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COVID-19 UPDATE: EXPERT Q&A WITH PUBLIC HEALTH, VACCINE, EPIDEMIOLOGY, AND LAB SPECIALISTS

Webinar date: **June 23, 2021**
Recording & Presentation Slides: https://ubccpd.ca/2021-06-23-expert-qa-public-health-vaccine-epidemiology-and-lab-specialists

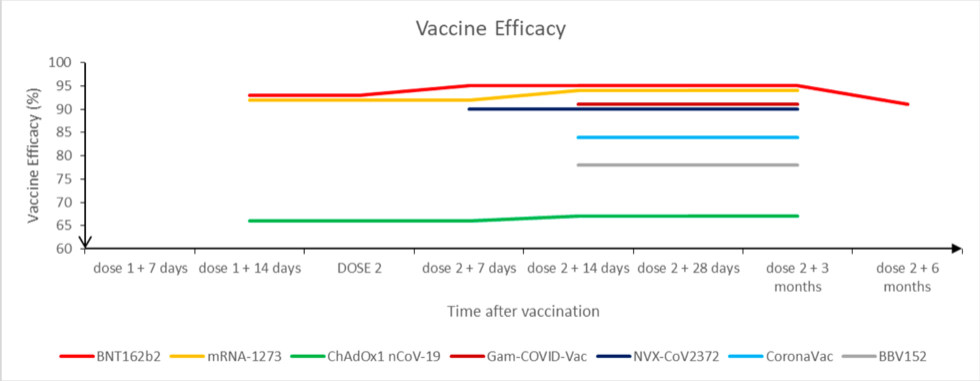
Disclaimer: Information on COVID-19 is changing rapidly and much of the research is preliminary. Assessment and management protocols are suggestions only; they do not take the place of clinical judgement. Please check with your own health authorities and local medical health officers as policies and support for the suggested approaches to patient care may vary between regions.

This summary was prepared by Dr. Birinder Narang and not by the speakers.

Webinar Summary

Overview

COVID 19 Vaccine Update – Dr. Sadarangani



Multiple effective vaccines

- **Clinical Trial Efficacy Data**
  - Gold line – Pfizer + Moderna mRNA efficacy; we have evidence for efficacy for both vaccines > 90% over 6 months
  - Green line – AstraZeneca; High efficacy any symptomatic disease, 65-70% after 1 dose maintained for 2-3 months, data not available on further yet post 3 months
  - Dark Blue Line – Novavax; 90% efficacy after 2 doses, have data for 2-3 months, showing remains effective

We have variants of concern (VOCs)

Name	Alpha	Beta	Gamma	Delta
Lineage	**B.1.1.7**	**B.1.351**	**P.1**	**B.1.617**
First detected	Sep 2020	Oct 2020	Dec 2020	Dec 2020
Country of first detection	UK	South Africa	Brazil	India
Number of spike mutations	10-13	10	11	2-6
Increased transmission	✓	✓	✓	✓
Increased disease severity	✖	✓	(✓)	?
Reduced serum neutralization	(✓) minimal	✓	✓	(✓) minimal
Impact on vaccine effectiveness	(✓) minimal	(✓) variable	(✓) minimal	(✓) minimal

- **Variants of Concern**
  - Alpha, Beta, Gamma Delta
  - There are lots of different mutations; all have increased transmission, some have increased severity

