

Changing the Way We Work

January 20, 2023: COVID Therapeutics

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Curated answers from CoP guest, panelists and co-hosts to in-session questions posed by participants, based on current guidance and information available at the time.

Paxlovid

- **Please comment on covid rebound and how to interpret/manage.**

A CDC advisory confirmed in May 2022 that some individuals who take Paxlovid experience a return of symptoms 2-8 days after finishing the 5-day treatment and testing negative for COVID-19. Please see also:

<https://www.nejm.org/doi/10.1056/NEJMc2205944>

- **How do the pharmacists prescribe Paxlovid without knowing the pt's eGFR?**

Paxlovid can be taken after dialysis and dosage can be adjusted based on eGFR (most recent) and weight. MDs and pharmacist can answer this better.

- **Comments on rebound of clinical symptoms after use of Paxlovid?**

A September 2022 letter in NEJM extracted data from Pfizer's EPIC-HR Phase III trial of about 2,200 "symptomatic, unvaccinated outpatient adults at high risk for progression to severe coronavirus disease." Half of the group was treated with Paxlovid; the other half was not. According to the authors:

- From baseline through day 14, viral load rebound occurred in 23 of 990 patients (2.3%) in the nirmatrelvir–ritonavir group and in 17 of 980 (1.7%) in the placebo group. In other words, there was not a statistically significant difference in the rate of rebound in the Paxlovid-treated and control groups.
- Although there is no definitive evidence that Paxlovid does not cause Covid rebound, there is, when taken as a whole, a convincing argument that this is true. And there is no evidence at all that it does.

- There is no data to support giving a second course of Paxlovid or other treatment, but in patients with severe symptoms or immunocompromising conditions, it might be worth considering.
- **Another Paxlovid question: Is the “expansion” to the Paxlovid guidance criteria based on new scientific data or due to increased supply?**

Paxlovid is an antiviral treatment for people with mild to moderate covid at high risk of becoming seriously ill from the virus. All adults 65 and up fall in that category. See: <https://www.nejm.org/doi/full/10.1056/NEJMoa2204919>

Conclusion: Among patients 65 years of age or older, the rates of hospitalization and death due to Covid-19 were significantly lower among those who received nirmatrelvir than among those who did not. No evidence of benefit was found in younger adults.

- **Does Paxlovid still work well for XBB 1.5?**

Evidence is still evolving. Not much is known.

- **What is the current evidence in terms of paxlovid decreasing the risk of long COVID?**

Please see here:

https://www.cmaj.ca/content/195/2/E80?utm_source=TrendMD&utm_medium=cpc&utm_campaign=CMAJ_TrendMD_0

<https://canjhealthtechnol.ca/index.php/cjht/article/view/RE0040sr>

More studies are needed however.

- **Basic question #2: how do patients physically GET the paxlovid if they are isolating? (many of my seniors don't have anyone who can pick it up for them)**

Meds are couriered to them in the trial - a great option! o/w some pharmacies deliver.

- **Patients with GFR below 60 are excluded according to Dr. Hosseini. This excludes a large number of elderly. Is this correct?**

Patients with GFR<60 need reduced dose of Paxlovid and for this study, dosage should be same for all participants.

- **Comment on the risk of hepatitis/liver issue on paxlovid**

Patients with known current severe liver impairment (characterized by severe ascites, encephalopathy, jaundice, or prolonged INR) will be excluded from randomizing to Paxlovid. People with liver disease without any of these features are eligible.

- **What about creatinine levels before paxlovid rx? Do pharmacists and or can treat staff arrange this?**

Patients with known moderate or severe renal disease (defined as CKD stage 3, 4 or 5 or current acute kidney injury or most recent eGFR in the past 6 months <60 ml/min) will be excluded from randomizing to Paxlovid

- **How come we can't prescribe Paxlovid to put on hold at a pharmacy for those high risk to be filled once COVID Positive confirmed by the pharmacist. It allows early treatment and prevents people scrambling for care.**

You can file a prescription with a pharmacy in advance. The pharmacy would then dispense when patient has positive test. etc.

