entire 28 days between the first and second dose, part of which is the first 14 days when vaccine may not yet have generated an immune response and the virus may already be incubating. Additional information from trial data is expected with regard to asymptomatic infection.

Assuming that the vaccine prevents asymptomatic infection and subsequent transmission with one dose, the level of vaccination to achieve prevention of transmission would be achieved faster when the second dose is delayed because more people can receive one dose sooner.

**Potential medical risks of delaying the second dose**

The following are potential medical risks of delaying the second dose and some considerations regarding these risks:

1) It is possible that some people will become infected/develop symptomatic COVID-19 after one dose when they may not have become infected or ill had they received a second dose, however vaccinating more people with a single dose will result in more people becoming vaccinated more quickly and possibly quicker indirect protection.
    - The efficacy of the first dose is estimated at approximately 92% compared to 94 to 95% for a two dose regimen, based on very limited evidence for the first dose efficacy for short periods of time.
    - Single doses will provide more individuals with protection against symptomatic COVID-19 more rapidly.
    - If transmission is prevented by single dose vaccination, more rapid indirect protection may be achieved for those individuals whose vaccination fails or who are unable to be vaccinated. The current evidence regarding the impact of vaccination on asymptomatic infection (and possibly on transmission) is very limited and is based on data for one dose of Moderna vaccine at approximately 28 days after vaccination.

2) The duration of protection with the first dose is unknown so breakthrough disease may begin to occur in the months before the second dose is given.
    - The duration of protection for two doses is only know for up to 14 weeks, while the duration of protection after one dose is unknown.

3) The impact of one or two doses of vaccine on new variants is unknown.
    - There is no evidence regarding how the vaccine will protect against potential new variants and whether that will be impacted by one or two doses. In addition, it is unknown how the number of people vaccinated with either one or two doses will influence pressure for new variants to emerge.

4) The immune response for the individual of a delayed second dose is unknown for these mRNA vaccines.
    - With other vaccines, individual immune response is either similar or improved when a longer interval between the first and second dose is compared to a shorter interval.

## Crude vaccine coverage targets for herd immunity:

Estimates of vaccine coverage targets are derived using the implied relationship between herd immunity and the basic reproduction number, R0, which represents the average number of secondary infections resulting from the introduction of an infectious person into a completely susceptible population. The epidemic threshold is the minimum proportion of the population that needs to be susceptible for the infection incidence to increase (R0>1). In relation to R0, this is defined as 1/R0. Following the same concept, the herd immunity threshold is the proportion of the population that needs to be immune (i.e. not susceptible) from infection such that incidence does not increase (R0≤1). In relation to R0, this is defined as 1 - 1/R0.

There is considerable uncertainty around the estimates of R0 for COVID-19 with mean estimated R0 ranging from 1.9 to 6.49.[1] One study has attempted to estimate a global convergence of R0 estimates and reported an estimated R0 of 4.5.[2] Elsewhere, a systematic review and meta-analysis based on 29 studies reported a reproduction number of 2.87 (95% CI: 2.39 – 3.34), albeit with a high degree of heterogeneity (99.5%).[3]

Two assumptions for R0 are used here:

1. R0 centered at 2.87 and ranging from 2.39 to 3.34.
2. R0 centered at 4.5 and ranging from 1.9 to 6.49.

### Crude vaccine coverage targets for herd immunity

The minimum proportion of the population that needs to be vaccinated to reach herd immunity is $\frac{1-\frac{1}{R0}}{ve}$, where *ve* is the vaccine efficacy against infection. Table 1 lists crude vaccine coverage targets to reach herd immunity based on this concept and using assumed ranges for R0 and vaccine efficacy.

### Vaccine efficacy

Efficacy after a full series (2-doses) of mRNA vaccines against symptomatic COVID-19 has been reported at 94.1% (89.3% - 96.8%) and 95% (90.3% - 97.6%).[4,5] Efficacy against symptomatic COVID-19 after the first dose (excluding the first 14 days of observation), have been estimated at approximately 92% (68% - 99%).[6,7]

The following vaccine efficacy assumptions are used in Table 1:

- 2-dose efficacy: 94.1% (89.3% - 97.6%)
- 1-dose efficacy: 90% (70-95%)

Assumed supply schedule

To provide a sense of the time to reach coverage targets, the following vaccine supply assumptions are used:

- 6M doses in Q1
- 18M doses in Q2
- 47M doses in Q3
- 9M doses in Q4

Times to target listed in Table 1 are derived by proportioning supply assumptions over each month and assuming a population of 37.5M in Canada. Time to second dose in the 1-dose scenarios is not included in the table.

**Table 1. Crude vaccine coverage targets after full series (2-doses) and partial series (1-dose) under different R0 and vaccine efficacy assumptions**

| Dosing | Assumed R0 (range) | Assumed Efficacy (ve) vs. Infection (range) | Estimated coverage target (1-1/R0)/ve (range) | Estimated time to target (months from Jan 1, 2021) |
|---|---|---|---|---|
| 2-dose (full series) | 4.5 (1.9 – 6.49) | 94.1% (89.3% - 97.6%) | 82.7% (48.5% - 94.7%) | 8.4 (6.8 – 10.0) |
| 2-dose (full series) | 2.87 (2.39 – 3.34) | 94.1% (89.3% - 97.6%) | 69.2% (59.6% - 78.5%) | 7.8 (7.3 – 8.2) |
| 1-dose (partial series) | 4.5 (1.9 – 6.49) | 90% (70% - 95%) | 86.4% (49.9% - 120%)* | 6.5 (5.1 – NA) |
| 1-dose (partial series) | 2.87 (2.39 – 3.34) | 90% (70% - 95%) | 72.4% (61.2% - 100%) | 6.2 (4.9 – 6.9) |

* Coverage targets > 100% indicate situations where vaccine efficacy is insufficient to reach herd immunity at a given R0.

