The rate of VITT in Canada appears to be extremely rare (1 in 100,000 doses of AstraZeneca), but ongoing investigations will improve estimation of the rate. VITT (also known as Vaccine-Induced Prothrombotic Immune Thrombocytopenia or VIPIT) is a rare adverse event that can follow adenovirus vector COVID-19 vaccines, including the AstraZeneca and Janssen COVID-19 vaccines. This condition is characterized by thrombosis (blood clots) and thrombocytopenia (low platelet levels) that appear 4-28 days after vaccination.

At this time, we don't know if certain patients are more likely to get VITT because it does not develop through the same process as more common types of bleeding or clotting problems. Most patients who developed VITT have been under 60 years old, and there have been more women than men diagnosed with VITT.

COVID-19 Vaccines in Yukon

11. Which COVID-19 vaccines are currently authorized for use in Canada?

There are currently four COVID-19 vaccines approved for use in Canada. Two are mRNA vaccines:

- Pfizer-BioNTech COVID-19 vaccine (additional information from manufacturer)
- Moderna COVID-19 vaccine (additional information from manufacturer)

Two are non-replicating viral vector vaccines:

- AstraZeneca/COVISHIELD vaccine (additional information from manufacturer)
- Janssen vaccine (additional information from manufacturer)

Yukon is using the Moderna COVID-19 vaccine because it can be transported between remote locations relatively easily. This makes it a good fit for Yukon and other northern territories. More information about the Moderna COVID-19 vaccine can be found here: Moderna COVID-19 vaccine: What you should know

Yukon has been using using the Pfizer-BioNTech COVID-19 vaccine to immunize youth between the ages of 12 and 17. More information about the Pfizer-BioNTech COVID-19 vaccine can be found here: Pfizer-BioNTech COVID-19 vaccine: What you should know

General questions

12. Will there need to be additional booster doses or a need for a yearly dose as given for influenza?

On September 28, 2021, the National Advisory Committee on Immunization (NACI) recommended a booster dose of a COVID-19 vaccine for all long-term care (LTC) residents and seniors living in other congregate settings who have completed a primary COVID-19 vaccine series.

On October 29, 2021, NACI recommended booster doses of COVID-19 vaccine for additional populations. As of November 1st, Yukon began offering booster doses in a phased approach starting with Yukoners ages 50 and older.

The booster dose should be offered at a recommended interval of at least 6 months after the primary series has been completed. The intent of a booster dose is to restore protection that may have decreased over time to a level that is no longer deemed sufficient in individuals who initially responded adequately to a complete primary vaccine series. In recent studies, a booster dose resulted in about a 10-fold reduction in confirmed infection rates. There are no data currently on the long-term effectiveness of booster doses so it remains unknown at this time how long benefit might last. Ongoing research will continue regarding booster doses for the general public.

Alongside a booster dose, NACI provided recommendations on an additional dose to complete a series for certain individuals. A third dose is different then a booster dose, and is given to immunosuppressed people so they can develop an adequate immune response. *In addition, the third dose is given four weeks after their second shot.*

September 2021, NACI recommended that "*for those who have not yet been immunized, moderately to severely immunocompromised individuals in the authorized age groups should be immunized with a primary series of three doses of an authorized mRNA vaccine*" and "*for those moderately to severely immunocompromised individuals in the authorized age groups who have previously received a 1- or 2-dose complete primary series, including*

those who received a mixed vaccine schedule, should be offered an additional dose of an authorized mRNA COVID-19 vaccine". In order to meet the criteria of this definition, the client must have one of the following conditions:

