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COVID 19 UPDATE: EXPERT Q&A WITH PUBLIC HEATLH, PRIMARY CARE, VACCINE, PHARMACOLOGY & EPIDEMIOLOGY SPECIALISTS

Webinar date: **April 6, 2022**
Recording & Presentation Slides: https://ubccpd.ca/2022-04-06-covid-19-update

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

Introduction & Observations from Australia – Dr. Birinder

- In Perth, Western Australia, borders closed for a long time. They opened with 95% 2-dose vaccine coverage and now 76% of those are boosted with 3 doses. Ongoing BA.2 surge right now with 8-10,000, with hospitalizations ranging from 200-250. No more than 10 in ICU despite high cases – a testament to high level of vaccine immunity
- 61% of vaccine doses (~36 million), in Australia overall, within Family Practice offices. We have not been able to do that in BC

Epidemiology Update – Dr. Reka Gustafson

Cases, Hospitalization and Death

- High numbers of cases and hospitalizations in January 2022. In December 2021, testing changed significantly as testing capacity had been reached
- Significant proportion of people in hospital with COVID, but not from COVID, hospitalization is representing prevalence of infection in community rather than severity

- Also similar to those who passed away with COVID, may be contributory, may not be overall cause

Variants of Concern

- BA.2, replaced BA.1 of Omicron over the last little while
- Variants come and go, they are inherent in the nature of coronavirus

Hospitalization

- Consistent pattern as well as deaths are significantly dependent on age

Age-Standardized Hospitalization, critical care and Death rates comparing vaccinated vs unvaccinated

- The effectiveness of vaccines may be misrepresented because when you have most of the people in a population immunized, even those hospitalized will immunized
- When you look at rates, vaccination retains strong effectiveness against hospitalization, critical care and death

COVID-19 Therapeutics – Dr. Jennifer Grant & Dr. Jolanta Piszczek

Currently Available Therapies

- Paxlovid (Nirmatrelvir/Ritonavir)
    - Take home oral direct acting antiviral (protease inhibitor)
    - 5-day course given within 5-7 days of symptom onset
    - Various drug-drug interactions (CYP 3A4 inhibitor) and contraindications
- Sotrovimab (Xevudy)
    - IV monoclonal antibody against SARS-COV-2 spike protein
    - Prone to loss of efficacy with emerging variants of concern, including BA.2
- Remdesivir (Veklury)
    - 3-day IV direct acting antiviral for those unable to take Nirmatrelvir/Ritonavir
- Evidence is similar for all drugs
    - RCT level data, Delta wave, unvaccinated participants with a risk-factor
    - Reduces progression of mild-moderate COVID to requiring hospitalization (6% to 1%)

Who to Treat?

- Risk of hospitalization cannot be characterized by a single variable
- Based on BCCDC Analysis:
    - Some risk factors include vaccination status and age

    - Most important thing to note, is that it is a combination of age, vaccination status and certain conditions and number of chronic conditions
    - There is an algorithm available through BCCDC
    - Treatment is recommended if risk ≥ 5%; Suggest if 3-4%
- Looking at BC Eligibility Criteria
    - Multitude of factors, varies between age, risk factor and vaccine status
    - E.g. anyone over age of 50, unvaccinated or partially vaccinated with >3 chronic conditions or indigenous are eligible
    - Need confirmed infection along with symptoms and have no drug-to-drug interactions/contra indications

Step by Step Assessment & Toolkits

- Probably best to take Paxlovid first line for those who can take it (including for medical reasons and for logistical reasons)
- Toolkit provides management strategies for interactions, there is also a 1800 line with pharmacists that can help support. The line is open Monday through Friday from 8:30-4:30 and accessible at: 1-866-604-5924

Question & Answers

VACCINATION

Q: What is the evidence behind 4th vaccine? Will this be an annual booster shot?

A: After the first booster (3rd dose for most people), effectiveness against BA.1 (original Omicron) infection was about 60-70%, and effectiveness against hospitalization was higher (about 10-20% higher), waning at about 10-12 weeks. Effectiveness against severe disease is more robust: 4 months after vaccination waning to about 40%. Another booster gives you about 2-4-fold increase in effectiveness against Omicron. If you look at absolute risk differences, you are looking at 4 vs 3, each subsequent dose has less incremental benefit.

The 4th booster right now is for the most at risk individuals who have the least robust immune response to start off with, and it wanes a bit quicker.

