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

Webinar date: **January 25, 2022**
Recording & Presentation Slides: https://ubccpd.ca/2022-01-25-covid-19-update-expert-qa-public-health-primary-care-vaccine-epidemiology-and-lab

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.

Webinar Summary

FAQS on RATs and Masks – Dr. Krajden

Rapid Antigen Tests (RATs)

- Recently a BMJ Meta-Analysis in children was conducted
  - For Omicron, RAT sensitivities were found to be in the 60-75% range relative to PCR (exact numbers are difficult to pinpoint)
  - Specificity is in the 97-99% range
- With early infection, RATs can be false negative
- If you are in a high prevalence scenario and the RAT is positive, consider it to be a true positive
- A negative rapid test does not eliminate the risk of transmission
- For consideration of therapeutics, if you have a negative RAT but think it may be positive, you should get confirmatory testing (PCR)

Masks

- They are transmission-reduction tools and quality does matter (i.e. medical vs. N95)
- Context is very important
    - Tools only work when used properly (i.e. a properly used medical mask is better than a poorly used N95)
    - In hospitals, we recognize transmission events include where health care workers are transmitting to other health care workers because they have left their guard down (e.g. at nursing stations or in-home settings)
        - However, wearing a mask is helpful even if it's not perfect
    - Eye wear is also important

BC Epidemiology Update – Dr. Gustafson

Cases versus Diagnoses

- The contact tracing strategy is changing
    - We tested less early on, then ramped up, and changed diagnosis rate
    - Periodically, blood samples have been looked at to see how much diagnoses underestimate infection, which could be 2-8-fold in the Lower Mainland depending on specific times
- Now with broad transmission, COVID-19 diagnoses represent a fraction of all the infections seen
- Overall, there is great coverage across the province; see slides for details

Hospitalizations

- Hospitalizations include people who have been admitted for and with COVID-19
- Over the past month, patients hospitalized with COVID-19 have gone up (i.e. they tested positive)
- Mortality is a reasonable measure, but we must look at those who die with COVID-19 as well as excess mortality
- Omicron emerged very rapidly; we now see that it has peaked in transmission based on cases and wastewater surveillance trends
    - Curves are similar around the world, which is the natural trajectory of the epidemic
- The types of public health measures that we have all gotten used to have a limited impact on transmission, as there is community level transmission that must be considered
- The strongest predictor of serious outcomes is still age
- Multiple comorbidities predict more serious outcome, but overall there is a trend of less severe illness with Omicron

Contact Tracing

- Contact tracing is an intervention used for a subset of communicable diseases
- Rationale:
  - Is there an intervention that contacts can take that is different from people who are not contacts to protect themselves or others?
  - Can we identify and reach contacts?
    - Can we define the contacts?
    - Do we have time to find them?
    - Do we have time to intervene?
- Examples:
  - STI, HIV, Hepatitis A, Measles → contact tracing works very well in these cases
  - Influenza, Norovirus, Invasive Pneumococcal disease → contact tracing does not work well in these cases
    - The reason is because it is either not possible or does not lend itself well to contact tracing
- Contact tracing can lead to contact specific intervention which can change the course of illness
  - Hepatitis A → Vaccination within 14 days
  - Measles → Vaccination within 3 days
  - COVID-19 in March 2020 → Quarantine for 14 days
  - COVID-19 now:
    - There is nothing available now for intervention, as it has a very short incubation period
    - There is very little opportunity to identify someone and give them meaningful intervention

Public Health Management

- We are moving towards:
  - Vaccination
  - Self-management
  - Testing
    - Limit transmission in high-risk settings
    - Identify those who benefit from treatment
  - Outbreak management in high-risk settings
  - Treatment

COVID-19 Vaccine Update – Dr. Sadarangani

Age	Comorbidities	Primary series*	Booster
<5 years	N/A	No vaccine available *(trials ongoing; data expected 2022Q2)*	
5-11 years	Moderate to severe immunosuppression**	3 doses Pfizer pediatric dose *(NACI recommendation; BC update pending)*	None
	None/other	2 doses Pfizer pediatric dose	
12-17 years	Moderate to severe immunosuppression**	3 doses mRNA	None
	None/other	2 doses mRNA *(Pfizer preferred)*	
18+ years	Moderate to severe immunosuppression**	3 doses mRNA	1 dose mRNA after 6 months *(Pfizer preferred for 18-29 yrs)*
	None/other	2 doses mRNA *(Pfizer preferred for 18-29 yrs)*	

