COVID-19 Community of Practice for Ontario Family Physicians

April 22, 2022

Dr. Andrew Morris
Dr. Sohal Goyal
Dr. Kelly Grindrod

All about Paxlovid

Family & Community Medicine
UNIVERSITY OF TORONTO

Ontario College of Family Physicians

All about Paxlovid

Moderator: Dr. Tara Kiran

Fidani Chair, Improvement and Innovation
Department of Family and Community Medicine, University of Toronto

Panelists:

- Dr. Andrew Morris, Toronto, ON
- Dr. Sohal Goyal, Mississauga, ON
- Dr. Kelly Grindrod, Waterloo, ON

The COVID-19 Community of Practice for Ontario Family Physicians is a one-credit-per-hour Group Learning program that has been certified for up to a total of 32 credits.

Land Acknowledgement

We acknowledge that the lands on which we are hosting this meeting include the traditional territories of many nations.

The OCFP and DFCM recognize that the many injustices experienced by the Indigenous Peoples of what we now call Canada continue to affect their health and well-being. The OCFP and DFCM respect that Indigenous people have rich cultural and traditional practices that have been known to improve health outcomes.

I invite all of us to reflect on the territories you are calling in from as we commit ourselves to gaining knowledge; forging a new, culturally safe relationship; and contributing to reconciliation.

STEP 1 ▶ Determine the risk of disease progression.

- **Higher risk** individuals are those who have a ≥5% risk of hospitalization if they develop COVID-19. **Standard risk** individuals are those who have a <5% of hospitalization.
- Indigenous people, Black people, and members of other racialized communities may be at increased risk of disease progression due to disparate rates of comorbidity, increased barriers to vaccination, and social determinants of health. They should be considered **priority populations** for access to COVID-19 drugs and therapeutics.

AGE (years)	NUMBER OF VACCINE DOSES			RISK FACTORS
	0 doses	**1 or 2 doses**	**3 doses**	
<20[1]	**Higher risk** if ≥3 risk factors[1]	Standard risk[1]	Standard risk[1]	• Obesity (BMI ≥30 kg/m^2) • Diabetes • Heart disease, hypertension, congestive heart failure • Chronic respiratory disease, including cystic fibrosis • Cerebral palsy • Intellectual disability • Sickle cell disease • Moderate or severe kidney disease (eGFR <60 mL/min) • Moderate or severe liver disease (e.g., Child Pugh Class B or C cirrhosis)
20 to 39	**Higher risk** if ≥3 risk factors	**Higher risk** if ≥3 risk factors	Standard risk	
40 to 69	**Higher risk** if ≥1 risk factors	**Higher risk** if ≥3 risk factors	Standard risk	
≥70	**Higher risk**	**Higher risk** if ≥1 risk factors	**Higher risk** if ≥3 risk factors	
Immunocompromised[2] individuals of any age	**Higher risk**: Therapeutics should always be recommended for immunocompromised individuals not expected to mount an adequate immune response to COVID-19 vaccination or SARS-CoV-2 infection due to their underlying immune status, regardless of age or vaccine status.[1,2]			
Pregnancy	**Higher risk**[3]	Standard risk	Standard risk	

1. Evidence for the safety and efficacy of sotrovimab and nirmatrelvir/ritonavir (Paxlovid) in children <18 years of age is limited. While early evidence on risk factors for moderate and severe COVID-19 in children is emerging, the ability to reliably predict disease progression in children remains very limited, and the frequency of progression is rare. While not routinely recommended in children <18 years of age, the use of these agents may be considered in exceptional circumstances (e.g., severe immunocompromise and/or multiple risk factors, clinical progression) on a case-by-case basis. Multidisciplinary consultation with Infectious Diseases (or Pediatric Infectious Diseases) and the team primarily responsible for the child's care is recommended to review the individual consideration of these medications.
2. Examples of immunocompromised or immunosuppressed individuals include receipt of treatment for solid tumors and hematologic malignancies (including individuals with lymphoid malignancies who are being monitored without active treatment), receipt of solid-organ transplant and taking immunosuppressive therapy, receipt of chimeric antigen receptor (CAR)-T-cell or hematopoietic stem cell transplant (within 2 years of transplantation or taking immunosuppression therapy), moderate or severe primary immunodeficiency (e.g., DiGeorge syndrome, Wiskott-Aldrich syndrome, common variable immunodeficiency, Good's syndrome, hyper IgE syndrome), advanced or untreated HIV infection, active treatment with high-dose corticosteroids (i.e., ≥20 mg prednisone or equivalent per day when administered for ≥2 weeks), alkylating agents, antimetabolites, transplant-related immunosuppressive drugs, cancer chemotherapeutic agents classified as severely immunosuppressive, tumor-necrosis factor (TNF) blockers, and other biologic agents that are immunosuppressive or immunomodulatory. These individuals should have a reasonable expectation for 1-year survival prior to SARS-CoV-2 infection.
3. Therapeutics should always be recommended for pregnant individuals who have received zero vaccine doses.

Changing the way we work

A community of practice for family physicians during COVID-19

At the conclusion of this series participants will be able to:

- Identify the current best practices for delivery of primary care within the context of COVID-19 and how to incorporate into practice.
- Describe point-of-care resources and tools available to guide decision making and plan of care.
- Connect with a community of family physicians to identify practical solutions for their primary care practice under current conditions.

Disclosure of Financial Support

This CPD program has received in-kind support from the Ontario College of Family Physicians and the Department of Family and Community Medicine, University of Toronto in the form of logistical and promotional support.

Potential for conflict(s) of interest:
N/A

Mitigating Potential Bias

- The Scientific Planning Committee has full control over the choice of topics/speakers.
- Content has been developed according to the standards and expectations of the Mainpro+ certification program.
- The program content was reviewed by a three-member national/scientific planning committee.

Planning Committee: Dr. Tara Kiran, Patricia O'Brien (DCFM), Susan Taylor (OCFP) and Mina Viscardi-Johnson (OCFP), Liz Muggah (OCFP)

Previous webinars & related resources:

https://www.dfcm.utoronto.ca/covid-19-community-practice/past-sessions

Dr. Andrew Morris– Panelist

Twitter: @ASPphysician

Medical Director, Antimicrobial Stewardship Program, Sinai Health System/University Health Network

Dr. Sohal Goyal– Panelist

Twitter: @sohalv

Family Physician, West Mississauga Medical

Dr. Kelly Grindrod– Panelist

Twitter: @kgrindrod

Pharmacist and Associate Professor, University of Waterloo School of Pharmacy

Dr. David Kaplan – Co-Host

Twitter: @davidkaplanmd

Family Physician, North York Family Health Team and Vice President, Quality, Ontario Health

Dr. Liz Muggah – Co-Host

Twitter: @OCFP_President

OCFP President, Family Physician, Bruyère Family Health Team

Speaker Disclosure

- Faculty Name: **Dr. Andrew Morris**
- Relationships with financial sponsors:
  - Grants/Research Support: Academic Health Sciences Alternate Funding Plan, Ontario College of Family Physicians
  - Speakers Bureau/Honoraria: N/A
  - Others: N/A

- Faculty Name: **Dr. Sohal Goyal**
- Relationships with financial sponsors:
  - Grants/Research Support: N/A
  - Speakers Bureau/Honoraria: CPD Network, Tamarind, ICEBM, HLS Therapeutics, Amgen, Abbott, Bausch, ICPDHM, Galderma, Astellas, Pfizer, Merck, Astra Zeneca, Tribute, Canadian Collective Research, Pediapharma, Duchesnay, Servier, Takeda, Aralez, Novonordisk, Sprout Pharma, Ardeane, GSK, Ontario College of Family Physicians
  - Others: N/A

- Faculty Name: **Dr. Kelly Grindrod**
- Relationships with financial sponsors:
  - Grants/Research Support:
  - Speakers Bureau/Honoraria:
  - Others:

Speaker Disclosure

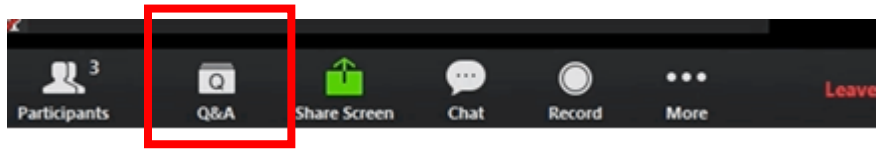
- Faculty Name: **Dr. David Kaplan**
- Relationships with financial sponsors:
  - Grants/Research Support: N/A
  - Speakers Bureau/Honoraria: Ontario College of Family Physicians
  - Others: Ontario Health (employee)
- Faculty Name: **Dr. Liz Muggah**
- Relationships with financial sponsors:
  - Grants/Research Support: N/A
  - Speakers Bureau/Honoraria: Ontario College of Family Physicians
  - Others: N/A
- Faculty Name: **Dr. Tara Kiran**
- Relationships with financial sponsors:
  - Grants/Research Support: St. Michael's Hospital, University of Toronto, Health Quality Ontario, Canadian Institute for Health Research, Ontario Ministry of Health, Gilead Sciences Inc (re: Hepatitis C), Staples Canada (re: Patient Engagement)
  - Speakers Bureau/Honoraria: Ontario College of Family Physicians, Ontario Medical Association, Doctors of BC, Nova Scotia Health Authority, Osgoode Hall Law School, Centre for Quality Improvement and Patient Safety, Vancouver Physician Staff Association, University of Ottawa, Ontario Health

Outline for today

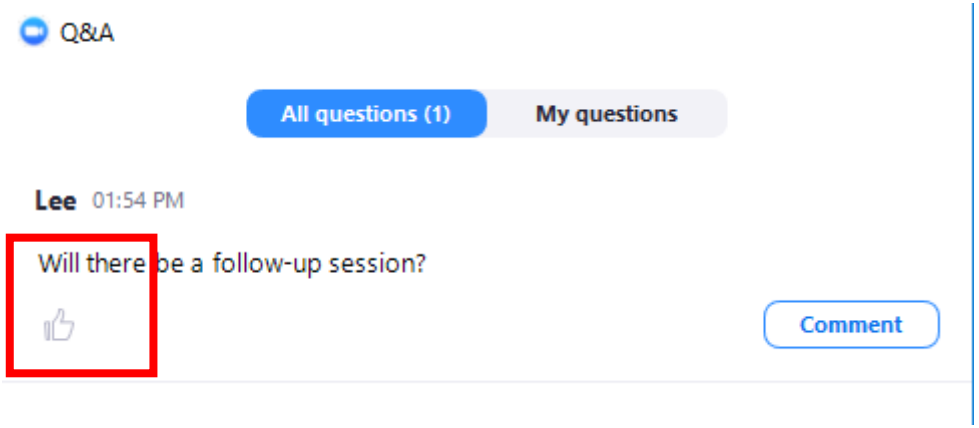
- Paxlovid—what it does, who might benefit
- Wisdom from a family physician
- Wisdom from a pharmacist
- Provincial tools to support prescribing
- Lots of Q&A

How to Participate

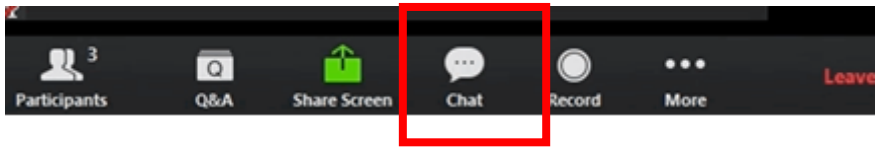
- All questions should be asked using the Q&A function at the bottom of your screen.



- Press the thumbs up button to upvote another guests questions. Upvote a question if you want to ask a similar question or want to see a guest's question go to the top and catch the panels attention.



- Please use the chat box for networking purposes only.



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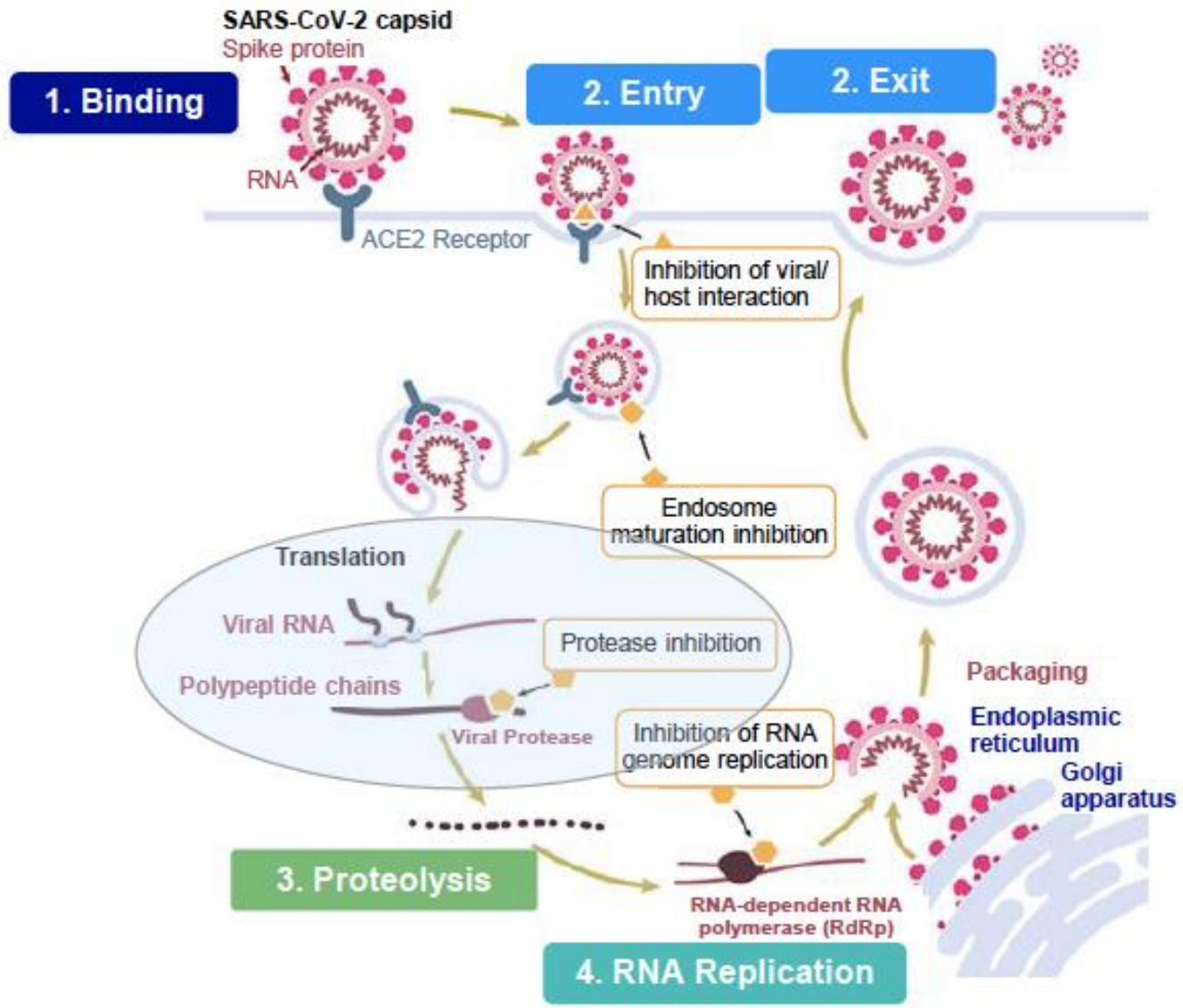
Pharmacist and Associate Professor, University of Waterloo School of Pharmacy

The drug

- I say NIR-muh-TREL-veer/rih-TON-a-VEER
- you can say PAX-loh-vid OR pax-LOH-vid
- acts on proteolysis by inhibiting the viral 3CL (M^{pro}) protease



Source: Dr. Tal Distelman-Menachem, Pfizer

Properties of an ideal COVID drug?