- Active treatment for solid tumour or hematologic malignancies
- Receipt of solid-organ transplant and taking immunosuppressive therapy
- Receipt of chimeric antigen receptor (CAR)-T-cell therapy or hematopoietic stem cell transplant (within 2 years of transplantation or taking immunosuppression therapy)
- Moderate to severe primary immunodeficiency (e.g., DiGeorge syndrome, Wiskott-Aldrich syndrome)
- Stage 3 or advanced untreated HIV infection and those with acquired immunodeficiency syndrome
- Active treatment with the following categories of immunosuppressive therapies: anti-B cell therapies (monoclonal antibodies targeting CD19, CD20 and CD22), high-dose systemic corticosteroids (e.g., a prednisone dose of ≥ 2 mg/kg per day or ≥ 20 mg per day if weight > 10 kg, for ≥ 14 days), alkylating agents, antimetabolites, or tumor-necrosis factor (TNF) inhibitors and other biologic agents that are significantly immunosuppressive (e.g., cancer chemotherapy, radiation therapy, cytotoxic drugs, calcineurin inhibitors, biological response modifiers and antibodies that target lymphocytes).

Multiple research and surveillance priorities are occurring with respect to the efficacy, effectiveness, immunogenicity, and safety of the COVID-19 vaccines. These priorities include population effectiveness and medium- and long-term duration of protection of the complete series of the COVID-19 vaccine. The level of protection provided by these vaccines against COVID-19 at one, two, or more years after vaccination will be determined with ongoing surveillance of vaccine effectiveness.

13. Once an individual is vaccinated will they need to continue practicing the recommended public health measures?

Yes. As of August 4, 2021, wearing a mask is no longer mandatory in indoor public spaces in the Yukon, however individuals are still encouraged to wear masks indoors to protect those who are not yet eligible to receive the COVID-19 vaccines or those who are higher risk. We should also continue to encourage practising the Safe 6 for the prevention and control of SARS-CoV-2 infection and transmission. There is currently not enough evidence on the duration of protection of COVID-19 vaccines in preventing infection and reducing transmission of SARS-CoV-2 to recommend discontinuation of public health measures. As we get more information about the impact of vaccination on COVID-19 transmission, there will likely be changes to the current prevention and control measures.

Please refer to Yukon.ca for the most up to date travel guidance.

14. How can I address false information clients have?

When addressing questions related to false immunization information, the first step is to acknowledge your clients' concerns. This helps build a trusting relationship between the client and health care provider.

Ex: "Thanks for bringing this to my attention. There is a lot of false information circulating and it can be difficult to distinguish from fact."

Discuss why the benefits of vaccination greatly outweigh the risks of Covid-19 infection and describe the trustworthiness of Canada's immunization system.

Ex: The vaccines are very effective at preventing severe illness, hospitalization, and death from COVID-19. Health Canada will only authorize a vaccine once the scientific and medical evidence shows the vaccine is safe and effective. The risks of a Covid-19 infection

Address the false information with a fact that is clear and relevant to help the client remember it.

Common concerns:

"I'm worried that these vaccines will change my DNA"

- Vaccines don't change your DNA. The mRNA vaccines cannot alter genetic material, its role is to teach the body to make an immune response against the COVID-19 pathogen.
- mRNA and DNA are different. The mRNA cannot enter the nucleus where DNA is stored and protected. Once the cell receives instructions from the mRNA to provoke an immune response, the mRNA will be destroyed.

"Can I get Covid-19 from the vaccine?"

- The vaccines cannot cause Covid-19 because they don't contain the virus that causes infection.
- mRNA vaccines do not contain the live virus to trigger an immune response, rather they teach your cells how to make antibodies that help fight off the real virus.

"mRNA vaccines are so new; how do we know they are not experimental?"

- Vaccines are rigorously tested and reviewed by Health Canada before they are approved for use.
- mRNA vaccines have been studied for years and could be developed faster because they were made in lab using materials that are easily available.
- Most adverse reactions to vaccines emerge within 6 weeks of immunization which is why vaccine manufacturers are required to produce 8 weeks of safety data.