Vaccine Updates

- Children under the age of 5:
  - No vaccine available yet
  - Trials are ongoing
- Children aged 5-11:
  - NACI recommends getting the pediatric dose (1/3 of the adult dose)
  - No recommendation for boosters right now
  - If you have moderate to severe immunosuppression, it's recommended to get a 3-dose primary series
  - This aligns with recommendations for those above the age of 12
- Youth aged 12-17:
  - Recommended to use the adult dose
  - Moderna is available, but is Pfizer preferred due to lower risk of myocarditis
- Interval for doses is typically 8 weeks, with a 6-month interval for boosters

Vaccine Effectiveness

- UK data – Symptomatic Disease
  - For people who received 2 doses against Omicron at 5-14 weeks post- vaccination, effectiveness starts at 50% and drops (much less than the Delta variant)
  - With mRNA Booster, this increases to 60-70% (still less than the Delta variant)
- UK data – Hospitalization
  - After two doses, effectiveness drops from ~60-40% against Omicron
    - Post-booster, we see a rapid increase to >90%, maintained at >80% after 10+ weeks

- US data – Hospitalization:
  - Delta variant:
    - We see a high vaccine effectiveness, with rates of 95% effectiveness against emergency and urgent care visits post-booster
  - Omicron variant:
    - After 2 doses of any mRNA within the last 6 months, we see a significant impact of the booster, getting to rates of about 80% effectiveness in preventing ER visits and 90% in preventing hospitalizations

COVID-19 Outpatient Oral Therapies – Dr. Narang

Repurposed & Novel Medications

- Colchicine:
  - Low power, low certainty, high adverse events
  - Not currently recommended
- Budesonide:
  - For symptomatic treatment, there is no impact in disease progression
  - Can be used in patients over the age of 65 with mild illness, or patients under the age of 50 with comorbidities
- Fluvoxamine:
  - A Brazilian RCT was shown to reduce emergency room visits over 6 hours and serves as a surrogate endpoint for hospitalizations
  - A Canadian fluvoxamine study stopped enrollment due to futility

Paxlovid – Nirmatrelvir/Ritonavir

- These are oral direct acting antivirals
- Recommended dosing: 300 mg of Nirmatrelvir alongside 100 mg Ritonavir, twice a day for 5 days
  - Ritonavir is being used to increase the half-life of Nirmaltrelvir
- It is metabolized by CYP 3A4 (high risk for drug-drug interactions)
- This treatment was approved by Health Canada January 17, 2022
- Phase 3 EPIC-HR study:
  - This has NOT been peer-reviewed
  - All data comes directly from Pfizer
  - It is double-blind placebo controlled, looking at unvaccinated and high-risk populations
    - Specifically looking at individuals aged 60 and above or those with a chronic condition such as diabetes, heart conditions, or chronic kidney disease

    - Relative risk reduction is 88%
    - Absolute risk reduction is 5.5%
- There are logistic and practical concerns regarding implementation

Molnupiravir

- This is a nucleotide analogue which, when incorporated into viral RNA, causes a base-pair mismatch thus leading to mutations
- The recommended dosing was 800 mg by mouth twice a day for 5 days
- A randomized double-blind controlled trial was conducted (MOVe-Out)
    - End point: all cases resulted in hospitalization or mortality
- The initial press release stated that risk reduction in severe outcomes (i.e. hospitalization/death) decreased from 9.7% to 6.8%.
    - A final analysis in December found that ARR declined to 3%, with concerns regarding statistical significance
- The BC CTC is reviewing
    - It is currently not approved for treatment by Health Canada
- The cost is expected to be over $500 for a 5-day treatment

Question & Answers

Q: Can someone explain the rationale around room sharing of COVID positive and negative patients in the hospital? Isn't that allowing for nosocomial infections to flourish?

A: The optimal design of hospitals to prevent nosocomial infections would be single-bed patient rooms. This is not our current state in BC where we are seeing 2- and 4-bed rooms. It is more of a a logistical issue.

There have been discussions about this, but ultimately the goal is that the people who are hospitalized for COVID get the management they need in the COVID ward, and others are to be managed in the area for why they are in hospital (maternity ward, surgical ward, etc.). The goal is to continue cohorting and isolating as much as possible. We have also considered that the disease is milder now. This is the approach that is used regularly for other respiratory pathogens.

Q: What are the indications and limitations of Rapid Testing? What are the false positive rates? Are we getting cross-reactivity?

A: The sensitivity is in the 60-75% range relative to PCR, and PCR itself is about 95% sensitive. The notion that you have a perfect test for PCR is false as there are very strict limitations. A comparison was conducted in the UK where a professional conducted a PCR test (i.e. a trained health care provider)

versus a non-professional, and it was found that there is a 15-20% splay in sensitivity depending on how well you do it. That said, if it is positive and the prevalence is high, the probability is that it is a true positive, since specificity is very high.

