BRITISH COLUMBIA
CENTRE *for* EXCELLENCE
in HIV/AIDS

BC Centre for Excellence in HIV/AIDS CDET Committee Statement Update on the use of COVID-19 vaccines in Persons Living with HIV

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1) Recommendation
2) Background
    a) COVID-19
    b) Health Canada approved vaccines
    c) Vaccine efficacy
    d) Vaccine safety
3) COVID-19 vaccines and HIV
4) Priority Populations for vaccine coverage in British Columbia
5) Contraindications
    a) Allergic reactions
    b) AstraZeneca vaccine
    c) Janssen vaccine
6) Precautions
    a) Allergic reactions
    b) Pregnancy and breastfeeding
    c) Acute febrile illness
7) References

1) Recommendation:

People living with HIV (PLWH) aged 18 years or older should be vaccinated for COVID-19 if they meet current Public Health criteria for priority groups and if they have no contraindications (see below). These vaccines are not expected to be associated with more serious or different adverse events among PLWH or other immunocompromised individuals. While the evidence is mixed, PLWH may be at increased risk of serious illness due to COVID-19, and in the absence of contraindications should receive any of the COVID-19 vaccines currently approved in Canada as appropriate for their age group, regardless of CD4 count (i.e.: Pfizer-BioNTech, Moderna, AstraZeneca, and Janssen vaccines).

PLWH who have CD4 counts <200 cells/μL or are not virologically suppressed should be counselled regarding the unknown efficacy and safety of the vaccines given that such subjects were not included in the vaccine licensing studies.

2) Background:

a) COVID-19

SARS-CoV-2 emerged in late 2019. The virus was named SARS-CoV-2 because of its similarity to the coronavirus responsible for the illness known as severe acute respiratory syndrome (SARS-CoV). This virus (SARS-CoV-2) is responsible for the clinical disease

COVID-19. The SARS-CoV-2 spike glycoprotein (S), which is a main target for neutralizing antibody, binds to cellular receptors to initiate infection. Disease symptoms may vary; however, respiratory infection is most common, with outcomes including pneumonia and acute respiratory distress syndrome (ARDS), leading to multiorgan failure and death (1). Morbidity and mortality are most strongly correlated with age, being highest in those with increasing age above 50 years, and particularly high above 80 years. Increased risk is also associated with additional medical comorbidities such as diabetes, hypertension, obesity and cardiovascular disease (2, 3).

b) Health Canada approved COVID-19 vaccines

Currently, there are 4 COVID-19 vaccines approved for use in Canada; 2 are mRNA vaccines and 2 are viral vector vaccines. The results of safety and immunogenicity studies for all 4 vaccines provided the basis for proceeding with efficacy and safety studies which are summarized below. Attempts to draw efficacy comparisons between the vaccines is limited by the different study designs, vaccinee populations, geographic location and prevalence of SARS-CoV-2 variants.

c) Vaccine Efficacy

i) Efficacy against virologically confirmed symptomatic COVID-19 infection in randomized controlled trials (RCTs)

- **The Pfizer-BioNTech (BNT162b2 mRNA) vaccine** consists of a modified messenger RNA (mRNA) molecule enclosed in a lipid nanoparticle. The mRNA encodes the SARS-CoV-2 spike protein. In a phase 2/3 clinical trial in 37,706 adults (age 16 years or older) randomized to receive either the active vaccine or placebo, receipt of the BNT162b2 mRNA vaccine, administered as two doses 21 days apart was found to have an efficacy for prevention of symptomatic, laboratory-confirmed COVID-19 of 95% (95% Credible Interval [CI] 90.3 to 97.6%) (4). Outcomes were similar across age groups. Individuals with underlying immune suppressive conditions or using immune suppressive therapy were excluded from study participation; however, PLWH on stable, effective antiretroviral therapy were included (see below).
- **The Moderna mRNA-1273 vaccine** also consists of mRNA encoding the SARS-CoV-2 spike protein and is enclosed in a lipid nanoparticle. A phase 3 trial involving 28,207 individuals randomized to receive vaccine or placebo dosed as two doses 4 weeks apart demonstrated efficacy of 94.1% (95% CI 89.3 to 96.8%) (5). When stratified by age group the efficacy was 95.6% (95% CI: 90.6 to 97.9%) for participants 18 to <65 years, and 86.4% (95% CI: 61.4 to 95.5%) for participants ≥65 years of age.
- **The AstraZeneca ChAdOx1 nCoV-19 vaccine (AZD1222)** consists of a replication-deficient chimpanzee adenoviral vector (ChAdOx1), containing the SARS-CoV-2 structural surface glycoprotein antigen (spike protein; nCoV-19). An interim analysis of the combined data from 4 randomized controlled trials (RCTs) conducted in Brazil, South Africa, and the UK included 11,636 participants who

