Clinical Guidance on COVID-19 Vaccines for People with Kidney Disease (Dialysis, Non-Dialysis with Advanced Disease, Glomerulonephritis)

This guidance is intended for nephrologists and other healthcare providers. It is based on known evidence as of November 8, 2022.

Background and Context

The risk of mortality from COVID-19 disease appears to be higher in patients with kidney disease. In a UK National Health Service study using a living risk predictor algorithm (QCOVID) for the risk of hospital admission and mortality due to COVID-19, chronic kidney disease (CKD) patients stage 5 (with or without dialysis or transplant) were found to be at increased risk of complications. Other risk factors included patients on oral steroids or immunosuppressive agents. The majority of these patients had multi-morbidities (including diabetes, heart disease, lung diseases) and many were over the age of 70.

Compounding these risk factors is the need for hemodialysis patients to travel to and receive dialysis care three times per week at hospital or community-based dialysis units where social distancing is more difficult and multiple exchanges with care teams and other patients occur.

This guidance is based on a review of the vaccines approved by Health Canada for the prevention of COVID-19 disease caused by the SARS-CoV-2 virus:

- **mRNA vaccines**: tozinameran (COMIRNATY, Pfizer-BioNTech), tozinameran and riltozinameran (COMIRNATY Bivalent original & BA.1, Pfizer-BioNTech), tozinameran and famtozinameran (COMIRNATY Bivalent original & BA.4/BA.4, 1Pfizer-BioNTech), elasomeran (SPIKEVAX, Moderna), elasomeran and imelasomeran (SPIKEVAX Bivalent original & BA.1, Moderna)

- **Viral vector vaccine**: ChADOx1-S (VAXZEVRIA, AstraZeneca), Ad26.COV2.S (JCVODEN, Janssen)

- **Recombinant protein vaccine**: COVID-19 Vaccine (recombinant protein, adjuvanted) (NUVAXOVID, Novavax)

- **Plant based virus-like particle (VLP) vaccine**: COVID-19 Vaccine ([VLP], recombinant, adjuvanted) (COVIFENZ, Medicago)

Currently, anyone in British Columbia (B.C.) who is aged 6 months and older is eligible for COVID-19 immunization. The mRNA vaccine SPIKEVAX (Moderna) and COMIRNATY (Pfizer-BioNTech) have been approved for children 6 months to 11
years of age, with young children getting a smaller dose of the same vaccine used for youth and adults.\textsuperscript{11} National Advisory Committee on Immunization (NACI) has released their statement for these age groups.\textsuperscript{12,13,14}

People who receive the mRNA vaccine (COMIRNATY [Pfizer-BioNTech] or SPIKEVAX [Moderna]) for their first dose, will be offered either mRNA vaccine for subsequent doses, with the exception of preferential recommendations based on age and immunosuppression.\textsuperscript{15,16} B.C. has taken the proactive step to expand booster doses for all individuals 5 years and older, not just those at high risk. However, it is particularly recommended for individuals 5-17 years of age who are at higher risk of severe illness due to COVID-19 infection.\textsuperscript{17,18} All booster doses will be mRNA vaccines.\textsuperscript{19} For those who are not able, or willing, to receive mRNA vaccines, Novavax is available as an alternative for individuals 18 years of age and older.

**Third doses as part of primary vaccine series:**

Recent studies demonstrate that some people who are immunocompromised develop an improved antibody response after a third dose of vaccine.\textsuperscript{20} Therefore, people who are moderately to severely immunocompromised in B.C. are eligible to receive a third dose of an mRNA COVID-19 vaccine as part of their primary vaccine series. NACI recommends the SPIKEVAX (Moderna) for children 6 months to 4 years of age.\textsuperscript{12,21} A minimum interval of 28 days between dose 2 and dose 3 is recommended for those eligible for a third dose. As per the B.C. Immunization Manual, SPIKEVAX (Moderna) is preferred for children 6 months to 4 years of age and COMIRNATY (Pfizer-BioNTech) is recommended for those 5-11 years of age. For individuals 12 years of age and older, SPIKEVAX (Moderna) is preferred for the third dose, but if it is unavailable (or if the individual prefers), COMIRNATY (Pfizer-BioNTech) may be provided.\textsuperscript{22}

