

NEW ANTI-VIRAL TREATMENTS FOR COVID-19 – PRIMARY CARE

March 1, 2022

LONDON MIDDLESEX PRIMARY CARE ALLIANCE (LMPCA)

Vision:

An inclusive network of primary care providers leading with a unified voice to improve the health of our community

Mission:

Create a strong and united primary care network to:

- **Lead** system change utilizing quintuple aim values
- **Drive** health equity and continuous quality improvement for the best possible experience and health outcomes
- **Advance** patient-centred equitable care in partnership with those we serve
- **Improve** integration of primary health services with public health and other social and health care partners

OBJECTIVES

Learn more about the new anti-virals:

- Mechanism
- Evidence and Clinical Trials
- Pharmacology
- How to access these drugs for your patients

OUR SPEAKERS

- Dr. Megan Devlin – Infectious Disease Specialist
- Dr. Sameer Elsayed – Infectious Disease Specialist
- Rita Dhami, BScPhm, Pharm.D, RPh
Clinical Pharmacist , Antimicrobial Stewardship/ Infectious Diseases
- Dr. Gord Schacter, London Middlesex Pandemic Clinical Lead

AGENDA

Time	Item	Speaker/Moderator
5 min	Welcome and Introduction	Dr. Vineet Nair
5 min	COVID Antiviral Therapy – Introduction to Outpatient COVID treatment	Dr. Megan Devlin
15 min	COVID Antiviral Therapy – Clinical Evidence	Dr. Sameer Elsayed
15 min	Pharmacology of Antiviral Therapy	Rita Dhami
5 min	Eligibility for Antiviral Therapy	Dr. Megan Devlin
15 min	How to get Antiviral Therapy for you patient	Dr. Gordon Schacter
30 min	Q & A Group Forum	All

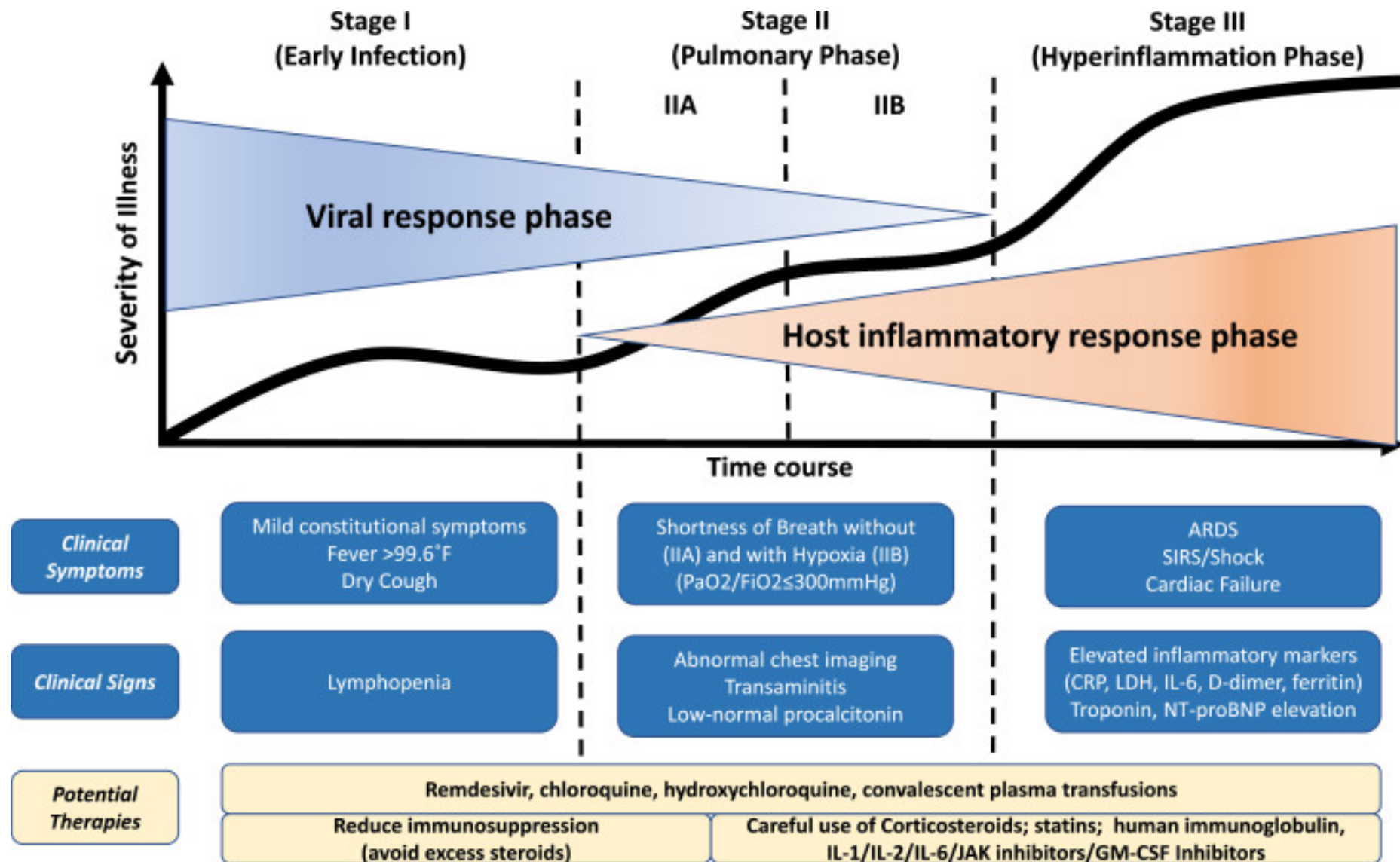
Brief Overview of Outpatient COVID Therapeutics

Dr. Megan Devlin, MD, FRCPC

Assistant Professor, Infectious Diseases

Co-Lead LHSC Urgent COVID Care Clinic (LUC3)