received two doses of either AZD1222 or control (meningococcal quadrivalent conjugate vaccine or saline), 28 days apart. Overall vaccine efficacy beyond 14 days after the 2nd dose was 70.4% (95% CI 54.8 to 80.6%) (6). The efficacy was higher at 81.3% (95% CI 60.3-91.2) for those participants who had a longer (≥12 weeks) prime-boost interval between 1st and 2nd doses compared to the 55.1% (95% CI 33.0-69.9) level of protection afforded by the shorter vaccination interval (≤6 weeks) (7).

- **The Janssen (Johnson and Johnson) COVID-19 vaccine (Ad26.CoV2.S)** is a replication-incompetent adenovirus serotype 26 (Ad26) vector encoding a full-length SARS CoV-2 spike (S) protein. The Ad26 vector is used in the Ebola vaccine that has been approved in Europe. Interim results from an international RCT of ~40,000 participants given a single dose of either Ad26.CoV2.S or placebo demonstrated vaccine protection at ≥14 and ≥28 days after vaccination of 66.3% and 65.5%, respectively (8).

ii) Efficacy against hospitalization and severe disease in RCTs.
Vaccine protection was generally higher for these less-common endpoints than the efficacy for prevention of symptomatic, laboratory-confirmed COVID-19 in the above-mentioned RCTs.

- **Pfizer BNT162b2 vaccine**. After the first dose, there were 10 cases of severe COVID-19, 9 of whom were in the placebo arm (4).
- **Moderna mRNA vaccine**. After ≥14 days following the 2nd dose, there were 30 cases of severe COVID-19, all in the placebo arm (5).
- **AstraZeneca ChAdOx1 nCoV19 vaccine**. After ≥21 days following the first dose there were 15 hospitalizations, all of whom were in the placebo arm (7).
- **Janssen vaccine Ad26.CoV2.S**. After ≥14 days or ≥28 days following this single dose vaccination, protection against hospitalization was present for 93.1% (95% CI, 71.1 to 98.4%) and 100% (95% CI, 74.3 to 100%), respectively (8).

iii) Efficacy against infection, hospitalization and severe disease in 'real world' surveillance. Factors that contribute to observed differences in vaccine efficacy and safety outside the context of a clinical trial include: i) differences in the characteristics of the populations vaccinated; ii) limited ability to collect data for clinical outcomes (e.g. hospitalization or death) by indirect means such as regional health care databases; iii) reliance upon passive rather than active data collection on adverse drug reactions (ADR); and iv) the greater likelihood of identifying rare ADRs with a much larger number of vaccinees.

- **Pfizer BNT162b2 vaccine**.
  - In **Israel**, the protection levels against symptomatic infection ≥14 days and ≥21 days after the 1st and ≥7 days after the 2nd dose were 57%, 91%, and 94%, respectively (9,10). The protection levels against hospitalization at >14 days

after the 1st and after >7 days after the 2nd dose were 74% and 87%, respectively (9).

- In **Scotland**, the protection provided against hospitalization at ≥28-34 days after the 1st dose was 85% (11).