Specifcics on current eligibility for a third dose may be reviewed here: [https://www2.gov.bc.ca/gov/content/covid-19/vaccine/register#immunocompromised](https://www2.gov.bc.ca/gov/content/covid-19/vaccine/register#immunocompromised)

**Booster doses:**

As part of the Fall 2022 booster dose program, B.C. is making plans to offer everyone 5 years and older a booster dose. NACI has been clear this approach will provide the best protection in the Fall and Winter when we’re all spending more time inside and respiratory illness is passed around our communities.\textsuperscript{23}

SPIKEVAX BIVALENT BA.1 (Moderna) (50 mcg) is the preferred product in B.C. for moderately to severely immunosuppressed individuals 12 years and older. SPIKEVAX original (Moderna) (100 mcg) primary series has been associated with a higher seroconversion rate among immunocompromised adult patients compared to COMIRNATY original (Pfizer-BioNTech) (30 mcg). In a general population of adults, booster vaccination with SPIKEVAX original (Moderna) (50 mcg) was also found to be more effective than COMIRNATY original (Pfizer-BioNTech) (30 mcg) during a period of Delta followed by Omicron variant dominance. However, these studies were conducted prior to the emergence of the Omicron BA.4/BA.5 Variant of Concern (VOC), and their applicability to all Omicron sublineages is uncertain.\textsuperscript{23} Health Canada has recently authorized an adapted version of the SPIKEVAX (Moderna) COVID-19 vaccine that targets the Omicron BA.4/BA.5 subvariants.\textsuperscript{24}

**Patients who have tested positive for COVID-19:**

Booster doses may be deferred in those who have tested positive for COVID-19 until 3-6 months from symptom onset or, for asymptomatic cases, from the time of the positive test.\textsuperscript{25} This suggested interval is based on immunological principles and expert opinion. When considering whether or not to administer vaccine doses following the suggested 3–
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6-month interval, biological and social risk factors for exposure (e.g., local epidemiology, circulation of VOCs, living settings) and severe disease should also be taken into account. As these intervals are to be used as a guide, clinical discretion is advised.

COVID-19 vaccination may be offered to individuals at any time following recovery from SARS-CoV-2 infection.

**Intervals between doses:**

Individuals requesting a shorter interval between doses should be informed that this actually offers less optimal protection, but their request for an earlier dose should be granted, without need for Medical Health Officer approval, provided the minimum interval between doses has been observed.26

The minimum interval between completion of the primary series, or a previous booster dose, and the Fall booster dose is 3 months. This revised minimum interval additionally applies to pregnant people and aligns with NACI’s updated guidance on COVID-19 vaccines for individuals who are pregnant or breastfeeding. The exception to this is JCVODEN (Janssen) for which the minimum interval is 8 weeks between the single dose of JCVODEN (Janssen) and the booster dose.27

**Other vaccines:**

**VAXZEVRIA (AstraZeneca)**

The VAXZEVRIA (AstraZeneca)7 vaccine program has been stopped in B.C. for first doses, unless there is a contraindication to the mRNA vaccines, or as advised by the Medical Health Officer or an allergist,15 due to infrequent (1:50,000) but serious Vaccine-Induced Thrombotic Thrombocytopenia (VITT) blood clotting events after the first dose.28 The Government of Canada is not securing additional VAXZEVRIA doses.

**JCVODEN (Janssen)**

The JCVODEN8 one-dose viral vector vaccine is now available in limited supply in B.C. However, mRNA vaccines are preferred over viral vector vaccines due to better effectiveness and immunogenicity of mRNA vaccines and the possible adverse effects specifically associated with viral vector vaccines (e.g., Thrombosis and Thrombocytopenia Syndrome [TTS]). A viral vector COVID-19 vaccine should only be considered when all other authorized COVID-19 vaccines are contraindicated or have been refused, due to the reduced effectiveness and the possible adverse effects associated with viral vector vaccines (e.g., TTS).

