National Transplant Consensus Guidance on COVID-19 Vaccine

Introduction

The following document provides expert consensus guidance based on available data and national/international recommendations, that can be used by provincial organ donation organizations and regional transplant and donation programs to guide the management of COVID-19 vaccination in transplant recipients.

It is understood that each organization, program, and jurisdiction will develop their own policies.
This document was last updated on September 20 2023 and will continue to be updated as new evidence and information becomes available.

What do we know about COVID-19 and transplant recipients?

COVID-19 is a disease caused by the SARS-CoV-2 virus that is predominantly a respiratory virus but can cause multi-system disease. Several organ transplant recipients have contracted COVID-19 and symptoms have ranged from mild disease to the need for ICU care and death. COVID-19 appears to have a greater severity in transplant recipients but the role of immunosuppression is unclear. Many transplant patients are older and have comorbid conditions such as chronic kidney disease, diabetes, and heart/lung disease that increases the risk of severe COVID-19 disease. Lung transplant patients also seem to be at particularly high risk of severe disease.
As the COVID-19 landscape has changed with the emergence of new SARS-CoV-2 variants and subvariants, protective immunity to SARS-CoV-2, either through past infection or vaccination and the use of early antivirals/monoclonal antibodies in the treatment, the disease severity has significantly improved in the transplant population.

What is the status of COVID-19 vaccines in Canada?

There are several formulations of the COVID-19 vaccine that have been authorized by Health Canada.

<u>mRNA Vaccines:</u>

Two mRNA vaccines (Pfizer/BioNTech and Moderna) have been authorized by Health Canada for use. Both vaccines are composed of mRNA in a lipid nanoparticle and have specific storage conditions and are approved for the use in individuals 6 months of age and older.

The current vaccine is a bivalent vaccine and is available in the following formulations:
- Pfizer-BioNTech bivalent (Original and Omicron BA.4/BA.5)
- Moderna (Original and Omicron BA1 or BA.4/BA.5)

On September 12, 2023, Health Canada authorized an XBB.1.5-containing mRNA COVID-19 vaccine that should be avaible in Canada in October of 2023.

Protein subunit vaccine

Novavax, is a combination of a purified full-length SARS-CoV-2 recombinant spike protein nanoparticle and adjuvant Matrix-M. Two doses are authorized by Health Canada for primary series in 12 years and older and 1 dose as a booster for individuals 18 years and older.

Adenovirus Vector Vaccines:

Two vaccines (University of Oxford/AstraZeneca and Johnson & Johnson) have been authorized for use by Health Canada for individuals 18 years and older. Both vaccines are adenovirus vector vaccines that can be stored at 2 to 8 °C, similar to standard vaccines. However, these vaccines were available as an interim solution and are no longer marketed.

What are the side effects of COVID-19 vaccine?

Local and systemic side effects can occur after any of the vaccines. These include tenderness, swelling, and redness at the injection site. Relatively common systemic symptoms include fever, myalgias, and headache. In the Pfizer vaccine trial, systemic symptoms were more common in younger age groups and after the second vaccine dose. Similarly, in the Moderna vaccine trial, there were more systemic events after the second dose.

For the mRNA vaccines, myocarditis and pericarditis are reported side effects, although incidence remains rare. These have been more frequently reported in males, younger adults under 30 years of age, and after a second dose of vaccine. The risk might be lower with Pfizer-BioNTech. The majority of these cases have been mild.

Systemic symptoms from vaccination are similar to COVID-19 disease so patients receiving vaccine should be counseled on the possibility of these symptoms occurring in the first few days after each dose.

What data are available about the COVID-19 vaccine in transplant recipients?

Multiple studies have assessed the safety and the response of mRNA-based vaccines in solid organ transplant (SOT) recipients. These studies show a lower antibody response to vaccine among SOT recipients when compared to the general population with a similar safety profile. Despite the lower antibody response, many patients develop detectable SARS-CoV-2 specific T-cells in response to vaccine and therefore, SOT recipients might derive clinical benefit from the vaccine despite an absent antibody response. This is likely the reason why the vaccine remains effective in preventing severe disease in transplant recipients. Data show that despite breakthrough infection, fully vaccinated SOT recipients have a significantly lower risk of severe disease compared to partial or no vaccine. The vast majority of data are derived from mRNA vaccination. Although less is known about the immunogenicity of Novavax vaccine in transplant recipients, it is an non-live, adjuvanted recombinant protein subunit vaccine that can be used as an alternative to mRNA vaccination.

How many doses constitute a primary vaccine series in transplant recipients?