- **AstraZeneca ChAdOx1 nCoV19 vaccine**.
  - In **Scotland**, the protection provided against hospitalization at ≥28-34 days after the 1st dose was 94% (11).

iv) Efficacy against both asymptomatic and symptomatic infection

- **Moderna mRNA vaccine and Pfizer BNT162b2 vaccine**.
  - In the **USA**, 3,950 health care and other frontline workers were given either the Moderna or Pfizer mRNA vaccine and then followed with self-collected mid-turbinate nasal swabs weekly for viral polymerase chain reaction (PCR). Protection levels against infection (with or without symptoms) after ≥ 14 days following the 1st and 2nd dose were 80% and 90%, respectively (12).
- **AstraZeneca ChAdOx1 nCoV19 vaccine**. In England and Wales, 129,529 weekly self-swabs yielded 435 positive cases among those who were asymptomatic or with unreported symptoms, corresponding to a vaccine efficacy of 7.8%, in contrast to overall vaccine efficacy of 70.4% for symptomatic COVID-19 (6).
- **Janssen vaccine (Ad26.CoV2.S)**. The vaccine appears to provide protection against the development of asymptomatic COVID-19 infection based upon documented seroconversion to a non-spike protein 71 days after vaccination among 0.7% of the vaccine group compared to 2.8% of the placebo group (estimated vaccine efficacy 74.2%; 95% CI, 47.1 to 88.6%) (8).

v) Efficacy against SARS-CoV-2 Variants of Concern (VOC).

- **Pfizer BNT162b2 vaccine.** Efficacy in regions where the UK B.1.1.7 VOC is the predominant virus such as the UK and Israel was 85% and 87%, respectively (9,11). Preliminary data from South Africa where the B.1.351 VOC is predominant suggests 91% protection against infection (13).
- **AstraZeneca ChAdOx1 nCoV19 vaccine.** Efficacy against infection with the UK B.1.1.7 VOC was 70.4% (14), but only 10% against the South African B.1.351 VOC (15).
- **Janssen vaccine (Ad26.CoV2.S).** Efficacy against infection was 72% for non-VOCs, 66% in Brazil (predominantly the Brazil P.1 VOC), and 57% in South Africa (predominantly B.1.351 VOC) (16).

d) Vaccine Safety

The most comprehensive safety monitoring system in US history has been implemented during the initial implementation phase of the COVID-19 vaccination program, which

depends upon the passive *Vaccine Adverse Event Reporting System* (VAERS) and also an active surveillance system (*v-safe*). All of the COVID-19 vaccines are frequently associated with mild local painful injection site reactions and/or constitutional symptoms such as fatigue, headache, myalgias, chills and fever. These reactions may be more prominent after the 2nd dose with the Pfizer and Moderna vaccines (17). The symptoms often resolve within 1-2 days and seldom persist beyond 7 days (18,19,20,21).

None of the 4 COVID-19 vaccines which are approved in Canada are considered to be "live virus vaccines", and consequently they are not anticipated to be associated with increased risks of adverse effects such as vaccine-virus induced infection in immunocompromised people. The 2 viral vector vaccines have been constructed with adenoviruses that have been modified so that they are unable to replicate. Previously, the Step and Phambili studies evaluated the efficacy of an adenovirus type 5 (Ad5) vector-based vaccine for the prevention of HIV disease, both of which demonstrated an increased risk of HIV-1 acquisition among vaccinated men (22). A subsequent National Institutes of Health (NIH) consensus conference warned that non-HIV vaccine trials that used similar vectors in areas of high HIV prevalence could lead to increased risk of HIV acquisition in the vaccinated population (23). This is relevant to the recent development of the recombinant adenovirus type-5 (Ad-5) vectored COVID-19 vaccine expressing the spike glycoprotein, from CanSino Biologics, China (22). However, neither of the two adenovirus vector COVID-19 vaccines approved in Canada use the type-5 adenovirus.

i) Pfizer BNT162b2 vaccine

- **Anaphylaxis**. During early surveillance following Emergency Use Authorization (EUA) in the US, between December 14-23, 2020 there were 21 reports of anaphylaxis among 1,893,360 first doses of the Pfizer BNT162b2 vaccine (11.1 cases per million doses). Among these cases, 85% occurred within 30 minutes of vaccination. Ninety percent were treated with epinephrine and no anaphylaxis deaths were reported (24).