**NUVAXOVID (Novavax)**

NUVAXOVID9 is a different class of vaccination, a protein subunit vaccine that will give British Columbians another option to protect themselves against COVID-19 infection. NUVAXOVID may be offered to individuals for whom COVID-19 mRNA vaccines are contraindicated or have been refused.29 This vaccine is available to people aged 18 years and older. It is a two-dose vaccine and a limited number of doses will be available in B.C.30
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**COVIFENZ (Medicago)**

COVIFENZ is a different class of vaccination, a plant-based virus-like particle vaccine that will give British Columbians another option to protect themselves against COVID-19 infection. COVIFENZ is approved for people who are 18 to 64 years of age. It is a two-dose vaccine and a limited number of doses will be available in B.C. This product is not yet available in Canada.

**Is COVID-19 immunization recommended for people with kidney disease?**

COVID-19 vaccines should be encouraged for people with kidney disease and are not contraindicated, including those who have had a COVID-19 infection.

This recommendation is based on the following review:

- The National Advisory Committee on Immunization recommends that immunosuppressed individuals may be offered the vaccine if the benefits of vaccine outweigh the potential risks.
- Patients with kidney disease have an increased risk of hospitalization and death related to COVID-19 infection.
- The Canadian Society of Nephrology supports the use of COVID-19 immunization in this population and has advocated to all provinces and the federal government for the urgent prioritization of dialysis patients for COVID-19 vaccinations.
- Aside from a very rare risk of an allergic reaction (only a handful of people to date), there is no concern that the vaccine will cause kidney patients harm. There is only uncertainty regarding its effectiveness for those who are immunosuppressed.

While data specific to the safety and efficacy of COVID-19 vaccines in people with kidney disease is currently limited, there are data to suggest that the currently available COVID-19 vaccines have efficacy. The authors of this guidance agree that the benefits of COVID-19 immunization with these vaccines outweigh any theoretical risks of immunization.

**Is the COVID-19 vaccine efficacious and safe for people with kidney disease?**

People living with chronic kidney disease, including those on dialysis, are less likely to mount an adequate immune response to the COVID-19 vaccines, which puts them at higher risk for COVID-19 infection and severe complication. There is one study that suggests that a third dose of COVID-19 vaccine in immunocompromised patients can increase antibody levels. Small studies on third doses of the mRNA COVID-19 vaccines have shown that immunogenicity (immunity measured in the blood) may increase with a third dose.

There are currently no known factors that would predispose individuals with chronic kidney disease to different or more frequent adverse events associated with the vaccines when compared to the general population.
Are there any specific contraindications or exceptions for kidney patients?

Individuals who have had a severe allergic reaction to an ingredient of one type of COVID-19 vaccine are still able to receive future doses of the other type of vaccine. BCCDC has a list of the individual components and their purpose in the vaccines. For a complete list of components in the vaccine, consult the vaccine monographs found at: www.bccdc.ca/health-info/diseases-conditions/covid-19/covid-19-vaccine/vaccines-for-covid-19.

For individuals with a history of anaphylactic reaction to a previous dose of an mRNA COVID-19 vaccine, re-vaccination (i.e., administration of a subsequent dose in the series when indicated) may be offered with the same vaccine or the same mRNA platform if a risk assessment deems that the benefits outweigh the potential risks for the individual and if informed consent is provided. Prior to revaccination, consultation with an allergist or another appropriate physician (e.g., Medical Health Officer) is advised. If re-vaccination is going ahead, vaccine administration should be done in a controlled setting with expertise and equipment to manage anaphylaxis, with an extended period of observation of at least 30 minutes after re-vaccination.

Health Canada continues to monitor any adverse events following immunization through their post-authorization surveillance process.