- ❑ it makes you feel better
- ❑ it prevents progression to severe disease
- ❑ it prevents transmission
- ❑ it prevents (+/- treats) Long COVID
- ❑ it is cheap and readily available
- ❑ it is easy to take (route, duration) with no drug/food interactions
- ❑ it doesn’t harm you

Does nirmatrelvir/ritonavir make you feel better?

- conservative answer: we don’t know
- skeptical answer:
  - it was measured in EPIC-HR (the study published in *NEJM*) and not reported
  - and there is that December 14, 2021 Pfizer press release ...

EPIC-SR Interim Results

Interim analyses of the EPIC-SR (Evaluation of Protease Inhibition for COVID-19 in Standard-Risk Patients) Phase 2/3 study, which included unvaccinated adults who were at standard risk (i.e., low risk of hospitalization or death) as well as vaccinated adults who had one or more risk factors for progressing to severe illness, showed that the novel primary endpoint of self-reported, sustained alleviation of all symptoms for four consecutive days, as compared to placebo, was not met.

Does nirmatrelvir/ritonavir prevent progression to severe disease?

A Outcomes According to Time Since Onset of Covid-19 Symptoms

	Treated ≤3 Days after Onset of Symptoms (modified intention-to-treat population)		Treated ≤5 Days after Onset of Symptoms	
	Nirmatrelvir+ritonavir (N=697)	Placebo (N=682)	Nirmatrelvir+ritonavir (N=1039)	Placebo (N=1046)
Patients with event — no. (%)	5 (0.72)	44 (6.45)	8 (0.77)	66 (6.31)
Hospitalization for Covid-19	5 (0.72)	44 (6.45)	8 (0.77)	65 (6.21)
Death from any cause	0	9 (1.32)	0	12 (1.15)
Average time at risk for event — days	27.29	26.19	27.05	25.97
Average follow-up — days	27.45	27.25	27.20	27.05
Estimated percentage with event (95% CI) — %	0.72 (0.30 to 1.73)	6.53 (4.90 to 8.68)	0.78 (0.39 to 1.56)	6.40 (5.06 to 8.08)
Difference (±SE) from placebo — percentage points	−5.81±1.01		−5.62±0.81	
95% CI of difference	−7.78 to −3.84		−7.21 to −4.03	
P value	<0.001		<0.001	

- in a study of unvaccinated high-risk adults with 6.2% hospitalized with placebo, nirmatrelvir/ritonavir reduced hospitalizations by 5.4% (RRR 88%) , giving a number needed to treat (NNT) of 18

NEJM 2022; **386**:1397-1408. DOI: 10.1056/NEJMoa2118542

Who was included in EPIC-HR (high risk)

- Median age: 46
- unvaccinated
- Only ~ 20% had more than 1 comorbidity
- <1% immunosuppressed

In fact, this study was massively under-represented by the very patients who we would mostly use it in.

NEJM 2022; **386**:1397-1408. DOI: 10.1056/NEJMoa2118542

What is the estimated NNT for various baseline risks?

Baseline risk of hospitalization	Absolute Risk Reduction (ARR) assuming 87.6% Effective	Number Needed to Treat (NNT) to Prevent a Hospitalization
1%	0.88%	114
3%	2.63%	38
5%	4.38%	23

What is the estimated NNT for various baseline risks?

AGE (years)	NUMBER OF VACCINE DOSES		
	0 doses	1 or 2 doses	3 doses
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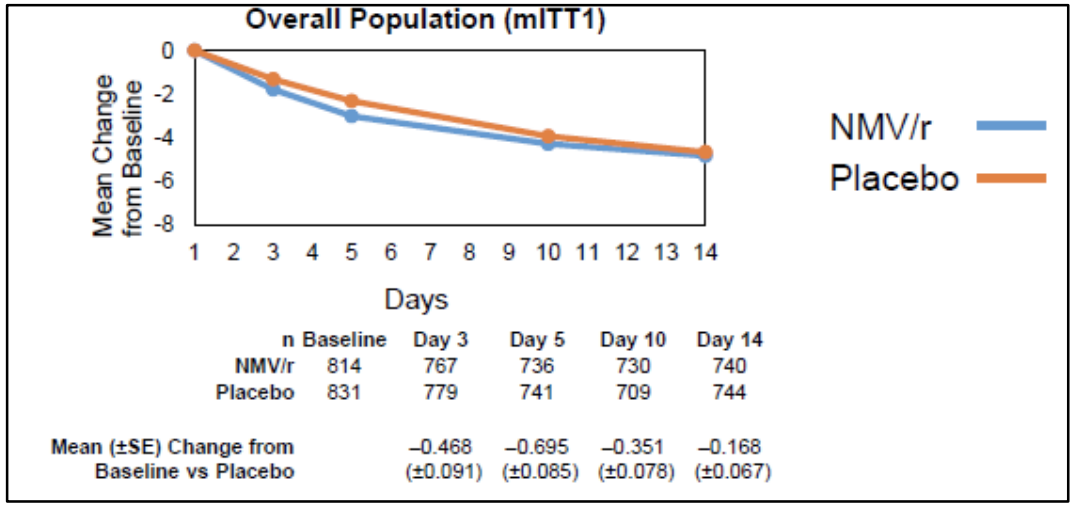
≥70	**Higher risk**	**Higher risk** if ≥1 risk factors	**Higher risk** if ≥3 risk factors
Immunocompromised[2] individuals of any age	**Higher risk**: Therapeutics should always be recommended for immunocompromised individuals not expected to mount an adequate immune response to COVID-19 vaccination or SARS-CoV-2 infection due to their underlying immune status, regardless of age or vaccine status.[1,2]		
Pregnancy	**Higher risk**[3]	Standard risk	Standard risk

- If we use very recent Alberta data, even with 1 or 2 doses of vaccine and Omicron, the risk is only greater than 3% if age >50 with 3 or more risk factors or >70 with 1 risk factor.

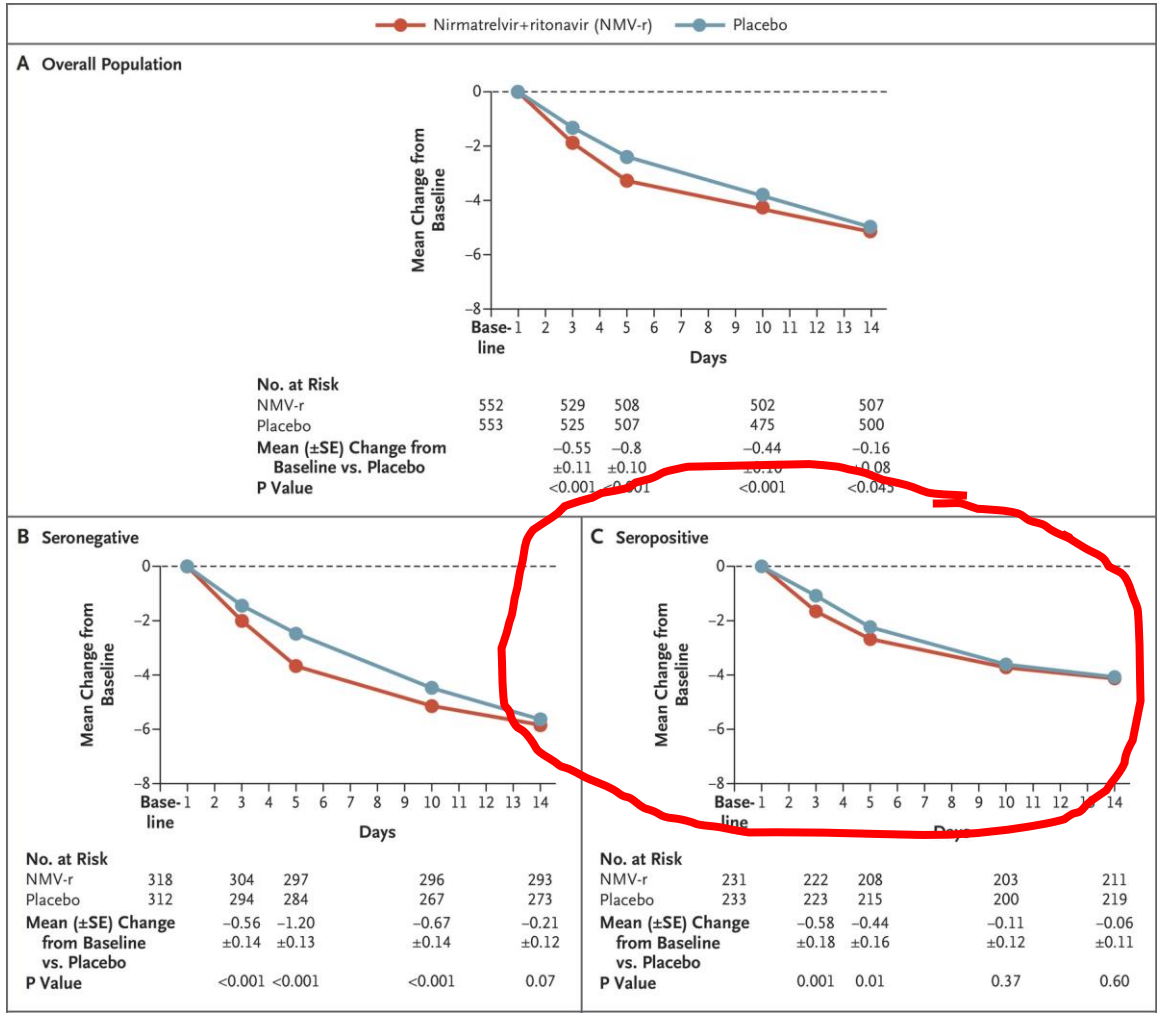
Paxlovid effects on Viral Load

Unadjusted VL



	n	Baseline	Day 3	Day 5	Day 10	Day 14
NMV/r	814		767	736	730	740
Placebo	831		779	741	709	744
Mean (±SE) Change from Baseline vs Placebo			–0.468 (±0.091)	–0.695 (±0.085)	–0.351 (±0.078)	–0.168 (±0.067)

Adjusted VL



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Cost-effectiveness of nirmatrelvir/ritonavir

		Number Needed to Treat			Cost per Hospitalization Prevented		
Drug	Cost/Patient	2.5% Risk	5% Risk	10% Risk	2.5% Risk	5% Risk	10% Risk
Fluvoxamine (meta-analysis)	14	160 (96–1334)	80 (48–667)	40 (24–334)	2244 (1346–18 709)	1122 (673–9355)	561 (337–4684)
Colchicine (meta-analysis)	37	182 (103–40 000)	91 (52–20 000)	46 (26–10 000)	6667 (3773–1 465 200)	3333 (1905–732 600)	1685 (952–366 300)
Inhaled corticosteroids (meta-analysis)[a]	132	143 (89–800)	72 (45–400)	36 (23–200)	18 819 (11 712–105 280)	9475 (5922–52 640)	4738 (3027–26 320)
Nirmatrelvir/ritonavir (meta-analysis)[b]	530	48 (44–57)	24 (22–29)	12 (11–15)	25 440 (23 320–30 210)	12 720 (11 660–15 370)	6360 (5830–7950)
Molnupiravir (meta-analysis)[a]	700	100 (72–236)	50 (36–118)	25 (18–59)	70 000 (50 400–165 200)	35 000 (25 200–82 600)	17 500 (12 600–41 300)
Remdesivir (phase 3)	1872	56 (45–160)	28 (23–80)	14 (12–40)	104 832 (84 240–299 520)	52 416 (43 056–149 760)	26 208 (22 464–74 880)

Lee, TC et al. Outpatient Therapies for COVID-19: How Do We Choose? *Open Forum Infectious Diseases* 2022. doi: 10.1093/ofid/ofac008

Drug Safety

Adverse Events during Treatment Period (safety-analysis population)

	Nirmatrelvir Group N=1109	Placebo Group N=1115
No. of adverse events	476	525
Patients with any adverse event — no. (%)	251 (22.6)	266 (23.9)
Serious adverse event	18 (1.6)	74 (6.6)
Maximum grade 3 or 4 adverse event	45 (4.1)	93 (8.3)
Maximum grade 5 adverse event	0	13 (1.2)
Discontinued drug or placebo because of adverse event	23 (2.1)	47 (4.2)
Had dose reduction or temporary discontinuation owing to adverse event	4 (0.4)	4 (0.4)

The New England Journal of Medicine

COMPARISON OF UPPER GASTROINTESTINAL TOXICITY OF ROFECOXIB AND NAPROXEN IN PATIENTS WITH RHEUMATOID ARTHRITIS

CLAIRE BOMBARDIER, M.D., LOREN LAINE, M.D., ALISE REICIN, M.D., DEBORAH SHAPIRO, DR.P.H., RUBEN BURGOS-VARGAS, M.D., BARRY DAVIS, M.D., PH.D., RICHARD DAY, M.D., MARCOS BOSI FERRAZ, M.D., PH.D., CHRISTOPHER J. HAWKEY, M.D., MARC C. HOCHBERG, M.D., TORE K. KVIEN, M.D., AND THOMAS J. SCHNITZER, M.D., PH.D., FOR THE VIGOR STUDY GROUP

Conclusions In patients with rheumatoid arthritis, treatment with rofecoxib, a selective inhibitor of cyclooxygenase-2, is associated with significantly fewer clinically important upper gastrointestinal events than treatment with naproxen, a nonselective inhibitor. (N Engl J Med 2000;343:1520-8.)

Expression of Concern: Bombardier et al., "Comparison of Upper Gastrointestinal Toxicity of Rofecoxib and Naproxen in Patients with Rheumatoid Arthritis," N Engl J Med 2000;343:1520-8.

Gregory D. Curfman, M.D., Stephen Morrissey, Ph.D., and Jeffrey M. Drazen, M.D.

N ENGL J MED 353;26 WWW.NEJM.ORG DECEMBER 29, 2005

Properties of an ideal COVID drug?