ii) Moderna mRNA-1273 vaccine

- **Anaphylaxis**. During early surveillance following Emergency Use Authorization (EUA) in the US, between December 21, 2020-January 10, 2021, there were 10 reports of anaphylaxis among 4,041,396 first doses of the Moderna mRNA-1273 vaccine (2.5 cases per million doses). Among these cases, 90% occurred within 15 minutes of vaccination. All 10 cases were treated with epinephrine and no anaphylaxis deaths were reported (25).
- **Delayed injection-site reactions**. Such reactions were reported in 0.8% of vaccinees after the 1st dose, defined as having an onset ≥8 days after the vaccination (5). A recent report describes 12 patients with large local reactions with a median onset of day 8 (range 4 to 11). Five of these patients had grade 3 plaques (≥10 cm in diameter). Symptoms resolved a median of 6 days after onset,

and all patients completed the 2nd dose of vaccine, although 50% had recurrence of similar symptoms (26).

iii) AstraZeneca ChAdOx1 nCoV19 vaccine

- **Vaccine-induced immune thrombotic thrombocytopenia (VITT).** The overall rate of thromboembolic events in the few weeks following ChAdOx1 nCoV19 vaccination is similar to that of the general population. However, rare types of thrombotic events such as cerebral sinus venous thrombosis (CSVT) and splanchnic-vein thrombosis associated with thrombocytopenia have been reported between 4-30 days (27) after vaccination, predominantly in women below the age of 60 years (28). However, in the UK experience of VITT there has been a broader age range (18-93 years) and a somewhat lower level of female predominance of 58%. It has also been referred to as thrombosis-thrombocytopenia syndrome (TTS). The frequency of this complication may be in the range of ~ 1/100,000 (29). Clinically, it resembles autoimmune heparin-induced thrombocytopenia (30). While awaiting further investigation of this rare complication, on March 29th, 2021 the National Advisory Committee for Immunizations (NACI) recommended that the AstraZeneca vaccine should not be used for Canadians under the age of 55 years (31). On April 23rd, 2021 the NACI recommendation was revised and now approves the use of the vaccine for those aged 30 years and older (32).

iv) Janssen Ad26.CoV2.S vaccine

- **Vaccine-induced immune thrombotic thrombocytopenia (VITT).** By April 12th, 2021, 6.8 million people had received the vaccine and there had been reports of 6 women between the age of 18-48 years who developed similar thrombotic complications to those reported with the AstraZeneca vaccine, as outlined above (CSVT and thrombocytopenia). In response to these findings, the US Centers for Disease Control (CDC)/Food and Drug Administration (FDA) temporarily paused the Janssen vaccination program while awaiting further review of the data (33). An additional 9 cases of VITT have subsequently been identified resulting in a total of 15 cases (estimated frequency of ~ 1/450,000). On April 23rd, 2021, the FDA and CDC recommended that the Janssen vaccine program should be resumed and that the vaccine is both safe and effective for those 18 years of age or older (34), but women younger than 50 years should be made aware of the risk of TTS. However, in Canada the NACI recommendation is that the Janssen vaccine may be offered to individuals 30 years of age and older without contraindications (35).

3) COVID-19 vaccines and HIV

Data for use of the mRNA vaccines in PLWH are currently limited. In the Pfizer BNT162b2 mRNA study, only one individual living with HIV and COVID-19 was included in data submitted to the FDA, although supplementary data from the clinical trial indicate 121 PLWH were enrolled (4, 36). In the Moderna mRNA-1273 study, 176 PLWH were included, with data for

vaccine efficacy available for 156 of these individuals in the FDA submission (37). Only one case of COVID-19 infection among PLWH was observed in this trial, in a placebo recipient. In the Ad26.COV2.S (Janssen) study, there were 1,218 PLWH in the full analysis (Ad26.COV2.S vaccine 601, placebo 617), 10 of whom developed moderate to severe COVID-19 (vaccine 5, placebo 5) (38). None of the 7 COVID-19 deaths occurred in PLWH.

PLWH are expected to have similar vaccine responses to those without HIV, although immune response may be sub-optimal in those with immune compromise. Further studies are underway to address this concern.

4) Priority Populations for vaccine coverage in British Columbia

At present, in Phase 3 (April to May 2021), priority populations identified for vaccination by the National Advisory Committee on Immunization (NACI) and adapted by BC Public Health include (39):

- People aged 79 to 60, in descending order of 5-year increments
- Indigenous peoples aged 64 to 18 years
- People aged 74 to 16 years who are clinically extremely vulnerable (CEV) (40) (defined and categorized as those with: organ transplants, cancer, severe respiratory conditions, certain rare blood diseases, other rare diseases, splenectomy, diabetes on insulin, developmental disabilities that increase risk, kidney/renal disease, pregnant with or without heart disease, neuromuscular or muscular conditions that require respiratory support, and immune suppression therapies including various biologics and corticosteroids).