There are no specific contraindications or exceptions for those with kidney disease. Health-care providers of those who have had a kidney transplant should refer to the clinical guidance on COVID-19 vaccines for people who have received an organ transplant.

Are there specific recommendations or considerations for safe and/or most effective administration?

Patients on kidney transplant waiting list

For those on the kidney transplant waiting list, there are some considerations related to immunization timing. It is recommended that immunization proceed as quickly as possible, given that the response to the vaccine is likely diminished in the immediate post-transplant period. Thus, completing immunization prior to transplant will be important for those high on the waiting list or those highly sensitized patients.

Patients on immunosuppressive therapy

People who take immunosuppressant/immunomodulating therapy were excluded in COVID-19 vaccine trials. Therefore, it is unknown if the COVID-19 vaccines are as efficacious in those who take immunosuppressants compared to those who are not considered immunosuppressed.

Kidney patients who take immunosuppressants (with or without transplants) should be informed there are not yet studies that examine the direct benefit and safety of COVID-19 immunization in this population, and that these
recommendations/clinical guidance are based on extrapolation of data from other viral infections, immunology of immunizations and from expert opinion.

The benefits of immunization are considered to outweigh the potential risks. Immunization is recommended in this group, preferably once ‘induction’ therapy has been completed.

People who may have severe systemic disease (lupus, vasculitis, etc.) who need to receive immunosuppressive therapy (Rituximab, Prednisone 20 mg/day or greater, Cyclophosphamide, Plasma Exchange) should complete that course of treatment before receiving the vaccine and should not delay treatment of their life threatening condition in order to be immunized. See special considerations for Rituximab and Prednisone below.

In general, it is preferred that patients complete immunization before starting high-dose immunosuppressive therapy, if possible, based on the timing of the treatments and the availability of vaccines at the time. This should ideally be at least 14 days after the second dose of any of the vaccines. Life-saving or prolonging therapy should not be delayed solely for the purposes of completing immunization.

Any other timing would require case-by-case assessment based on:

a. Risk of morbidity related to COVID-19 infection (including local prevalence of the pandemic, comorbidities that confer higher risk categories in general population, etc.).

b. Suboptimal immunity protection due to insufficient time between immunization and immunosuppressive therapy.

Special considerations for Hepatitis B vaccination and IGRA testing in the context of COVID-19 vaccination for hemodialysis patients

The following considerations and recommendations for HD care should be taken into account as hemodialysis patients begin receiving vaccination against COVID-19:

- COVID-19 vaccines can be given concomitantly with, or any time before or after any other indicated vaccine.36-39

- For new hemodialysis patients requiring TB screening:
  - Blood samples may be sent for IGRA testing if the patient has not had a COVID-19 vaccine dose in the last 28 days.
  - IGRA testing should be deferred until 28 days after the most recent COVID-19 vaccine dose.

Special considerations for immunotherapy: Rituximab and Prednisone

Patients receiving these agents may have a blunted immune response to vaccines in general that can extend to up to six months following treatment completion.

- For patients on rituximab, COVID-19 immunization should ideally be timed four to five months after their last infusion and 2 to 4 weeks prior to their next infusion, when possible, in order to optimize vaccine response.
However, in patients that require immediate infusion or who are unable to optimize timing of infusion product and vaccine, treatment is paramount. Patients should be counselled to get the vaccine as soon as it is available to them, but to not delay rituximab treatment for the sake of a vaccine appointment.

- For patients on **prednisone** 20mg/day or higher (or equivalents), consider waiting until the prednisone dose is tapered to below 20mg/day to receive both vaccine doses, but only if the time needed to taper the prednisone dose below 20mg/day is short. Pediatric patients on high-dose steroids should consult with their pediatric rheumatologist to decide on the best time to receive the vaccine.40

### References

1. BMJ 2020; 371:m3731. Living risk prediction algorithm (QCOVID) for risk of hospital admission and mortality from coronavirus 19 in adults: national derivation and validation cohort study. [https://www.bmj.com/content/371/bmj.m3731](https://www.bmj.com/content/371/bmj.m3731).
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