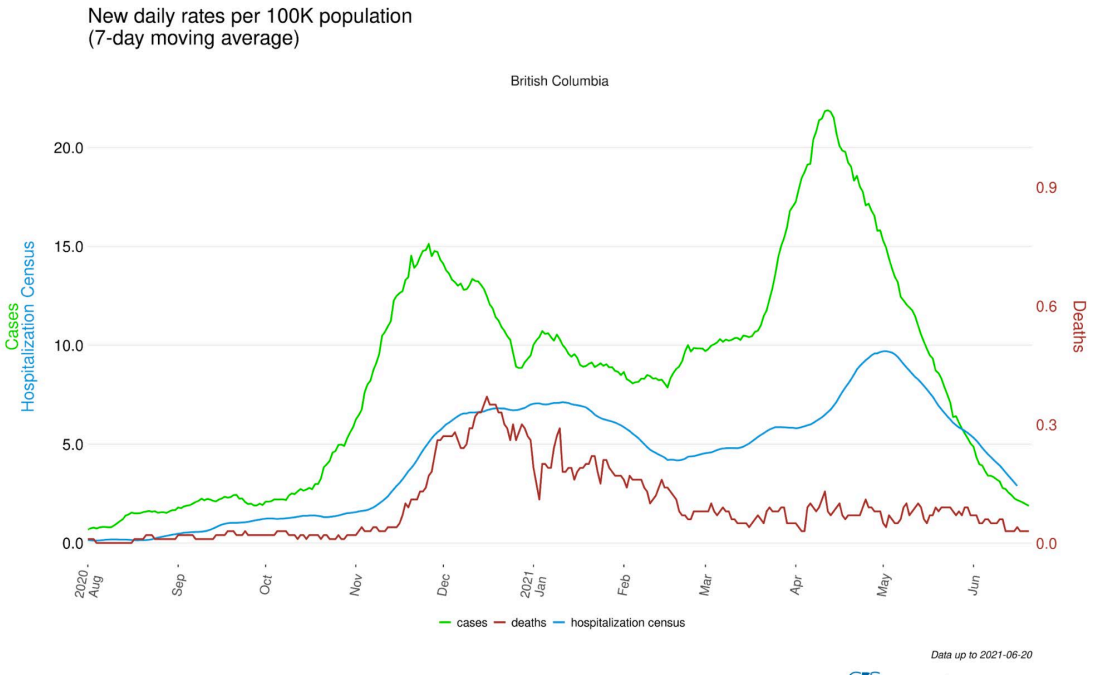
- **BC Data on vaccine effectiveness against gamma variant**
  - From 1 dose, in adults over age 70, we saw 60-70% estimates of vaccine effectiveness for Pfizer & Moderna
  - For Non-Variants of Concern (Alpha & Gamma variants) we have not seen any significant reduction in the effectiveness of mRNA vaccines against these variants from BC data

Vaccine effectiveness against delta variant

		Alpha			Delta		
Vaccination status		OR vs symptomatic disease	HR vs hospitalisation	VE vs hospitalisation	OR vs symptomatic disease	HR vs hospitalisation	VE vs hospitalisation
Any vaccine							
	Dose 1	0.51 (0.48-0.55)	0.44 (0.28-0.70)	78% (65-86)	0.69 (0.64-0.75)	0.37 (0.22-0.63)	75% (57-85)
	Dose 2	0.13 (0.1-0.15)	0.64 (0.24-1.72)	92% (78-97)	0.20 (0.18-0.23)	0.29 (0.11-0.72)	94% (85-98)
Pfizer							
	Dose 1	0.53 (0.47-0.58)	0.32 (0.14-0.73)	83% (62-93)	0.64 (0.54-0.77)	0.10 (0.01-0.76)	94% (46-99)
	Dose 2	0.06 (0.05-0.08)	0.88 (0.21-3.77)	95% (78-99)	0.12 (0.1-0.15)	0.34 (0.10-1.18)	96% (86-99)
Astrazeneca							
	Dose 1	0.51 (0.48-0.55)	0.48 (0.30-0.77)	76% (61-85)	0.70 (0.65-0.76)	0.41 (0.24-0.70)	71% (51-83)
	Dose 2	0.26 (0.21-0.32)	0.53 (0.15-1.80)	86% (53-96)	0.33 (0.28-0.39)	0.25 (0.08-0.78)	92% (75-97)

- **Vaccine Effectiveness against Alpha & Delta Variant**
  - Pfizer Vaccine – 50% reduction in symptomatic disease after 1 dose, and >90% reduction after 2 doses against alpha variant; similar rates for the Delta Variant
  - AstraZeneca – as seen for both Alpha & Delta Variants, we are seeing >90% vaccine effectiveness against hospitalization from Astra Zeneca Vaccine
  - We are seeing high effectiveness after 2 doses for both vaccines