With Omicron, it was attempted in several parts of the world to improve sensitivity by doing oral and bilateral nasal swabs. The challenge with that is that the studies are small, and there is already evidence that if you drink fluids (i.e. put water into the test), you can get a false positive. So with these tests, it can be falsely negative early on, you can get infected very quickly with Omicron (incubation of a few days), and it's not practical to use it to determine if you can go to an event or visit someone as it doesn't necessarily prevent transmission.

The province will have a lot of kits and will try to distribute them. It will be important to use them where they can impact outcomes. You may want to use a PCR if you need to identify someone who is at risk of severe disease and could benefit from the therapeutic. This is also what is behind the push to focus PCR capacity in supporting people where it will impact outcome.

Q: Are we spending too much on rapid tests? Do we have enough of them?

A: As mentioned, rapid tests are being distributed by the province and there has been a lot of procurement. Every province has a slightly different strategy. In BC, it initially became available to help industries, especially where there are large congregate settings to help support business continuity. As demand and supply increased, rapid tests were used to manage that demand at testing sites. Now as more tests are becoming available, rapid test kits are being targeted to other sites such as schools, rural and remote Indigenous communities, post-secondary institutions and childcare settings.

Is it a useful or harmful intervention? It's a new technology, so we are hoping to have the ability to evaluate their benefit. If someone has access to one, it is convenient. You can use it to make decisions about care; that is why the testing recommendations are so focused on people who work in high-risk settings or may be eligible for treatment.

As a self-management tool and where it lands on the harm/benefit spectrum, we don't know that yet. Symptoms overlap with other conditions, especially in winter months. It provides us with another piece of information to decide if they have symptoms. Other Point-of-care tests have been important in helping with treatment, such as HIV testing. So, this is another tool that may help us transition to an endemic state where we manage COVID-19 as we manage other respiratory infections, and move to testing only when it effects management.

Q: What is the science behind the CDC guidelines that unvaccinated youth under 18 are able to return to society in 5 days but not unvaccinated adults? Can vaccinated people transmit the virus? Are youth less likely to transmit the virus?

A: At all times in the pandemic, we have to look at both risk from the virus as well as harm from measures, and we try to balance that. Children are less likely to acquire COVID, to transmit COVID and to have severe complications from COVID. They are also more likely to be around other children in these

settings. For those reasons, we felt it was safe for children to go back to school and resume their activities after 5 days even if they are not fully vaccinated. A longer isolation time wasn't worth increasing the harm from staying away from school.

The policy is a combination of science about COVID transmission as well as the harms and benefits of the intervention itself. Isolating children at home has significant impacts on their educational outcomes. The primary goal of testing right now is identifying people that would benefit from treatment and to identify people that may transmit in a high-risk setting.

The vast majority of people who have Omicron will not be diagnosed with Omicron. It did not make sense to put specific isolation recommendations for a subset of people who are diagnosed. It is becoming a question of incremental benefits and incremental harm.

If you keep the children at home, transmission within the household is higher than school settings. A study that is under peer-review right now estimates it at 4-5x higher in the household setting than the school setting. Children who are socially isolated at home with worsening mental health are instead on their tablets, playing video games which are not good for their development.

About two weeks ago, there was a UBC CPD webinar that looked at different aspects of COVID in youth specifically. Dr. Choi, one of the panelists, highlighted some studies from Vancouver Coastal Health looking at community transmission versus school transmission. It is an important point to consider here. Also, data presented from a Canadian study looking at >1,000 parents and 400 youth aged 10-18 found that stress from social isolation was the strongest risk factor for mental health deterioration. So, when looking at the risk of transmission, we must make sure that factors into the decision.

As for adults, there is some evidence that unvaccinated adults can transmit Omicron for a longer period, hence the longer isolation requirement.

Q: What are your thoughts on phasing to endemic from pandemic?

A: 'Pandemic' is a global definition, so we do not decide that. It looks at outbreaks on the global scale. Endemic refers to a known pathogen that ebbs and flows, sometimes seasonally and sometimes based on an increase in susceptibility in a population. Pertussis comes in waves, but it comes every few years. There is a predictable pattern of transmission.

Locally, in BC, we have a very transmissible virus where a large proportion of our population will have been infected by the virus or have been vaccinated. We are in that transition period, but we are not aiming for COVID-Zero.

A good reminder to keep in mind is that the goal of pandemic management is to reduce serious illness, reduce death and to minimize societal disruption. We have the tools available to do the first of these two things. We must work hard together to minimize societal disruption, which will take a lot of work over the next few months.