✗ it makes you feel better

✓ it prevents progression to severe disease

? it prevents transmission

? it prevents (+/- treats) Long COVID

✗ it is cheap and readily available

✗ it is easy to take (route, duration) with no drug/food interactions

✓ it doesn’t harm you

COVID treatment in primary care

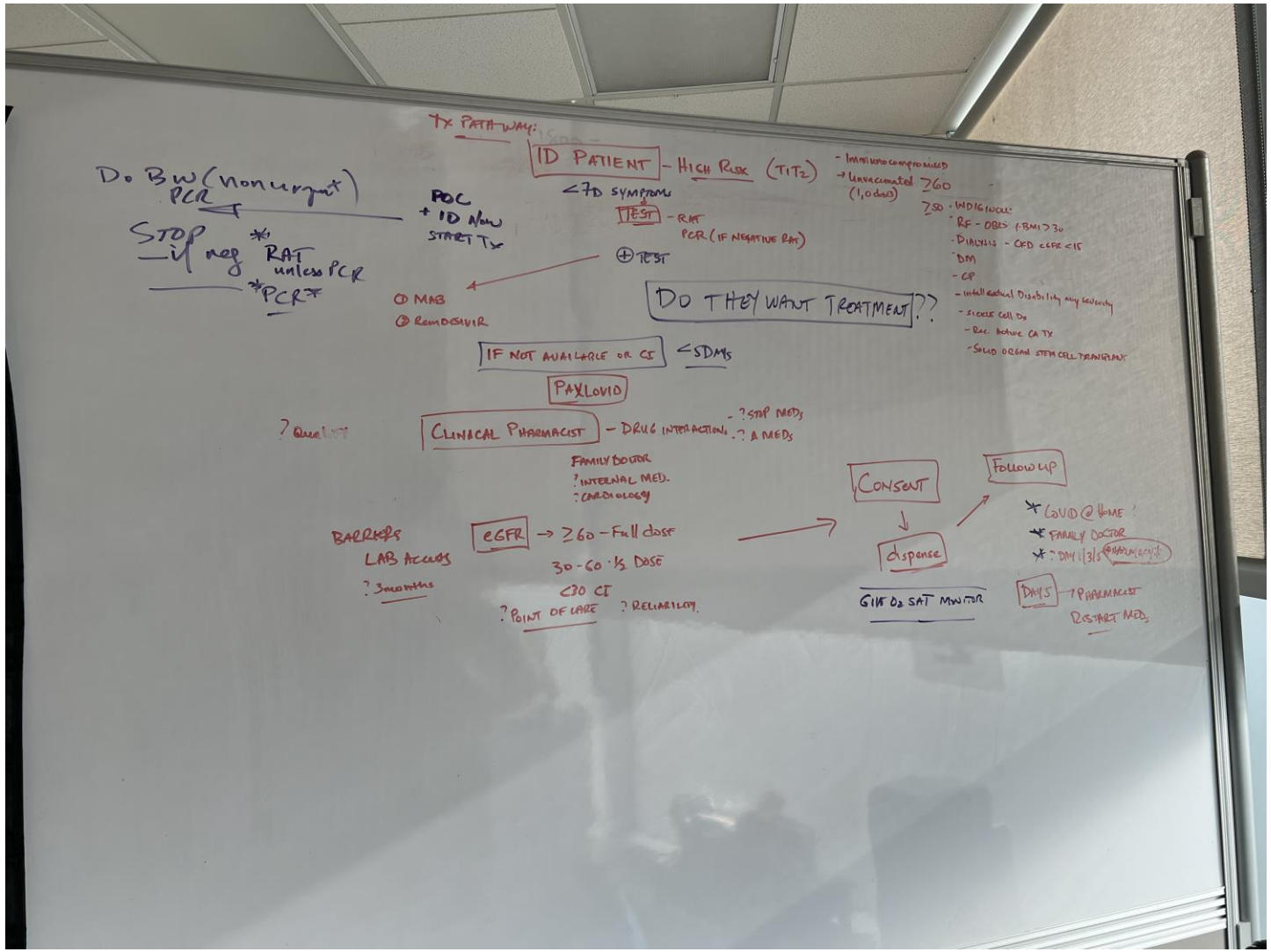
COVID Cold and Flu Care Clinic, Mississauga

Sohal Goyal, Family Physician

Our Journey

- Started October 25, 2021
- Testing, Assessments
- Treatment Jan 31, 2022
- Team based care – nurses, family physicians, pharmacists

Our initial pathway



Clinical Case

- 47 y.o. with diabetes type 2, lives alone
- Sore throat x 4d, fever, chills
- 2 covid shots or 3?
- Home rapid test positive or negative?
- Meds – atorvastatin 10, metformin 500 bid, amlodipine 10 mg, candesartan 16 mg
- Blood work done 1 year ago – egfr - 61

Practical considerations

Criteria Feb 23, 2022 – OST

2)	Number of Vaccines		
Age	0 doses	1 or 2 doses	3 doses
< 20	Higher risk if ≥ 3 risk factors	Standard risk	Standard risk
20 to 39	Higher risk if ≥ 3 risk factors	Higher risk if ≥ 3 risk factors	Standard risk
40 – 69	Higher risk if ≥ 1 risk factors	Higher risk if ≥ 3 risk factors	Standard risk
≥ 70	Higher risk	Higher risk if ≥ 1 risk factors	Higher risk if ≥ 3 risk factors
Pregnancy	Higher risk	Standard risk	Standard risk

Eligibility April 11, 2022

2)	Number of Vaccines		
Age	0 doses	1 or 2 doses	3 doses or 4 doses
18-59	□ Eligible if ≥ 1 risk factors	□ Eligible if ≥ 1 risk factors	Not Eligible
60-69	□ Eligible	□ Eligible	Not Eligible
≥ 70	□ Eligible	□ Eligible	□ Eligible
Pregnancy	□ Eligible	Not Eligible	Not Eligible

RISK FACTORS

Obesity (BMI over 30), DM, Heart disease (HTN, CHF), Chronic Respiratory disease (inc. cystic fibrosis), cerebral palsy, intellectual or developmental disability, sickle cell disease, moderate severe kidney disease (eGFR≤60mL/min) , moderate or severe liver disease (e.g., Child's Pugh Class B or C cirrhosis)

Clinical case

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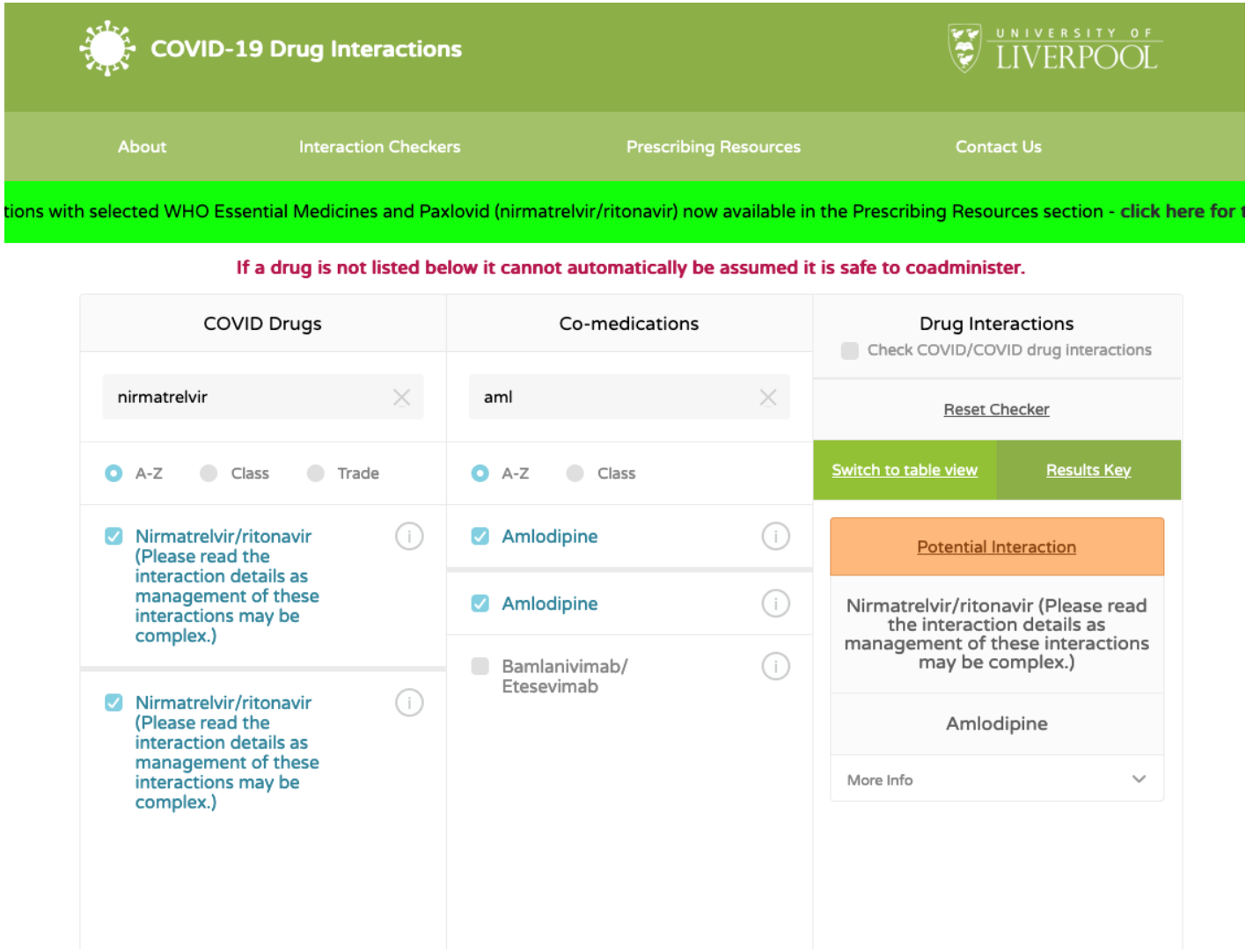
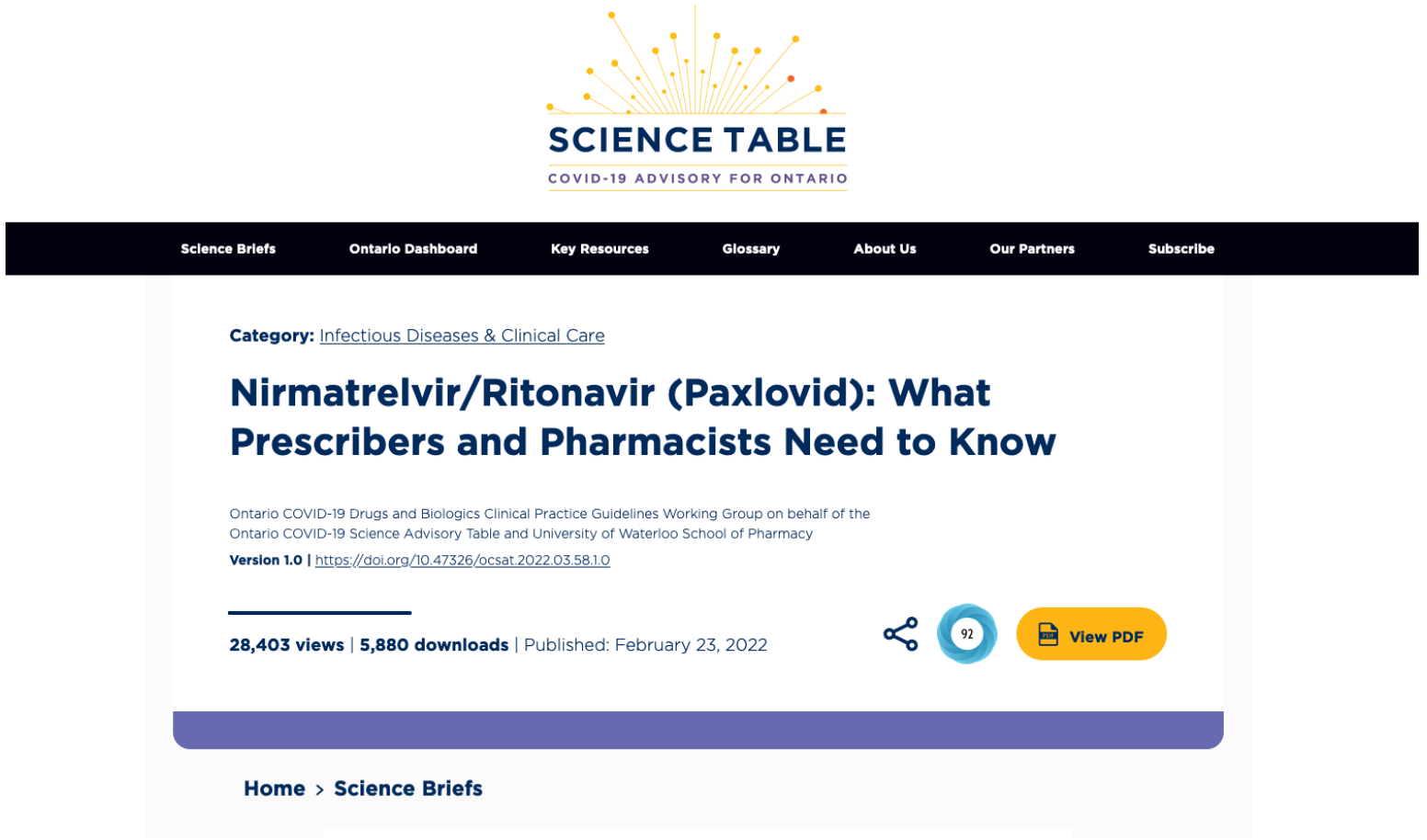
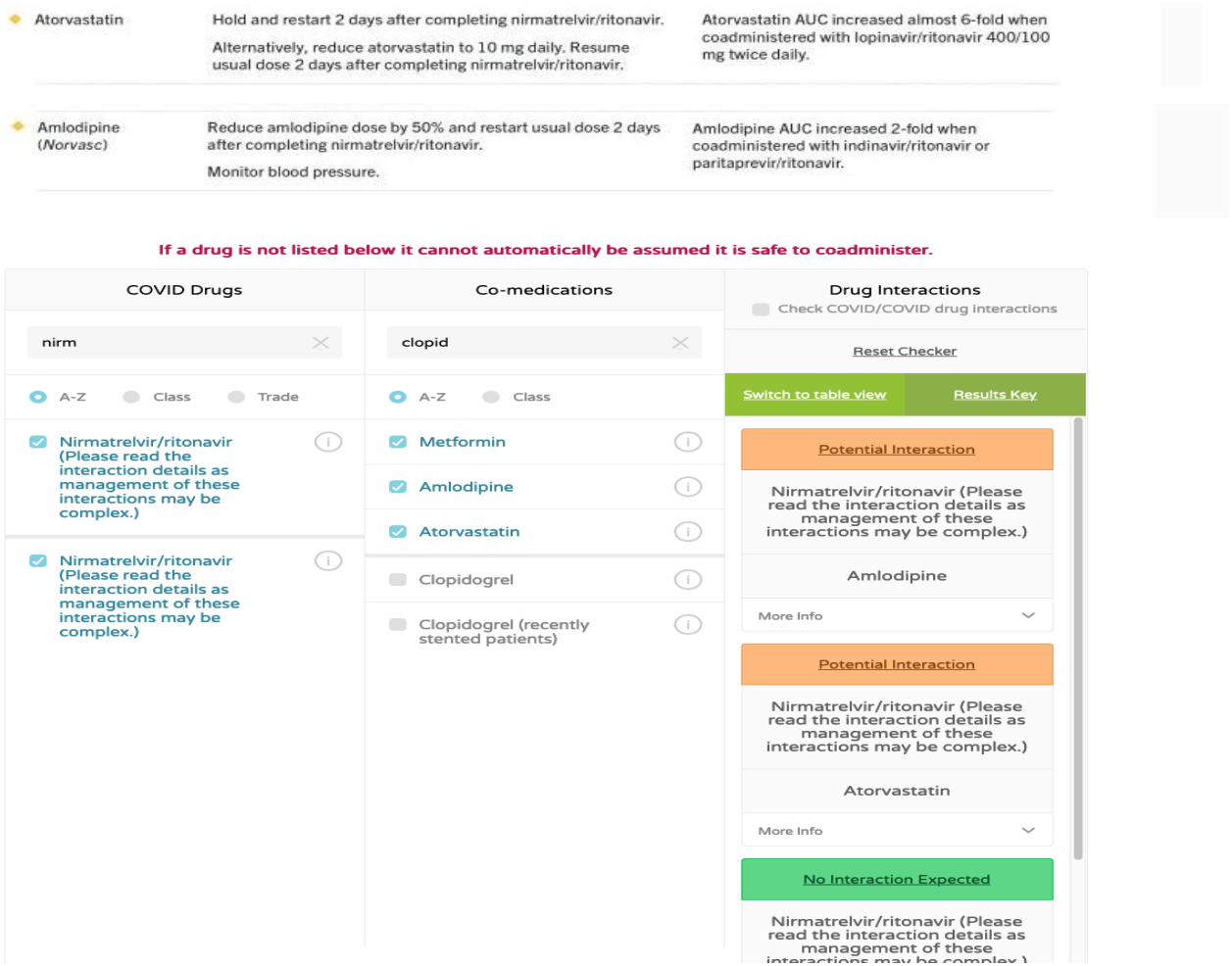
Drug interactions



Interactions



Interactions



Clinical case

- 47 y.o. with diabetes type 2, lives alone
- Sore throat x 4d, fever, chills
- 2 covid shots or 3?
- Home rapid test positive or negative?
- Meds – atorvastatin 10, metformin 500 bid, amlodipine 10 mg, candesartan 16 mg, CLOPIDOGREL
- PMHx – Afib ?, Stroke?, ACS?
- Blood work done 1 year ago – egfr - 61