PLWH who meet any of these criteria should be evaluated for vaccination, register with the BC Covid-19 vaccination program, and book an appointment when indicated by public health. Phase 4 of the vaccine roll-out (May to June 2021) will be directed to adults aged 59 to 18 years in descending order of 5-year increments.

Most earlier studies did not demonstrate an increased COVID-19 mortality risk among PLWH relative to the general population. In a recent meta-analysis of 22 studies, PLWH had a higher risk of SARS-CoV-2 infection (Relative Risk [RR] 1.24, 95% CI 1.05 to 1.46) and COVID-19 mortality (RR 1.78, 95% CI 1.21 to 2.60) compared to HIV-negative individuals (41). However, this meta-analysis has important limitations, particularly the lack of detailed clinical and socio-demographic information which precluded subgroup and meta-regression analyses to explore the influence of stage of HIV, levels of CD4 counts or HIV viral load, and antiretroviral therapy regimen and treatment adherence on the incidence and severity of COVID-19 among PLWH, and thus, residual confounding by comorbid conditions cannot be excluded entirely. The BC-CfE continues to prospectively monitor COVID-19-related morbidity and mortality

among individuals engaged in highly active antiretroviral therapy (HAART) and pre-exposure prophylaxis (PrEP) programs in British Columbia.

It is expected that the above vaccine eligibility criteria will be updated based on vaccine supply and as further vaccine trial data become available. Any modifications in vaccine eligibility will be available at the BC Centre for Disease Control as new recommendations are made: Vaccine Eligibility (bccdc.ca)

5. Contraindications

a) **Allergic reactions**. None of the 4 currently approved vaccines listed above should be administered if there is a history of **severe allergic reaction** (e.g., anaphylaxis) or other **immediate allergic reaction** of any severity (e.g., hypersensitivity signs or symptoms such as urticaria, angioedema, respiratory distress such as wheezing or stridor, occurring within 4 hours) (42) to either:

i) a previous dose of a COVID-19 vaccine which uses the same platform

- mRNA platform (Pfizer and Moderna)
- adenovirus vector platform (AstraZeneca and Janssen)

or

ii) any component of the vaccine (e.g. polyethylene glycol [PEG] or polysorbate). PEG is an ingredient of both mRNA vaccines for the purpose of stabilizing the lipid nanoparticle which contains the mRNA. Polysorbate 80 is an ingredient used to increase water solubility of both the Janssen and AstraZeneca COVID-19 vaccines. PEG and polysorbate are structurally related and cross-reactivity may be observed (43,44).

b) **AstraZeneca (ChAdOx1 nCov-19) (AZD1222) vaccine** should **not** be administered to individuals aged less than 30 years (32) due to the rare adverse effect of vaccine-induced immune thrombotic thrombocytopenia (VITT) (27,28, 29,30). Vaccinated individuals should be instructed to seek immediate medical attention if they develop any of the following symptoms between 4 to 30 days after vaccination: severe or persistent headaches, blurred vision, shortness of breath, chest pain, persistent abdominal pain, leg swelling or pain, easy bruising, tiny spots under the skin (petechiae), or bleeding.

Patients who have a history of VITT following the 1st dose of the vaccine should not receive the 2nd dose. Until the risk factors and pathophysiology of VITT have been determined, the mRNA COVID-19 vaccines (Pfizer or Moderna) are preferred in individuals with a history of rare thrombosis (e.g., cerebral sinus venous thrombosis [CSVT]), heparin-induced thrombocytopenia [HIT]), or who are receiving active treatment for low platelet counts (thrombocytopenia). In these individuals, the adenovirus vector vaccines (AstraZeneca or Janssen) should be avoided, unless the mRNA vaccines are not available.

c) The Janssen COVID-19 vaccine (Ad26.COV2.S). Following a pause in the US vaccination program related to investigating 15 cases of VITT, the program was resumed with a recommendation to offer the vaccine to individuals aged 18 years and older (34). Vaccinated individuals should be instructed to seek immediate medical attention if they develop any of the following symptoms between 4 to 30 days after vaccination: severe or persistent headaches, blurred vision, shortness of breath, chest pain, persistent abdominal pain, leg swelling or pain, easy bruising, tiny spots under the skin (petechiae), or bleeding.