- **How come Paxlovid rebound has not been addressed: i.e) longer duration needed.**

Will be discussing when we explore CanTreatCOVID and subsequent arms of the study.

Vaccines

- **Are covid bivalent booster vaccinations (i.e. second bivalent shots) recommended? If so when is the best time to get these?**

Bivalent vaccines still perform better than monovalent vaccines against XBB.1.5.

- **If someone has 4 doses, last early Sept 2022, and has asthma and epilepsy, and is a healthcare worker, would that warrant earlier booster? They had COVID x2, last March 2022, with significant increase in Seizures thereafter...**

If under age 50, the 2 conditions noted would not result in impaired immunogenicity to vaccine so I would not advocate for a shorter boosting period.

- **Once you have the vaccine, isn't there memory effect? Why do we have to boost so often?**

Great question. Why some viruses do not induce prolonged immunity, another example is RSV, may relate to the nature of the Abs produced along with the evolution of subtle mutations in the primary antigenic epitopes of those viruses.

- **Is there any recommendation for a second bivalent booster after 3-6 months after 1st one?**

NACI is also starting to emphasize that the 6 month interval post vaccine or confirmation infection (to get another booster) is most optimal. The 3 month (as per their October statement) was mostly to get people caught up in the fall - it wasn't intended to be an ongoing 3 month interval). NACI is looking at if/when future boosters may be required.

- **Re: the patient with the positive RAT - what should I advise them re getting a bivalent booster? Should they have one at 3 months post-positive RAT, since their last vaccine was 12 months ago? Or should they wait til 6 months for their vaccine?**

I would consider they be boosted as you indicated at 3-4 months post +RAT.

- **How often should vulnerable patients receive Covid boosters?**

Most < 65 are recommended to get their booster six months after their last dose or following a COVID-19 infection. People at high risk are recommended three-month interval. As per the discussion this 3 month interval was to try to get people boosted in the Fall. NACI is looking at the ongoing 3vs6 months intervals. Here is the Ontario eligibility <https://www.ontario.ca/page/covid-19-vaccines#:~:text=Most%20people%20under%20the%20age,fall%2Fwinter%20respiratory%20illness%20season>

- **Should vulnerable patient who received the bivalent BA1-2 vaccination receive the BA 4/5? If so after how long?**

Not at this point.

- **Is there a role for Novavax as a universal booster?**

Please see here: <https://www.cdc.gov/media/releases/2022/s1019-novavax.html>

Nothing more recent, however.

- **If you had a first generation Moderna BA 2 bivalent vaccine can you get a BA 5 bivalent vaccine booster post 3-6 months? Is it recommended? Many physicians /health care professions got the first generation BA2 moderna vaccine.**

The National Advisory Committee on Immunization (NACI) is currently reviewing if/when future booster doses may be required. The mRNA COVID-19 vaccines provide good protection against hospitalization and severe illness within the 3 to 6 months following vaccination.

- According to NACI, it is not expected that a booster dose be routinely given every three months. With informed consent, an additional booster dose may be given at a shortened interval of at least 3 months for people at high risk of severe illness from COVID-19.

See: <https://www.toronto.ca/home/covid-19/covid-19-vaccines/covid-19-vaccine-eligibility-doses/>

- **What is the risk to the unboosted after 6 months?**

There is data from an Israeli study to show that protective immunity falls from 80% to 39% at >6 months from last vaccine dose.

- **Would suggest getting the Pfizer bivalent in the elderly if they had the Moderna bivalent greater than 3 months previously to give them better protection?**

There is no evidence to support that as a recommendation. I would not suggest it as a strategy.

- **Could the strokes after vaccination with Pfizer age 65 be consequence from prior COVID Infection.**

This is what is being looked at, but numbers are too low to be able to determine causation at this point.

- **Please clarify if bivalent vaccine significantly reduces risk of infection with new variants vs decreasing risk of serious illness from Covid?**

Yes there is evidence of sterilizing immunity (prevention of infection) with the bivalents that lasts for 3-4 months post administration.

