



THE UNIVERSITY OF BRITISH COLUMBIA

Continuing Professional Development

Faculty of Medicine

UBC CPD

The Division of
Continuing Professional Development
Faculty of Medicine
City Square, 200-555 W 12th Ave
Vancouver BC Canada V5Z 3X7
T 604.675.3777
ubccpd.ca

COVID 19 UPDATE: Q&A WITH BC AND QUEBEC EXPERTS ON THE CLINICAL MANAGEMENT OF COVID19

Webinar date: **March 29, 2022**

Recording & Presentation Slides: <https://ubccpd.ca/2022-03-29-covid-19-update-qa-bc-and-quebec-experts-clinical-management-covid-19>

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

Everyday Business In Family Practice – Dr. Rita McCracken

Questions to Consider:

- Does this person have COVID? How sick are they? Should they get treated?
- What treatments are available? Contraindications?
- How do I actually prescribe?
- There are BC tools to help decide who may benefit from treating mild/moderate symptoms

Predictors of Serious Illness

- Age is most reliable predictor
- Vaccination status also an important predictor
- Co-morbidities may be a significant predictor of serious illness

BCCDC Risk Assessment:

- http://www.bccdc.ca/Health-Professionals-Site/Documents/COVID-treatment/PracticeTool1_AssessmentGuideforClinicians.pdf
 - Tool can help to assess risk from <1% to >20% risk of hospitalization
 - If hospitalization risk is:
 - 3 points or less → treatment not recommended
 - 4 points: Slightly increased risk (3-4%), treatment recommended
 - 5 or 6 points: treatment recommended

Paxlovid – Nirmatrelvir/ritonavir – Oral Anti-viral

- Treatments approved based on RCT results drugs compared to placebo during delta wave on unvaccinated adults ≥55 yo or ≥1 health complication
- RCTs designed to test effect of drug on preventing hospitalizations (for COVID) or death within 28 days (any cause)
- Treatment
 - Risk of hospitalization or death = 0.8% (79/1046)
- Placebo
 - Risk of hospitalization or death = 6.3% (8/1039)
- No information yet about how this drug may benefit vaccinated people in Omicron wave or later.

Who should I offer treatment to?

- If patient has:
 - >3% estimated benefit (use the risk calc tool)
 - Is symptomatic, with positive test (in BC RAT is okay)
 - Been sick ≤5 days (first day of symptoms = Day Zero)
- Then consider Nirmatrelvir/ritonavir
- But there are significant drug-to-drug interactions
- See resources for information on how to contact treatment line
 - Statins, Novel Anti-coagulants, Anti-epileptics, Calcium Channel Blockers, Certain Antipsychotics, Fentanyl, Amiodarone, Tacrolimus & Cyclosporine.

Clinical Pearls – Dr. Omar Ahmad

Therapeutics Through COVID – ER + ICU

- Dexamethasone – for patients who are sick enough to be admitted to hospital, not for outpatients
- Remdesivir – for people who are being admitted as well (recommendation may change)

Reflections – Dr. Srinivas Murthy

- At the beginning of the pandemic, relied on supportive care
- 1 year into pandemic, steroids for inpatients
- 2 years into pandemic, into a confusing place of both inpatient and outpatient treatment pathways
- Main recommendation is not to know the therapeutics but to know how to find out what is available in your jurisdiction as the evidence continues to change
- [BC COVID 19 Therapeutics Committee](#) continues to review evidence and give recommendations

COVID 19 & Thrombosis – Dr. Susan Kahn

Thrombosis in COVID 19 Infection

- COVID 19 → high incidence of venous thromboembolism and arterial thrombosis (stroke, heart attack), despite standard use of thromboprophylaxis (ie low dose anti-coagulant)

Mechanisms of Thrombosis in COVID19

- Multiple factors that contribute including intense inflammation can induce thromboinflammation in both small and large blood vessels

Rationale for anticoagulation as an intervention in COVID-19

- Several lines of evidence support potential efficacy of therapeutic parenteral anticoagulation with heparin for the treatment of COVID-19
 - COVID-19 associated with hypercoagulable state
 - Heparin induces conformational changes in the SARS-COV-2 Receptor spike protein (may limit cellular invasion and improve acute lung injury)
 - Heparin has direct anti-inflammatory effects
 - Easy scalability (ubiquitously available)
- 75 clinical trials registered on clinicaltrials.gov
- Recent meta-analysis from a few months ago also

Bottom Line (results so far)