Mar. 1, 2022



Prescribing for COVID-19 Outpatients

Prescribing to reduce ED visits/Hospitalizations/Death

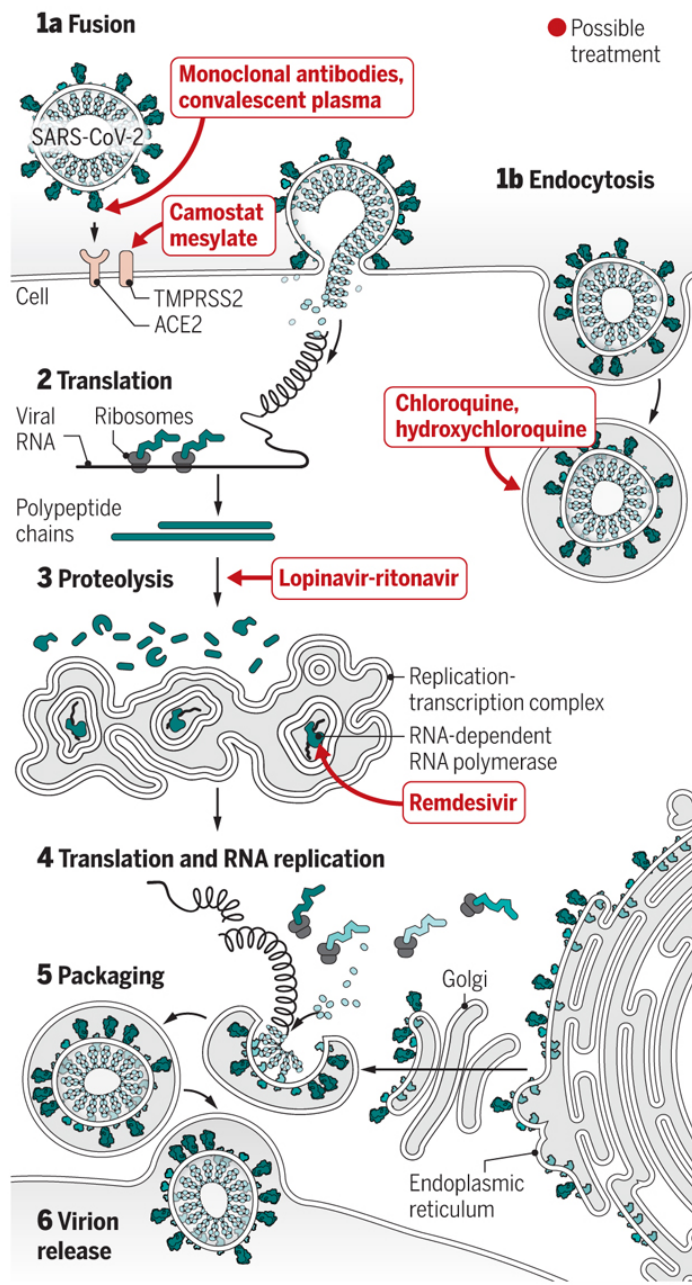
- Viral Effect
 - Oral
 - Nirmatrelvir-ritonavir (Paxlovid)
 - Molnupiravir
 - IV
 - Sotrovimab (monoclonal antibody)
 - Remdesivir (Anti-viral)
- Other
 - Fluvoxamine
 - Budesonide

Prescribing to ameliorate symptoms:

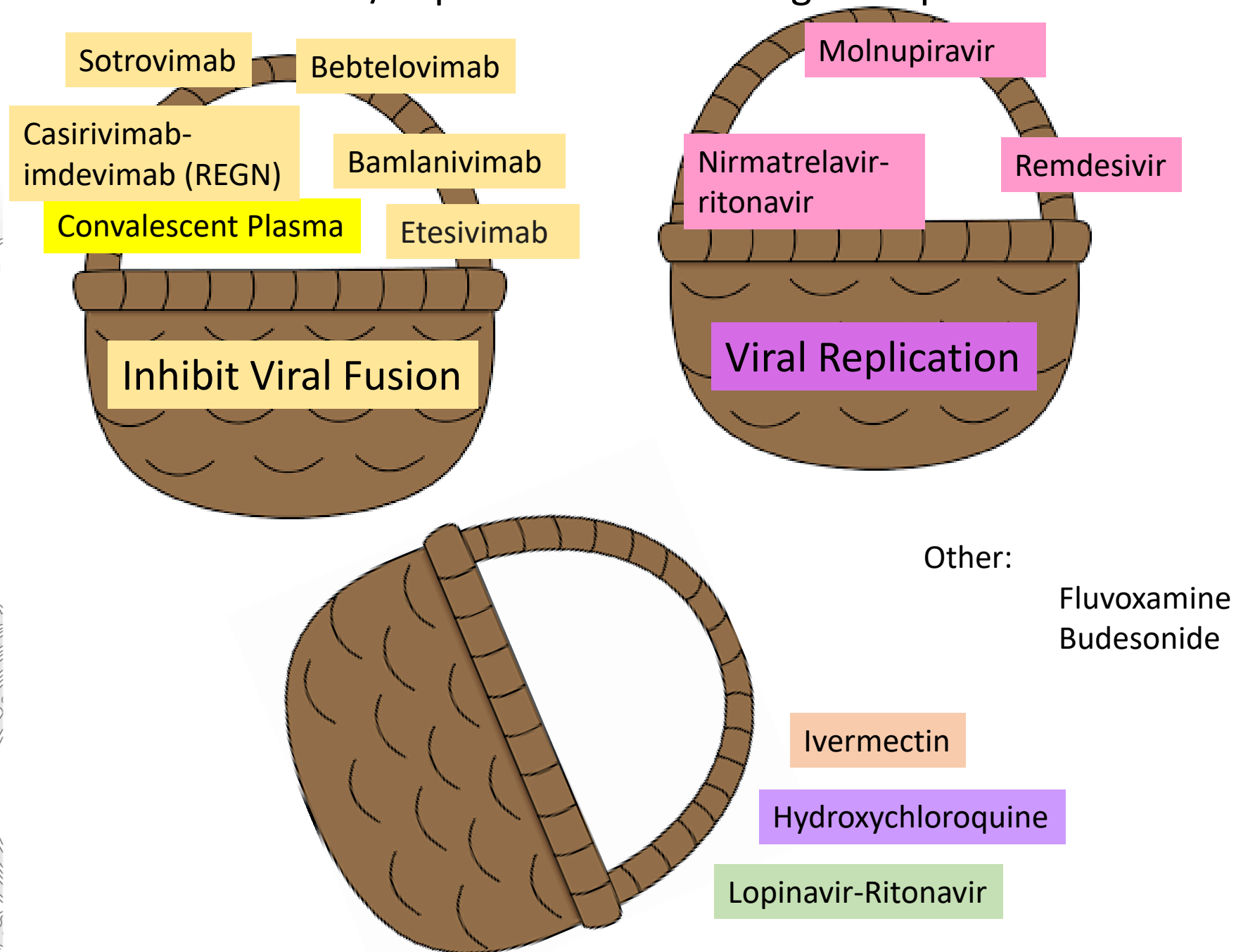
- Nausea:
 - Gravol
 - Ondansetron
- Cough/Dyspnea
 - Cough Syrup
- Headache
 - Acetaminophen/Ibuprofen

Lines of attack

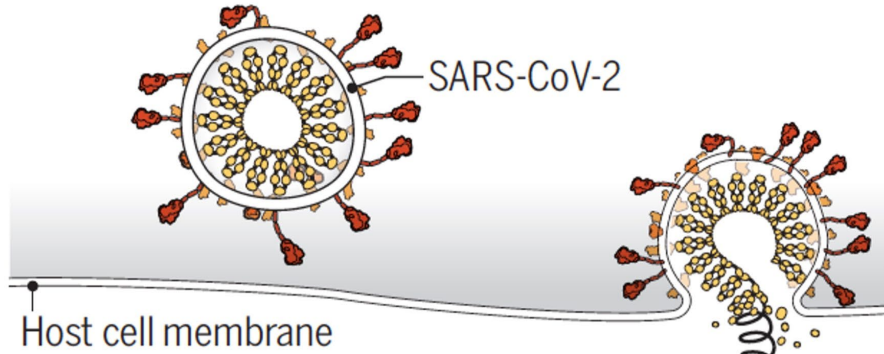
Experimental treatment strategies attempt to interfere with different steps (numbered) in the coronavirus replication cycle.