- **Please comment about boosters after Covid infections.**

Timing of COVID booster after infection depends on the population and current #s. Most can wait 3-6 months. See pgs 14-15 here:

https://www.health.gov.on.ca/en/pro/programs/publichealth/coronavirus/docs/vaccine/COVID-19_vaccine_administration.pdf

- **Basic question: why can't we target an area on the virus that doesn't mutate and make a vaccine for that?**

We are looking at that strategy, but SARS-CoV-2 mutates all antigenic regions, so it's finding one that has the lowest mutation frequency AND results in viral neutralization.

Clinical Trial

- **Is the study unblinded if a patient develops severe covid or is hospitalized in the study?**

CanTreatCOVID is an open label trial (unblinded).

- **Re the blinded trial: Paxlovid tastes incredibly bitter. Will patients be able to tell this way if they got the real thing? People are starting to know about the bitter taste.**

CanTreatCOVID is an open-label trial (unblinded), and participants will be randomized to either usual care or study therapeutics.

- **Who does the testing for Covid in this trial?**

It will be done by participants and they need to send us a picture of positive test (via email/ text).

- **In this study will there be a crossover e.g. if someone is in the no treatment group and symptoms worsen...and is still within the 5day symptom onset?**

No crossover but the study is designed to be flexible; i.e. modifications to the arms based on interim analysis.

- **Does the study follow patients daily?**

Participants need to complete online diaries for day 1- day 14. We have safety calls at day 1 and day 4 to make sure there is no adverse effects.

- **For this study is there any exclusion based on creatinine clearance?**

Patients with known moderate or severe renal disease (defined as CKD stage 3, 4 or 5 or current acute kidney injury or most recent eGFR in the past 6 months <60 ml/min) will be excluded from randomizing to Paxlovid.

- **How most recent for the GFR? last 6 months?**

Patients with most recent eGFR in the past 6 months <60 ml/min) will be excluded from this study.

- **I have an 85 year old female with multi-morbidities and 2 covid vaccines whose daughter refused paxlovid treatment even though eligible. Instead, she wanted high dose of Vitamin C, Vitamin D, Zinc, multivitamin and a naturopathic anti-inflammatory. Will your study be looking at these alternate treatments?**

There has been some discussion to also add an antioxidant therapy (high dose of vitamin C, Zinc, Selenium and Lycopene) as an arm to CanTreatCOVID. This has to be approved by study therapeutic committee before we can proceed.

- **Is there going to be a placebo arm in the trial.**

There is no placebo for this trial. It is an open-label trial, and participants will be randomized to either usual care or study therapeutic.

- **Do patients need official ref. or they can self-refer?**

They can reach out to us at our Toll-free line: 1-888-888-3308

Email: info@CanTreatCOVID.org

Website contact form: <https://cantreatcovid.org/contact/>

- **Please confirm: is vaccine status relevant as inclusion/exclusion criteria for RCT?**

We include both vaccinated and unvaccinated individuals.

- **Do you feel the shelter population may benefit from this study?**

Yes, indeed. We are including all eligible people regardless of housing and we are trying to be equitable with this study.

- **Is the cantreat study assessments all virtual**

Yes, there will be no in-person visit.

Other

- **PANEL POLL: Can the doctors on the panel let us know how they practice to see any patients or even in the community? N95 or KN95 or surgical mask? Would be nice to know what experts actually do.**

I've continued to wear an N95 most of the time in clinic so that I'm not having to switch my mask when seeing pts with COVID-like symptoms.

You're likely familiar with current PPE recommendations, summarized here:

<https://www.ontariofamilyphysicians.ca/tools-resources/covid-19-resources/clinical-care-office-readiness/ipac-ppe-tools-suite.pdf>

- **Has everyone tried the new AI chat GPT? It is incredible and scary at the same time. Unfortunately, it is not up-to-date with the COVID pandemic.**

I would suggest posting this into the chat to see if others have used this AI! Personally I have.

- **Is <https://cantreatcovid.org> a 24/7 service? Can patients expect to be contacted within 24 hrs?**

Yes, they can also contact us at 1-888-888-3308.