BC Epidemiology update



- The green line indicates case rates in BC, blue indicates hospitalizations, and red indicates deaths
- We saw a precipitous decline in cases in mid-April, when immunizations started to roll out in a complete way
- When we opened up substantially at the end of May, the decline of cases continued, as has hospitalizations
- There wasn't a particular peak in mortalities related to the 3rd wave
    - Because the majority of people who were likely to die from COVID-19 were already immunized (i.e. the frail and elderly), we did not see wave 3 related increases in death, although there was increased hospitalization
    - At this time, most people who were hospitalized were those over 50 and not fully immunized
- BC immunization
    - 76% of all eligible immunizations have been vaccinated with one dose as of June 23rd, 2021
    - When looking at ages > 18, the number is 78%
    - There are some differences amongst health authority, with still some way to go in Northern and Interior Health

Understanding BC's Restart Plan

- Step 3 is upcoming, with a plan to change the paradigm for the pandemic
- As the percentage of population that is vaccinated increases, the ability of the virus to spread is greatly reduced along with the ability to cause severe illness
- Now that the virus is unlikely to overwhelm the healthcare system, we don't need societal measures and can rely on regular public health actions: case identification, isolation, cluster management (focused measures), etc.
- During Step 3:
    - Masks will go from required to recommended indoors
    - We will not recommend physical distancing in public or private
    - Most type of events will be able to restart without restrictions
- There will be some restrictions on high risk events – i.e. those involving lots of people, stadium-type events
- Adjusting may be hard on population as they are used to wearing masks and being distant from others
    - May take some convincing that immunization works

Question & Answers

Transmission

Q: How serious of a threat is the Delta Variant? For partially and unvaccinated populations?

A: Variants have been a source of news for a while (i.e. more transmissible variants will dominate). The biggest threat we have right now is communicating the impact of the delta variant. We have been going through the pandemic through a well-defined plan including testing and public health measures until vaccination could be delivered. Our ability to measure and monitor variants will give us a chance to monitor vaccine effectiveness. The threat is no different than the previous ones.

Naturally for viruses to occur, there is a lambda variant that people have on their radar. Viruses can only evolve to a certain degree before it loses its ability to replicate. Vaccines target the entire spike protein, while there are some changes in neutralizing antibody. Even Pfizer believes that neutralizing the antibody itself is not the right marker for what is the new protection.

This virus is going to be corralled by the fact that the vaccines are predominantly spike-based. Even if there is a variant, the probability there is sufficient immunity from vaccination is high.

Though there has been a resurgence of the Delta Variant in the UK, we are in a different place in BC. Whereas in the UK 1/3 of people < 40 years old were vaccinated when the resurgence occurred, at the same time we had 2/3 in that group vaccinated with their first dose. Due to different strategies, we had an already protected population.

Q: Now that we know fomite transmission is low, will we change directions for Physician offices?

A: The whole world has been disinfecting high touch surfaces and requiring workplaces to have a COVID safety plan, with a singular focus in trying to control it. As we transition into Step 3, a transition from our COVID Safety plan to more general communicable disease plans will occur. The recommendation will be to return to routine cleaning practices. This does not mean we will need to have enhanced cleaning procedures. Different sectors will have to fine-tune for their own specific places.

Q: Will the recommendations change soon for Doctors and their offices?

A: The first thing that will change is non-clinical areas. As of July 1st, people will not be required to wear masks in non-clinical areas. In physician offices, it can be difficult to manage with distancing. If someone is symptomatic, we should keep distance from them and they should wear a mask. The recommendations around PPE will be slower to change during clinical encounters.

Additionally, it's important for primary care providers to help write these guidelines. We are seeing trends move away from additional measures. What are the negative consequences of extra infection control measures? We need to work on this now.

We will need to rebalance to come up with a more logical model in the future. If we 'package' people with masks and eye protection, we can eliminate RSV and influenza. Therefore, we have to think about what the right balance is going forward, and what the right amount of protection needed for symptomatic and asymptomatic people is.

Vaccine Considerations

Q: Is myocarditis a risk in adolescents as a result of vaccination?

A: Vaccination is not just meant to protect you today or for the next week of next month, but also over several months and the future. ACIP reviewed data from US CDC and has put out statements on the likely association between mRNA vaccine and myocarditis, with both mRNA vaccines.

In 12–39 year-olds, 12 cases of myocarditis occur per one million doses of vaccine. In BC that would translate to ~20 cases. Most of the cases of myocarditis are very mild. In the US, 6% cases went to ICU, so if we apply this percentage to BC, 1 person would go to the ICU in this age group from COVID. We have had 200 ICU admissions and 17 deaths in the context of less than 5% of the BC population affected.