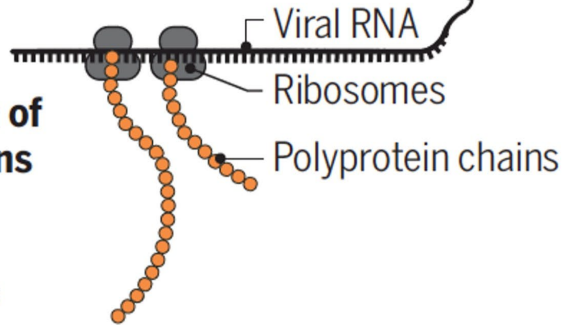
Virus Adhesion/Replication Modulating therapies



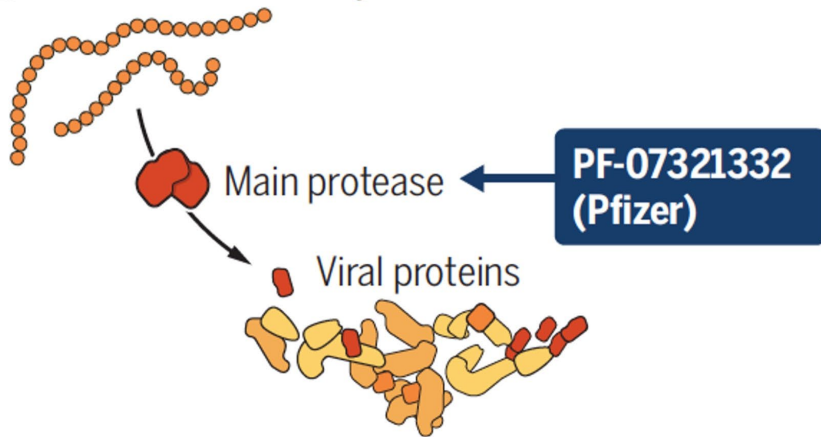
1 Attachment and entry



2 Translation of viral proteins

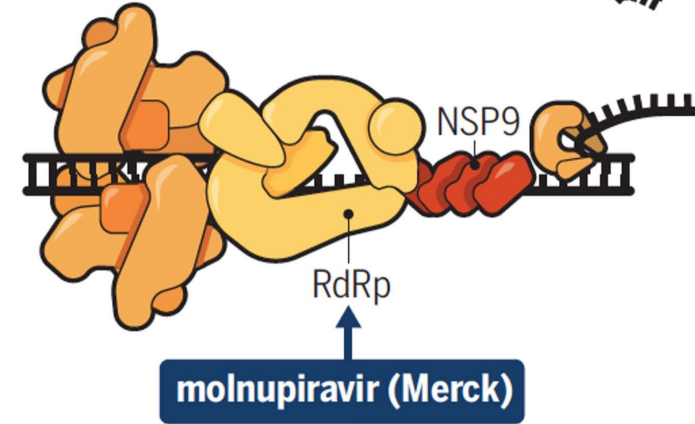
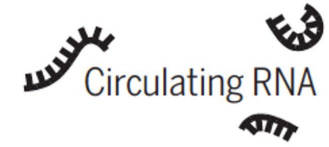