**Caveats**

The formula, $\frac{1-\frac{1}{R0}}{ve}$, used to estimate vaccine coverage thresholds for herd immunity carries the assumption that contact/mixing and vaccine efficacy are uniform throughout the population. Social mixing surveys have shown that younger populations tend to have higher contact rates.[8] Thus, vaccine coverage targets estimated here are provided for general guidance.

Relating herd immunity thresholds to R0 ignores the proportion of the population that has acquired immunity from infection and represents herd immunity in the absence of continued public health measures.

The duration of protection after a single dose is unknown. Vaccine coverage thresholds described here do not account for waning protection.

The degree to which the mRNA vaccines provide protection from infection is still uncertain. Note that the minimum efficacy required for herd immunity is 1 – 1/R0 (with the aforementioned caveat applied).

Times to vaccine coverage target are predicated on uncertain supply assumptions and assuming 100% uptake (i.e. vaccine confidence).

Legal and Contractual Risks:

*Off-label use from a contract perspective:*

- When the issue of off-label use first arose in early December PHAC sought input from legal services on the potential implications on the Pfizer and Moderna vaccine supply contracts. In the absence of supplier consent or clear NACI advice on off-label use, it is not clear how the suppliers (Pfizer and Moderna) would respond to a PT's decision to use the vaccine off-label at a program level.

- There may be a risk that other suppliers under contract with Canada could refuse to deliver, or may alter the expected delivery.

- Legal Counsel's recommendation was that PHAC use extreme caution in this matter. Likely the best course of action would be to seek the views and consent of the vaccine suppliers before adopting broad off-label use.

NACI advice to date:

- On December 23, 2020, Canada's National Advisory Committee on Immunization (NACI) updated their *Recommendations on the Use of COVID-19 Vaccine(s)* to include guidance on the use of Moderna's vaccine, as well as an ethical analysis of the options for the delivery of a second dose of COVID-19 vaccines in the context of limited vaccine supply.

- There are ethical arguments on both sides, particularly given the escalating case counts in many jurisdictions. In this case, wider distribution of initial doses to protect more Canadians, especially those at increased risk of exposure and severe disease, could be beneficial. However, there is a high level of scientific uncertainty around the level of protection COVID-19 vaccines provide during an extended interval between vaccine doses.

- Currently NACI recommends the vaccine series be completed with the same COVID-19 vaccine and administered according to authorized or alternate intervals (time between first and second dose).
  - Moderna vaccine has an authorized interval of 28 days.
  - Pfizer/BioNTech vaccine has an authorized interval of 21 days, with an alternate interval of 28 days to allow for harmonization of immunization schedules.
  - The same product should be used for both doses; but if not available, the other mRNA vaccine
  - There is no maximum dose interval, but there are minimum intervals between doses (19 days for Pfizer or 21 days for Moderna).

- Negative impact on public confidence in the COVID-19 immunization program, the COVID-19 response, and vaccines in general could be impacted by constant change in vaccine policy.

- The lack of consistency in approaches between jurisdictions in the initial phases of roll-out of the COVID-19 immunization program could erode public trust in the recommendations and process.

**Annex A – International Strategies**

| Country | Strategy | Date | Source |
|---|---|---|---|
| Belgium | • Considering single-dose vaccine strategy in order to provide a first vaccination to the whole population before summer<br>• Experts are advising the second dose can be extended up to six months<br>• Currently, referring to Pfizer and Moderna | December 28, 2020 | The Brussels Times https://www.brusselstimes.com/news/belgium-all-news/health/147286/coronavirus-belgium-considers-single-dose-vaccination-strategy-pierre-van-damme-group-immunity-vaccine/ |
| Germany | Appears to be doing 2 doses on schedule | December 28, 2020 | |
| Denmark | Appears to be doing 2 doses on schedule | December 28, 2020 | |
| United Kingdom | • UK immunization campaign is shifting to provide as many (vulnerable) people as possible their first dose of vaccine<br>• The JCVI advises that vaccinating more people with the first dose is prioritised above offering others their second dose, to maximise benefits from the vaccination programme in the short term.<br>  • For the Pfizer-BioNTech vaccine, the second vaccine dose can be offered between 3 to 12 weeks after the first dose. For the AstraZeneca vaccine, the second dose can | December 30, 2020 | Press release - JCVI issues advice on the AstraZeneca COVID-19 vaccine. Public Health England.<br><br>https://www.gov.uk/government/news/jcvi-issues-advice-on-the-astrazeneca-covid-19-vaccine |

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|---|---|---|---|
| | be offered 4 to 12 weeks after the first dose.<br>• There are some data from the AstraZeneca vaccine trials suggesting that extending the time to the second dose may be better than having the second dose earlier. | | |
| United States | US- Fauchi<br>• On Friday Jan 1 2021, Dr Fauci told CNN that the United States would not be following in the UK's footsteps and would follow Pfizer and BioNTech's guidance to administer the second dose of its vaccine three weeks after the first.<br><br>US- CDC<br>• Second doses administered within a grace period of ≤4 days from the recommended date for the second dose are considered valid; however, doses administered earlier do not need to be repeated. The second dose should be administered as close to the recommended interval as possible. **However, there is no maximum interval between the first and second dose for either vaccine.** | December 30, 2021 | https://www.theguardian.com/world/2021/jan/02/dr-anthony-fauci-says-us-will-not-delay-second-doses-of-covid-vaccine<br><br>https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html |

**References for crude vaccine coverage targets for herd immunity**


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