Public health statement on deferral of second dose COVID-19 vaccine in BC

27 January 2021

Summary:
We have highly effective vaccines for COVID-19, but a limited supply. At this stage in the pandemic, providing a first dose to as many vulnerable people as possible will avoid more hospitalisations and deaths than providing a second dose within 21-28 days to a smaller number of people. A two-dose vaccination series remains important to provide long-term protection.

Situation:
- Current community transmission of SARS-CoV-2 in BC is relatively high. There is minimal population immunity, leaving the vast majority of the BC population susceptible to COVID-19.
- **Priority groups** are at increased risk of serious health outcomes and death following a COVID-19 infection.
- There will be limited vaccine supply in BC between January and March. Supply is expected to increase substantially between April and June.
- Our current vaccine supply is insufficient to vaccinate everyone in the priority groups by end of March if we hold back vaccine doses so that each individual receives 2 doses within 21-28 days.

What we know about vaccines in general:
- It takes about 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, or boosters, extend protection over the long-term and are often given months or even years apart.
- For most vaccines, antibody levels decline gradually over time and 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 booster dose results in higher antibody levels. High antibody levels are 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.

Clinical trials data for COVID-19 vaccines that have been approved in Canada:
- Both vaccines approved for use in Canada have high (>94%) efficacy against COVID-19 disease after the second dose; both vaccines are also highly effective after the first dose, at least in the short term.
• **Moderna vaccine** efficacy is estimated as 94% 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.
  o 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. The risk of acquiring COVID-19 does not drop immediately after vaccination (most COVID-19 infections were observed in the first 14 days, and some would have included individuals who were infected and incubating the virus just prior to receiving the vaccine).
• Single-dose vaccine efficacy can be approximated from clinical trial data submitted by the manufacturers to regulatory agencies by looking at the period from 14 days after dose 1 (by which point full immune response is expected) to dose 2:

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Efficacy (protection against COVID-19 disease)</th>
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<tbody>
<tr>
<td></td>
<td>14 days after dose 1 and before dose 2 (estimated)</td>
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<tr>
<td>Pfizer</td>
<td>93% (95% CI 69–98%)</td>
</tr>
<tr>
<td>Moderna</td>
<td>94% (95% CI 76–99%)</td>
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</tbody>
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*CI=confidence interval*

• Vaccine efficacy for both vaccines was reported to be above 94% after two doses. The second dose appears to provide little additional short-term benefit for either mRNA vaccine.

• Other considerations:
  o The interval between the first and second doses was not studied for periods longer than 6 weeks and thus the optimal interval between doses remains unknown.
  o The duration of protection is unknown for either single or two-dose regimens since studies have only lasted a few months to date.
  o Not everyone in Pfizer’s and Moderna’s clinical trials received the second dose vaccine exactly on schedule. The per-protocol analyses 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.
  o For the *AstraZeneca vaccine* (not yet approved in Canada, currently under review), which is made using a different technology, delaying the second dose to 3 months or more after the first dose resulted in higher antibody levels, suggesting improved response with a longer interval between doses.

• Overall, evidence to support decision making about optimal interval between doses is limited and expert opinion based on clinical and scientific judgement, as well as logistical, ethical, legal, and other considerations play a role.
BC’s current approach:

- The current approach aims to balance limited supplies with minimizing serious COVID-19 related outcomes in the population and will be revisited regularly as more scientific evidence becomes known and as vaccine supply increases.
- BC is fully committed to a two-dose regimen. A two-dose vaccination series remains important to provide long-term protection.
- Evaluation of the protection from COVID-19 vaccination will continue. Internationally, clinical trials will continue to follow vaccine recipients for at least 2 years. In BC, vaccine effectiveness will be assessed regularly after a sufficient number of people are vaccinated.

**Clinical Note**

You are the head of an emergency department of 100 staff. You know that vaccine protection in the short term exceeds 90% whether you get one dose (93%) or two doses (95%). We don’t know how long protection lasts thereafter for either one or two doses, but the pandemic risk is elevated now. We have enough vaccine supply now to give you 100 doses to last the winter (Jan-Mar). We expect to get more doses beginning in April. Based on the above, how would you allocate those 100 doses: would you give one dose to give 93% protection to all 100 staff or two doses to 50 staff who would get the maximal 95% protection?

Option 1 (single dose) would leave 7 of your staff unprotected (i.e. 100 * 0.07); Option 2 (two dose) would leave 52 of your staff unprotected (i.e. 50 + 50 * 0.05 = 52).

How BC’s approach compares nationally and internationally:

- Scientific advisory committees in the UK and QC recommended that a second dose deferral is permitted anywhere between 3 and 12 weeks (or even later) after the first dose – advice that governments of these jurisdictions have accepted.
- Canadian National Advisory Committee on Immunization (NACI), European Medicines Agency and World Health Organisation support deferral of the second dose up to 42 days (6 weeks) after the first dose. Denmark, France and the Netherlands have adopted this approach.
- US Centers for Disease Control and Prevention has recommended that manufacturer’s schedule should be followed as indicated whenever possible (21 days apart for Pfizer vaccine, 28 days apart for Moderna vaccine), but administration of second dose could be deferred up to 6 weeks.