It is recommended that 3 doses of mRNA vaccine is a 'primary series' in adult transplant recipients. This is based on a published randomized controlled trial, and other observational studies in SOT recipients that have shown that a third dose of mRNA vaccine increased both SARS-CoV-2-specific humoral and cellular responses, with an acceptable safety profile. Despite full vaccination, some SOT recipients will continue to have poor immune responses and potentially remain unprotected. Therefore, it is critical that household contacts and healthcare workers be fully vaccinated. Moreover, transplant recipients should continue to follow infection control measures and be considered for early therapy.

The best studied timing for third dose vaccine is 2 months after the second dose. There is no need to do serology testing before or after a third dose of vaccine. This is because: a) there is no threshold currently that predicts protection; b) the antibody threshold for protection will vary depending on the circulating variant; c) T-cell responses may increase after vaccination despite a low antibody response ,and are shown to be conserved across variants.

Should transplant patients receive booster doses of vaccine ?

Data in the general population suggest waning vaccine effectiveness over time after primary series. A booster dose may provide more durable short term protection against infection, and severe disease in some populations with similar safety profile as with second or third doses. In SOT a 4th mRNA dose (booster) increased T cell response and BA.4/5-specific neutralization.

When and what type of booster vaccines should transplant patient consider?

Starting this fall, any XBB.1.5-containing mRNA COVID-19 vaccine can be given as a booster, regardless of previous type and number of COVID-19 vaccines. This should be a least 6 months after their previous vaccine dose (primary series or previous booster doses) or SARS-CoV-2 infection.

Can transplant patients receive a different type of vaccine for their subsequent and booster dose?

Persons who received Oxford/AZ vaccine may receive the mRNA vaccine for their subsequent dose. The mRNA vaccines' immune response appears to be better than for the adenoviral vector vaccines in transplant recipients. Having said this, mRNA vaccines are generally interchangeable

For optimum vaccine efficacy, it is recommended that:

- It is recommended that vaccines be administered in the pre-transplant setting, with the final dose at least 1 to 2 weeks prior to transplant whenever possible. Pre-transplant patients should follow the recommendation for the general population for primary series and t Booster.
- In post-transplant patients, wait at least 1 month after transplant to continue the vaccine series, regardless of induction therapy.
- In post-transplant patients, 3-doses mRNA vaccine constitute the primary series and patients should also receive subsequent booster doses >6 months later consistent with booster recommendations for high-risk groups. If the patient undergoes transplantation before the vaccines are complete, the remaining doses can be given starting at > 1 month after transplant.
- In patients undergoing active treatment for acute rejection, vaccination can be deferred for a 1-month period.
- Delay giving vaccine for at least 3 months after rituximab for improved efficacy.
- For patients with previous COVID-19 infection the next dose of vaccine should be given 6 months post-infection
- If a patient has received monoclonal antibodies such as sotrovimab for treatment of COVID-19 disease, COVID-19 vaccination should be deferred until at least 90 days after therapy.
- COVID-19 vaccines and other vaccines can be given on the same day, as well as co-administered within 14 days.
- Vaccine should not be given to patients that have had an anaphylactic reaction to a known component of the vaccine (i.e., polyethylene glycol in mRNA vaccines).
- Antibody testing is not recommended after vaccination. The levels of protective antibody and association with vaccine effectiveness are not known.
- Since efficacy is expected to be lower than the general population, it is strongly recommended that patients continue to practice infection control measures. In addition, household contacts of the transplant recipient should also be vaccinated when possible.

What are the recommendations for pediatric transplant patients?

Pediatric SOT recipients at least 6 months of age should be encouraged to receive a primary series of COVID-19 vaccine using the vaccine dose and product recommended for their age. Pediatric SOT recipients 6 months of age and over can receive XBB.1.5-containing mRNA booster doses of COVID-19 vaccine, with the product recommended for their age as recommended for immunocompromised children.

What are the national and international recommendations?

The CDC Advisory Committee on Immunization Practices (ACIP;U.S.) and the Joint Committee on Vaccination and Immunisation (JCVI; U.K.) prioritizes the immunocompromised population for vaccination. The AST (American Society of Transplantation) and ISHLT (International Society for Heart and Lung Transplantation) have also recommended COVID-19 vaccine for transplant patients.

The National Advisory Committee on Immunization in Canada states that complete three dose vaccine series and booster doses with a XBB.1.5-containing mRNA COVID-19 vaccine should be offered to individuals in authorized age groups, including those who are immunosuppressed. Efficacy may be lower in the immunosuppressed state so immunocompromised patients should continue to practice infection control measures against COVID-19 and receive early therapy until further notice.