Eligibility

15. Who is eligible and how are priority populations chosen to receive the COVID-19 vaccination?

NACI's Preliminary guidance on key populations for early COVID-19 immunization guides planning for the equitable allocation of COVID-19 vaccines once they are authorized for use in Canada. NACI recommends that key populations in whom vaccine is deemed safe and effective based on clinical evidence available at the time of vaccine availability should be prioritized for COVID-19 immunization. These groups are not mutually exclusive and may overlap. Sequencing of populations and sub-prioritization within these populations will be based on:

- A population-based risk-benefit analysis taking into consideration risk of exposure, risk of transmission to others, risk of severe illness and death, and the safety and effectiveness of vaccine(s) in key populations
- Vaccine supply (number of available vaccine types, number and timing of available doses, number of doses required)
- COVID-19 epidemic conditions when the vaccine(s) become(s) available

COVID-19 mRNA Vaccines

16. What are COVID-19 mRNA vaccines?

mRNA stands for messenger RNA and is the "blueprint" used by cells to synthesize proteins. The two COVID-19 mRNA vaccines approved in Canada use mRNA contained inside a lipid nanoparticle (LNP). The mRNA contains the synthetic nucleotide sequence that codes for the SARS-CoV-2 spike protein. After injection, the LNP is taken up by the body's immune system cells and, once inside the cell, the mRNA provides the instructions for the cell to manufacture the spike protein. After being manufactured, the spike protein exits the cell and becomes anchored onto the cell's surface. The immune system gets activated to recognize the spike protein as foreign and initiates an immune response. The mRNA is then cleared by the cell's natural mRNA degradation process. The estimated half-life for mRNA after injection is about 8-10 hours before the native RNases (enzymes that break up DNA) complete degradation in the body. The expressed spike protein continues to be present in the body for several days and during this time continues to stimulate the immune response. mRNA vaccines are not live vaccines and cannot cause infection in the host. The delivered mRNA does not replicate, does not enter the cell nucleus, or interact with or alter the recipient's DNA in any way.

Several mRNA vaccines are under development for other infections such as cytomegalovirus, human metapneumovirus, parainfluenza virus type 3, Zika and influenza viruses.

The manufacturing of mRNA vaccines began a decade ago. The process is cell-free, meaning it does not use human or other animal cells, and does not use vectors (like other viruses), animal products, preservatives, or adjuvants.

17. How effective is the Moderna mRNA vaccine against COVID-19 disease?

The estimated vaccine efficacy at least 14 days after Dose 2 was 94.1% (95% CI: 89.3 to 96.8%), with 11 confirmed COVID-19 cases identified among vaccine recipients (n=14,134) compared to 185 confirmed COVID-19 cases among placebo recipients (n=14,073). In the clinical trial involving adolescents between the ages of 12 and 17 (n=3,732), the vaccine was 100% effective against the development of COVID-19 14 days after Dose 2.

When stratified by age, vaccine efficacy against COVID-19 from 14 days after Dose 2 for those:

- 12 to 17 years of age = 100%
- 18 to 65 years of age = 95.6% (95% CI: 90.6% to 97.9%).
- > 65 years of age = 86.4% (95% CI: 61.4 to 95.2%).
- > 75 years of age = 100%, however this must be interpreted with caution as there were few cases identified in this group.

18. How effective is the Pfizer-BioNTech vaccine against COVID-19 disease?

The estimated efficacy at least 7 days after Dose 2 was 94.6% (95% CI: 89.9 to 97.3%), with 9 laboratory-confirmed symptomatic COVID-19 cases identified among vaccine recipients (n=19,965) compared to 169 cases among placebo recipients (n=20,172). The vaccine efficacy at least 14 days after Dose 2 in this population was comparable. In the clinical trial involving adolescents between the ages of 12 and 15 (n=2,260), the vaccine was 100% effective against the development of symptomatic COVID-19 7 days after Dose 2.