- Hospitalized non-ICU patients with COVID-19 – Therapeutic dose anticoagulation (AC) better than sub-therapeutic (prophylactic or intermediate) dose AC
- Hospitalized ICU patients with COVID-19
 - No benefit of therapeutic dose AC vs sub-therapeutic dose AC and may cause harm
 - No benefit of intermediate dose AC vs prophylactic dose
 - So: Prophylactic dose seems best
- Vaccine-Induced Thrombosis with Thrombocytopenia (VITT)

- Rare but serious complication of AstraZeneca and Johnson & Johnson COVID vaccine (but not Pfizer and Moderna vaccines)
- A prior history of thrombosis or having thrombosis risk factors does NOT increase the risk of this rare complication

The Post COVID-19 Condition– Dr. Emilia Falcone

- At least 10% of COVID-19 survivors will have long-term sequelae (~300K Canadians)

Terminology & Definition

- Post COVID-19 condition
- Post-acute sequelae of COVID-19 (PASC)
- **WHO Definition (Oct 6, 2021)**
 - History of probable or confirmed SARS-CoV-2 infection
 - 3 months from the onset of COVID-19
 - Symptoms that last for at least 2 months and not explained by an alternative diagnosis
 - Common symptoms include fatigue, shortness of breath, cognitive dysfunction but also others which generally have an impact on everyday functioning.
 - Symptoms may be of new onset following initial recovery from acute COVID-19, or persist from the initial illness
 - Symptoms may fluctuate or relapse over time

Potential Risk Factors

- Occurs irrespective of initial severity of infection
- Having more than >5 symptoms during the acute infection
- Higher BMI
- Being Female
- Having asthma
- Having poor pre-pandemic mental health
- Having poor general health
- Being older or middle aged (20-70 years)
- Type 2 Diabetes
- SARS-CoV2 RNAemia
- EBV viraemia
- Specific autoantibodies

Post COVID 19 Condition: Common signs and symptoms

- Could be post ICU, or post admission with other medical comorbidity that occurred and those who did not have a severe course of illness in acute phase, can be trickier to diagnose
- Most common symptoms: (>200 have been found)

- Fatigue – 58%
- Headache – 44%
- Attention disorder – 27%
- Hair Loss – 25%
- Dyspnea – 24%

Clinical Evaluation and Management

- Determine if current condition is due to:
 - Sequelae from acute COVID-19
 - An exacerbation of an existing comorbidity
 - Must assess/appreciate what mental, physical health was like pre-COVID diagnosis and functional changes that have occurred
- Eliminate all conditions unrelated to COVID-19
- Symptoms are often not associated with objective findings on initial evaluation
- Management:
 - May differ if patient had severe COVID-19
 - Should be symptom-based, personalized and ideally evidence-based
 - May include promoting a progressive return to activity when safe to do so
 - Multi-disciplinary approach will be important, if profile is similar to chronic fatigue syndrome, then one key is to teach them about post-exertional malaise and pacing
 - May include self-management of certain symptoms

IRCM post COVID-19 (IPCO) Research Clinic

Objectives

- Comprehensively evaluate the long-term complications of COVID-19
- Establish a biobank
- Elucidate the pathophysiological mechanisms underlying the post-COVID 19 condition
- Uncover novel therapeutic targets to treat the post-COVID 19 condition

COVID-19: From pandemic to here for a long time? – Dr. Karl Weiss

- “It will take years to fully quantify the economic costs of the pandemic, but they are enormous. Early estimates suggest that lockdowns cost the United States between \$20 and \$35 billion per day. Preliminary estimates of the pandemic’s total economic impact – separate from the health costs – will be over \$7.5 trillion in losses.”
- With Omicron started seeing a lot of reinfections, if you have had COVID in the past, you will not necessarily have protection forever.

- Effects of reinfection are not known yet, we are not looking at severe outcomes, but still learning about things like Long COVID
- Have a lot of experience with regards to safety in vaccination now
- Omicron Variant
 - Quite different from what seen before
 - BA.1 and BA.2 now, very quickly in late December BA.1 took over, now BA.2 is taking over
 - Seeing very quick spread of BA.2 subvariant, Fitness is key to this virus over virulence
- Hospitalization
 - Roughly 40-50% of patients admitted with COVID, don't really have COVID as their primary diagnosis, must rethink how we look at hospitalizations
- Highlights
 - Omicron came into a population that was highly immune in Canada, generally we did very well
 - Between Nov 22 and December 25, 2021, 0.03% matched Omicron cases died, compared to 0.12% Delta cases
 - 0.5% were hospitalized or died compared to 1.6% among Delta cases
 - 0.06% Omicron cases were admitted to ICU or died, compared to 0.42% Delta cases
 - For Omicron compared to Delta:
 - Risk of hospitalization or death was 65% lower, while risk of ICU admission or death was 83% lower
 - Significant impact on healthcare system could be present due to sheer volume of cases, despite probable reduction in severity
- Masks
 - Are effective and useful in certain settings
 - Even surgical and cloth masks will reduce risk of testing positive by 50-60% based on CDC MMWR data
 - Masks will likely be here to stay for institutions (i.e. for travel)
- Time to infection
 - If neither person is wearing a mask, time to infection is about 15 minutes
 - If both people wear typical cloth masks ~26 minutes
 - If both people wearing typical surgical masks ~1 hour
 - If both have FIT tested N95s, time goes up to 25 hours

