

Public health statement on extension of the interval between first and second doses of COVID-19 vaccines in BC

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Summary:

There is good scientific evidence from clinical trials and real-world experience of a high degree of protection following a single dose of COVID-19 vaccine. Providing a first dose to as many people as possible saves more lives and avoids more cases and hospitalizations and supports a return to essential functions in our communities. This aligns with recommendations from the Canadian National Advisory Committee on Immunization. Completion of the 2 dose COVID-19 vaccination series remains important to provide long-term protection.

Situation:

- Initially, the pace of our COVID-19 vaccine supply was insufficient to vaccinate everyone right away and we had limited supply of COVID-19 vaccine.
- Prior to the vaccination campaign, there was minimal population immunity, leaving the vast majority of the BC population susceptible to COVID-19.
- While older adults and people with certain medical conditions are at increased risk of serious health outcomes and death due to COVID-19, adverse events have been observed in all age groups.

What we know about vaccines in general:

- It generally takes at least 2 weeks to mount an immune response to a vaccine dose.
- For most vaccines, the first dose contributes the most towards short-term protection. Additional doses extend protection over the long-term and are often given months or even years apart.
- For most vaccines, antibody levels decline gradually over time. They do not suddenly fall below protective levels. Even months or years later, another vaccine dose can boost antibodies to higher levels.
- For many vaccines, a longer interval to the second dose results in higher antibody levels after the series has been completed. Higher antibody levels are generally associated with longer duration of protection.
- Generally, vaccine manufacturing companies and national vaccine advisory bodies specify a *minimum* interval between vaccine doses but do not specify maximum intervals. Delay in receipt of a scheduled dose does not require restarting a series.

Vaccine efficacy¹ based on clinical trial data for COVID-19 vaccines approved for use in Canada:

- Both mRNA vaccines approved for use in Canada have high ($\geq 94\%$) efficacy against COVID-19 disease after the second dose; both vaccines are also highly efficacious after the first dose, at least in the short term (see Table below). For either mRNA vaccine, the second dose provides relatively little additional short-term benefit.
- [Moderna vaccine](#) efficacy is reported as 92% in the period from day 14 after dose 1 up to administration of dose 2.
- [Pfizer-BioNTech vaccine](#) efficacy is [estimated as 93%](#) in the period from day 14 after dose 1 up to administration of dose 2.
 - Pfizer reported vaccine efficacy of 52% from day 1 after dose 1 to before dose 2. This is an important reminder that it takes time for the full immune response to be mounted. Therefore, the risk of acquiring COVID-19 does not drop immediately after vaccination with the first dose (in the clinical trials, most COVID-19 infections were observed in the *first* 14 days, and would have included individuals who were infected and incubating the virus just prior to receiving the vaccine).
- The interval between the first and second doses was not studied for long periods in most clinical trials and thus the optimal interval between doses remains unknown.
- The duration of protection is unknown for either single or two-dose regimens since studies have only lasted a few months following vaccination to date.
- Not everyone in Pfizer's and Moderna's clinical trials received the second dose of vaccine exactly on schedule. The protocol allowed an interval of up to 42 days after the first dose. Therefore, reported results reflect vaccine administration within and beyond the recommended 21-28 day schedule.
- It is also important to note that because vaccines are not 100% efficacious, infections can still occur even after both doses. However, the risk of severe outcomes such as hospitalizations and death is significantly reduced after vaccination.
- AstraZeneca vaccine is made using a different technology (viral vector) but also requires two-doses for optimal protection.
 - The efficacy of one dose of the AstraZeneca vaccine is 76% from day 22 up to day 90 after it was administered.
 - Delaying the second dose for 3 months or more after the first dose [led to higher vaccine efficacy](#) (82%) compared with the administration of second dose within 6 weeks of the first (55%), suggesting an improved response with a longer interval between doses.