Interactions

Clopidogrel (*Plavix*)	**Acute coronary syndrome (ACS)/percutaneous coronary intervention (PCI):** • **If <1 month since ACS:** Use alternative COVID-19 agent. • **If <3 months since ACS or <1 month since PCI (no ACS):** Consider switching clopidogrel to prasugrel (if age <75, weight >60 kg, and no history of stroke/TIA) and resume clopidogrel 2 days after completing nirmatrelvir/ritonavir; • **If >3 months since ACS or >1 month since PCI (no ACS):** Continue clopidogrel with acetylsalicylic acid (ASA) during nirmatrelvir/ritonavir therapy. If not taking ASA, consider switching to prasugrel (if age <75, weight >60 kg, and no history of stroke/TIA) and resume clopidogrel 2 days after completing nirmatrelvir/ritonavir.	Coadministration will decrease the antiplatelet effect of clopidogrel. Clopidogrel active metabolite AUC decreased by 51 to 69% when coadministered with ritonavir.
Apixaban (*Eliquis*)	If possible, use alternative COVID-19 agent. If not possible, ensure stable renal function, then in: **Acute venous thromboembolism (VTE):** Hold apixaban and restart 2 days after completing nirmatrelvir/ritonavir. While apixaban is on hold, start therapeutic dosing of a subcutaneous low molecular weight heparin (LMWH) such as: • Dalteparin 200 units/kg daily OR 100 units/kg every 12 hours if >90 kg; • Enoxaparin 1 mg/kg every 12 hours (preferred) or 1.5 mg/kg once every 24 hours; • Tinzaparin 175 anti-Xa units/kg once daily. **Atrial fibrillation:** Decrease apixaban to 2.5 mg twice daily, then resume usual dose 2 days after completing nirmatrelvir/ritonavir. If patient is taking 2.5 mg twice daily, use an alternative COVID-19 agent.	Canadian monograph states that coadministration with ritonavir is contraindicated. However, US product monograph suggests to decrease 5 mg twice daily dose to 2.5 mg twice daily when combined with strong inhibitors of CYP3A4 and P-glycoprotein. Eliquis (U.S.) Prescribing Information. Accessed February 8, 2022. https://www.accessdata.fda.gov/drugsatfda_docs/label/2012/202155s000lbl.pdf Observational data from Italy found a 70 to 490% increase in apixaban levels in combination with *antivirals* containing ritonavir in hospitalized patients. Testa S, Prandoni P, Paoletti O et al. Direct oral anticoagulant plasma levels' striking increase in severe COVID-19 respiratory syndrome patients treated with antiviral agents: The Cremona experience. *J Thromb Haemost.* 2020;18:1320–1323. https://doi.org/10.1111/jth.14871

Renal dosing

Ontario Health
Ontario Renal Network

COVID-19 Supplemental Clinical Guidance #4: Nirmatrelvir/Ritonavir (Paxlovid) Use in Patients With Advanced Chronic Kidney Disease and Patients on Dialysis with COVID-19

April 13, 2022

Current Recommendation		**Proposed Dosing guidance**	
Kidney Function	*Dosing schedule*	*Kidney Function*	*Dosing schedule*
GFR > 60	300 mg nirmatrelvir + 100 mg ritonavir both twice a day for 5 days	GFR > 60	300 mg nirmatrelvir + 100 mg ritonavir both twice a day for 5 days
GFR 30 - 60	150 mg nirmatrelvir + 100 mg ritonavir both twice a day for 5 days	GFR 30 - 60	150 mg nirmatrelvir + 100 mg ritonavir both twice a day for 5 days
GFR < 30	Do not use	GFR < 30	300 mg nirmatrelvir + 100 mg ritonavir both on day 1 then 150 mg nirmatrelvir + 100 mg ritonavir once a day for 4 more days
Dialysis	Do not use	Dialysis	300 mg nirmatrelvir + 100 mg ritonavir both on day 1 then 150 mg nirmatrelvir + 100 mg ritonavir once a day for 4 more days, to be dosed after dialysis[1]

Questions?

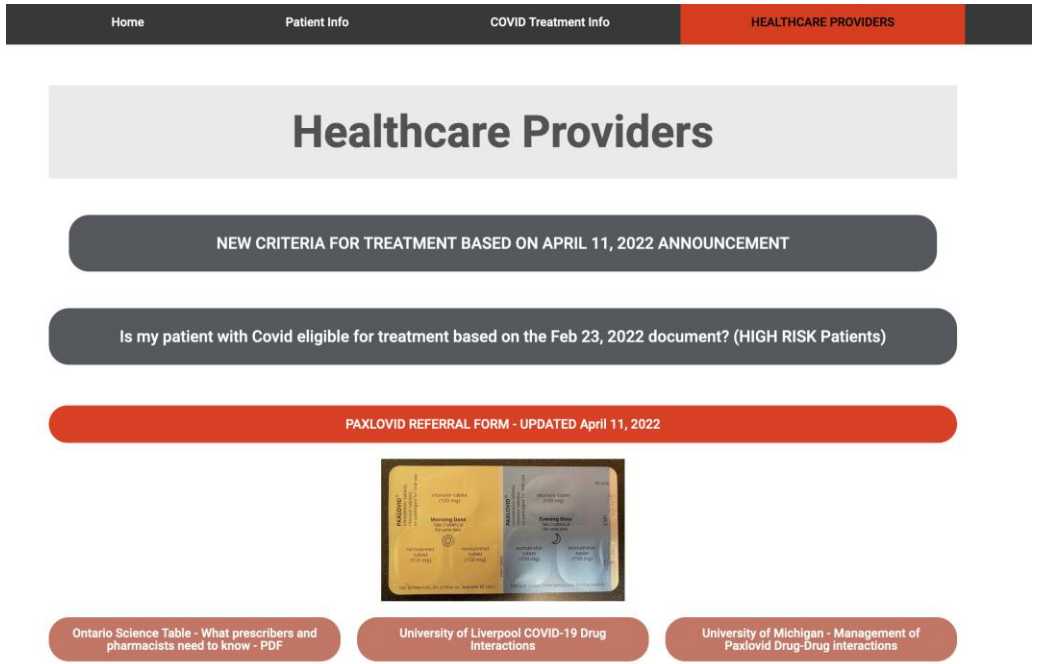
- Are they at high risk?
- Are they getting better?
- Do they want treatment?
- Are they aware that some of their meds may be stopped or may not work?
- Side effects?

PRO TIPS

- eGFR in your high risk patients
- RAT tests for your high risk patients
- Consider an oximeter
- Ensure that your patients keep med lists ready
- Herbals and supplements
- Reach out early, when the symptoms first start

Challenges

- Biggest challenge – Identification of the patient
- Testing
- Consent – Does the patient want treatment?
- Drug interactions
- Creatinine
- Access to other therapies
- Follow-up



Covidinfo.ca – updated regularly with tools

Paxlovid™ in Ontario Pharmacies

Kelly Grindrod BScPharm PharmD MSc

Associate Professor, University of Waterloo School of Pharmacy

April 18, 2022

STARTING PAXLOVID™
TIMELINES

SYMPTOMATIC PHASE:

DAY 0
First day of symptom onset

DAY 5
Last day eligible to start Paxlovid™

What to do:

- Confirm diagnosis (rapid antigen test/PCR)
- Confirm eligibility
- Obtain best possible medication history
- Assess for drug interaction(s)
- Counsel on expected side effects

TREATMENT PHASE:

DAY 1
First day of Paxlovid™ treatment

DAY 5
Last day of Paxlovid™ treatment

DAY 7
Resume usual dosing of other treatments

What to do:

- Day 2-3: Follow-up with patient to assess tolerability, need for further interaction dose adjustments, etc.
- Day 5: Ensure treatment completion, remind patient when to resume normal dosing of interacting co-medications.

UNIVERSITY OF WATERLOO | SCHOOL OF PHARMACY

Dosing Paxlovid

How do I dose nirmatrelvir/ritonavir for treatment of COVID-19?

1. Paxlovid consists of 2 drugs packaged together:
   - Nirmatrelvir (pink) 150 mg tablet
   - Ritonavir (white) 100 mg tablet
2. Each carton contains 5 blister cards. One blister card is used each day. The full course of treatment is 5 days.
3. Take 2 pink tablets of nirmatrelvir and 1 white tablet of ritonavir (3 tablets total) together at the same time, once in the morning and once in the evening for 5 days (i.e., 6 tablets per day).
   - Nirmatrelvir/ritonavir may be taken with or without food.

Special Dosing Considerations:

eGFR† 30 to 59 mL/min:
The dose is 1 each of nirmatrelvir 150 mg and ritonavir 100 mg, with both tablets taken together orally BID x 5 days.

eGFR† <30 mL/min:
Nirmatrelvir/ritonavir is not recommended.

Severe hepatic impairment (Child-Pugh Class C):
Nirmatrelvir/ritonavir is not recommended.

Practical Tips

- Pills cannot be split or crushed
- Take with or without food
- Bad taste in mouth and diarrhea common
- Renal dosing: pharmacist can remove extra nirmatrelvir pill
- Pharmacist can add pills to blister packing
- Pharmacy can delivery to patient home, may charge fee

Updated: February 23, 2022

SCIENCE TABLE
COVID-19 ADVISORY FOR ONTARIO

UNIVERSITY OF WATERLOO | SCHOOL OF PHARMACY

Nirmatrelvir/ Ritonavir (*Paxlovid*)

What Prescribers and Pharmacists Need to Know

Why is nirmatrelvir/ritonavir used to treat COVID-19?

COVID-19 has an initial phase of viral replication and a significant inflammatory response in moderate illness. This inflammation can lead to poor outcomes, including hospitalization, invasive ventilation, and death. However, treatments that target SARS-CoV-2 replication, if administered before the inflammatory phase of COVID-19, can improve outcomes.

Nirmatrelvir works by binding to the SARS-CoV-2 3CL protease, which ultimately causes viral replication to stop. Ritonavir is a potent CYP3A4 inhibitor. It is not active against SARS-CoV-2 but is administered as a "boosting agent" to slow the metabolism of nirmatrelvir, thus increasing concentrations of nirmatrelvir.

Nirmatrelvir/ritonavir is a highly effective outpatient therapy based on available data, but there is uncertainty about effect magnitude in target populations and high certainty for harm with ritonavir **if drug interactions are not mitigated.**

What is the benefit of nirmatrelvir/ritonavir for COVID-19?

The EPIC-HR study[1] has shown a benefit from treatment of adult outpatients with laboratory-proven SARS-CoV-2 infection who were not on supplemental oxygen and were within 5 days of symptom onset. The study suggests that nirmatrelvir/ritonavir may reduce the risk of hospitalization in these patients by 88%.

Research on nirmatrelvir/ritonavir was done in unvaccinated patients and prior to circulation of the Omicron variant. However, a study suggests that nirmatrelvir/ritonavir retains activity against the Omicron variant in vitro.[2] The Ontario Science Advisory Table recommends the use of nirmatrelvir/ritonavir in COVID-19 patients who are not on supplemental oxygen but are at high risk of progression to moderate or severe COVID-19.[3]

Who should receive nirmatrelvir/ritonavir?

Nirmatrelvir/ritonavir should be offered to patients at **higher risk** of severe COVID-19 *(proven by PCR* or a provider-administered rapid test),* who are not yet on supplemental oxygen, and who are within 5 days of symptom onset.

*PCR = polymerase chain reaction

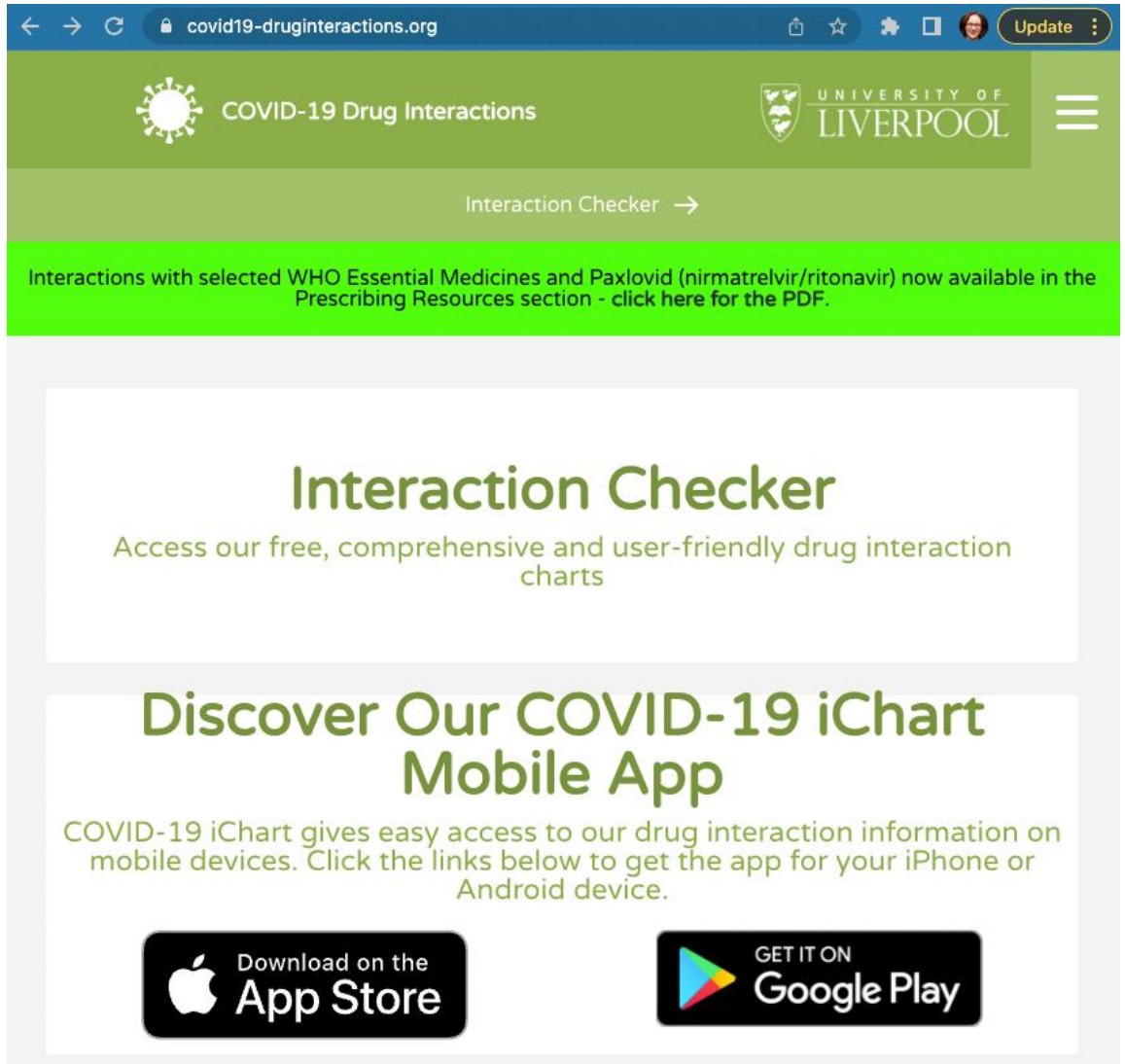
AGE (years)	NUMBER OF VACCINE DOSES			RISK FACTORS
	0 doses	1 or 2 doses	3 doses	
<20[1]	**Higher risk** if ≥3 risk factors[1]	Standard risk[1]	Standard risk[1]	• Obesity (BMI ≥30 kg/m²) • Diabetes • Heart disease, hypertension, congestive heart failure • Chronic respiratory disease, including cystic fibrosis • Cerebral palsy • Intellectual disability • Sickle cell disease • Moderate or severe kidney disease (eGFR <60 mL/min) • Moderate or severe liver disease (e.g., Child Pugh Class B or C cirrhosis)
20 to 39	**Higher risk** if ≥3 risk factors	**Higher risk** if ≥3 risk factors	Standard risk	
40 to 69	**Higher risk** if ≥1 risk factors	**Higher risk** if ≥3 risk factors	Standard risk	
≥70	**Higher risk**	**Higher risk** if ≥1 risk factors	**Higher risk** if ≥3 risk factors	
Immunocompromised[2] individuals of any age	**Higher risk**: Therapeutics should always be recommended for immunocompromised individuals not expected to mount an adequate immune response to COVID-19 vaccination or SARS-CoV-2 infection due to their underlying immune status, regardless of age or vaccine status.[1,2]			
Pregnancy	**Higher risk**[3]	Standard risk	Standard risk	