Vaccines

- New study from New England Journal of Medicine, overall for healthcare workers, likely will not be very benefit, may have marginal benefit
 - Better than third dose for those over age of 60, limited in protection ~10 weeks max.
 - Not a very big impact on severe illness

Treatments

- Almost 100 medications in trial right now including anti-virals
- In USA – CTAP (Coronavirus Treatment Acceleration Program)
 - At least 15 anti-viral in clinical trials right now
 - Including cellular therapies, antivirals, immunomodulators, neutralizing antibodies
- Stages of COVID-19 Therapeutics
 - Outpatient
 - COVID 19 vaccines
 - mABs (monoclonal antibodies) for PrEP (Pre Exposure prophylaxis for high risk)
 - Post exposure prophylaxis (mABs)
 - Therapy: Paxlovid
 - Inpatient
 - Remdesivir, Tocilizumab, Dexamethasone, Baricitinib

The Future

- Reduce Transmission (Surveillance, Testing)
- Reduce Severity
 - Target the high-risk population
 - Test
 - Treat

Question & Answers

Q: How concerned should we be about BA.2?

A: Believes there is a wave coming. Lots of surges in wastewater surveillance in BC and Ontario. The challenge will be what the disease will be and how many susceptible people are out there. BA.1 infection provides some protection from BA.2, expect some residual protection. 3 doses of a good vaccine will provide some protection. Not sure how much against BA.2. We have a lot of population immunity (but not complete) and a lot of public health knowledge. Difficult to implement.

From an ICU perspective, feel a much less level of concern than before. Hospitalizations continue to drop in many places around the world. This could change.

We also have a lot better treatments now including with steroids, thromboprophylaxis and treatments.

Q: BC seems to have been have a lower incidence of morbidity and mortality than Quebec. Any comments?

A: In Quebec, the first wave was a disaster, especially in the Long-Term Care Facilities. Unfortunately, many deaths occurred in the initial wave and in second wave, which may be skewing the numbers in

that way. The Quebec population is likely older than BC population on average. Structure of the Long-Term Care Facility also needs to be considered - very limited human resources and terrible architectural conditions.

In BC, at least in the first wave, the March break and Spring break was offset, and we had a delayed spring break compared to Quebec.

Q: What are thoughts of another variant and wave in coming months? Any specific recommendations that you would suggest in preparing?

A: Now we are getting to a place of endemicity. COVID is a respiratory virus, that is cyclical, with peaks/troughs of transmission throughout the year. We are better prepared with vaccinated population and from virus perspective, there is no real reason to change to a variant that is different. Might have ongoing subvariants, but unlikely to have a brand-new variant in the short term. As two variants emerged from African countries, we must continue to help support global vaccine equity. There are a lot of immunocompromised patients in these lower socio-economic conditions can breed new variants.

Q: It is said that Long COVID has similarities to post-concussion syndrome, do we know much about pathophysiology and neural inflammation?

A: May be similarities clinically, but we different physiologically. One is post infection. There are some signals with auto antibodies, some related to Lupus and G protein coupled receptors. Possibilities of tissues that could be affected are vast. Another hypothesis that has been raised is about the microbiota. There is a perturbation of the intestinal microbiome, that perturbation can be impacted for months. Leaky gut could lead to bacterial translocation that could have an impact on end organs. Another hypothesis is around microclots which could have an impact on nerve endings manifesting in neurological symptoms.

Q: Should primary care clinicians be encouraging their fully vaccinated at risk patients to present early to access therapy?

A: For those patients who are chronically at risk, we have patients in our primary care practices that may have medical and social risk, would recommend a mechanism of outreach to check on them, to let them know that there is a mechanism to get assessed and access treatment. Don't need to send out messaging to all patients though. Applying treatments to a population that is different than those studied in the RCTs that led to approval. Comes down to clinical judgment.

Some parallels that were seen with oseltamivir, the earlier you give the drug, the better. Ideally, if you give it very quickly within the first 36 hours, the impact on outcome will be much more than if you give it on day 5 of symptoms.