When stratified by age, vaccine efficacy against COVID-19 from 7 days after Dose 2 for those:

- 12 to 16 years of age = 100%

- 16 to 55 years of age = 95.6%
- > 55 years of age = 93.7%
- > 65 years of age = 94.7% (95% CI: 66.7 to 99.9%)
- > 75 years of age = 100% (95% CI: -13.1 to 100%), however this must be interpreted with caution as there were few cases identified in this group.
- In all subgroups stratified by "at-risk" status (presence of 1 or more comorbidities = 91%

19. How long does it take for immunity to develop following vaccination?

For both the Moderna mRNA vaccine and the Pfizer-BioNTech vaccine, SARS-CoV-2 binding and neutralizing antibodies were both induced by one dose of the vaccine and boosted by the second dose of the vaccine. Maximal immune response was seen 7 days after the second dose.

20. How long does immunity after vaccination last?

From the phase 3 clinical trials, the median period of follow-up of vaccine and placebo recipients was 2 months. Further clinical trials showed consistent efficacy at the 6 month mark.

Recent Canadian studies show that although two doses of mRNA vaccine elicit a strong initial antibody response in LTC residents, a majority of these individuals fail to demonstrate detectable neutralizing antibody titers at six months following the primary series. While the clinical significance of this is unclear, waning antibodies may indicate susceptibility to SARS-CoV-2 infection, while still being protected against severe outcomes.

Additional information about the duration of protection will continue to be gathered in the clinical trials, which will gather data for at least two years after the vaccination. Vaccine effectiveness information will be gathered from post-marketing surveillance evaluations including studies using the test-negative design in populations being targeted for early vaccination, such as health care workers.

Dosing and Scheduling

21. What if a client presents later than the recommended interval for the COVID-19 mRNA vaccines? How important is the timing for the second dose?

Vaccine history tells us that when further doses are required, the subsequent doses are designed to boost the immune response as well as to confer long-term immunity. NACI has spent a lot of time deliberating on the importance of timing the second dose according to manufacturer recommendations versus waiting for a longer period in order to reach as many people as possible with first doses given the limited supplies.

Our aim is to strike the best balance. On October 22, 2021 NACI recommended an 8 week interval between dose 1 and dose 2 of the COVID-19 vaccine primary series. This change was made in Yukon Immunization Manual shortly after the NACI recommendation.

NACI tells us that the short-term effectiveness from the first dose is likely very good, and that limited delays up to 4 months will not be expected to affect overall immune response. Vaccine history with other vaccines shows us that giving subsequent doses after the recommended interval does not compromise long-term immunity and may even improve it. We can be very confident therefore in the effectiveness of a 4 to 6-week interval between dose #1 and dose #2, and potentially even longer.

If administration of the second dose of the COVID-19 vaccine is delayed (8 weeks or longer), the second dose should still be provided as soon as possible. The series does not need to be restarted. In general, regardless of the time between doses, interruption of a vaccine series does not require the restarting of the series. Delays between doses do not cause a reduction in final antibody concentrations for most other vaccines requiring more than one dose in a series. Maximum protection may not be attained until the complete vaccine series has been administered.

22. What is the minimum interval for the second dose for each of the mRNA vaccines?

For optimal response, immunizers should follow the recommended intervals as much as possible. Doses given earlier than recommended may still be considered valid and need not be repeated if minimum intervals are observed.

23. What are the differences in the primary series schedules, doses and administration between the two COVID-19 mRNA vaccines being used in the Yukon?

Product	Pfizer-BioNTech COVID-19 vaccine	Moderna COVID-19 vaccine
Authorized for use	12 years of age and older	12 years of age and older**
Dose	0.3 mL (30 mcg of mRNA)*	0.5 mL (100 mcg of mRNA)
Route	Intramuscular (IM)	Intramuscular (IM)
Primary Series Schedule* **	2 doses, 8 weeks apart	2 doses, 8 weeks apart
Diluent Required	Yes Dilute with 1.8 mL of sodium chloride (0.9% NS)	No Ready for use
Formats available	Multi-dose vial (6 doses) After dilution, vaccine must be used within 6 hours	Multi-dose vial (10 doses OR 14 doses) Must be used within 24 hours of first puncture

*It is important to note that the dose for this vaccine (0.3 mL) is unique compared to that of most routine vaccinations. Special precautions should be taken to ensure the correct dose is taken from the multi-dose vial.