3 Proteolysis

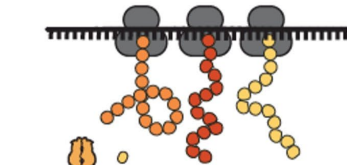


4 RNA replication

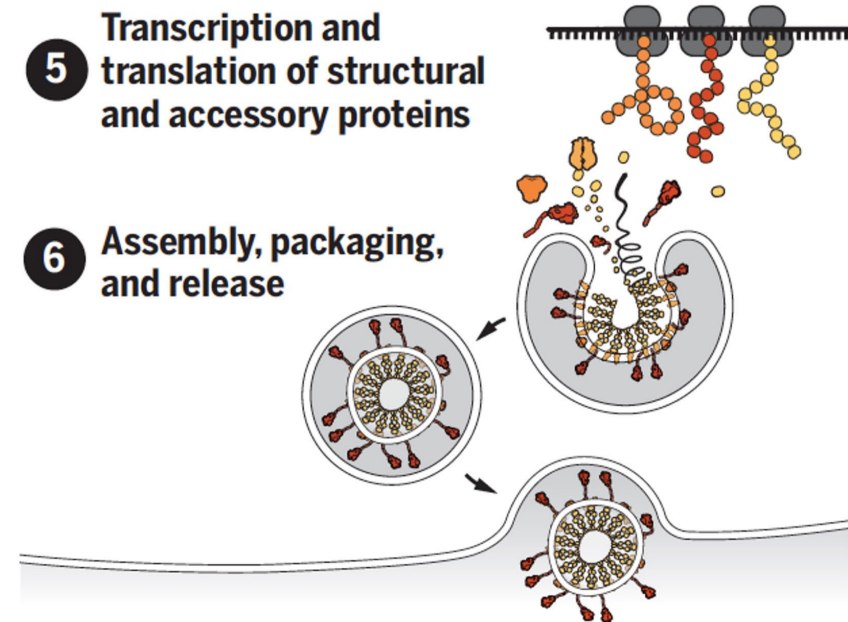
Replication transcription complex



5 Transcription and translation of structural and accessory proteins

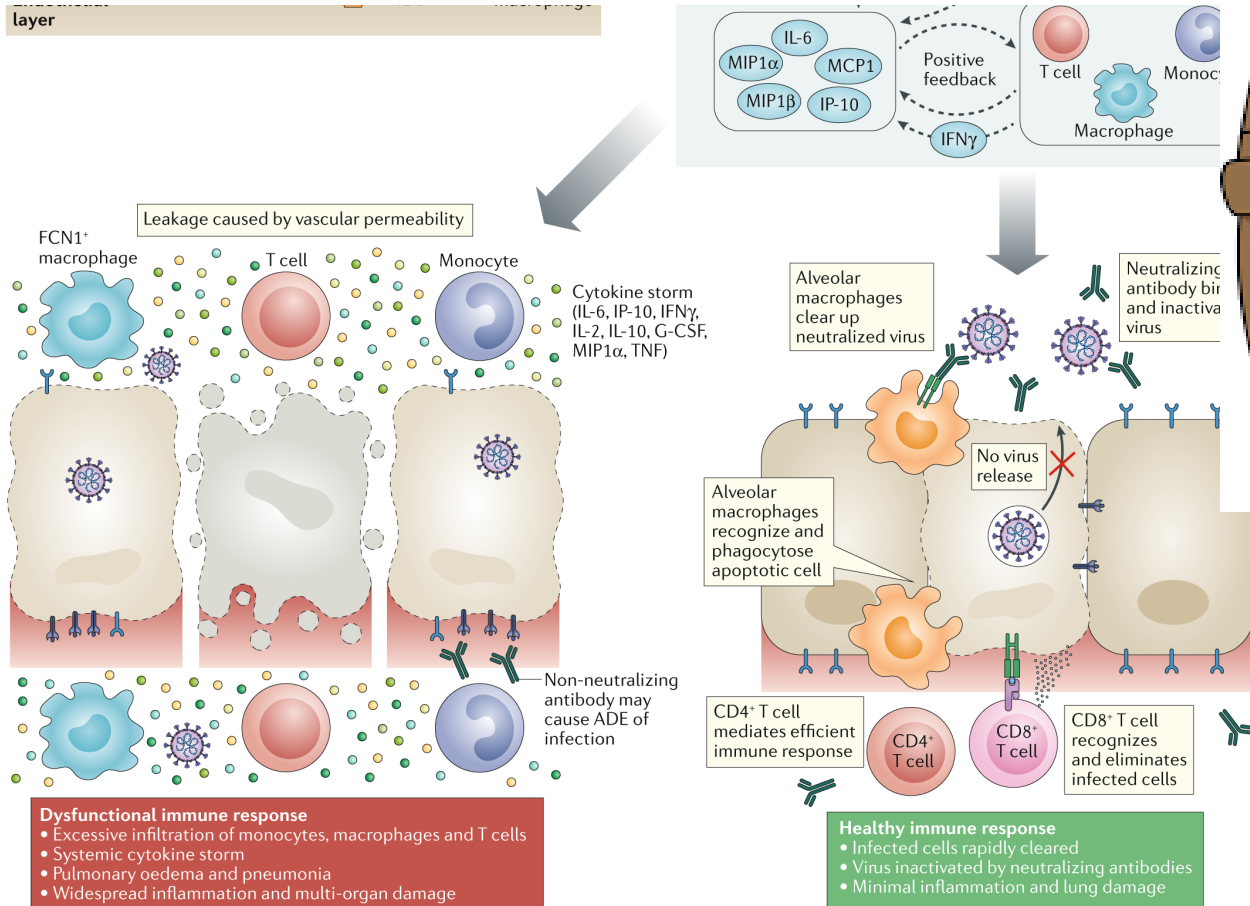


6 Assembly, packaging, and release



Immunologic Effect

layer



Dexamethasone

Steroids

Baricitinib

JAK
Inhibitors

Tocilizumab

Sarilumab

IL-6
Inhibitors

Prescribing for COVID-19 Outpatients

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- Viral Effect
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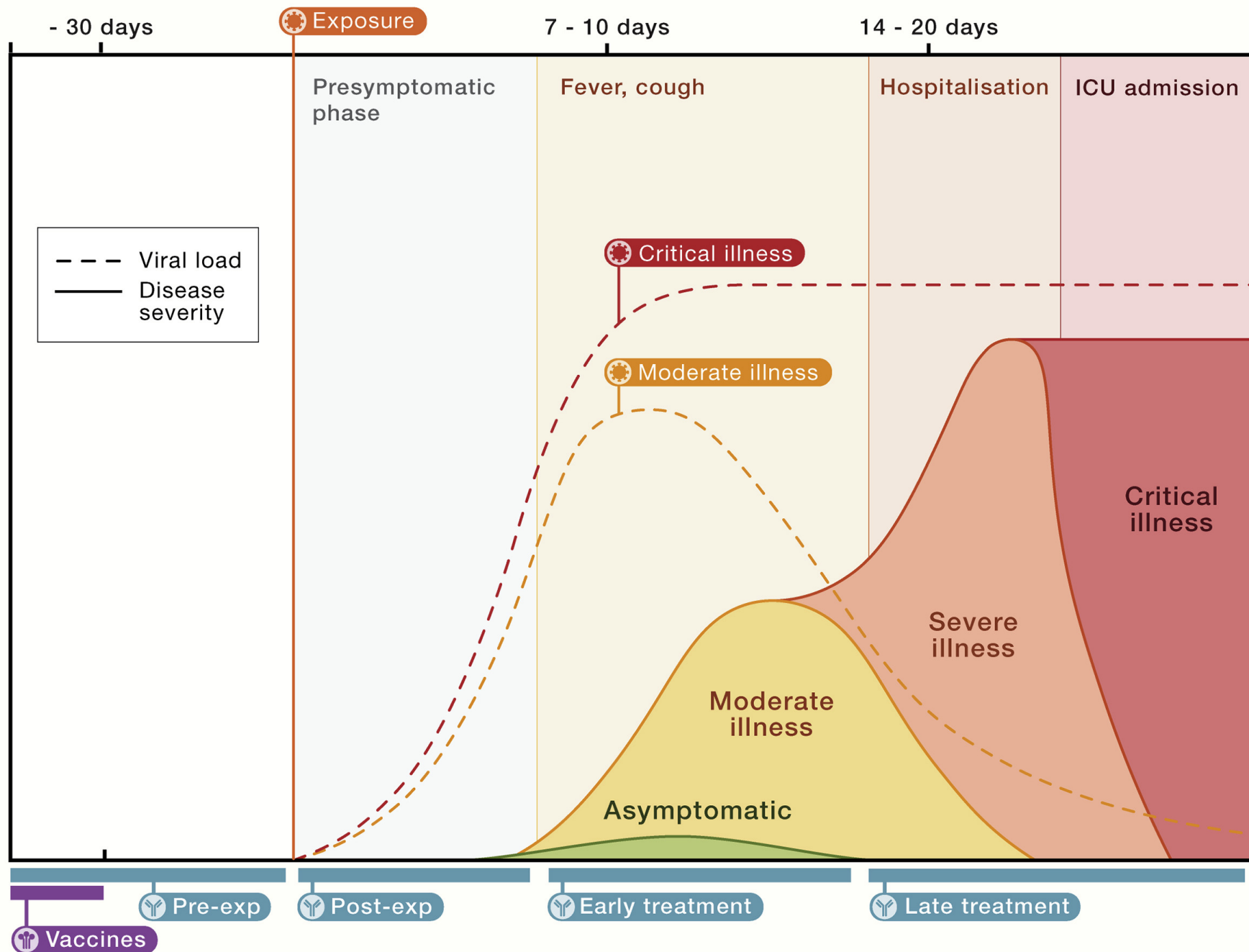


COVID-19 Therapeutics: The Evidence

Sameer Elsayed MD, MSc, FRCPC

London Health Sciences Centre/St. Joseph's
Healthcare London/Western University

March 1, 2022



Vaccines

mRNA-1273 (Moderna)
 BNT162b2 (Pfizer/BioNTech)
 ChAdOx1-S (Astrazeneca)
 Ad26.COV2.S (Johnson&Johnson)
 Sputnik V (GRIEM)

Pre-exposure

AZD8895+AZD1061 (Ph. 3)

