Q&A regarding third dose planning for clinically extremely vulnerable – moderately to severely immunocompromised populations (Groups 1 & 2)

1. ***Why were these specific groups selected for a third dose?***

The groups we are recommending to receive a third dose of COVID-19 vaccines are those whose conditions and/or specific treatments generally result in much lower immune response after two COVID-19 vaccine doses than healthy individuals. Research has shown that a third dose will provide a higher proportion of these individuals with an immune response considered likely to be protective against COVID-19.

2. ***Why do the groups recommended for a third dose in BC differ from the National Advisory Committee on Immunization (NACI) recommendations?***

Third dose eligibility in B.C. is inclusive of all of the groups suggested for a third dose by NACI. The one major difference is that in B.C. we have made the decision to make patients who are on dialysis and/or with severe kidney/renal disease to be eligible for a third dose. This decision is based on rapidly growing literature that some patients undergoing hemodialysis had a poor antibody response to vaccinations (JAMA Network Open. 2021;4(9):e2123622. doi:10.1001/jamanetworkopen.2021.23622). We are also seeing within our BC data that dialysis patients who have completed a two dose COVID-19 vaccine series are being infected with COVID-19, indicating that their immune response may be insufficient. Other provinces, such as Quebec and Ontario, have been offering third doses to dialysis patients.

Radiation therapy is commonly used for patients with solid or haematological malignancies. Radiation therapy can suppress lymphocyte counts for months to years after treatment in a dose - and volume dependent fashion. After consultation with BC Cancer's radiation oncologists, it was decided that people who are undergoing radiation therapy would be eligible for a third dose to ensure that they develop a sufficient immune response.

There are also some slight differences in wording between the groups eligible in B.C. and those suggested by NACI. All patients included in the NACI recommendations are included in our planning. Our definition is clear and inclusive based on the clinical terminology and criteria we use here in B.C.

3. ***Why aren't all the CEV groups getting a third dose at this time?***

The clinically extremely vulnerable or CEV group described in March 2021 included those people who would be more at risk of serious illness or hospitalization if they got COVID-19. However, many of the people in this group do mount a good immune response to the vaccine and are protected.

Data now supports a recommendation to provide a third dose to a group of moderately or severely immunocompromised people whose immune response to a two-dose series is likely to be lower than the general population; a third dose will increase their chances of having a protective immune response with their initial vaccine series.

Within the CEV group, there are people whose conditions made them at risk of serious illness if they got COVID-19 but whose condition does not prevent them from getting good protection against COVID through an appropriate immune response from the two vaccine doses. CEV individuals with conditions which do not have a moderately or severely compromised immune response do not require a third dose to complete their vaccine series. The evidence of vaccine effectiveness is being looked at closely for all CEV subgroups and the general population. If the evidence changes over time that will be considered in the vaccine strategy as we move forward.

4. ***Are children who are moderately to severely immunocompromised receiving a third dose?***

Children aged 12 and above (born in 2009 and earlier) with the eligible conditions that make them moderately or severely immunocompromised will be offered a third dose. Clinical trials of COVID-19 vaccines for younger children (i.e., those born later than 2009) are still being conducted.

5. ***Who is included in the first and second group of moderate to severely immunocompromised to receive a third dose?***

People who are moderate to severely immunocompromised and require a third COVID-19 vaccine dose to complete their vaccine series are listed below. Eligible patients are born in 2009 or earlier.

- Have had a solid organ transplant. May include a heart, lung, liver, kidney, pancreas or islet cells, bowel or combination organ transplant.
- Since January 2020 have received an anti-CD20 drug for a malignant condition.
- Since March 2020, have received or are receiving systemic therapy (including chemotherapy, molecular therapy, immunotherapy, targeted therapies including CAR-T, monoclonal antibodies, hormonal therapy for cancer). This includes solid tumours as well as hematologic cancers within this time period.
- Since October 2020, have received or are receiving radiation therapy for cancer.
- Since September 2019, have had bone marrow or stem cell transplant or are still taking immunosuppressant medications related to transplant.
- Have combined immune deficiencies affecting T cells, immune dysregulation (particularly familial hemophagocytic lymphohistiocytosis) or those with type 1 interferon defects (caused by a genetic primary immunodeficiency disorder or secondary to anti-interferon autoantibodies).
- Have a moderate to severe primary immunodeficiency which has been diagnosed by an adult or pediatric immunologist and requires ongoing immunoglobulin replacement therapy (IVIG or SCIG) or the primary immunodeficiency has a confirmed genetic cause (e.g., DiGeorge syndrome, Wiskott-Aldrich syndrome).
- On dialysis (hemodialysis or peritoneal dialysis) or have stage 5 chronic kidney disease (eGFR <15ml/min or have glomerulonephritis and receiving steroid treatment.