**In the Yukon Moderna vaccine will only be offered to adults 18 years of age and older.

*** A third dose may be required to complete a series in certain immunocompromised groups. See criteria here.

24. Can other vaccines be administered at the same time as COVID-19 vaccine?

As of Aug 24, 2021 in the Yukon, COVID-19 vaccines can be administered concomitantly or at any time before or after the administration of inactivated or live vaccines. On Sept 28, 2021 NACI recommended COVID-19 vaccines may be given at the same time as, or any time before or after, other vaccines, including live, non-live, adjuvanted or unadjuvanted vaccines.

Administration

25. What if there is remaining vaccine in the vaccine vial after 10 or 14 doses from the Moderna vaccine vial, or 6 doses from the Pfizer-BioNTech vaccine vial have been removed?

Some vials have been shown to have an additional dose. If there is enough vaccine left in the vial for a complete dose (0.5 mL Moderna, 0.3mL Pfizer), another dose can be drawn and administered.

If there is less than a full dose of vaccine remaining in a vial, discard the leftover vaccine. It is not recommended to draw vaccine from two separate vials to make up a full dose.

26. Are the COVID-19 mRNA vaccines interchangeable?

On June 1, 2021, NACI updated their recommendations on the interchangeability of COVID-19 vaccines. These recommendations are based on current scientific evidence and NACI's expert opinion. NACI recommends that people who received a first dose of an mRNA vaccine should be offered the same mRNA vaccine for their second dose. If the same mRNA vaccine is not readily available or unknown, another mRNA vaccine can be considered interchangeable and should be offered to complete the vaccine

series at least 8 weeks after the first dose. This series should be considered valid, without the need to restart a two-dose series with a new product. The spike proteins that encode the authorized mRNA vaccines have the same sequence and are stabilized in the same manner to remain in pre-fusion confirmation. Other vaccine components such as the lipid nanoparticle may be different between the vaccines.

People who received a first dose of the AstraZeneca/COVISHIELD vaccine may receive either an Astra/Zeneca/COVISHIELD vaccine or an mRNA vaccine for their second dose, unless contraindicated. This recommendation considers the risk of severe blood clots with low blood platelets associated with the viral vector vaccine (AstraZeneca) but not the mRNA vaccines, the possibility of increased short-term side effects when mixing COVID-19 vaccine schedules, and all available data on the immune responses produced by a first dose of the AstraZeneca vaccine follow by a second dose of an mRNA vaccine.

Getting the same vaccine for first and second dose or a mixed schedule are both considered valid options, and both will count as a completed series. More results from ongoing studies, including Canadian data, on mixing vaccine schedules are expected in the coming months.

27. Are prophylactic oral analgesics or antipyretics recommended before or at the time of vaccination?

Prophylactic oral analgesics or antipyretics (e.g., acetaminophen or non-steroidal anti-inflammatory drugs such as ibuprofen) should not be routinely used before or at the time of vaccination. While these medications may be used after vaccination, it is not known whether these may blunt the antibody response to vaccine. This phenomenon has been observed in some studies of other vaccines in children, although the clinical significance is still unknown.

If an individual has taken one of these medications before immunization, they should still be immunized.

Oral analgesics or antipyretics may be used for the management of symptoms attributed to the vaccine (e.g., pain, fever, headache, myalgia) if the symptoms cannot be addressed using non-pharmaceutical strategies.

28. Is there a recommendation on the size of needle to be used to dilute the Pfizer-BioNTech vaccine?

Yes. A 21-gauge needle or narrower is recommended to prevent a larger opening in the vial stopper that may allow the vaccine to leak.

29. When diluting the Pfizer-BioNTech vaccine, is there a need to expel air from the vial to equalize the pressure?

Yes. After adding the diluent into the vaccine vial, withdraw 1.8 mL of air from the vaccine vial into the empty diluent syringe prior to removing the needle and attached syringe from the vial. This will prevent loss of vaccine from the vial through forceful expulsion under pressure.