1. Evidence for the safety and efficacy of sotrovimab and nirmatrelvir/ritonavir (Paxlovid) in children <18 years of age is limited. While early evidence on risk factors for moderate and severe COVID-19 in children is emerging, the ability to reliably predict disease progression in children remains very limited, and the frequency of progression is rare. While not routinely recommended in children <18 years of age, the use of these agents may be considered in exceptional circumstances (e.g., severe immunocompromise and/or multiple risk factors, clinical progression) on a case-by-case basis. Multidisciplinary consultation with Infectious Diseases (or Pediatric Infectious Diseases) and the team primarily responsible for the child's care is recommended to review the individual consideration of these medications.
2. Examples of immunocompromised or immunosuppressed individuals include receipt of treatment for solid tumors and hematologic malignancies (including individuals with lymphoid malignancies who are being monitored without active treatment), receipt of solid-organ transplant and taking immunosuppressive therapy, receipt of chimeric antigen receptor (CAR)-T-cell or hematopoietic stem cell transplant (within 2 years of transplantation or taking immunosuppression therapy), moderate or severe primary immunodeficiency (e.g., DiGeorge syndrome, Wiskott-Aldrich syndrome, common variable immunodeficiency, Good's syndrome, hyper IgE syndromes), advanced or untreated HIV infection, active treatment with high-dose corticosteroids (i.e., ≥20 mg prednisone or equivalent per day when administered for ≥2 weeks), alkylating agents, antimetabolites, transplant-related immunosuppressive drugs, cancer chemotherapeutic agents classified as severely immunosuppressive, tumor-necrosis factor (TNF) blockers, and other biologic agents that are immunosuppressive or immunomodulatory. These individuals should have a reasonable expectation for 1-year survival prior to SARS-CoV-2 infection.
3. Therapeutics should always be recommended for pregnant individuals who have received zero vaccine doses.

From: "Clinical Practice Guideline Summary: Recommended Drugs and Biologics in Adult Patients with COVID-19. (Version 10.0)" https://covid19-sciencetable.ca/sciencebrief/#infectious-diseases-clinical-care.

Indigenous persons (First Nations, Inuit, or Métis), Black persons, and members of other racialized communities may be at high risk of disease progression due to disparate rates of comorbidity, increased vaccination barriers, and social determinants of health, and should be considered priority populations for access to COVID-19 therapeutics. Nirmatrelvir/ritonavir may be considered in pregnant or lactating patients on an individual basis if the benefits of treatment outweigh the potential risks.

[1] Hammond J, Leister-Tebbe H, Gardner A, Abreu P et al. Oral Nirmatrelvir for High-Risk, Nonhospitalized Adults with Covid-19. *NEJM*. doi: 10.1056/NEJMoa2118542
[2] Vangeel L, Chiu W, De Jonghe S, Maes P, et al. Remdesivir, Molnupiravir and Nirmatrelvir remain active against SARS-CoV-2 Omicron and other variants of concern. *Antiviral Res.* 2022;198:105252. doi: 10.1016/j.antiviral.2022.105252.
[3] Ontario COVID-19 Science Advisory Table. Clinical Practice Guideline Summary: Recommended Drugs and Biologic in Adult Patients with COVID-19. (Version 10.0). Accessed February 23, 2022. https://covid19-sciencetable.ca/sciencebrief/#infectious-diseases-clinical-care.



Examples of Drugs to Adjust

- Easy: Amlodipine
  - Reduce by 50%, monitor BP
- Easy: Viagra, Cialis prn
  - Hold or lower dose
- Moderate: Zopiclone, aripiprazole
  - Reduce by 50%, monitor hangover effect—may need to reduce more
- Difficult: clopidogrel, DOACs, transplant meds, chemo meds
  - Consider remdesivir

Examples of Drugs To Hold

🛑	Do not coadminister	Hold and restart 2 days after completing nirmatrelvir/ritonavir.

- Atorvastatin, rosuvastatin
- Alfuzosin, tamsulosin
- Salmeterol
  - Use only steroid for week or switch LABA to formoterol/vilanterol

Examples of Drugs to Switch

🛑	Do not coadminister	Hold and restart 2 days after completing nirmatrelvir/ritonavir.

- Clopidogrel
  - Options based on time since ACS/PCI: hold, Prasugrel, CI
- Apixaban, Edoxaban, Riviroxaban
  - Consider remdesivir
  - Options based on risk: hold, half dose, or bridge w/LMWH
- Clonazepam, diazepam, flurazepam
  - Switch to: Lorazepam, oxazepam, temazepam

Examples of Contraindicated Drugs

- Inducers in last 2 weeks
  - St. John's wort
  - Carbamazepine, phenytoin
- Narrow therapeutic window (risk of overdose or serious reaction)
  - Fentanyl, Clozapine
- Too long acting for Paxlovid 5-day treatment window
  - Amiodarone, IM risperidone, lurasidone

▲	Contraindicated	Use alternative COVID agent. **Do not use nirmatrelvir/ritonavir.**
▲	Contraindicated (use within past 14 days)	

Tips for Prescribers

- Confirm that an eligible patient will also benefit from treatment
  - *“You have reduced your risk so much through vaccination that we don’t know if you benefit from this treatment.”*
  - If a patient has complex drug interactions but is low risk (e.g., has had all eligible vaccines and otherwise healthy), consider advising against treatment
- Partnership between pharmacy & primary care
  - You are not alone
  - Give enough info for pharmacist to assess (eGFR, eligibility)
  - Treatment window is 5 days from symptom onset
  - Many patients coming to the pharmacy at day 4 or 5
  - If the prescriber is unreachable, the patient will miss the treatment window
  - Call ahead or give a number where you can be reached in next 24h

Paxlovid™ Tools for Primary Care

DAVID KAPLAN MD, MSc, CCFP, FCFP | APRIL 22, 2022

VP Quality, Clinical Institutes and Quality Programs

Ontario Health

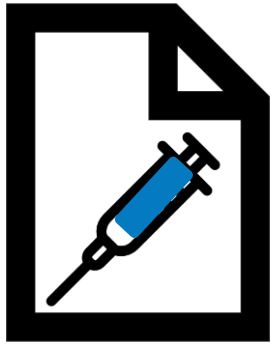
What We Heard

Family Doctors and Nurse Practitioners are contributing significantly to Paxlovid uptake and access, however report challenges including:

- Patient-facing communication
- Identification of high-risk patients who may benefit from Paxlovid but are not aware/informed
- Trepidation surrounding drug interactions
- Prescribing supports

Tools for Identifying High Risk Patients

1



IDENTIFICATION

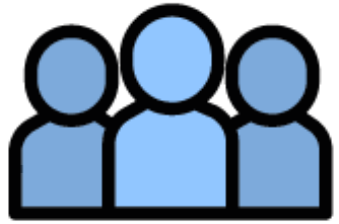
Primary care providers can use the reports available through COVaxON to identify 70+ unvaccinated patients who may benefit from Paxlovid

2

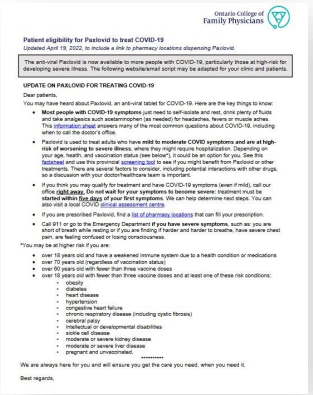
COMMUNICATION

Use the EMR searches created for the 3 main primary care EMRs and identify age, immunocompromised individuals and those with risk factors such as obesity, diabetes, hypertension

3



Send an email template to patients identified during steps 1 and 2 (e.g., OCFP adaptable script)



Patient eligibility for Paxlovid to treat COVID-19

Updated April 19, 2022. *to include a link to pharmacy locations dispensing Paxlovid.*

The anti-viral Paxlovid is now available to more people with COVID-19, particularly those at high-risk for developing severe illness. The following website/email script may be adapted for your clinic and patients.

UPDATE ON PAXLOVID FOR TREATING COVID-19

Dear patients,

You may have heard about Paxlovid, an anti-viral tablet for COVID-19. Here are the key things to know:

- **Most people with COVID-19 symptoms** just need to self-isolate and rest, drink plenty of fluids and take analgesics such acetaminophen (as needed) for headaches, fevers or muscle aches. This information sheet answers many of the most common questions about COVID-19, including when to call the doctor's office.
- Paxlovid is used to treat adults who have **mild to moderate COVID symptoms and are at high-risk of worsening to severe illness**, where they might require hospitalization. Depending on your age, health, and vaccination status (see below*), it could be an option for you. See this factsheet and use this provincial screening tool to see if you might benefit from Paxlovid or other treatments. There are several factors to consider, including potential interactions with other drugs, so a discussion with your doctor/healthcare team is important.
- If you think you may qualify for treatment and have COVID-19 symptoms (even if mild), call our office right away. **Do not wait for your symptoms to become severe; treatment must be started within five days of your first symptoms.** We can help determine next steps. You can also visit a local COVID clinical assessment centre.
- If you are prescribed Paxlovid, find a list of pharmacy locations that can fill your prescription.
- Call 911 or go to the Emergency Department **if you have severe symptoms**, such as: you are short of breath while resting or if you are finding it harder and harder to breathe, have severe chest pain, are feeling confused or losing consciousness.

*You may be at higher risk if you are:

- over 18 years old and have a weakened immune system due to a health condition or medications
- over 70 years old (regardless of vaccination status)
- over 60 years old with fewer than three vaccine doses
- over 18 years old with fewer than three vaccine doses and at least one of these risk conditions:
  - obesity
  - diabetes
  - heart disease
  - hypertension
  - congestive heart failure
  - chronic respiratory disease (including cystic fibrosis)
  - cerebral palsy
  - intellectual or developmental disabilities
  - sickle cell disease
  - moderate or severe kidney disease
  - moderate or severe liver disease
  - pregnant and unvaccinated.

We are always here for you and will ensure you get the care you need, when you need it.

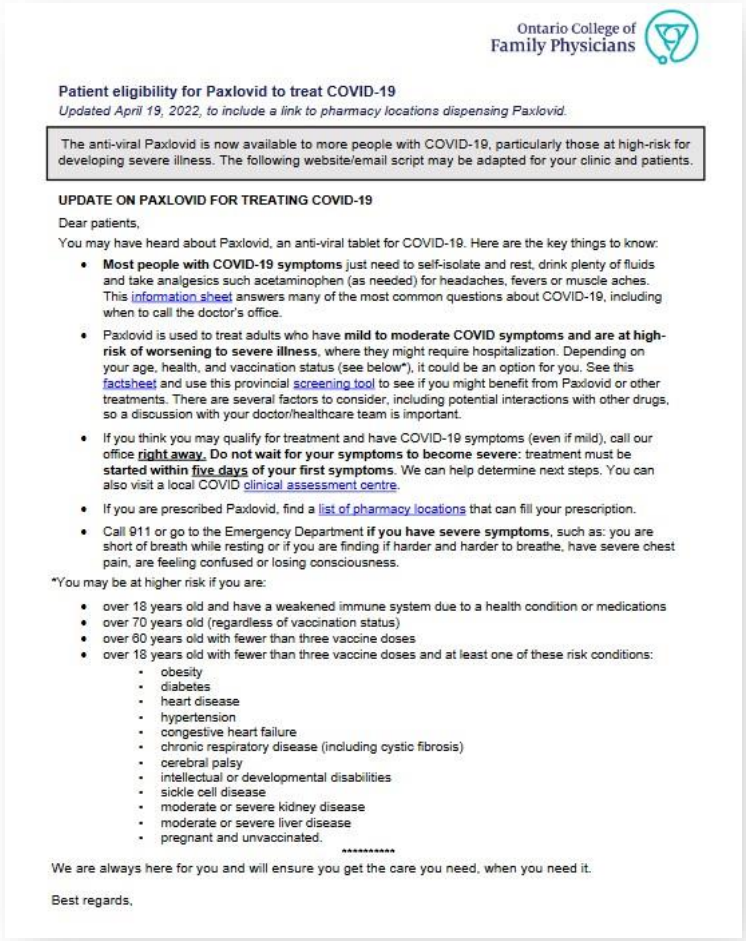
Best regards,

Ontario Health

OMD, eCE and other partners assisting with supports

Tools for Communicating

OCFP Adaptable Script



Ontario College of Family Physicians

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  - moderate or severe kidney disease
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  - pregnant and unvaccinated.

****

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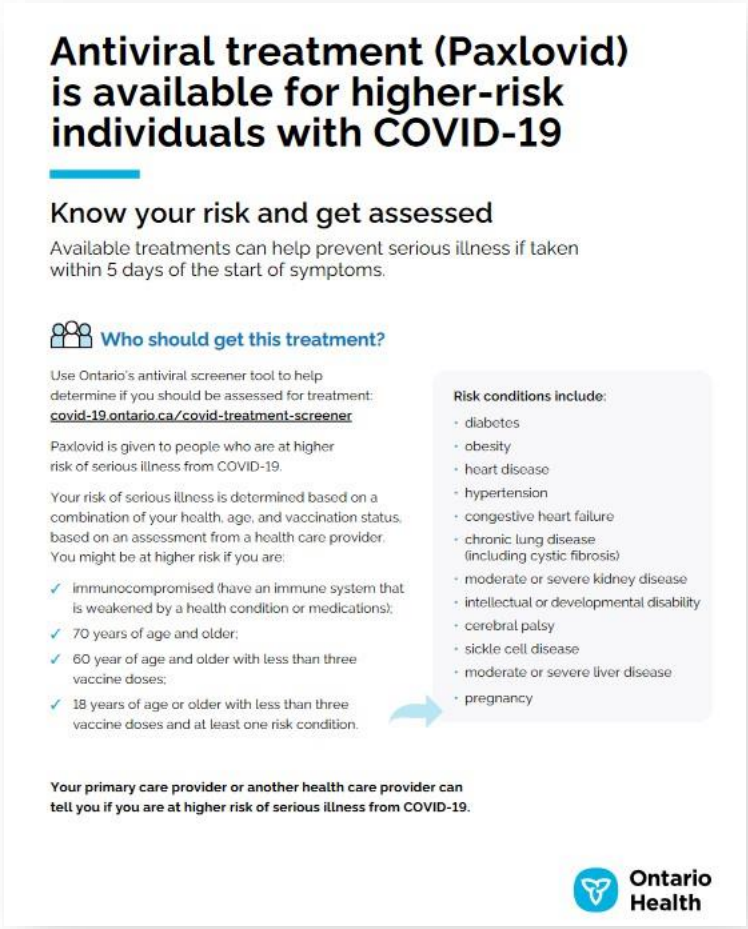
Best regards,

OH Patient Information Sheet



Antiviral treatment (Paxlovid) is available for higher-risk individuals with COVID-19

Know your risk and get assessed

Available treatments can help prevent serious illness if taken within 5 days of the start of symptoms.

Who should get this treatment?