Post-exposure

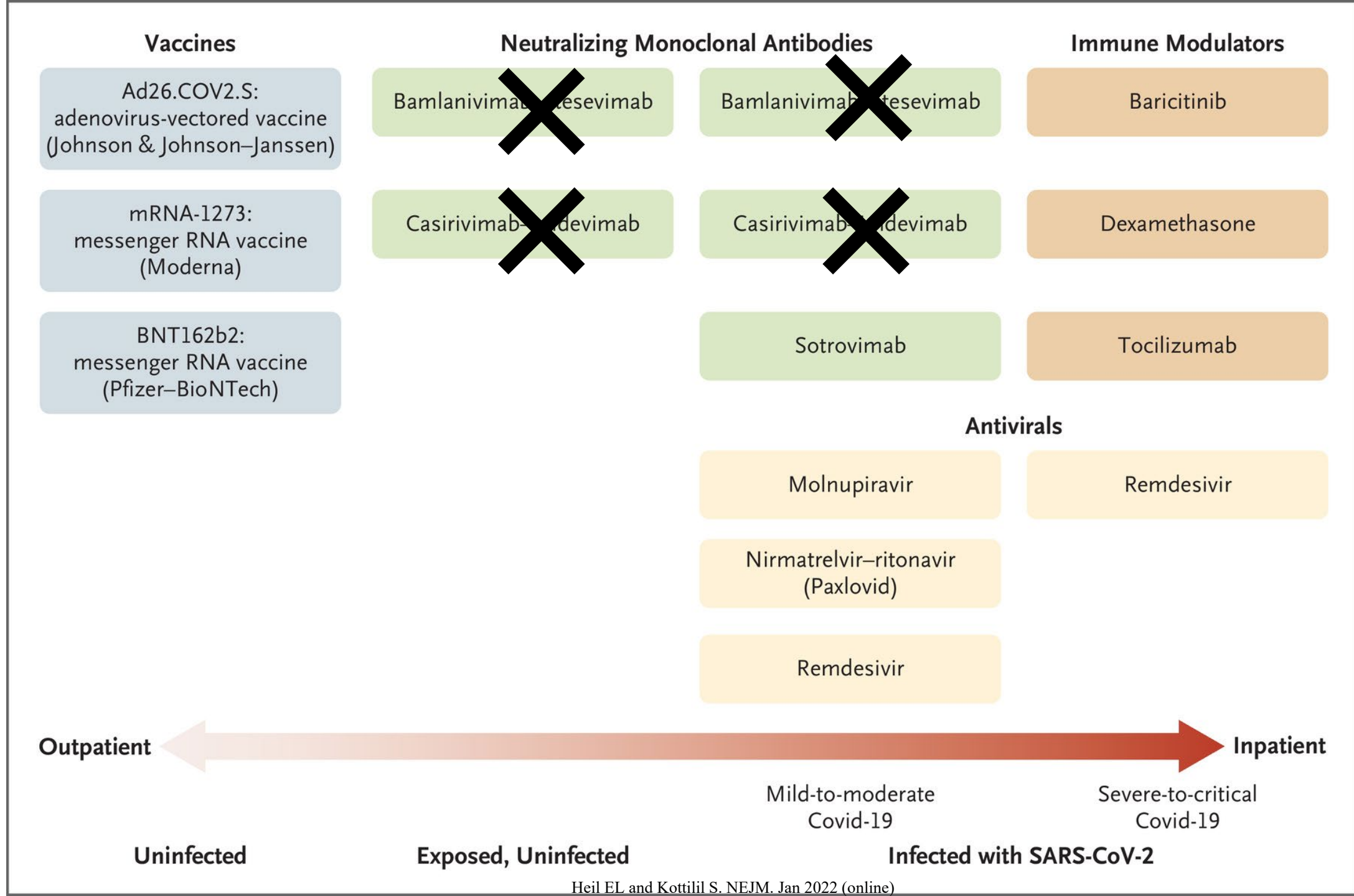
Casirivimab+imdevimab (Ph. 3)
 Etesevimab+bamlanivimab (Ph. 3)
 AZD8895+AZD1061 (Ph. 3)

Early treatment

Bamlanivimab (EUA)
 Etesevimab+bamlanivimab (EUA)
 Casirivimab+imdevimab (EUA)
 Regdanvimab (EUA in South Korea)
 Sotrovimab (EUA)
 AZD8895+AZD1061 (Ph. 3)

Late treatment

Casirivimab+imdevimab (Ph. 3)
 AZD8895+AZD1061 (Ph. 3)



COVID-19 Treatments

Paxlovid (PO)

Sotrovimab (IV)

Remdesivir (IV)

Molnupiravir (PO)

Tocilizumab/Sarilumab (IV)

Baricitinib (PO/NG)

Dexamethasone (PO/IV)

ORIGINAL ARTICLE

February 16, 2022

Oral Nirmatrelvir for High-Risk, Nonhospitalized Adults with Covid-19

Jennifer Hammond, Ph.D., Heidi Leister-Tebbe, B.S.N.,
Annie Gardner, M.P.H., M.S.P.T., Paula Abreu, Ph.D., Weihang Bao, Ph.D.,
Wayne Wisemandle, M.A., MaryLynn Baniecki, Ph.D., Victoria M. Hendrick, B.Sc.,
Bharat Damle, Ph.D., Abraham Simón-Campos, M.D., Rienk Pypstra, M.D.,
and James M. Rusnak, M.D., Ph.D., for the EPIC-HR Investigators*

EPIC-HR

- Industry-sponsored, multicentre RCT
- 202 study locations, 2246 participants
- Oral Paxlovid vs. Placebo in unvaccinated, high-risk symptomatic adult outpatients with COVID-19 (within 5 days of symptom onset)
- Study Period: July 16, 2021 to December 9, 2021
- Primary Outcome: COVID-19 related hospitalization, OR death from any cause (Day 1 –28)

EPIC-HR: Main High-Risk Groups

Smokers

Diabetes

Hypertension

**Cardiovascular
Disease**

COPD

BMI \geq 25

EPIC-HR: Results

Paxlovid (n=1039)

- # of Events: 8
- Hospitalizations: 8 (0.77%)
- Deaths: 0
- Relative Risk of Event = 0.77%

Placebo (n=1046)

- # of Events: 66 (6.31%)
- Hospitalizations: 65 (6.21%)
- Deaths: 12 (1.15%)
- Relative Risk of Event = 6.3%

Relative Risk Reduction: 87.8%
Absolute Risk Reduction: 5.53%
Number Needed to Treat: 18

ORIGINAL ARTICLE

N ENGL J MED 385;21 NEJM.ORG NOVEMBER 18, 2021

Early Treatment for Covid-19 with SARS-CoV-2 Neutralizing Antibody Sotrovimab

Anil Gupta, M.D., Yaneicy Gonzalez-Rojas, M.D., Erick Juarez, M.D., Manuel Crespo Casal, M.D., Jaynier Moya, M.D., Diego R. Falci, M.D., Ph.D., Elias Sarkis, M.D., Joel Solis, M.D., Hanzhe Zheng, Ph.D., Nicola Scott, M.Sc., Andrea L. Cathcart, Ph.D., Christy M. Hebner, Ph.D., Jennifer Sager, Ph.D., Erik Mogalian, Pharm.D., Ph.D., Craig Tipple, M.B., B.S., Ph.D., Amanda Peppercorn, M.D., Elizabeth Alexander, M.D., Phillip S. Pang, M.D., Ph.D., Almena Free, M.D., Cynthia Brinson, M.D., Melissa Aldinger, Pharm.D., and Adrienne E. Shapiro, M.D., Ph.D., for the COMET-ICE Investigators*

COMET-ICE

- Industry-sponsored, multicentre RCT
- 37 trial sites in U.S., Canada, Brazil, and Spain, with 583 participants
- IV Sotrovimab vs. Placebo in unvaccinated, high-risk symptomatic adult outpatients with COVID-19, and within 5 days of symptom onset
- Study Period: August 7, 2020 to March 4, 2021
- Primary Outcome: COVID-19 related hospitalization, OR death from any cause (Day 1 – 29)

COMET-ICE: Main High-Risk Groups

**Age \geq 55
years**

Diabetes

Obesity

Asthma

COMET-ICE: Results

Sotrovimab (n=291)

- # of Events: 3 (1.03%)
- Hospitalizations: 3 (1.03%)
- Deaths: 0
- Relative Risk of Event = 1.03%

Placebo (n=292)

- # of Events: 21 (7.19%)
- Hospitalizations: 21 (7.19%)
- Deaths: 1
- Relative Risk of Event = 7.19%

Relative Risk Reduction: 85.7%
Absolute Risk Reduction: 6.16%
Number Needed to Treat: 16

The NEW ENGLAND JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

JANUARY 27, 2022

VOL. 386 NO. 4

Early Remdesivir to Prevent Progression to Severe Covid-19 in Outpatients

R.L. Gottlieb, C.E. Vaca, R. Paredes, J. Mera, B.J. Webb, G. Perez, G. Oguchi, P. Ryan, B.U. Nielsen, M. Brown, A. Hidalgo, Y. Sachdeva, S. Mittal, O. Osiyemi, J. Skarbinski, K. Juneja, R.H. Hyland, A. Osinusi, S. Chen, G. Camus, M. Abdelghany, S. Davies, N. Behenna-Renton, F. Duff, F.M. Marty,* M.J. Katz, A.A. Ginde, S.M. Brown, J.T. Schiffer, and J.A. Hill, for the GS-US-540-9012 (PINETREE) Investigators†