With regards to annual booster, we are unsure at this point. For flu, we do have an annual program and the interval is usually about 6 months. Right now, we have variants coming and going much faster than that.

Q: At what point do we stop giving boosters and let natural immunity take effect?

A: There is still benefit from boosters, just that incrementally the added benefit is less than the previous one. No safety concerns have been identified with the boosters and the risk of the vaccine is much less than getting the disease.

Q: When would you recommend giving 3rd dose after COVID infection, in previously healthy double vaccinated adults with some minor residual symptoms?

A: The prolonged symptoms and potential of long covid does not correlate well to the immune response to vaccination and T cell activity against the virus. The symptoms should not impact the timing of the next shot. The recommendation is mainly based on expert advice, vaccinology, and immunology, that if you get infected you will get some boost in your immunity from the infection, so it is reasonable to delay next dose. The recommendation is to wait 3 months if you are 6 months from 2nd dose.

Alternatively, if you get infected before completing the primary series, it is generally recommended to wait 2 months before getting the next dose.

The nuance is that if you need to, you can get the vaccine sooner, i.e. if you are going to a place where you won't be able to get vaccinated in a reasonable time frame. If people who are immune compromised or other health reasons, then safety wise it is okay to give sooner. There was some indication that a shorter interval between 1 and 2 doses may have contributed to increased risk of myocarditis in young male adults.

Q: My patients don't trust the officially reported adverse side effects and can cite numerous examples of people who have had stroke, bells palsy and other concerns. In the clinic, how would you address these concerns?

A: The adverse reporting is only as strong as the reports submitted. When primary care providers discuss this with patients, we should encourage patients and their acquaintances to make sure that these side effects are reported. We need to be mindful of when we look back earlier in the pandemic, looking at VITT (vaccine induced thrombotic thrombocytopenia) and myocarditis, those signals were identified within weeks of vaccine roll out. On a large scale the monitoring systems have worked, the idiosyncratic or not as common adverse events were also reported. They are listed in CDC reports. We must also remember that temporal correlation does not mean it is caused by the vaccine.

Q: Re mRNA vaccines, any comment on tinnitus as a side effect?

A: Haven't seen a strong correlation from it. If we were to ask our ENT colleagues, they would say that tinnitus is one of the more difficult conditions as there are such multi-factorial aetiologies. As a primary care physician, look at low hanging fruit, is it infectious in etiology, is it related to hearing loss, or is it previous damage from exposure?

Q: What are the current recommendations for future booster doses for those who have had documented myocarditis after 2nd or 3rd dose of vaccine?

A: Right now, NACI recommendations those who have had myocarditis after vaccination should defer it. US recommendations are a bit more open in that scenario. We are a bit more on the cautious side. A lot of people who are referred for myocarditis for vaccination who have not had myocarditis following the vaccination, they had chest pain, but testing does not support it. First thing is to make sure if you suspect it, then investigate it appropriately, i.e. with ECG and bloodwork. For those where diagnosis was not clear, or maybe a bit soft, have recommended revaccination and it has gone okay.

As new vaccines become available, recommendations that may shift.

Q: Should we be expecting a vaccine booster in the winter, and any special consideration for health care workers?

A: Reinforce the current recommendations, the 2nd booster is for adults > age of 80 and for residents of long-term care or congregate settings, and discretionary recommendation for those 70-79. In BC, the recommendation is for those 70 and older, Indigenous people 55 years and older. Health care workers have been a relatively high priority group, it will probably come at some point, timing is unknown at this point. Winter will depend on emerging variants, disease, and the epidemiology over the coming months.

With the latest NACI and BC recommendations for the 2nd booster, we have started seeing some parallels with the influenza program (targeting those at highest risk). There was a mention from PHO not to extend 2nd booster to general population unless the evidence supports it.

PERSONAL PROTECTIVE EQUIPMENT

Q: How can the PHO justify removing mandatory masking in crowded enclosed spaces? Mask-wearing reduces virus transmission.

A: For public health, the burden of proof is on us to implement and maintain measures that are necessary to prevent a health hazard. We no longer meet that threshold to continue keeping the public health order active. The large majority of the BC population is no longer at significant risk from this virus. We no longer have a completely susceptible population as we had 2 years ago, and a less intrusive and more effective measure is in place now. The goal was not to prevent exposure as we cannot do that sustainably.

The virus itself has also changed; it has become much more infectious. The behavioural maneuvers we could use to limit transmission for a less infective virus are less effective now. When the likelihood of being exposed was quite low, going to significant measures to prevent exposure in the community could overall reduce exposure, with the currently infectious variant, exposure is almost a certainty, population level maneuvers are not as effective.