Special Considerations

30. Are there groups in which the approved vaccines have not been specifically studied?

People who are pregnant or lactating, immunocompromised, or those with autoimmune disorders were originally not included in large numbers as participants in early clinical trials. Additional evidence is now available from real-world use of COVID-19 vaccines, primarily mRNA vaccines, in these populations. For example, recently published safety analyses included 35,691 pregnant women in the United State who received an mRNA COVID-19 vaccine without any obvious safety signals. This evidence showed that COVID-19 vaccines are safe in these populations so NACI recommendations for these populations are now the same as for the general adult population.

31. How should I counsel my pregnant patients about COVID-19 vaccine?

The latest NACI recommendations states that an mRNA COVID-19 vaccine is preferentially recommended for individuals who are pregnant. NACI's latest statement includes the following:

- *NACI preferentially recommends that a complete two-dose vaccine series with an mRNA COVID-19 vaccine (Pfizer-BioNTech, Moderna) should be offered to individuals in the authorized age group, including those who are immunosuppressed, have an autoimmune condition, are pregnant or are breastfeeding. If they are not able to receive an mRNA vaccine, for example because of an allergy, another authorized COVID-19 vaccine should be offered. mRNA vaccines are preferred for use during pregnancy, due to recently published data from a study in the United States indicating the mRNA COVID-19 vaccines are safe in pregnant women. In addition, treating Vaccine-Induced Immune Thrombotic Thrombocytopenia (VITT) during pregnancy, should it occur following the administration of a viral vector vaccine, can be complex.*

There is no concerning red flag or hypothesized mechanism for potential harm associated with the administration of an mRNA vaccine during pregnancy. Other inactivated vaccines have a long history of administration during pregnancy without concern as to adverse effects.

Other considerations should include the potential for more severe COVID-19 disease. The majority of individuals, including pregnant women, who become infected with COVID-19 have mild symptoms or are asymptomatic. However, current data suggest that symptomatic pregnant patients with COVID-19 are at an increased risk of severe illness when compared to their non-pregnant peers. In addition, pregnant patients with underlying co-morbidities such as diabetes or obesity may have an even higher risk of severe illness.[1]

[1] https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2020/12/vaccinating-pregnant-and-lactating-patients-against-covid-19

Both the Society of Obstetricians and Gynaecologists of Canada and the American College of Obstetrics and Gynecology have published statements on the use of COVID-19 vaccines in pregnancy. Both medical groups acknowledge the unvaccinated pregnant individual is at risk for acquiring COVID-19 and they are at an increased risk for severe outcomes compared to non-pregnant individuals. They recommend that pregnant individuals should be offered vaccination at any time during pregnancy or while breastfeeding, if no contraindications exist.

32. My patient is considering pregnancy and wondering about timing vis-a-vis COVID-19 vaccine. What should I advise?

The latest NACI statements also address this question. There are several points that the NACI statement covers to guide advice to your patients considering pregnancy. The following are direct comments from the NACI statement:

- *Recently published safety data suggests mRNA vaccine administration within 30 days of conception is safe.*
- *Individuals who become pregnant during their vaccine series or shortly thereafter should not be counselled to terminate pregnancy based on having received the mRNA vaccine.*
- *Vaccine recipients and health care providers are encouraged to report COVID-19 vaccine during pregnancy or breastfeeding to the local public health authority as well as to the vaccine manufacturer for follow-up. Active surveillance in these vaccine recipients is strongly encouraged. NACI will monitor the evidence as it evolves, and update recommendations as needed.*

The Society of Obstetricians and Gynaecologists of Canada recommends that vaccination series should be completed if pregnancy is detected during their vaccine series. Ideally, an individual would be immunized against COVID-19 ahead of conception to benefit from maximal vaccine efficacy throughout the entire pregnancy.