PINETREE

- Industry-sponsored, multicentre RCT
- 64 trial sites in the U.S., U.K., Spain, and Denmark
- IV Remdesivir (3 days) vs placebo in unvaccinated outpatients (age ≥ 12 years) with COVID-19, ≤ 7 days of symptoms
- Study Period: September 18, 2020 to April 8, 2021
- Primary Outcome: COVID-19 related hospitalization, OR death from any cause (Day 1 –28)

PINETREE: Main High-Risk Groups

Diabetes

Obesity

Hypertension

**Cardiovascular
Disease**

COPD

Other

PINETREE: Results

Remdesivir (n=279)

- # of Events: 2 (0.72%)
- Hospitalizations: 2 (0.72%)
- Deaths: 0
- Relative Risk of Event = 0.72%

Placebo (n=283)

- # of Events: 15 (5.30%)
- Hospitalizations: 15 (5.30%)
- Deaths: 0
- Relative Risk of Event = 5.30%

Relative Risk Reduction: 86.5%
Absolute Risk Reduction: 4.58%
Number Needed to Treat: 22

The NEW ENGLAND JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

FEBRUARY 10, 2022

VOL. 386 NO. 6

Molnupiravir for Oral Treatment of Covid-19 in Nonhospitalized Patients

A. Jayk Bernal, M.M. Gomes da Silva, D.B. Musungaie, E. Kovalchuk, A. Gonzalez, V. Delos Reyes,
A. Martín-Quiros, Y. Caraco, A. Williams-Diaz, M.L. Brown, J. Du, A. Pedley, C. Assaid, J. Strizki, J.A. Grobler,
H.H. Shamsuddin, R. Tipping, H. Wan, A. Paschke, J.R. Butters, M.G. Johnson, and C. De Anda,
for the MOVE-OUT Study Group*

MOVE-OUT

- Industry-sponsored, multicentre RCT with 1433 participants
- 78 trial sites in 15 countries
- Molnupiravir vs. Placebo in unvaccinated, high-risk symptomatic adult outpatients with COVID-19 within 5 days of symptoms and ≥ 1 risk factor
- Study Period: May 6, 2021 to November 4, 2021
- Primary Outcome: COVID-19 related hospitalization, OR death from any cause (Day 1 –29)

MOVE-OUT: Main High-Risk Groups

Age \geq 55 yr

Diabetes

BMI \geq 30

Asthma

MOVe-OUT: Results (mITT)

Molnupiravir (n=709)

- # of Events: 48 (6.77%)
- Hospitalizations: 3 (1.03%)
- Deaths: 1
- Relative Risk of Event = 6.77%

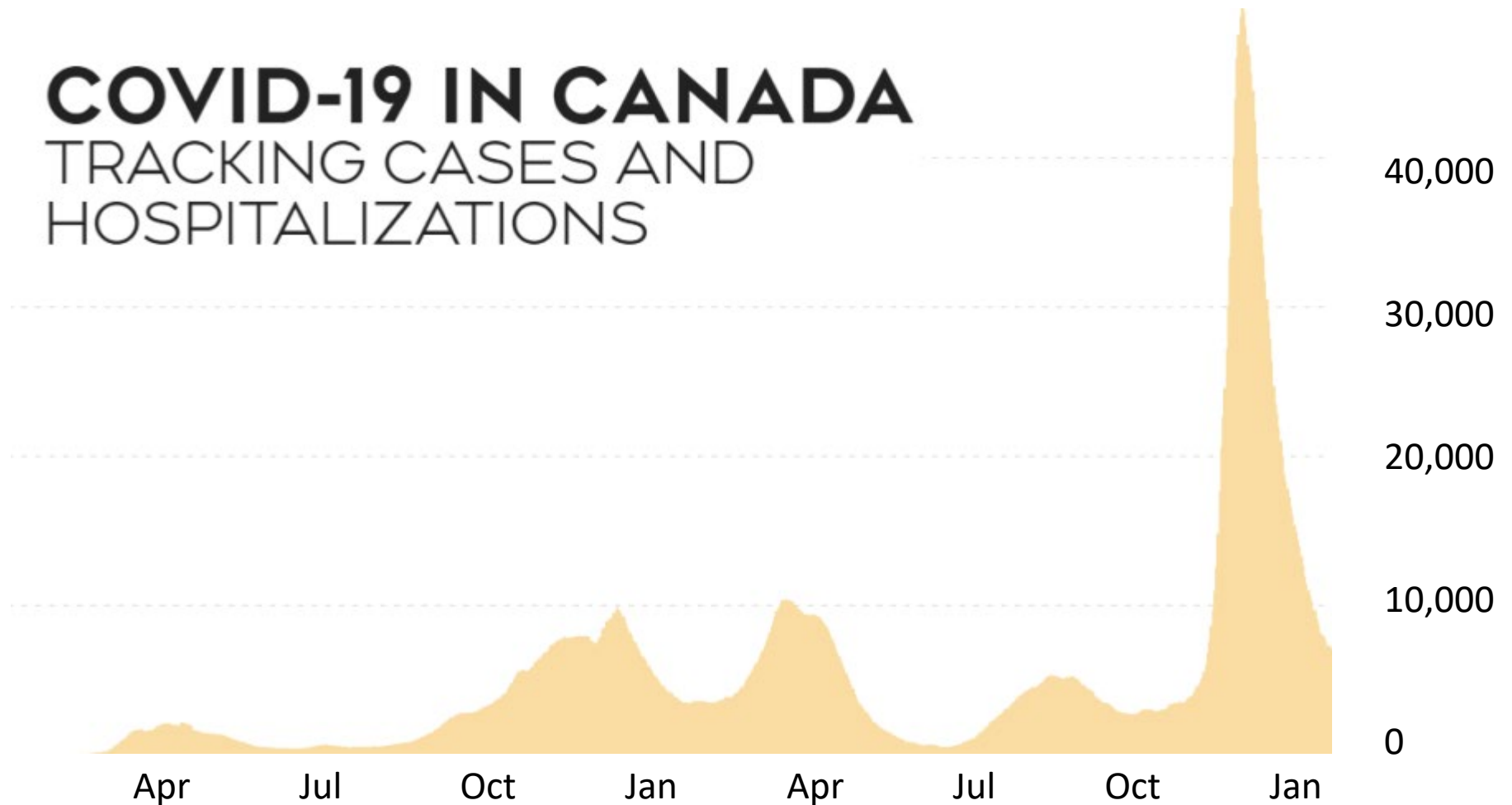
Placebo (n=699)

- # of Events: 68 (9.73%)
- Hospitalizations: 21 (7.19%)
- Deaths: 9
- Relative Risk of Event = 9.73%

Relative Risk Reduction: 30.4%
Absolute Risk Reduction: 2.96%
Number Needed to Treat: 34

SARS-CoV-2 Waves

COVID-19 IN CANADA TRACKING CASES AND HOSPITALIZATIONS



THANK YOU!

Pharmacology

Health Canada Approval Paxlovid®

- For adults with mild to moderate COVID-19 in patients who:
 - have a positive result from a SARS-CoV-2 viral test AND
 - who have a high risk of getting severe COVID-19, including hospitalization or death.
- PAXLOVID IS NOT approved for any of the following:
 - To treat patients who are hospitalized due to severe or critical COVID-19.
 - To prevent COVID-19.
 - To be used for longer than 5 days in a row.
 - For use in children and adolescents less than 18 years of age.