Efficacy of masks, when worn well, are effective as part of a general approach. We have published studies; medical staff has same rate as general population. Dr. Grant has worked on the COVID ward and in ICU and has worn basic masking procedures and has not been infected.

If someone is at risk, a surgical mask likely gives a good amount of protection in that setting, along with washing hands and other protective measures.

Important to distinguish difference in discussion regarding masking in general to protect individuals rather than a mandate that is there at a policy level.

People get COVID from the people that they know and spend a lot of time with, i.e. their family, friends and co-workers. It continues to be unlikely to get COVID from strangers in public making it more difficult to justify these mandates/measures.

Q: What is the best way to protect ourselves in the office when we see people?

A: Throughout the pandemic many physicians have been seeing patients in clinic including Family Practice clinics, consultant specialty clinics and hospital-based clinics, both symptomatic and asymptomatic patients, wearing surgical masks, face shields, gowns, and other equipment. The majority of people have been wearing surgical masks and there haven't been chains of transmission that have been reported or recognized in these spaces. I (Dr. Narang) have never been able to be FIT Tested (beard). Was testing people with masks with original variant, not wearing a face shield.

Now going forward, we are in a highly immune population, know that the basics of PPE have been effective. When we look at the future of care, take some of the learnings from the last 2 years i.e. if someone is symptomatic whether COVID or other viruses, we need to ask do they need to be seen in person at this time or can we use effective telehealth measures knowing that there are both patient risks and staff risks.

Must make sure infrastructure is in place to support clinics to do this effectively.

TESTING

Q: What is the sensitivity of rapid antigen test for BA.2? Should we recommend daily repeat testing? What should we tell people who has cold symptoms, and their test is negative?

A: The sensitivity is about the same as other variants. The RAT are slightly less analytically sensitive than PCR, but that may give better accuracy on how much "high level" virus you have. When that antigen is positive it's because you have more virus. If you have symptoms, it is 90% sensitive, after 2-3 days. If you have symptoms and test on day 1 or 2 you may have a false negative. If you have cold symptoms, whether it is COVID or not, stay away from high-risk people. In these high-risk populations, other viruses such as influenza, human metapneumovirus, are all dangerous to these populations.

Another question to consider is, do you need to be tested? Right now, the real value of testing is to connect you to treatment.

CDC report MMWR last week looking at what they had seen with regards to testing. At home testing was highest in those who identified as white, adults age 30-39, annual incomes $150K, those with post

graduate degrees and New England division residents, a picture of young affluent lower risk individuals. We need to be mindful now, and even though our test at home strategy took a while to get off the ground, it has likely been more equitable. With regards to testing-to-treat model, we need to make sure that those eligible for treatment are accessing it in a low-barrier way. Throughout the pandemic we have seen much disparity within testing, vaccines in racialized communities, how do we make sure that people who need treatment can get access to it now.

Q: Is there a role of using nasal swabs for collecting specimen from both mouth and nasal passage for rapid tests?

A: Would discourage doing that as this would likely decrease sensitivity. Whenever a test is created it is validated for a specific body part and using it in other places that could interact with buffers and other chemicals that could alter test sensitivity. Especially in the throat as there are some enzymes that could impact test sensitivity. If it says nose, then do nose.

Q: How can it be that the BC CDC recommends back to work in 5 days when my rapid antigen test was positive for 10 days?

A: The first thing is that it is not recommended to continue testing once a test has come back positive. The test is used to diagnose an infection, it is not used to tell you when you are infectious or not. For most cases they will no longer be infectious at the end of that 5-day window. Some will test positive by a rapid test after but it won't tell you how long you are infectious for. For some people they may be infectious longer. Ultimately the goal is to reduce risk not eliminate risk.

Rapid antigen tests are testing an antigen, it lives on in dead cells even after the virus has been killed and cleared. Antigen does not mean you have viable virus (along with PCR). When you are infected, the mucosal cells at the bottom must work their way up. The better data is from viral viability studies; most viable virus is gone by day 5.

EPIDEMIOLOGY

Q: What percentage of BC residents do you estimate have been infected with SARS-COV-2?

A: The proportion of BC residents infected with SARS-COV-2 increased during Omicron wave with the latest estimate at about half of British Columbians. This is informed by Life Labs studies on lab samples that have been submitted for other reasons, and that are used for antibody prevalence (can distinguish between infection induced and vaccine induced antibodies). Some samples are skewed as they are not random. We have not been testing at a population level, we were when there was a lower prevalence, now the number is different.