Almost everyone will get vaccinated or infected, and clear benefit exists from vaccination. The benefit of vaccine far outweighs the current risk.

In particular, a publication in JAMA Cardiology looked at young athletes after they became COVID-infected, and found a subclinical myocarditis rate of 2%. So the Myocarditis risk could be estimated at 2% if you have had COVID (i.e. 1/50), and the risk of myocarditis from vaccine is 1/50-100,000, again supporting the risk/benefit in favour of vaccine.

Q: Should we have lower doses of vaccine for youth?

A: Clinical trials that are released were done with adult doses. For younger children, trials are now being done with a lower dose. We have seen very high immune responses with both mRNA vaccines, with high efficacy. Logistically, it is also easier if can use the vials as adults. We may see different dosages for younger kids but cannot assume that side effects/adverse events are dose-dependent.

Q: If patients got AstraZeneca as their first dose, what are they being told for their 2nd dose, with respect with mix and matching?

A: In Vancouver, the recommendations for getting what is first available vaccine has made sense still. NACI has changed the wording of their recommendation, which has made it a bit difficult. NACI recommends having the mRNA vaccine as a second dose, although we have already been providing it as an option. People may still and are still choosing to get AZ as their second dose. We have to appreciate that there are limited supplies of AstraZeneca in BC, so if people do want that as an option, they should get it soon.

When NACI changed their recommendation, it was based on a relatively small study measuring cellular immunity and antibodies. In looking at that recommendation, we must look at the entire body of evidence. The efficacy & safety of AstraZeneca vaccine has not changed recently; the importance of that change was overstated. The study compared Antibody responses of 2 doses of AstraZeneca vs 2 doses of Pfizer vs 1st dose AstraZeneca, second dose Pfizer. The antibody response for the mix were equivalent to 2 Pfizer doses and higher than 2 AstraZeneca vaccines. We don't have a correlate of protection from these antibody levels. Effectiveness against hospitalization for 2 doses of AstraZeneca was still 90%. Any of those combinations will be likely highly effective.

We have to take the antibody data in the context of the clinical data that trumps antibody data.

The risk of VITT is ~1/600,000 in the 2nd dose of Astra Zeneca, though we are not yet sure what NACI is doing about the myocarditis risk. There should be no hesitation in taking AstraZeneca to be highly protected.

Q: What will be the policy for Canadians received AstraZeneca and who want to travel?

A: There are national conversations happening on what proof of vaccination should look like in Canada. These types of requirements are being created as we speak and are quite haphazard, and we expect that the recommendations will converge and become more sensible. Right now, these recommendations have not been made by science, but mainly based on logistical decisions it seems. As a reminder, Prime Minister Justin Trudeau received an AstraZeneca dose.

Q: What about mixing Moderna & Pfizer vaccines?

A: In the next few weeks, mass clinics will have a lot more Moderna. Both are mRNA-based vaccines, and we believe they can be interchanged without any impact on efficacy. Potential side effects from both are very similar. There may be some more delayed local reactions from Moderna.

We have a lot less Pfizer coming than initially expected, and are expecting to give most people Moderna over the next few weeks to months.

It's important that everyone receives 2 doses, so we do not recommend people wait for a preferred dose.

Q: Will we need a 3rd vaccine?

A: We don't know right now. We can see high efficacy >90% up to 6 months, and do not expect it to drop off. We can't predict right now how long it will last. We don't know what infection looks like yet in the context of vaccination; if it ends up being a very mild infection, one could speculate that this may provide a boost in your immunity to keep your ongoing protection going, so you don't need additional boosters. If there is still a lot of severe disease in community, then maybe we will need it.

At NACI they are not discussing this yet.

As with any vaccination, we monitor long term efficacy data. For example, in the not-so-distant past, we recommended a 2nd dose of MMR to those people who only got a single dose as children. So will have to see what the clinical trials show and compare that to the burden of illness.

Boosters may not be for everyone and may be just for certain high-risk populations.

BC is going to be tracking what is happening with one dose as well as two doses and is looking at what is the risk of symptomatic and severe infection with a variant. Large cohort studies are happening to understand the correlates of protection. This type of research will help inform future recommendations.