Use Ontario's antiviral screener tool to help determine if you should be assessed for treatment: covid-19.ontario.ca/covid-treatment-screener

Paxlovid is given to people who are at higher risk of serious illness from COVID-19.

Your risk of serious illness is determined based on a combination of your health, age, and vaccination status, based on an assessment from a health care provider. You might be at higher risk if you are:

- ✓ immunocompromised (have an immune system that is weakened by a health condition or medications);
- ✓ 70 years of age and older;
- ✓ 60 year of age and older with less than three vaccine doses;
- ✓ 18 years of age or older with less than three vaccine doses and at least one risk condition.

Risk conditions include:

- diabetes
- obesity
- heart disease
- hypertension
- congestive heart failure
- chronic lung disease (including cystic fibrosis)
- moderate or severe kidney disease
- intellectual or developmental disability
- cerebral palsy
- sickle cell disease
- moderate or severe liver disease
- pregnancy

Your primary care provider or another health care provider can tell you if you are at higher risk of serious illness from COVID-19.

Ontario Health

Ontario Health

Potential Longer Term Actions

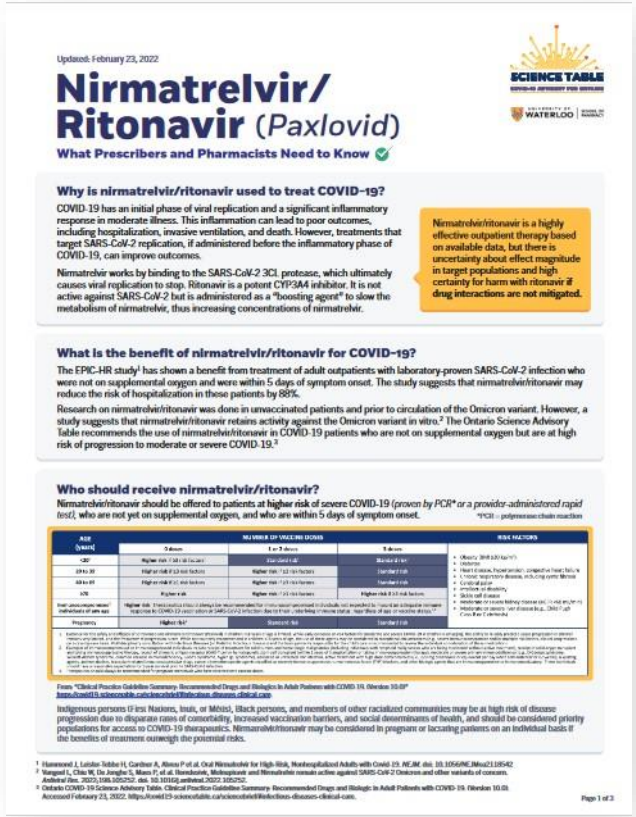
Action
Optimize EMR tools to identify high risk patients to benefit from Paxlovid – expand to all vendors and skill level of clinical users. eCE and OMD collaborating on EMR support and tool development.
Change management facilitation through comprehensive OMD and eCE supports (e.g. Peer Leaders, webinars, one-on-one support)
Create materials about 'best practice" workflows on how to incorporate the tools/searches/forms into the office workflow and provide sample templates for reach out to patients with a goal as indicated to reduce stress on clinicians and their clinics
OMD/eCE to collaborate on ongoing improvements to EMR tools incorporating feedback
Consolidate all resources to "one look" that can be recreated in multiple places

Tools for Prescribing and Identifying Drug Interactions

Approaches from the field

- EMR prescribing tools, such as a provider assessment and prescribing tool in PS Suite
- A “prescription favorite” in PSS to aid in Paxlovid prescribing and use auto EMR drug interaction identification
- EMR KT Tool & Rx all-in-one available in OSCAR, TELUS PSS and Accuro EMRs

Ontario Science Table
What Prescribers and Pharmacists Need to Know



Updated: February 23, 2022

Nirmatrelvir/ Ritonavir (Paxlovid)

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*PCR = polymerase chain reaction

AGE (YEARS)	NUMBER OF VACCINE DOSES			RISK FACTORS
	0 doses	1 or 2 doses	3 doses	
<30	Higher risk if ≥1 risk factor	Paxlovid[1]	Standard risk	• Obesity (BMI ≥30 kg/m²) • Diabetes • Heart disease, hypertension, congestive heart failure • Chronic respiratory disease, including cystic fibrosis • Sickle cell disease • Immune disorders • Stroke or cerebrovascular disease • Moderate or severe liver disease (e.g., Child-Pugh Class B or C cirrhosis)
30 to 39	Higher risk if ≥2 risk factors	Higher risk if ≥1 risk factors	Standard risk	
40 to 49	Higher risk if ≥1 risk factors	Higher risk if ≥1 risk factors	Standard risk	
≥50	Higher risk	Higher risk if ≥1 risk factors	Higher risk if ≥3 risk factors	
Pregnancy	Higher risk[2]	Standard risk	Standard risk	

From "Clinical Practice Guideline Summary: Recommended Drugs and Biologics in Adult Patients with COVID-19, Version 10.0" https://covid19-sciencetable.ca/sciencebrief/infectious-diseases-clinical-care

Indigenous persons (First Nations, Inuit, or Métis), Black persons, and members of other racialized communities may be at high risk of disease progression due to disparate rates of comorbidity, increased vaccination barriers, and social determinants of health, and should be considered priority populations for access to COVID-19 therapeutics. Nirmatrelvir/ritonavir may be considered in pregnant or lactating patients on an individual basis if the benefits of treatment outweigh the potential risks.

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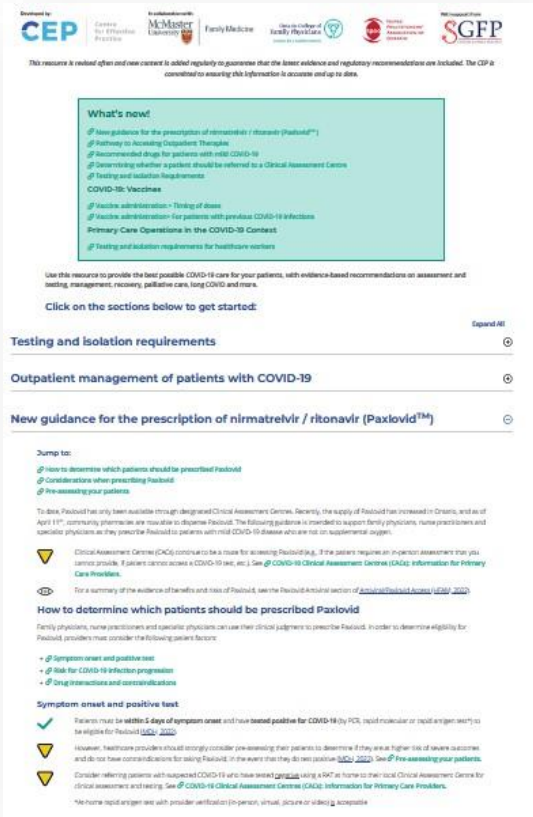
Page 1 of 3

Centre for Effective Practice
COVID-19: Clinical Guidance for Primary Care Providers



CEP | McMaster University Family Medicine | SGFP

What's new!

- New guidance for the prescription of nirmatrelvir / ritonavir (Paxlovid™)
- Pathway to Accessing Outpatient Therapies
- Recommended drugs for patients with mild COVID-19
- Determining whether a patient should be referred to a Clinical Assessment Centre
- Testing and isolation Requirements

COVID-19: Vaccines

- Vaccine administration – Timing of doses
- Vaccine administration– For patients with previous COVID-19 infections

Primary Care Operations in the COVID-19 Context

- Testing and isolation requirements for healthcare workers

Use this resource to provide the best possible COVID-19 care for your patients, with evidence-based recommendations on assessment and testing, management, recovery, palliative care, long COVID and more.

Click on the sections below to get started:

Expand All

Testing and isolation requirements

Outpatient management of patients with COVID-19

New guidance for the prescription of nirmatrelvir / ritonavir (Paxlovid™)

Jump to:

- How to determine which patients should be prescribed Paxlovid
- Considerations when prescribing Paxlovid
- Pre-assessing your patients

To date, Paxlovid has only been available through designated Clinical Assessment Centres. Recently, the supply of Paxlovid has increased in Ontario, and as of April 11th, community pharmacies are now able to dispense Paxlovid. The following guidance is intended to support family physicians, nurse practitioners and specialist physicians as they prescribe Paxlovid to patients with mild COVID-19 disease who are not on supplemental oxygen.

Clinical Assessment Centres (CACs) continue to be a route for accessing Paxlovid (e.g., if the patient requires an in-person assessment that you cannot provide, if patients cannot access a COVID-19 test, etc.). See COVID-19 Clinical Assessment Centres (CACs): Information for Primary Care Providers.

For a summary of the evidence of benefits and risks of Paxlovid, see the Paxlovid Ministry section of Ministry/Paxlovid Access (MSAC 2022).

How to determine which patients should be prescribed Paxlovid

Family physicians, nurse practitioners and specialist physicians can use their clinical judgment to prescribe Paxlovid. In order to determine eligibility for Paxlovid, providers must consider the following patient factors:

- Symptom onset and positive test
- Risk for COVID-19 infection progression
- Drug interactions and contraindications

Symptom onset and positive test

Patients must be within 5 days of symptom onset and have tested positive for COVID-19 (by PCR, rapid molecular or rapid antigen test) to be eligible for Paxlovid (MOH, 2022).

However, healthcare providers should strongly consider pre-assessing their patients to determine if they are at higher risk of severe outcomes and do not have contraindications for taking Paxlovid, in the event that they do test positive (MOH, 2022). See Pre-assessing your patients.

Consider referring patients with suspected COVID-19 who have tested negative using a RAT at home to their local Clinical Assessment Centre for clinical assessment and testing. See COVID-19 Clinical Assessment Centres (CACs): Information for Primary Care Providers.

*At-home rapid antigen test with provider verification (in-person, virtual, picture or video) is acceptable

Ontario Health

(Nirmatrelvir-Ritonavir) Paxlovid™ Prescription

MUST include accurate medication list with Form

Please fax completed form AND patient's medication list to patient's preferred pharmacy

Prescriber Information		Patient Information			
First Name	**Last Name**	**First Name**	**Last Name**	**Sex (at birth)** ☐ Male ☐ Female	**DOB**
Address		**Address**		**Health Card No.**	**Version**
		City		**Postal Code**	
City	**Postal Code**	**Telephone**		**Preferred Language** ☐ EN ☐ Other	
Telephone	**Fax**	**Height (cm)**		**Weight (Kg)**	

INCLUSION CRITERIA: MUST MEET CRITERIA TO PROCEED WITH TREATMENT

Date of positive COVID test: **Date of symptom onset (must be 5 days or less):**

AGE (YEARS)	NUMBER OF VACCINE DOSES	
	0, 1, OR 2 DOSES	3 DOSES
18 to 59	❑ Eligible if 1 or more risk factors	Not Eligible
60 to 69	❑ Eligible	Not Eligible
70 or greater	❑ Eligible	❑ Eligible
Immunocompromised individuals of any age (18 years of age and older)	❑ Eligible: Therapeutics should always be recommended for immunocompromised individuals not expected to mount an adequate immune response to COVID-19 vaccination or SARS-CoV-2 infection due to their underlying immune status, regardless of age or vaccine status.	
Pregnancy	0 DOSES	1,2, OR 3 DOSES
	Eligible	Not Eligible

Indigenous persons (First Nations, Inuit, or Métis), Black persons, and members of other racialized communities may be at high risk of disease progression due to disparate rates of comorbidity, increased vaccination barriers, and social determinants of health, and should be considered priority populations for access to COVID-19 therapeutics.

Risk Factors: (Check all that apply)
- ☐ Obesity (BMI greater than or equal to 30 kg/m^2)
- ☐ Diabetes
- ☐ Heart disease, hypertension, congestive heart failure
- ☐ Chronic respiratory disease, including cystic fibrosis
- ☐ Cerebral palsy
- ☐ Intellectual disability
- ☐ Sickle cell disease
- ☐ Moderate or severe kidney disease (eGFR less than 60 ml/min)
- ☐ Moderate or severe liver disease (e.g. Child-Pugh Class B or C)

*** Evidence for less than 18 years of age is limited. Multidisciplinary consultation with infectious diseases and primary care is recommended**

Immunocompromise Factors: (Check all that apply)
- ☐ Solid organ or bone marrow transplant **(*)**
- ☐ CAR T-cell therapy
- ☐ Anti-CD 20 agent
- ☐ Alkylating agents, anti-metabolites **(*)**
- ☐ Advanced or untreated HIV
- ☐ Congenital immunodeficiency
- ☐ Anti-TNF blockers or other biologic agents **(*)**
- ☐ Taking chronic oral corticosteroid (greater than 20mg/d prednisone equivalent for greater than 2 weeks)
- ☐ Other: Name of Immune modifying Drug _____

(*) Depending on absolute contraindications

Note: These individuals should have a reasonable expectation for 1-year survival prior to SARS-COV-2 infection

(Nirmaltrevir-Ritonavir) Paxlovid™ Assessment:	
☐ Attach current medication, herbal, OTC list	Existing liver impairment: ☐ YES ☐ NO ☐ UNKNOWN
☐ Patient's home pharmacy	Existing renal impairment: ☐ YES ☐ NO ☐ UNKNOWN
☐ Home pharmacy phone number	If YES, enter Serum Creatinine and eGFR if available
☐ Allergies ☐ NKA	❑ Serum Creatinine (µmol/L):_____ _ Date:_____
Is the patient pregnant? ☐ YES ☐ NO ☐ N/A	❑ eGFR (ml/min): Date:

Note pharmacist will review eligibility, assess drug interactions and confirm dosing prior to releasing the medication. Any recommended changes to the therapeutic regimen will be communicated back to the prescriber.

Medication Order

Standard Dose (eGFR above 60ml/min)

☐ Paxlovid (Nirmatrelvir 150mg and Ritonavir 100mg): Take 2 pink tablets of nirmatrelvir and 1 white tablet of ritonavir once in the morning and once in the evening for 5 days

Reduced Dose (eGFR between 30-59ml/min)

☐ Paxlovid (Nirmatrelvir 150mg and Ritonavir 100mg): Take 1 pink tablet of nirmatrelvir and 1 white tablet of ritonavir once in the morning and once in the evening for 5 days

By prescribing this medication, the referring prescriber assumes responsibility for all follow up.

Physician/NP Registration Number _____ Signature _____ Date _____

Paxlovid™ Prescription Form – Version 1

Ontario Health

Resources

Clinical/Prescriber Guidance

- Centre for Effective Practice (CEP) New Guidance for the Prescription of Nirmatrelvir / Ritonavir (Paxlovid™)
- Ontario Science Table Clinical Practice Guideline Summary: Recommended Drugs and Biologics in Adult Patients with COVID-19
- Ontario Science Table Nirmatrelvir/Ritonavir (Paxlovid): What Prescribers and Pharmacists Need to Know
- University Health Network/Women's College Hospital COVID Therapeutics Overview
- Ontario Health Access to COVID-19 antiviral treatment (Paxlovid): Information for primary care providers and other health care providers caring for patients in the community

Patient and Public Information

- Ontario Health Patient Fact Sheet

Comprehensive Websites

- Ontario College of Family Physicians Prescribing Paxlovid, Patient Resources and More
- Ontario Ministry of Health COVID Antiviral Treatment (public information, screening tool and dispensing pharmacy list)
- Government of Canada COVID-19 Vaccines and Treatments Portal: Paxlovid (information for health care providers, consumers and researchers

Templates for Patient Communication

- Ontario College of Family Physicians Patient Eligibility for Paxlovid to treat COVID-19 template

eHealth Centre of Excellence - Paxlovid Resources

Paxlovid Resources

Developed in collaboration with Partnering For Quality, the eHealth Centre of Excellence has developed several resources to help with Paxlovid prescriptions and referrals. These resources are available for PS Suite, Oscar and Accuro.