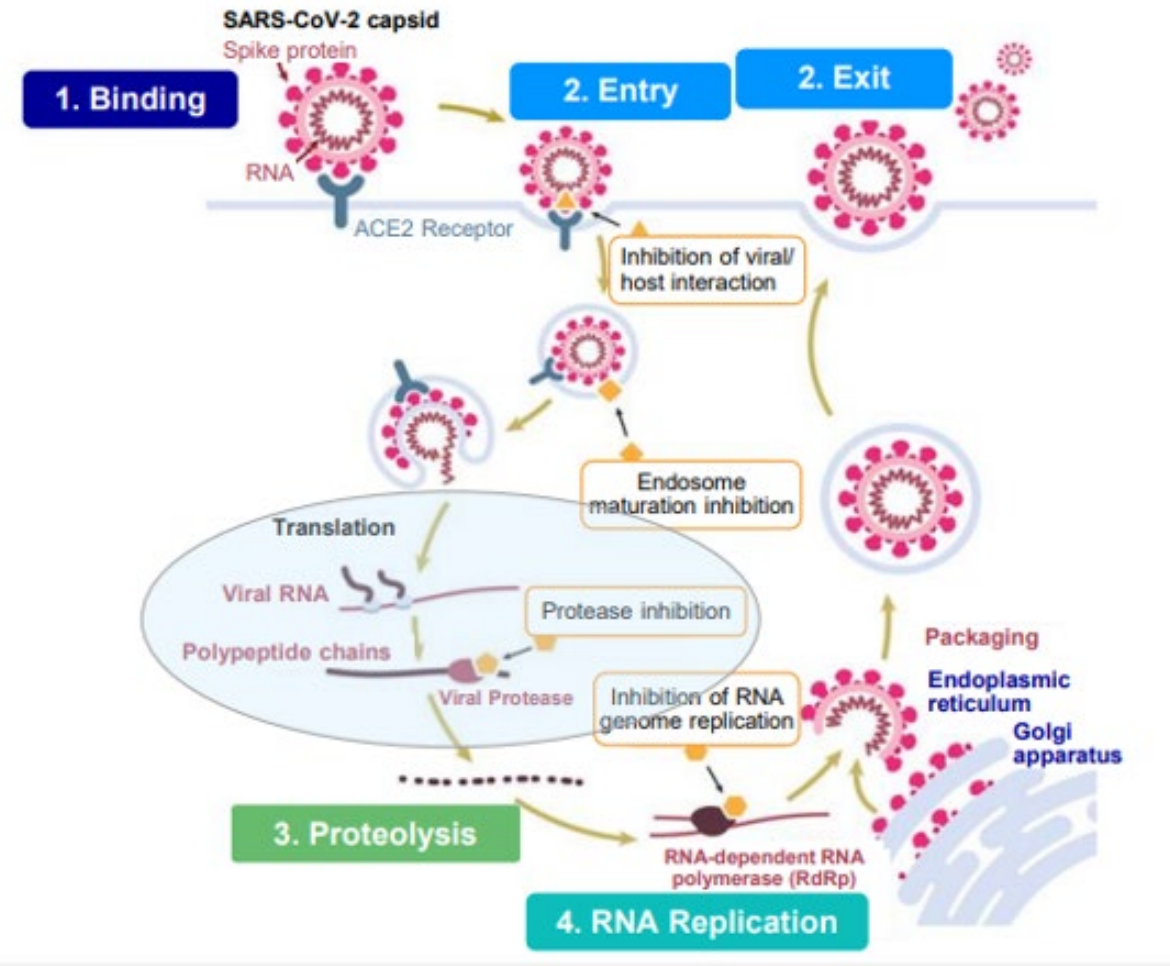
Pharmacology

Nirmatrelvir

- SARS-CoV-2 3CL protease inhibitor which leads to the prevention of viral replication

Ritonavir

- HIV protease inhibitor
- No intrinsic activity against SARS-CoV-2
- “boosting” agent



Administration

- Supplied
 - nirmatrelvir (pink) 150 mg tab
 - ritonavir (white) 100 mg tab
- Administration
 - Initiate within 5 days of symptom onset
 - Swallow whole, do not chew, break or crush
- Adverse Reactions
 - dysgeusia, diarrhea, hypertension, myalgia, vomiting and headache



Dosing

- Standard Dosing
 - assuming eGFR > 60 mL/min
 - Nirmatrelvir 300 mg + Ritonavir 100 mg BID x 5 days
- Renal Impairment
 - eGFR 30-59 mL/min
 - Nirmatrelvir 150 mg + Ritonavir 100 mg BID x 5 days
 - eGFR less than 30 mL/min
 - Not recommended
- Hepatic Impairment
 - Not recommended beyond Child-Pugh Class C

Special Populations

- Pregnancy/Lactation
 - No safety data available
- Paediatrics
 - Canadian labelling authorized ≥ 18 years old, weight ≥ 40 kg
- Geriatrics
 - No specific safety concerns
 - In EPIC-HR, 13% were 65 years of age and older and 3% were 75 years of age and older

Drug interactions

- Nirmatrelvir

- substrate: CYP3A4, P-gp
- inhibitor (potential): CYP3A4, P-gp, OATP1B1
- inducer: does not induce any CYPs

'Victim' of
Drug
Interactions

- Ritonavir

- substrate: CYP3A4, 2D6, P-gp
- inhibitor: CYP3A4 >> 2D6 (lesser extent), P-gp, OATPs, MATE1
- inducer: UGT, CYP3A4, 1A2, 2C9, 2C19, 2B6
- dose and time-dependent inhibition/induction effects

'Perpetrator'
of Drug
Interactions

ON Science Table Drug Interaction Resource

Symbol Interaction



Contraindicated



Contraindicated (current and recent use within past 28 days)



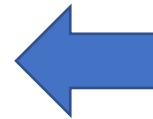
Contraindicated (significant increase in drug concentrations expected)



Significant increase in drug concentrations expected



Drug interaction not likely to be clinically relevant



Nirmatrelvir/Ritonavir (Paxlovid) Drug Interactions:			
This is not an exhaustive list. Consultation with a pharmacist who can obtain a complete medication, recreational, and natural health product history from the patient is recommended prior to prescribing nirmatrelvir/ritonavir.			
Symbol	Severity	Recommendation	Rationale
▲	Contraindicated	Use alternative COVID agent. Do not use nirmatrelvir/ritonavir.	Stopping the drug will not mitigate the interaction (e.g., prolonged half-life, narrow therapeutic index, prolonged enzyme-inducing effects which may decrease effectiveness of nirmatrelvir/ritonavir). Do not coadminister due to risk of serious toxicity.
▲	Contraindicated (use within past 14 days)		
●	Do not coadminister	Hold and restart 2 days after completing nirmatrelvir/ritonavir.	Significant ↑ in drug concentrations expected. Do not coadminister due to risk of serious toxicity.
◆	Caution	Therapy modification required (see Appendix).	Significant ↑ in drug concentrations expected, which may lead to serious toxicity or impaired efficacy. Only coadminister if the interacting drug can be safely held or dose-adjusted and closely monitored (see Appendix). Expert consultation may be useful.
✓	Drug interaction not likely to be clinically relevant	Continue with standard dosing.	Although mentioned in the monograph, clinically relevant interaction is not anticipated (e.g., minimal impact on certain metabolic pathways, wide therapeutic index, and short course of nirmatrelvir/ritonavir).