Q: How strongly should Primary Care Physicians be encouraging the use of this medication? What is the relative risk, benefit, and cost?

A: The first step is use the step-by-step assessment to determine risk. High risk has a different definition to different people. You would want to recommend treatment in those who have that >5% risk of being hospitalized within Omicron wave. Looking at the thermal map and point system, and if they score >5 points on scale, then they are at high risk and they are likely to benefit. 5% risk means 1/20 chance of going to hospital.

In terms of relative benefit from side effects, if you take someone who has an absolute risk of 5% and apply and EPIC-HR study results to it, can expect a benefit of 4%. That would be a 4% absolute risk reduction or an 80% relative risk reduction. Would need to treat 20-25 people to prevent 1 hospitalization.

Cost is free to patient and the Public Health Agency of Canada has procured it (cost is about $600 per treatment). The cost-benefit analysis is likely supportive as the use of this drug prevents 1 in 20 hospitalizations.

Side effects are nausea/diarrhea, and they are usually tolerable. Benefit in high-risk patients outweighs the side effects.

Regarding equitable access to medications, it has always been the case that lower socio economic status and racialized communities have decreased access. Has been a lot of work done by the Ministry to make sure that approaches are equitable across BC and that there are numerous ways to access the medication. Would love for people to go to their Family Physician, recognizing that this is not always possible.

Health Authorities have physicians available that can do telehealth consults. Patients can self-refer through Government of BC website.

There is also access through testing sites as the testing team follows up on every positive test to assess for treatment, it is not just a reactive process.

Q: How concerned should we be with Omicron BA.2 and future variants?

A: The emergence of new variants is how the new coronaviruses behave. The focus on the new variants on an individual level is not entirely necessary. We need to monitor it at public health and clinical level for multiple reasons. We need to look at immune evasion or a change of the epidemiology of the infection (i.e. greater severity or different populations being impacted). We are not particularly worried regarding BA.2 and it doesn't change the approach at the population level. It is behaving the same as the other Omicron variants.

From a therapeutic perspective, we are learning about new variants of concern and how the therapeutic landscape has changed. Therapeutically speaking, the monoclonal antibodies are vulnerable to changes in the spike protein. The BA.2 has been significant for therapy and has had to decommission a monoclonal antibody that was relatively useful for BA.1 and other variants. The direct acting antivirals have been very stable against these new variants and can expect that the therapeutics we are using today will continue to be effective.

The UKHSA data comparing BA.1 vs BA.2: looked at 3 shot vaccine effectiveness vs hospitalization. At 70 days post vaccine, 81% effective vs BA.1 and 83% effective vs BA.2. Past 70 days there was a drop to 73% for BA.1 and 71% for BA.2 Not seeing a lot of difference in vaccine effectiveness against severe outcomes.

Q: Should we redraw the 4th, 5th and 6th curves for the recent waves, as we have not had PCR testing as available for the general population?

A: We won't redraw the epi-curves as they represent what we know about cases, hospitalizations and people who have died within 30 days of a test. They are point in time estimates of the overall number of people who have been exposed and cannot be translated into a curve. When we do modeling there will be error bars and shades that confer estimates. For most transient respiratory infections we don't know how many people have had it. The shorter the incubation and milder the infection, the less we can expect to know on the exact number infected with a pathogen. The epidemic curve is giving us a trend.

If we want to look at the curves that represent transmission, the weekly surveillance contains wastewater surveillance reports on COVID that is detected in the lower mainland. Have had it through recent waves. That is published by BC CDC.

MISCELLANEOUS

Q: Do you recommend wearing a mask in public places, transit, and airplanes?

A: Depends on a few things: in places like airplanes you are required to wear masks, you are not necessarily required in other public places. There is also an issue of risk tolerance, some people can tolerate more risks than others.

These are conversations we will be having with patients for a while now, we need to be clear on that as well, that different mandates and what someone chooses to do on an individual level are not the same. We need to be promoting a culture of acceptance and tolerance, may not be a right answer for a patient, but want to make sure it is being discussed respectfully amongst families and patients/work etc.

Q: Seeing people coming back to work 5 days after COVID looking unwell, coughing, and wearing only a surgical mask. Are there better guidelines, should they have a negative rapid antigen test before returning to the Emergency Department?