Paxlovid Prescription Form

PS Suite: (Designed by PFQ)

1. Download the package: **Click here**
2. Unzip the .cfm file to your Desktop
3. Import the .cfm file into PS Suite

Oscar: (Developed by eCE)

1. Download the package: **Click here**
2. Import the full .zip package into Oscar

Accuro: (Designed by PFQ)

Found in the global forms list
Name: Paxlovid Prescription- 04122022- DC
Publisher: wejerrett
Date: April 13, 2022

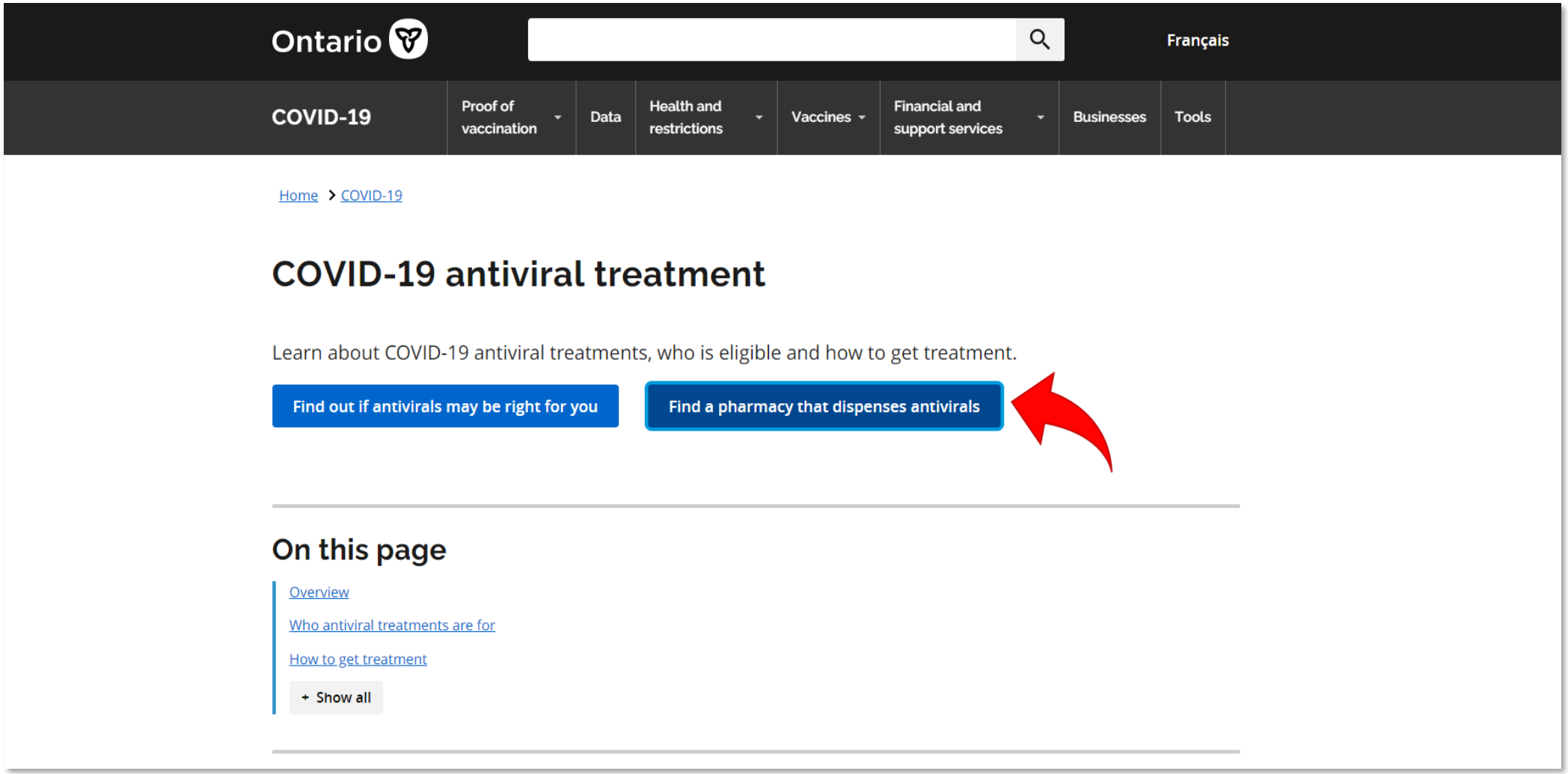
PDF version: **Click here**

Pharmacy Master List

1. **https://covid-19.ontario.ca/covid-19-antiviral-treatment**
2. Click on the button **"Find a pharmacy that dispenses antivirals"**

https://ehealthce.ca/COVID-vax.htm#Paxlovid%20Resources

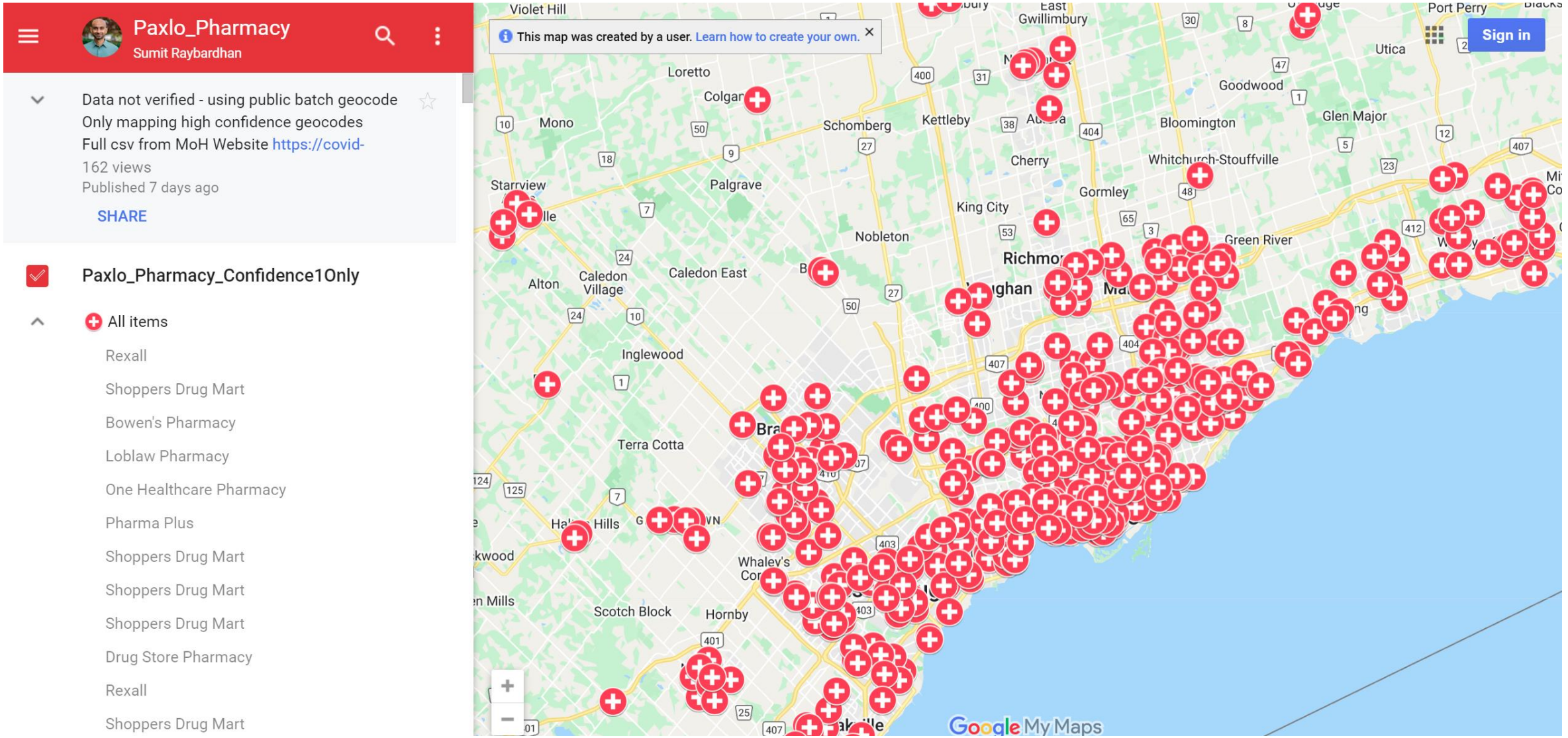
Pharmacies for COVID-19 antiviral treatment



https://covid-19.ontario.ca/covid-19-antiviral-treatment

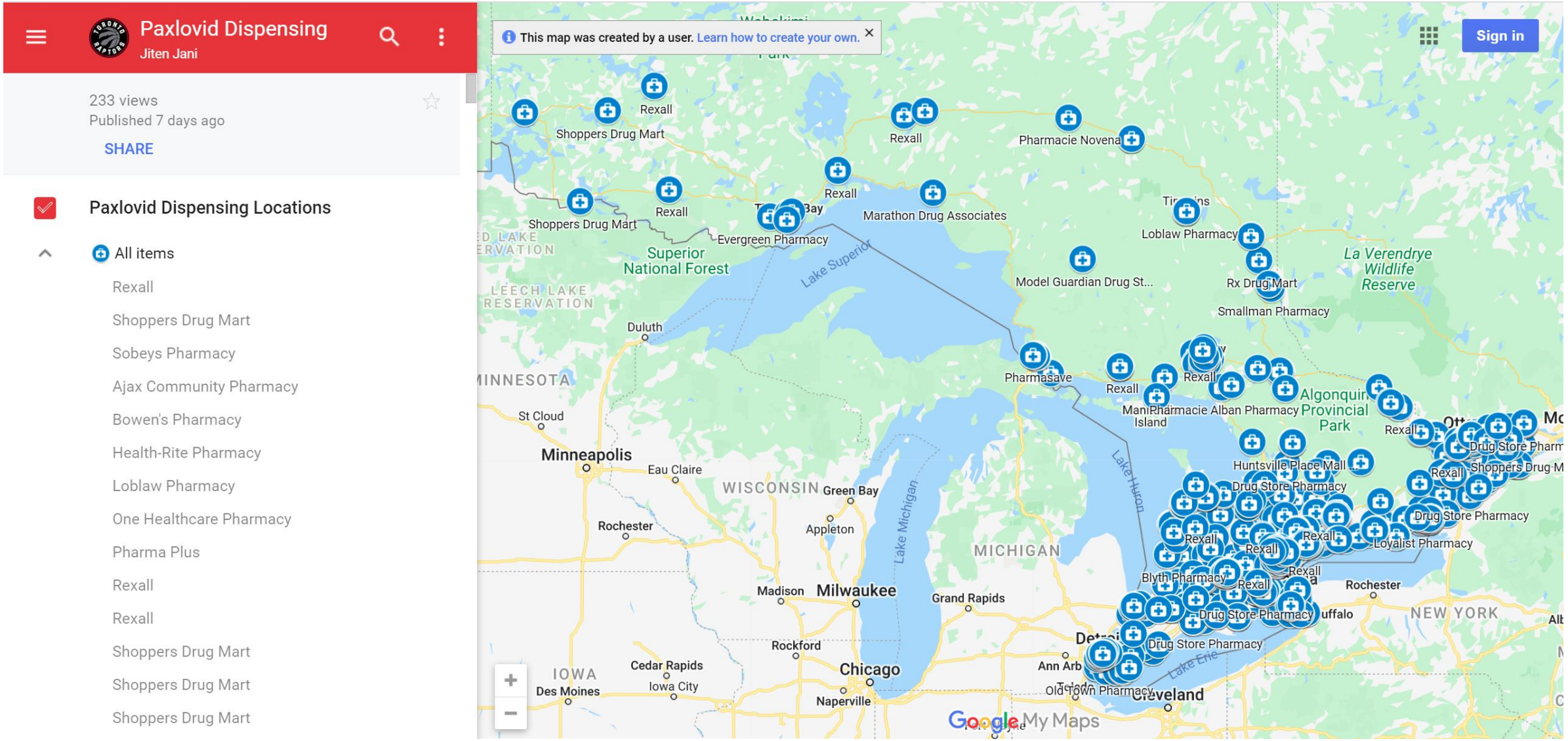
Pharmacies dispensing Paxlovid

https://www.google.com/maps/d/u/0/edit?mid=1_zXBQgh2TK2tm_mVmNwByeDtD0xs8Bcr&ll=43.77302208707974%2C-79.47531803905962&z=10



Pharmacies dispensing Paxlovid

https://www.google.com/maps/d/viewer?mid=1PdhbqFxXXfkgV4upoX64E1Fu6xLtJhDt



Prescribing Paxlovid

- ✓ **Mild to moderate disease, no supplemental oxygen**
  - ➢ positive COVID-19 test: PCR, rapid molecular or rapid antigen test.
  - ➢ self-administered RAT, verified by provider is acceptable
- ✓ **Higher risk of severe disease**
  - ➢ see next slide: SAT's "Who should receive nirmatrelvir/ritonavir"
  - ➢ will patient benefit from treatment?
- ✓ **Within 5 days of symptom onset**
- ✓ **No cost to Ontario patients | Health Card not required**
- ✓ **Assess drug-drug interactions**
- ✓ **Patient may be referred/self-refer to COVID Clinical Assessment Centre**

- Ministry of Health (Ontario eligibility for Paxlovid): COVID-19 antiviral treatment | COVID-19 (coronavirus) in Ontario
- Science Advisory Table
- List of pharmacy locations dispensing Paxlovid (Excel, updated regularly): https://covid-19.ontario.ca/covid-19-antiviral-treatment
- Map of pharmacy locations dispensing Paxlovid (Google map): https://www.google.com/maps/d/u/0/viewer?mid=1PdhbqFxXXfkgV4upoX64E1Fu6xLtJhDt&ll=46.214375048778656%2C-84.5458116&z=6

Who Should Receive Paxlovid?

Who should receive nirmatrelvir/ritonavir?

Nirmatrelvir/ritonavir should be offered to patients at **higher risk** of severe COVID-19 *(proven by PCR* or a provider-administered rapid test),* who are not yet on supplemental oxygen, and who are within 5 days of symptom onset.