Until the risk factors and pathophysiology of VITT have been determined, the mRNA COVID-19 vaccines (Pfizer or Moderna) are preferred in individuals with a history of rare thrombosis (e.g., cerebral sinus venous thrombosis [CSVT]), heparin-induced thrombocytopenia [HIT]), or who are receiving active treatment for low platelet counts (thrombocytopenia). In these individuals, the adenovirus vector vaccines (AstraZeneca or Janssen) should be avoided, unless the mRNA vaccines are not available.

6. Precautions

a) Allergic reactions.

i) Those who have a past history of immediate allergic reactions (as defined under *Contraindications*) have a precaution for use of either of the COVID-19 vaccines which are based upon the other platform which they have not yet received. For example, if there is a contraindication to one of the mRNA vaccines or mRNA vaccine ingredients (e.g., PEG), then there is a precaution for the use of either of the adenovirus vector COVID-19 vaccines, and vice versa. In this situation, it is recommended that the person consult their physician before receiving the vaccine. The **management** of these individuals should include: COVID-19 risk assessment; consideration of allergy consultation (which may include PEG or polysorbate skin testing); informed consent prior to vaccination; and a 30-minute period of observation (rather than the standard 15 minutes) following vaccination (42).

or

ii) Those who have a past history of immediate allergic reactions to any other vaccines or injectable therapy (other than "allergy shots") should be counselled regarding their possible greater risk of vaccine allergic reaction compared to others without an allergy history and have a 30-minute period of observation (rather than 15 minutes) following vaccination (42).

Epinephrine should be immediately available for potential anaphylactic reactions for all vaccinees, not just those with an allergic reaction history.

b) Pregnancy and breastfeeding. Pregnancy is associated with increased risk of COVID-19-related maternal and fetal complications. Among pregnant women with COVID-19, 8-11% require hospitalization, and 2-4% require intensive care unit support (45). In a recent

statement on April 15th, 2021, the **Society of Obstetricians and Gynecologists of Canada (SOGC)** recommended that pregnant women be given priority for COVID-19 vaccination (46). On May 4th, 2021, in British Columbia pregnancy was included in the list of conditions considered to be a priority for Covid-19 vaccination.

Pregnant and breastfeeding mothers were excluded from licensing clinical trials of the COVID-19 vaccines. There is no clinical trial experience to date which clarifies the safety of COVID-19 vaccines during pregnancy. However, preliminary observations from surveillance in the US included 3,958 pregnant persons who received either of the mRNA vaccines (Pfizer or Moderna) and had similar incidence of adverse pregnancy and neonatal outcomes compared to those reported in studies of pregnant women prior to the Covid-19 pandemic (47). However, among the 827 participants who had reported a completed pregnancy (v-safe pregnancy registry) at the time of analysis, 84.6% had received their 1st mRNA vaccination during the 3rd trimester (47). There is also no current evidence indicating fetal toxicity related to COVID-19 vaccination during pregnancy. Pregnant or breast-feeding individuals should be offered COVID-19 vaccination after informed consent and counselling regarding the risk/benefit considerations for the individual and the fetus or infant. Guidance regarding Covid-19 vaccination during pregnancy is provided by the BCCDC (48).

The following is the **consensus statement of the Society of Obstetricians and Gynecologists of Canada:** *Women who are pregnant or breastfeeding should be offered vaccination at any time if they are eligible and no contraindication exists. The decision is based upon the women's personal values and an understanding that the risk of infection and/or morbidity from COVID-19 outweighs the theorized and undescribed risk of being vaccinated during pregnancy or while breastfeeding. Women should not be precluded from vaccination based on pregnancy status or breastfeeding* (49).

c) Acute illness. Vaccination should be postponed until there is complete resolution of the acute illness, whether or not this may be suspected or proven to be due to Covid-19. Postponing the vaccination will avoid confusion associated with the inability to differentiate vaccine-related adverse effects from those caused by the acute illness. It will also reduce the risk of infection transmission (COVID-19 or others) to vaccine health care providers.

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