A: Rapid antigen test does not indicate whether one is infectious or not. Most who are health care workers, are not infectious after 5 days, and even in the health care environment they are wearing PPE that will protect patients. They will need to decide whether they are well enough to be at work or not. Many people have a cough long after they are infectious with COVID.

Q: Should those with children under the age of 5 continue to take extra precautions such as limiting contact, masking or only doing virtual meetings?

A: People will have to make their own decisions based on their own risks and risk tolerance. Children under 5 have not been at risk of serious disease through the pandemic and limiting contact with others can have real harms.

We must also look at the social development, mental health, and substance use issues that have arisen in conjunction with the pandemic.

A lot of research being conducted on adverse childhood experiences and the downstream impacts into adulthood. We are seeing COVID babies, the lack of exposure to what we would consider normal interactions with family, friends and experiences and an increase in anxieties early on. The data won't be here to support it in a while, we need to be intuitive about it and we need to balance it in a rational manner.

Adverse effects from public health interventions is cumulative amongst all age groups in youth, evidence is emerging of cumulative impact.

Q: Is there evidence about remdesivir being more effective than sotruvimab for BA.2?

A: Do have evidence that remdesivir is more effective. Sotruvimab is a monoclonal antibody that binds to the spike protein which has been mutated in BA.2. Animal studies have shown that the effect of a monoclonal antibody like this is reduced 16-30 fold in different studies. Remdesivir is a nucleoside analog, it is difficult to mutate a RNA polymerase in a virus and have a viable virus, so we do have direct evidence that remdesivir kills BA.2 effectively. All of this is knowledge is from Delta (clinically), these trials take time to get set-up and enrol participants when waves are on the way down. RCT takes about 18 months to come out in a peer-reviewed journal.

Q: To what extent does facial hair compromise mask effectiveness?

A: FIT testing it is challenging if you have a beard, but for surgical masks FIT testing is not required. When you are using a surgical mask, the barrier is protecting you from droplets. All mask wearing depends on how well individuals wear the masks.

With N95s, it is very difficult to get fit tested with a beard, but there are ways. From a Sikh perspective, a surgeon in the UK was published for tying up their beard tightly, by using a "Thattha" (cloth/band) to tie it close to face, and then wore a mask and was able to pass fit testing. In Australia, a surgical registrar, using some type of elastic type material, tied their beard up and passed fit testing (more information can be found in the resource section below).

I was dismayed when I saw stories early in the pandemic of Sikhs, for whom having unshorn hair is an article of faith, felt pressured to shave their beards for their employment. If you are working in a setting where you're at risk for aerosols, institutions must provide you with a PAPR or find a way to help you pass fit test. We need to make sure our environments are well prepared for this.

Resources

- Summary – https://ubccpd.ca/2022-04-06-covid-19-update
- For patients – How to request and get treatment: https://www2.gov.bc.ca/gov/content/covid-19/vaccine/treatments#request
- Safety reporting: https://health-infobase.canada.ca/covid-19/vaccine-safety/
- Pharmacy Support is available for prescribers. This line is staffed by clinical pharmacists from Primary Care Networks who are specifically trained to assist with these complex interactions and are funded through the Ministry of Health. The line is open Monday through Friday from 8:30-4:30 and accessible at: 1-866-604-5924 Source: http://www.bccdc.ca/Health-Professionals-Site/Documents/COVID-treatment/PracticeTool1_AssessmentGuideforClinicians.pdf
- Drug interactions for Paxlovid and Remdesir: http://www.bccdc.ca/Health-Professionals-Site/Documents/COVIDtreatment/PracticeTool3_DrugInteractionsContraindications.pdf
- Assessment Guide for Clinicians: Step-by-step instructions: http://www.bccdc.ca/Health-Professionals-Site/Documents/COVID-treatment/PracticeTool1_AssessmentGuideforClinicians.pdf
- Under-Mask beard cover (Singh Thattha technique) – https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7532752/

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. Manish Sadarangani** (Director, Vaccine Evaluation Center at BC Children's Research Institute),
- **Dr. Jolanta Pisczcek –** (Co-Chair BC COVID-19 Therapeutics Committee, Infectious Disease Pharmacist)
- **Dr. Jennifer Grant** (Co-Chair BC COVID-19 Therapeutics Committee, Infectious Disease Physician & Medical Microbiologist, Vancouver Coastal Health)
- **Dr. Birinder Narang** (Family Physician, Clinical Assistant Professor, UBC Family Practice)
- Moderator: **Simon Moore** (Family Physician, UBC CPD Medical Lead)