Q: Since the mRNA vaccine involves the expression of spike protein on transfected cells and a subsequent inflammatory cell, what is the risk to the host of developing auto-immune disease? Wouldn't host proteins be potential antigens to antibody protection?

A: With respect to mRNA vaccines, we have mRNA in our muscles and have spike proteins and other proteins that are expressed. They are already there through part of the evolution of the immune system and you are self-selected to not react against those. It's not the case that the vaccines are giving you any extra host proteins. With local inflammatory response, if there are concerns against making host proteins, the whole way B cells and T cells develop, those sequences (billions in your repertoire), are deleted through development of immune cells in utero or early life. It shouldn't be possible for people to produce ongoing T cell responses. Clearly, there will be some people who are at risk of developing autoimmune disease, though there have been no signals so far.

Q: If offered a 3rd mRNA Vaccine, i.e. if someone is going to USA and has that opportunity, should they get it?

A: We would discourage it, as we don't know what the point of it is. You don't know if there is any incremental benefit, and there is a possibility of additional side effects.

Q: Should we encourage people who have had COVID to get vaccinated? Shouldn't their antibodies be protective and lasting?

A: We know that people who have natural infections and have immunity believe they are protected. We know the people that receive vaccines are protected. We have adequate supplies of vaccine to get protected. As of now, we can't predict the length of protection from natural infection. The goal is to get the population protected by getting them as immune as possible. People may only need one vaccine post natural infection but we can't say that definitively yet.

In Brazil last year when a lot of endemic related infections occurred, by some estimates 60-70% of the population were infected. It was clear that even though they were protected, the population was still heavily affected by the Gamma P1 Variant that was isolated from Brazil. Vaccines give you a more potent immune response, although we don't know what the threshold of immunity is yet.

With normal coronaviruses, the protection from natural infection lasts 1-2 years, so the notion of having a more immune response is likely to protect you for longer.

Q: What is the research on infants born to women who have had the vaccine? Do we know about antibody levels in fetus, fetal cord blood, or breast milk?

A: A NEJM study looked at 35,000 people who were pregnant and vaccinated. The short answer from this study is that the side effect profiles are very similar. Pregnancy outcomes were not different based on background rates of various things such as pre-term birth. There is no evidence that these vaccines are harmful in pregnancy to pregnant persons vs infants. We also know that pregnant people are at higher risk of severe complications from COVID-19. We do see antibody transfer to newborn post-delivery, which will likely last a few months, but we are not seeing high infection rates in this patient population.

We have a long history of safe vaccinations during pregnancy. We often have a cautionary statement as studies are not often done in pregnant populations.

Even the risks of vaccines that should not be given to pregnant women (i.e. live virus vaccines) are theoretical. The reality of these infections in pregnant women and severity of them are real.

Q: Do we know when the safety data on vaccinations in children age 6-11 will come out?

A: We are expecting that data later this year.

Q: Regarding workers, students, and travellers who have had vaccines that are not approved in Canada (i.e. Sputnik & Sinovac), do we know what the message will be for them? Will they be revaccinated?

A: By large, WHO-approved vaccines will be accepted as proof of vaccination in Canada. The vaccines don't necessarily have to be approved in Canada for you to be considered vaccinated. We are continuing to monitor effectiveness. Sometimes vaccination schedules in other countries are different to here (i.e., if you received MMR at 9 months, in Canada we don't recommend for that dose to be counted for long term protection).

As these are new vaccines though, the effectiveness will need to be monitored over time.

Q: Is there a higher risk of flying soon after vaccination (i.e. with blood clots)? There are some reports of airline pilots dying within a few days of vaccination.

A: When clots were being looked at with regards to AstraZeneca, there was no other risk factor identified. This was found to be an immune mediated response, not related to other risk factors for blood clotting.

BC Specific Considerations

Q: Is the blood test at LifeLabs used to assess post-vaccination the same blood test that we use to assess antibodies for previous infections?

A: The original LifeLabs test was an antibody that could detect IgM, IgG, IgA against the nucleic capsid. This capsid is only present in natural infections (e.g. COVID-19), or in the Chinese Sinovac vaccine which used a killed virus. Several physicians have sent patients to get their antibodies post vaccine and were surprised the test was negative. The test WILL be negative if never exposed to natural infection.