¹ Efficacy refers to how well vaccine works under controlled clinical trial conditions

Table. Summary of reported vaccine efficacy for COVID-19 vaccines approved for use in Canada

Vaccine	Efficacy (protection against COVID-19 disease defined as percentage of symptomatic COVID-19 cases prevented)	
	14 days after dose 1 and before dose 2 (95% CI)	7 to 14 days after dose 2 (95% CI)
Pfizer	Estimated 93% (69–98%)	95% (90–98%)
Moderna	92% (69–99%)	94% (89–97%)
Astra-Zeneca	76% (59-86%)*	67% (57-74%)

CI=confidence interval; * from day 22 up to day 90 after dose 1

Vaccine effectiveness² based on real-world data for COVID-19 vaccines approved for use in Canada:

- Growing scientific evidence from real-world experience shows a high degree of protection against symptomatic COVID-19 disease following a single dose of vaccine.
- In Canada, early vaccine effectiveness [results from BC](#) showed that the first mRNA vaccine dose reduced the risk of COVID-19 in long-term care residents and health care workers by 80% within 2-3 weeks of receiving the shot. Data from [Quebec](#) demonstrated similar results.
- More recently, [analysis of BC data](#) showed that a single dose of mRNA vaccine reduced the risk of infection by about two thirds, with protection minimally reduced against B.1.1.7 (Alpha) and P.1 (Gamma) variants.
- Globally, data from [England](#), [Scotland](#), [Israel](#), [Denmark](#), [South Korea](#), [Italy](#), and the [US](#) on the effectiveness of the vaccines show a strong level of protection, especially against more severe outcomes (like hospitalizations and death), following the first dose, albeit somewhat lower than what is reported based on clinical trial data. For a more comprehensive list, see this [table](#) of studies.
- Lower vaccine performance based on data from real-world settings is typical and expected, generally reflecting different population demographics, health status profiles, and setting.
 - In other words, characteristics of people who participate in clinical trials are not necessarily the same as characteristics of people who live in places where the vaccine is used in real life – they can be different in many ways, such as age distribution or the types of health conditions they have.
 - In addition, circulating viral strains in places where clinical trials were conducted could be different from strains circulating in places at the time when vaccine is being administered, which could also lead to differences in how well vaccine works.
- There is no indication to date that protection after the first dose declines rapidly over time.

² Effectiveness refers to how well vaccine works in the real world, i.e. outside of the clinical trial setting

BC's current approach:

- The goal of BC's COVID-19 immunization program is to minimize serious COVID-19 outcomes. To achieve this goal, BC has adopted the [recommendation](#) by the Canadian National Advisory Committee on Immunization (NACI) to extend dose intervals.
- Providing a first dose faster to as many people as possible saves more lives and avoid cases, hospitalisations and deaths.
- Completion of the COVID-19 vaccination schedule (currently set at 2 doses) remains important to provide long-term protection.

How BC's approach aligns nationally and compares internationally:

- In Canada, most jurisdictions have adopted NACI's [recommendation](#) and extended the interval for the second dose to up to 4 months.
- In the United Kingdom, Quebec, and Finland, the practice of extending the interval to the second dose up to 12 weeks (or even later) after the first dose has been in place for months. Argentina, Estonia, and Hungary also switched to this approach relatively more recently.
- [European Medicines Agency](#) and [World Health Organisation](#) support using a longer interval up to 6 weeks.
- The [US Centers for Disease Control and Prevention](#) has recommended that manufacturer's schedule should be followed whenever possible, but administration of second dose could be extended up to 6 weeks.

In conclusion

- On balance, using a longer interval between the first and the second dose is ethical and justifiable public health policy to maximize population level benefit in the context of limited supply and relatively high community transmission of the SARS-CoV-2 virus.
- Evaluation of the level of protection provided by COVID-19 vaccination will continue. Internationally, clinical trials will continue to follow vaccine recipients for at least 2 years.
- In Canada and BC, vaccine effectiveness will be assessed regularly and the approach to vaccination will be revisited as more scientific evidence becomes known and as vaccine supply increases.