Lot of indication creep for drugs like paxlovid and how the study was done and how it is applied it is very different. Hopes that it does bear fruit, does worry that it was only one study. The benefit is so impressive that it seems a bit too good to be true.

Q: A COVID-19 patient, that was on the ward, that is now transferred to ICU, should therapeutic anticoagulation be continued or not?

A: Certainly, within the trials that looked at therapeutic dose in hospital wards and were then transferred to ICU, they remained on the allocated intervention, i.e. would have remained on therapeutic dose if that was randomized to initially.

Don't have any direct data yet. The practice is quite variable. In Dr. Kahn's hospital, keep them on therapeutic dose, some other centres downscale to prophylactic dose.

Q: With respect to ICU management, are more patients surviving now than earlier in the pandemic?

A: Management has changed significantly, the rush to intubate has decreased. Has gone back to common practice, using fluid management, better sedation, and ventilation strategies. Have been using dexamethasone and the addition of interleukin 6 antagonists have made a big difference. Have learned that there is a group of patients called "stalled" patients, looking at other issues have developed such as Ventilator associated pneumonia, Tuberculosis/Aspergillosis. Overall management has changed, that has led to better improved outcomes. The virulence of Omicron is not as severe, and vaccination has had a massive impact, including in ICU patients with decreased mortality in vaccinated compared to unvaccinated

Q: For COVID19 related persistent cough, how would you treat it?

A: Need to approach it as any cough, not a very common post covid symptom, could last few weeks to a couple of months. Address common causes through your clinical approach.

Q: Given the low incidence of COVID in children and adolescents, how aggressive should we pursuing vaccination in these age groups?

A: Haven't done very well in Canada in vaccinating the 5-11 age range. We are still stuck in the 40-60% depending on jurisdiction. We do not want to be this low. While we think COVID in children that are unremarkable, when we look at other diseases in kids, that we have routine vaccinations for, ie polio, meningococcal, pneumococcal etc. These are also exceptionally rare to have severe outcomes from, even more rare than from COVID 19. For protecting individuals and populations from COVID19, vaccinations is one of our biggest bangs for our bucks. Lots of policy makers are looking at ways to incentivize family members to help vaccinate children, looking at ways to discuss relative benefit.

Q: Long COVID incidence 10-30%, does not seem to being represented in clinical practice, especially during Omicron?

A: The nuance is, the definition of Long COVID, is not very clear cut, need one persistent symptom. The problem is one of these symptoms is common to other diseases as well. Prevalence will vary the further out you are from time from infection. The numbers come from UK Office of national statistics, and WHO. Data is based on earlier forms of the virus, and not necessarily in the post vaccination era. When you get to 3 months, looking at 10-13%. A Quebec study that came out in healthcare workers, not all

vaccinated, the prevalence was 40-45%. Preliminary data does suggest that vaccination does prevent you from developing Long COVID, perhaps up to 50%. Will likely see Long COVID with Omicron, hope that proportion impacted patients will be lower.

Resources

- <https://ubccpd.ca/2022-03-29-covid-19-update-qa-bc-and-quebec-experts-clinical-management-covid-19>

Thanks to the speakers on the video:

- **Dr. Omar Ahmad**, Dept. Head, Emergency Medicine and Critical Care Medicine, Island Health; Clinical Associate Professor, University of British Columbia
- **Dr. Emilia Liana Falcone**, Director, Microbiome and Mucosal Defence Research Unit, Montréal Clinical Research Unit; Assistant Professor, Department of Medicine, Université de Montréal
- **Dr. Susan Kahn**, Canada Research Chair in Venous Thromboembolism; Director, Jewish General Hospital Centre of Excellence in Thrombosis and Anticoagulation Care (CETAC); Professor of Medicine, McGill University
- **Dr. Rita McCracken**, Family Physician; Assistant Professor, Department of Family Practice, University of British Columbia
- **Dr. Srinivas Murthy**, Investigator, BC Children's Hospital; Clinical Associate Professor, Department of Pediatrics, Faculty of Medicine, University of British Columbia
- **Dr. Karl Weiss**, Chief, Division of Infectious Diseases, Jewish General Hospital, Professor of Medicine, McGill University, Department of Medicine; Clinical Professor, Department of Microbiology, Infectiology and Immunology, Faculty of Medicine, Université de Montréal
- **Moderator: Dr. Bob Bluman**, Executive Medical Director, UBC CPD; Clinical Professor, Department of Family Practice
- **Moderator: Dr. Sam Daniel**, CPD Director, Fédération des médecins spécialistes du Québec; Director, Otolaryngology–Head and Neck Surgery, Montreal Children’s Hospital; Professor, Pediatric Surgery and Otolaryngology, McGill University