*PCR = polymerase chain reaction

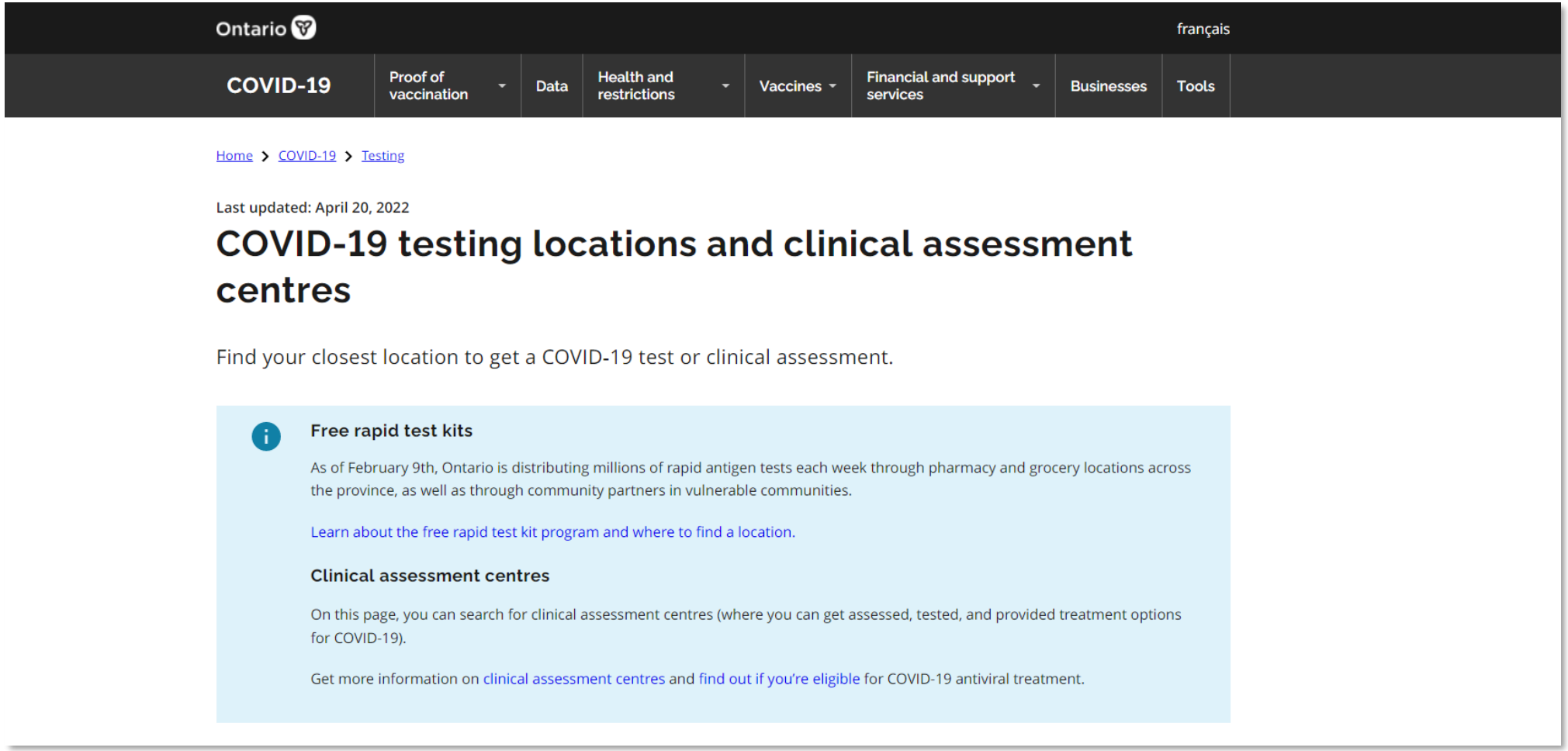
AGE (years)	NUMBER OF VACCINE DOSES			RISK FACTORS
	0 doses	1 or 2 doses	3 doses	
<20[1]	**Higher risk** if ≥3 risk factors[1]	Standard risk[1]	Standard risk[1]	• Obesity (BMI ≥30 kg/m²) • Diabetes • Heart disease, hypertension, congestive heart failure • Chronic respiratory disease, including cystic fibrosis • Cerebral palsy • Intellectual disability • Sickle cell disease • Moderate or severe kidney disease (eGFR <60 mL/min) • Moderate or severe liver disease (e.g., Child Pugh Class B or C cirrhosis)
20 to 39	**Higher risk** if ≥3 risk factors	**Higher risk** if ≥3 risk factors	Standard risk	
40 to 69	**Higher risk** if ≥1 risk factors	**Higher risk** if ≥3 risk factors	Standard risk	
≥70	**Higher risk**	**Higher risk** if ≥1 risk factors	**Higher risk** if ≥3 risk factors	
Immunocompromised[2] individuals of any age	**Higher risk**: Therapeutics should always be recommended for immunocompromised individuals not expected to mount an adequate immune response to COVID-19 vaccination or SARS-CoV-2 infection due to their underlying immune status, regardless of age or vaccine status.[1,2]			
Pregnancy	**Higher risk**[3]	Standard risk	Standard risk	

1. Evidence for the safety and efficacy of sotrovimab and nirmatrelvir/ritonavir (Paxlovid) in children <18 years of age is limited. While early evidence on risk factors for moderate and severe COVID-19 in children is emerging, the ability to reliably predict disease progression in children remains very limited, and the frequency of progression is rare. While not routinely recommended in children <18 years of age, the use of these agents may be considered in exceptional circumstances (e.g., severe immunocompromise and/or multiple risk factors, clinical progression) on a case-by-case basis. Multidisciplinary consultation with Infectious Diseases (or Pediatric Infectious Diseases) and the team primarily responsible for the child's care is recommended to review the individual consideration of these medications.
2. Examples of immunocompromised or immunosuppressed individuals include receipt of treatment for solid tumors and hematologic malignancies (including individuals with lymphoid malignancies who are being monitored without active treatment), receipt of solid-organ transplant and taking immunosuppressive therapy, receipt of chimeric antigen receptor (CAR)-T-cell or hematopoietic stem cell transplant (within 2 years of transplantation or taking immunosuppression therapy), moderate or severe primary immunodeficiency (e.g., DiGeorge syndrome, Wiskott-Aldrich syndrome, common variable immunodeficiency, Good's syndrome, hyper IgE syndrome), advanced or untreated HIV infection, active treatment with high-dose corticosteroids (i.e., ≥20 mg prednisone or equivalent per day when administered for ≥2 weeks), alkylating agents, antimetabolites, transplant-related immunosuppressive drugs, cancer chemotherapeutic agents classified as severely immunosuppressive, tumor-necrosis factor (TNF) blockers, and other biologic agents that are immunosuppressive or immunomodulatory. These individuals should have a reasonable expectation for 1-year survival prior to SARS-CoV-2 infection.
3. Therapeutics should always be recommended for pregnant individuals who have received zero vaccine doses.

From: "Clinical Practice Guideline Summary: Recommended Drugs and Biologics in Adult Patients with COVID-19. (Version 10.0)"
https://covid19-sciencetable.ca/sciencebrief/#infectious-diseases-clinical-care.

Ontario Science Table: [Nirmatrelvir/Ritonavir (Paxlovid): What Prescribers and Pharmacists Need to Know - Ontario COVID-19 Science Advisory Table (covid19-sciencetable.ca)](https://covid19-sciencetable.ca) (February 23, 2022)

COVID-19 Assessment Centres



https://covid-19.ontario.ca/assessment-centre-locations

List of sites distributing Paxlovid

COVID-19 Clinical Assessment Centres (CACs): Information for Primary Care Providers

UPDATED List of Clinical Assessment Centres

The Ministry of Health's COVID-19 testing locations and clinical assessment centres webpage contains contact information for all Assessment Centres (ACs) and Clinical Assessment Centres (CACs) in the province. To find CACs, check off the "Provides clinical assessments" box under Services Available on the left side of the page.

https://tools.cep.health/tool/covid-19/#listCAC

Eligible for Fourth Dose

Recommended interval 5 months (140 days) after 3rd dose (minimal interval 84 days):

- Ontarians 60+;
- Indigenous residents and their non-Indigenous household members aged 18 or older

3 months (84 days) after their 3rd dose for 18+; or 6 months (168 days) for 12-17:

- long-term care and retirement home residents, those who live in First Nation elder care lodges and older adults in other congregate care settings that have health and assisted living services
- People who are immunocompromised including:
  - People on dialysis, those receiving cancer treatment, those with previous organ or stem-cell transplants, those with advanced or untreated HIV, people with rare genetic disorders that impair the immune system, people taking immunosuppressant medications

For people who are immunocompromised: 18+ and living in a group setting; or 18+ and First Nations, Inuit or Métis; or 60+ and received three primary doses plus 1st booster (4th dose) are eligible for a 2nd booster (5th dose)

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

Immunocompromised

Examples:

- transplant recipient (including solid organ transplant and hematopoietic stem cell transplants)
- receiving stable, active treatment (chemotherapy, targeted therapies, immunotherapy) for a malignant hematologic disorder or solid tumor
- receiving chimeric antigen receptor (CAR)-T-cell treatment
- have moderate or severe primary immunodeficiency (for example, DiGeorge syndrome, Wiskott-Aldrich syndrome)
- stage 3 or advanced untreated HIV infection or acquired immunodeficiency syndrome
- in active treatment with any of these immunosuppressive therapies:
  - anti-B cell therapies (monoclonal antibodies targeting CD19, CD20 and CD22)
  - high-dose systemic corticosteroids
  - alkylating agents
  - antimetabolites, or tumor-necrosis factor (TNF) inhibitors and other biologic agents that are significantly immunosuppressive taking specific immunosuppressant medications

Confused about COVID?

Home › Quality & Innovation › COVID-19 Community of Practice › *Confused about COVID? Family doctors answer your questions*

As Omicron sweeps through communities across Ontario, Canada and beyond, patients are grappling with a large amount of confusing information and new uncertainties about COVID.

To cut through the confusion, family doctors have come together to help patients and the public make sense of the current COVID rules and realities. The **'Confused about COVID? Family doctors answer your questions'** series offers patients and the public trustworthy advice about protecting their health and how family doctors can help.

https://dfcm.utoronto.ca/confused-about-covid

"I think I have COVID. When should I call my doctor?"

Most people with COVID can manage at home. You should:

- ✓ Rest.
- ✓ Drink plenty of fluids.
- ✓ For fever, headaches, and muscle aches: use over-the-counter pain and fever medications. Acetaminophen (Tylenol) is the best choice if you can take it.
- ✓ For a cough: try a teaspoon of honey (except if you have diabetes or if it is for a child under 12 months) or turn on a humidifier.
- ✓ For a sore throat: try lozenges or gargle with warm salt water.
- ✓ For mild discomfort when breathing: keep the room cool, open the window, try relaxation exercises and shifting your position.

If you have COVID, you must self-isolate. If you need care, you should not hesitate to call your doctor. Learn more here: rebrand.ly/Feeling-Unwell.

Call your doctor for an appointment if:

01 You have a medical condition that needs attention.

COVID can worsen medical problems such as diabetes, asthma, heart disease, lung disease, high blood pressure or other long-term conditions. If you get COVID and have one of those health problems, your treatment might have to change. Call your doctor if you are unsure about how to manage these conditions while you have COVID.

If pregnant, your risk of more serious illness from COVID increases. Call your pregnancy care provider for advice and follow-up.

CONFUSED ABOUT COVID? FAMILY DOCTORS ANSWER YOUR QUESTIONS.

"If I get COVID, is there a medication I can take?"

If you have COVID, you must self-isolate. If you need care, you should not hesitate to call your doctor. Learn more here: rebrand.ly/Feeling-Unwell.

Most people who get COVID can recover at home without treatment. To find out how to care for yourself at home or when to call your doctor, visit rebrand.ly/When-To-Call.

People who are sick enough to go to hospital will be given medications to help them recover. For people who are at higher risk of serious illness, medications are available that can help prevent them from needing to be cared for in hospital.

Who can get these medications?

Medications to treat COVID are for people who are at higher risk of getting seriously ill. That's because the research on these medications was generally done on people who were at higher risk of serious illness.

If you have COVID, please call your family doctor right away to discuss potential treatment if ANY of the following apply to you:

- ✓ **You have an immune system that is weakened by a health condition or medications.**
  For example, DiGeorge Syndrome, cancer chemotherapy or high-dose steroid treatment.
- ✓ **You are 70 or older.**
- ✓ **You have not had any doses of a COVID vaccine.**
- ✓ **You have any of the following chronic conditions:**
  Diabetes, obesity, high blood pressure, heart disease, heart failure, lung disease including cystic fibrosis, serious liver or kidney problems, intellectual disability, cerebral palsy or sickle cell disease.
- ✓ **You are pregnant.**
  Call your pregnancy care provider.

Updated: Apr. 5, 2022
For other questions, please visit ConfusedAboutCOVID.ca.
Family & Community Medicine UNIVERSITY OF TORONTO
Ontario College of Family Physicians
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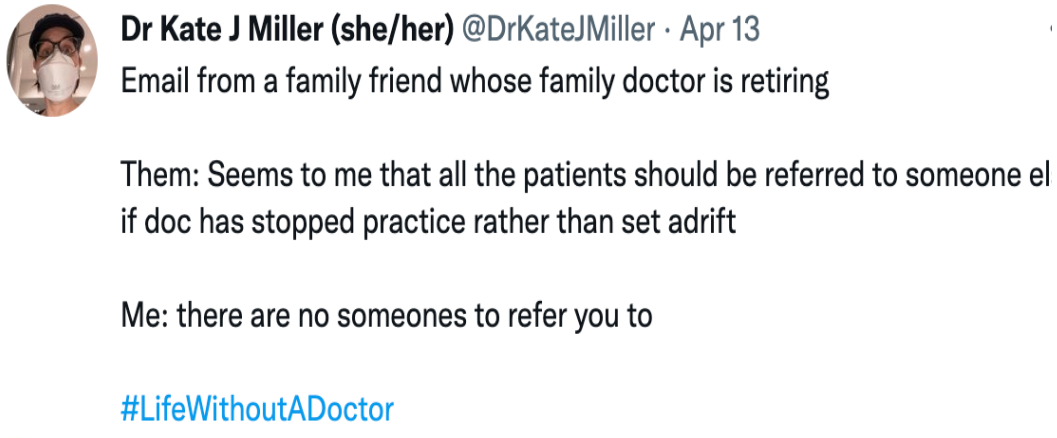
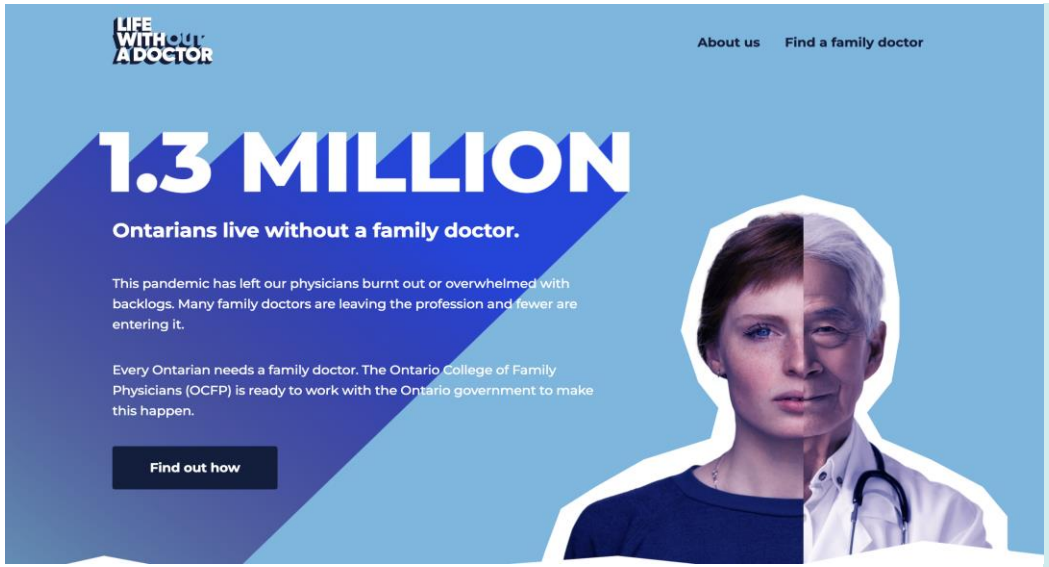
ADVOCACY CAMPAIGN UPDATE





LifeWithoutADoctor.ca

OCFP/SGFP Virtual Advocacy Town Hall For Members

Mark your calendars:

Monday, May 2, 7:00pm – 8:00pm

Questions?

Webinar recording and curated Q&A will be posted soon
https://www.dfcm.utoronto.ca/covid-19-community-practice/past-sessions

Our next Community of Practice: **Friday, May 13, 2022**

Contact us: *ocfpcme@ocfp.on.ca*

Visit: https://www.ontariofamilyphysicians.ca/tools-resources/covid-19-resources

The COVID-19 Community of Practice for Ontario Family Physicians is a one-credit-per-hour Group Learning program that has been certified for up to a total of 32 credits..

Post session survey will be emailed to you. Mainpro+ credits will be entered for you with the information you provided during registration.

Family & Community Medicine
UNIVERSITY OF TORONTO

Ontario College of Family Physicians
Leaders for a healthy Ontario