Vaccination and masking of health care providers taking care of transplant patients

As the efficacy of vaccines is lower in SOT, and SARS-CoV-2 and other respiratory viruses continue to circulate, we strongly support vaccination for health care (HC) providers (physicians, surgeons and allied health professionals) involved in the care of solid organ transplant candidates and recipients; to decrease the risk of transmission to their patients. We also strongly support ongoing masking of HC providers when in the care of transplant patients.

What is the rationale for strongly recommending COVID-19 vaccines pre-transplant?

We strongly recommend that transplant candidates receive age appropriate vaccines including COVID-19 vaccine prior to transplantation. Individual organ groups where COVID-19 continues to have increased morbidity and mortality may have mandatory vaccine requirements. The rationale is as follows:

1. Solid organ transplant (SOT) candidates and recipients are at increased risk of severe COVID-19 disease and death compared to the general population – despite the general improvement in outcomes over time.
2. COVID-19 vaccines are immunogenic in patients with end stage renal disease on dialysis and patients with liver cirrhosis and can reduce COVID-19 infections while on the transplant waitlist.
3. COVID-19 vaccines are much less immunogenic when given in the post-transplant period.
4. SOT candidates and recipients have greater healthcare interactions and can spread SARS-CoV-2, when infected, to other inpatients or outpatients who are immunosuppressed or have chronic illnesses.
5. The Canadian Society of Transplantation, the American Society of Transplantation and the International Society for Heart and Lung Transplantation have recommended vaccination pre-transplant.

6. Transplantation involves scarce resources and organs are offered to those in which appropriate care of the organ is possible post-transplant.
7. Transplant candidates are assigned many responsibilities and requirements in the pre-transplant setting in order to be eligible for listing. Adherence to medical measures is an important factor when programs determine listing.
8. In general, if safety requirements cannot be met pre- and post-transplant, then alternative therapies for organ failure may be preferable (eg, dialysis, ventricular assist devices, medical management).
9. There may be additional considerations in pediatric populations as less data are available, but the vaccine is still strongly recommended in approved pediatric age groups.
10. Transplant candidates that choose not to be vaccinated need to be educated about the risk of severe COVID-19 including death post transplant.

Recommendations regarding the implementation of a pre-transplant vaccination mandate

Transplant centres may choose to have a pre-transplant vaccination mandate for specific organ groups. In this case, we recommend the following:

1. Any policy that makes the COVID-19 vaccine mandatory should be transparent and be announced with enough time for transplant candidates and healthcare staff to adhere to the mandate.
2. Candidates should have time to obtain their vaccines before the policy is implemented, as is done for healthcare professionals.
3. The healthcare system has a duty to maximize efforts at education and reassurance of vaccine hesistant candidates.
4. Transplant programs should endeavour to address any uncertainties, concerns, or misperceptions candidates may have through evidence-based patient education.
5. The vaccine policy should be reassessed on a regular basis.

Summary

Given that: (a) COVID-19 can cause serious illness in a transplant recipient, (b) transplant recipients often have comorbidities, (c) the safety of SARS-CoV-2 vaccine has been demonstrated, and (d) transplantation is not a contraindication to COVID-19 vaccine, we recommend that vaccine should be given to the pre- and post-transplant patient population. Based on available data, the potential benefits of vaccine outweigh any theoretical risks or concerns about graft dysfunction. Due to the severity of COVID-19 in this population, we also recommend that transplant patients remain a priority for ongoing booster doses of vaccine. Transplant patients should be made aware that they may not have adequate protection from vaccine alone and advised to continue infection control measures. In addition, household contacts of the transplant recipient should be vaccinated.

Disclaimer

The guidance provided is not meant to replace clinical judgement. The field also continues to evolve and as such the guidance may change over time. Any clinical decisions should be made in consideration of the latest available information.

Endorsement

These guidelines were written by the Canadian Society of Transplantation's Transplant Infectious Diseases Group, reviewed by the CST Ethics Committee and endorsed by the Canadian Society of Transplantation.

Version number	Effective date	Modification
1		
2		
3	June 1 2021	Addition of side effects Oxford/AZ vaccine with rare cases of thrombosis and thrombocytopenia Addition of pediatric approval of vaccines
4	August 18 2021	Addition of 3rd dose vaccine and addition of small risk of pericarditis as side effects in younger male adults
5	November 2021	Addition of booster dose (4th dose)
6	Jan 9 2022	Addition of rationale and implementation of vaccine mandate and health care vaccination
7	Septmber2023	Addition of Biavlent booster and XBB.1.5-containing mRNA Modification in mandate to strongly support but that certain organ groups can maintain vaccine mandate. Masking in transplant areas strongly recommended.

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