- **I noticed at the preadmission clinic, in they have added, "Have you tested for Candida in the last 6 months?" This was at the end of the Covid questions. Have they noted a connection between Candida and Covid?**

Yes. Please see here: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8918595/>

- **Is testing sewage for COVID variants more effective at the airport to look for foreign variants?**

Interestingly, a lot of countries are moving to test wastewater from international flights, which makes a lot of sense to detect new variants.

- **If you have no symptoms are you less infective?**

Please see: <https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2774707>

Conc: Asymptomatic individuals can still shed the virus

- **What does the future hold for this virus?**

A slow evolution to endemicity, which will take another 3-5 years.

- **Is cantreat available on weekends and evenings?**

Currently, we operate Monday- Friday from 8am- 6pm.

- **How accurate are the rapid tests re xbb1.5**

So far, there is no evidence of tests not working on COVID variants like Kraken.

- **Is there a new, specific diagnostic code for long covid?**

There is a new diagnostic code for Post COVID condition ie. long COVID which is 081

- **Can you please comment on isolation recommendations? I feel like I can't keep track.**

The Confused About COVID series summaries current guidance well. For non-immunocompromised patients/those in high risk settings, isolate until symptoms are improving for at least 24 hrs. (48 for GI symptoms) and no fever and take precautions (masking, avoid high risk settings, etc) for 10 days.

<https://dfcm.utoronto.ca/sites/default/files/assets/files/q1feelingunwellennew.pdf>

- **Is there a new, specific diagnostic code for long covid?**

No, to my knowledge it is still 080 for COVID and that includes acute infection and long COVID.

- **Are Covid-19 assessment centres going to remain open after March 31, 2023?**

Not yet clear what will happen with the CACs

These additional questions were answered live during the session. To view responses, please refer to the session recording.

- How come Paxlovid rebound has not been addressed: i.e.) longer duration needed.
- What criteria are used to decide if a patient requires a second round of paxlovid?
- Please speak to new concerns re: bivalent vaccine in the elderly.
- Has everyone tried the new AI chat GPT? It is incredible and scary at the same time.
- Has anyone come across patients testing positive on RAT without actually having Covid? I have one patient who tested positive for 17 days with no symptoms and tested positive 3 months later for 9 days with no symptoms. No one was sick around them, and they are good mask wearers. They had 3 doses of vaccine - the last one was a year ago, I think.
- Risk factor ">6 mo since a COVID vaccination" is a very large heterogeneous group. Was there enough statistical power to analyze which subset of people in that group is the most at risk? 30 yo vs 60 yo?
- Can you comment on the reliability of RAT testing with current variants? Specifically a negative RAT despite symptoms. Thx.
- How effective is the pediatric Pfizer bivalent booster against the XBB.1.5 sub-variant?
- Does Moderna have a BA5 bivalent available in pharmacies? Which is better Moderna or Pfizer?
- What do we know about the protection Moderna BA1 bivalent provides?

- Can you comment on the change in interval to 6 months post covid for vaccination?
- In the last 4 months, PHO hospitalizations due to covid have been clustered mainly in those over 80, and even more so in unvaccinated elderly patients. Assuming we all keep up to date with our vaccines, has severe covid become mainly an elderly and immunocompromised patient issue?
- Since the upcoming variant XBB1.5 is more related to the BA.2 variant, wouldn't the first generation of Moderna bivalent vaccine be preferred?
- Should health care providers get boosters every 3-4months regardless of age?
- For booster dose, is sixth dose available or suggested 6months after the fifth dose?
- In Peterborough we do not yet have access to Moderna BA 4,5 and are being sent Moderna BA 1 to use it up[!]
- It is coming close to 6 months since getting the Bivalent vaccine for some people. When should the next vaccine be, for health care workers for example? Should they get another bivalent vaccine after 3-6 months?
- Dr. Tara Kiran: can you please give me a reference that says I can prescribe Paxlovid in advance that I can show the pharmacist. (I saw the response from Jason.) I am getting resistance to this from most pharmacists and family doctors.