The test that can be used to detect Spike Protein. There are different tests available that can measure neutralizing antibody and can test IgG, IgM etc.

It is not justified right now as there is no immune correlate. Right now, it won't tell you what you need to know, and in a study population it makes sense to look at immunosuppressed and other special populations.

At a population level we are seeing with higher antibodies, responses have been related to vaccine effectiveness. However, at individual levels this can vary, and we are not measuring T-cell responses. We also may or may not get this information, as it is not available for some preventable diseases that are quite common.

This falls under the category of 'don't order at test if you don't know what you are going to do with the result.'

AstraZeneca vaccines are slowly driving up antibody + T cell responses. The problem with the patients is that they get this mixed information that they cannot tease apart.

Q: Regarding COVID-19 in BC, who is still in hospital and what is their vaccination status?

A: Vast majority of those who have had no vaccination or only one vaccine are in hospital. It is difficult to calculate right now as the denominator keeps changing (the number of people who have been vaccinated from 1-2 has changed). People who have had 2 vaccines who are hospitalized comprise a very small proportion. The pattern of disease of those who are hospitalized who are immunized is the same as others. People who are older tend to be the ones requiring hospitalization.

We started measuring breakthrough cases on December 27. We have had about 90,000 infections in those who are unimmunized, 2600 with one dose and 200 with 2 doses. It is not a very good measure of vaccine effectiveness. If you start measuring proportion of breakthrough cases, then by definition, if you immunized everyone then 100% of cases would be breakthrough cases and that would be a gross misrepresentation of vaccine effectiveness.

Q: Will large testing sites stay open, or will they be shut down?

A: Less and less people are coming for testing, and positivity rates are coming down, so sites are closing and operating at reduced hours. As part of the switch from a pandemic response to a normal endemic virus response, there will be a shift in the testing strategy, including where they get tested. We are not sure if that shift will happen before this year's respiratory season or after those discussions happen.

The testing centres are partially concerned with public health, but also are part of public expectation. WHO has said that *test, test, test* is the way to control the pandemic. That was the right thing to do when case and contact tracing was the primary method of controlling the pandemic. When testing for case-finding, the goal was to identify every case. In an immunized population, not everyone will require a test.

We also have to be able to justify the utility of using health care resources for a testing a centre that is not being used.

Q: Are we expecting COVID infections to increase this winter?

A: Typically, coronaviruses are seasonal, and we have seen that seasonality played out globally. When there is a new infection, the behaviour is changed, though we are not sure what we will see in the fall. If we get enough people vaccinated, this will prevent significant symptomatic and severe disease.

Q: What is the plan for healthcare workers who have not been able to get vaccinated yet or refuse to get vaccinated?

A: That is still being discussed. For other vaccines, we have asked people to report their vaccination status before, which may be considered. We have also asked people to take certain actions if they are not immunized (i.e. asked to wear a mask), so this may also become a rule.

Q: Is BC going to start vaccinating youth under the age of 12 before we have results of Phase 3 trials with mRNA Vaccines?

A: We wouldn't think so, as we need to receive trial data before Health Canada approves it. It likely wouldn't be used without Health Canada approval. What we have learned in BC is we did not need to vaccinate this age group to control the pandemic. We will have to continue to look at epidemiology and the length of protection from vaccines going forward.

Q: What is happening with other routine youth vaccines in BC such as the Grade 6 and 9 ones?

A: There are plans in place on how to catch-up kids on these vaccines. Vancouver Coastal Health is converting one of the test sites into a mass school-based immunization centre through the summer to help kids catch up. We will be planning to engage Family Physicians in this as well.

Part of the pandemic recovery process involves catching up on these vaccines and screening programs, so there is work being done for this at the provincial level.

Thanks to the speakers on the video:

- **Dr. Reka Gustafson**, Vice President, Public Health and Wellness and Deputy Provincial Health Officer

- **Dr. Mark Lysyshyn**, Deputy Chief Medical Health Officer, Vancouver Coastal Health
- **Dr. Mel Krajden,** Medical Director of the Public Health Laboratory, BCCDC
- **Dr. Manish Sadarangani,** Director, Vaccine Evaluation Center at BC Children's Research Institute
- **Ms. Nomi Mate,** Public Health Nurse
- **Simon Moore**, Family Physician, UBC CPD Medical Lead