- Prior AIDS defining illness or CD4 count ≤ 200/mm3 or CD4 fraction ≤ 15% or detectable plasma viral load since January 2021 or HIV infection and ≥ 65 years old or perinatally acquired HIV infection.
- On active treatment with immunosuppressive therapies such as:
    - Since January 2020, been treated with anti-CD20 agents: rituximab, ocrelizumab, ofatumumab, obinutuzumab, ibritumomab, tositumomab.
    - B-cell depleting agents taken since January 2020: epratuzumab, MEDI-551, belimumab, BR3-Fc, AMG-623, Atacicept, anti-BR3, alemtuzamab
    - Biologics taken since December 15, 2020: abatacept, adalimumab, anakinra, benralizumab, brodalumab, canakinumab, certolizumab, dupilumab, etanercept, golimumab, guselkumab, infliximab, interferon products (alpha, beta, and pegylated forms), ixekizumab, mepolizumab, natalizumab, omalizumab, resilizumab, risankizumab, sarilumab, secukinumab, tildrakizumab, tocilizumab, ustekinumab, or vedolizumab
    - Oral immune-suppressing drugs since December 15, 2020: azathioprine, baricitinib, cyclophosphamide, cyclosporine, leflunomide, dimethyl fumerate, everolimus, fingolimod, mycophenolate, siponimod, sirolimus, tacrolimus, tofacitinib, upadacitinib, methotrexate, dexamethasone, hydrocortisone, prednisone, methylprednisolone, or teriflunomide
    - Steroids orally or by injection on an ongoing basis since December 15, 2020: dexamethasone, hydrocortisone, methylprednisolone, or prednisone
    - Immune-suppressing infusions/injections taken since December 15, 2020: cladribine, cyclophosphamide, glatiramer, methotrexate

6. There are specific dates mentioned in the criteria for inclusion. Why were those dates chosen (e.g., January 2020 for anti-CD agents and January 2021 for active treatments)?

The decision to provide third doses to severely immunocompromised people to complete their vaccine series was made after evidence from the literature showed these groups would have less protection from two doses of the COVID-19 vaccines than the rest of the population. The evidence in the literature, guidelines from the National Advisory Committee on Immunization (NACI), and input from clinical experts caring for these people helped to inform these decisions. It is known that some medications can suppress the body's ability to make an immune response for some time after an individual stops taking them, and ongoing effects from the medication should be considered. If someone took one of those medications at an earlier date than listed, their response to their two-dose vaccine series should not be affected, and they should not require a third dose at this time to complete their series.

7. What is the recommended timeframe between the second and third dose?

The third dose should be offered at a minimum of 28 days (four weeks) following Dose 2. Most of the studies of a third dose were done with an interval of 2-3 months and evidence shows that an interval longer than the minimum 28 days between doses is likely to result in a better immune response. However, a longer interval also increases the period of time that an individual may be sub-optimally protected and risk factors for exposure (including the level of local community spread and circulation of variants of concern) and risk of severe disease should also be taken into account in the Dose 3 timing

decision. Even with a third dose, it is important that those who are severely immunocompromised take precautions to protect themselves against COVID.

We will keep learning about these vaccines in the coming months and years, which means we will adjust our vaccine plan accordingly if new evidence emerges.

8. Why isn't this third dose called a booster shot?

A booster shot is given in the situation where a full vaccine series has been given, it gives a good level of protection, but then that level of protection starts to decline, or wane. A booster then gets immunity back up to a desirable level of protection for an extended period of time.

However, a third vaccine dose is given to people whose conditions or treatments caused them to not develop the same level of immunity as the rest of the population after the recommended vaccine series (two doses). This is why a third dose is recommended for moderately to severely immunocompromised individuals, as a third dose will help increase their level of protection from COVID-19 to give them similar protection the rest of the population achieves after two doses. This group of immunocompromised people who have not been immunized against COVID-19 yet would now receive a total of three doses of vaccine. If booster doses are recommended at a later date, those would be considered separately, and would be given to 'boost' immunity that has declined or waned.

9. Should my family members get a third dose to protect me as a moderately to severely immunocompromised patient?

The good news is that people who are healthy should have ample protection from their two COVID-19 vaccine doses. At this time, the best thing family members can do to protect their vulnerable family member is to ensure they receive both doses of the COVID-19 vaccine and follow directions from public health.

10. What about if I am about to start a future treatment that could make me moderately to severely immunocompromised? Should I get a third dose now?

The decision to issue a third dose to someone who starts a new immunosuppressing treatment should be made by the patient on the advice of their health care team so that the timing is optimized to give the best protection possible.

11. Do I need to have a third dose to be considered fully vaccinated on my BC Vaccine Card?

No, the BC Vaccine Card is currently based on receipt of a two doses of any approved COVID-19 vaccine, separated by a minimum interval. It doesn't require a third dose even for those who are moderately to severely immunocompromised and recommended to receive a 3rd dose.