Vaccination alone cannot be used to eliminate the virus. Vaccination does not entirely prevent transmission; we are not in those conditions but we are fortunate that it reduces the harms. We must look at switching from risk-elimination strategies to risk-reduction strategies. When you apply risk-elimination strategies at a population level, which is when you start seeing the impact on individual freedoms, their social determinants of health, and other problems. At this stage of the pandemic, the majority of people are going to be protected from severe illness.

We will likely be living in an endemic phase while the pandemic continues. The global inequity to testing, treatments, and vaccines will continue. Western Australia & New Zealand have been aiming for COVID-Zero approaches but are starting to recognize it is not possible with Omicron. We can expect future variants but due to our population immunity it should not cause the same amount of societal disruption.

Q: Should we give the 3rd dose of vaccine immediately after someone recovers or wait for a few months?

A: Post-COVID infection, you will have some immunity that will last a few months. This varies a lot between people. Before Omicron, people with milder infections had less of an antibody and immune response, and we are not sure how long of a protection that leads to. We are not yet sure about antibodies on the nature of Omicron.

Regarding when to get the "next vaccine", the first question asked should be whether or not there are there any safety concerns. Even when looking at initial trials, most of them were immune naïve, but some people did swab positive and were kept in the trials. No safety signals emerged. There is no evidence there is any disadvantage of getting it after you have recovered from illness.

When you look at whether there is benefit, it was found that with a 7-8-week interval you will have a better immune response and better protection. There is still a good baseline interval at the 3-4-week interval. It may be optimal to wait for 7-8 weeks, as you may get more of an immune and memory response.

Whether you previously contracted COVID should not be the predominant reason behind whether you decide to get a booster and when. For example, if you are going somewhere where a booster may not be available or is mandated for certain activities, then it is reasonable to get it.

It's hard to generalizes across age groups. When you look at risks, they are not the same across these groups; conversations with 65-year-old versus 18-year-old patients may be very different.

Q: With the Clinically Extremely Vulnerable (CEV), the list is restrictive, meaning some may not have access to testing and treatment. What is the plan to protect those who are vulnerable, but cannot access these?

A: Paxlovid was approved just last week, with 4,000 treatment doses made available. We must look at the most medically vulnerable and move down the list. Very fortunately, the gradient of risk has been shortened by immunization. Many CEV individuals received very good protection and were prioritized for vaccination. The limitations are practical, as medications that are made more broadly available must

look at who it will be useful for. The skewing of risk is towards the elderly and those with multiple co-morbidities (e.g. solid organ transplant patients). As we gain more experience with the medications, they will be made appropriately available. If you are looking at Tamiflu, this requires a lot more assessment of drug-to-drug interactions and other risks.

There have been plans to have direct messaging with CEV individuals regarding criteria for therapeutics and an automatic report out to link to the case indications for therapeutics. If rapid antigen testing is helpful then it can be used, but if it is negative then we will need PCR access across the province to help implement therapeutics.

The initial CEV group that was identified earlier in the pandemic included populations at risk for many conditions, but that doesn't mean the risk for COVID-19 is higher. With Paxlovid, you have a medication that will be most effective in a population where it may be hardest to safely give. However, it is not a substitute for vaccination.

The CEV group is recommended to get an extra vaccine. As CEV individuals were prioritized for vaccine roll-out, they should be due for boosters soon.

Q: What do we know about long COVID? How long do individuals with Long COVID need to be off work?

A: Certain estimates project that 10-30% of cases can lead to long COVID. It doesn't correlate well to severity of symptoms (analogous to multi-inflammatory syndrome in children). It likely is contributing to a lot of uncertainty and stress in the public with limitations in access to testing. Symptoms can be similar to Central Sensitivity Syndromes and Post-Concussion syndromes. With regards to long COVID, it is coming from immunonaive patients earlier in the pandemic. Lots of lab-based research and real-world data is starting to emerge indicating that patients who get vaccinated after showing long COVID symptoms are likely to have a significant improvement in their long COVID symptoms.

With regards to length of time off work, this must be individualised based on severity of illness and how recovery is going. We must assess symptoms and the impact on function and ability to work, and then plan accordingly.

Resources

- **BMJ Study:** https://ebm.bmj.com/content/early/2022/01/04/bmjebm-2021-111828
- **NEJ Study:** https://www.nejm.org/doi/full/10.1056/NEJMcp2117115
- **UBC CPD 2022-01-11 COVID-19 Pandemic: Preventing and Managing the Health Impacts on Kids Webinar:** https://ubccpd.ca/2022-01-11-covid-19-pandemic-preventing-and-managing-health-impacts-kids

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),
- **Dr. Birinder Narang** (Family Physician, Clinical Assistant Professor, UBC Family Practice)
- **Dr. Simon Moore** (Family Physician, UBC CPD Medical Lead)