<ul style="list-style-type: none"> Abemaciclib (Verzenio) Alfuzosin (Xatral) Alprazolam (Xanax) Amiodarone Amtripyline Amlodipine (Norvasc) Apalutamide (Erleada) Apixaban (Eliquis) Aripiprazole (Abilify), oral Atorvastatin (Lipitor) Atovaquone Bosentan (Tracleer) Bosutinib (Bosulfir) Brexiprazole (Rexulti) Budesonide Bupropion Buspirone (Buspar) Carbamazepine (Tegretol) Ceritinib (Zykadia) Cisapride Citalopram Clarithromycin Clozapine (Clozaril) Clozapine (Clozaril) Cobimetinib (Cotellic) Colchicine in renal/hepatic impairment Cyclosporine (Neoral) Dabigatran Dabrafenib (Tafinlar) Dasatinib (Sprycel) Dexamethasone Diazepam (Valium) Digoxin Diltiazem (Tiazac, Cardizem) 	<ul style="list-style-type: none"> Divalproex Dofetilide Dronabinol Dronedaron (Multaq) Edoxaban (Lixiana) Elafox (Onilissa) Encorafenib (Braftovi) Enzalutamide Ergot alkaloids (e.g., dihydroergotamine, ergonovine) Escitalopram Ethinyl estradiol Everolimus (Certoan) Felodipine Fentanyl (Duragesic) Flecainide Fluoxetine Flurazepam Fluvoxamine Fostamatinib (Tavalisse) Fusidic acid, topical Glecaprevir/Pibrentasvir (Maviret) Hydrocodone Ibuprofen (Motrin) Imipramine Itraconazole Ketocanazole Lamotrigine Lomitapide (Lupatid) Lorlatinib (Lorbrena) Lovastatin Lurasidone (Latuda) Maprotiline Maraviroc Meperidine (Demerol) Methamphetamine 	<ul style="list-style-type: none"> Metoprolol Midazolam, oral Milofen (Lysodren) Modafinil Neratinib (Nerlynx) Nifedipine Nilotinib (Tasigna) Nitrazepam (Mogadon) Nortriptyline Oxcarbazepine Oxycodone (Percocet, OxyNEO) Paroxetine Phenobarbital Phenytoin (Dilantin) Pimozide Primidone Propafenone Quetiapine (Seroquel) Quinine Raltegravir Ranolazine (Corzyne) Rifabutin Rifampin Rifapentine Risperidone (Risperdal, oral) Risperidone, long-acting injection (Risperdal Consta) Rivaroxaban (Xarelto) Rosuvastatin (Crestor) Salmeterol (Serevent, Advair) Sertraline Sildenafil for ED (Viagra) Sildenafil for PAH (Revatio) 	<ul style="list-style-type: none"> Sildenafil (Rapaflo) Simvastatin Sirolimus (Rapamune) Sonidegib (Odomzo) St. John's wort (Hypericum perforatum) Tacrolimus (Prograf, Advagraf, Envarsus) Tadalafil for ED (Cialis) Tadalafil for PAH (Adcirca) Tamsulosin (Flomax) Tapotinin (Tepmetko) Theophylline Ticagrelor (Brilinta) Timolol Tramadol Triazolam (Halcion) Trimipramine Vardenafil (Levitra) for ED Vardenafil (Levitra) for PAH Venetoclax (Venclexta) Venlafaxine Verapamil Vinblastine Vincristine Voriconazole Warfarin Ziprasidone (Zeldox) Zolpidem (Sublinox, Ambien) Zopiclone (Imovane)
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Click here for the Liverpool COVID-19 Interaction Checker
Or visit: <https://www.liverpool-liv.ac.uk/covid-19-interaction-checker/>

Appendix:

Drug	Recommendation	Comments
<ul style="list-style-type: none"> Clopidogrel (Plavix) 	<p>Acute coronary syndrome (ACS)/percutaneous coronary intervention (PCI):</p> <ul style="list-style-type: none"> • 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/transient ischemic stroke) and resume clopidogrel 2 days after completing nirmatrelvir/ritonavir. 	<p>Coadministration will decrease the antiplatelet effect of clopidogrel.</p> <p>Clopidogrel active metabolite AUC decreased by 51 to 69% when administered with ritonavir.</p>
<ul style="list-style-type: none"> Clozapate 	<p>Hold and restart 2 days after completing nirmatrelvir/ritonavir.</p> <p>If an anxiolytic is needed, use lorazepam, oxazepam, or temazepam at usual doses.</p>	<p>Due to prolonged benzodiazepine half-life, coadministration is not recommended.</p>
<ul style="list-style-type: none"> Cobimetinib (Cotellic) 	<p>Hold cobimetinib and start nirmatrelvir/ritonavir 24 hours after the last cobimetinib dose. Restart cobimetinib 2 days after completing nirmatrelvir/ritonavir.</p>	<p>Decisions to hold or dose-adjust should be made in conjunction with the patient's oncologist.</p> <p>Cobimetinib AUC increased 6.7-fold when administered with ketoconazole.</p>
<ul style="list-style-type: none"> Colchicine in renal/hepatic impairment 	<p>Coadministration is contraindicated in patients with renal and/or hepatic impairment.</p> <p>In patients with normal renal/hepatic function, colchicine may be administered at a lowered dose if practical:</p> <ul style="list-style-type: none"> • Treatment of gout flares: 0.6 mg x 1 dose, then 0.3 mg (½ tablet) 1 hour later. Repeat dose no earlier than 3 days. • Prevention of gout flares: <ul style="list-style-type: none"> a) If originally on 0.6 mg twice daily: decrease to 0.3 mg once daily; b) If originally on 0.3 mg twice daily, decrease to 0.3 mg once every 2 days. • Treatment of Familial Mediterranean fever: maximum 0.6 mg (or 0.3 mg twice daily). <p>In all cases, resume usual colchicine dose 2 days after completing nirmatrelvir/ritonavir.</p>	<p>Drug interaction could lead to potentially life-threatening/fatal adverse events.</p>
<ul style="list-style-type: none"> Cyclosporine (Neoral) 	<p>Reduce cyclosporine total daily dose by 80% and start nirmatrelvir/ritonavir 12 hours after the last cyclosporine dose. Continue at reduced dose throughout nirmatrelvir/ritonavir therapy.</p> <p>Resuming transplant immunotherapy after the last dose of nirmatrelvir/ritonavir should be guided by therapeutic drug monitoring and in conjunction with the patient's transplant provider.</p>	<p>Check cyclosporine concentrations 1 to 2 days after the last dose of nirmatrelvir/ritonavir.</p> <ul style="list-style-type: none"> • If subtherapeutic: increase cyclosporine dose. Consider resumption of twice daily dosing. • If therapeutic: continue with current cyclosporine dose. • If supratherapeutic: reduce or hold current cyclosporine dose. <p>In all cases, repeat cyclosporine level in 2 to 4 days and continue to dose-adjust accordingly.</p>

Contraindicated: Do not use Paxlovid®

- Anticonvulsants
 - Carbamazepine
 - Phenobarbital
 - Phenytoin
 - Pimozide
 - Primidone
- Anti-arrhythmics
 - Amiodarone
 - Dronedarone
 - Flecainide
 - Propafenone
 - Quinidine
- Anti-anginal
 - Ranolazine
- PDE5 Inhibitors for Pulmonary HTN
 - Sildenafil
 - Tadalafil
 - Vardenafil
- Endothelin Receptor antagonist
 - Bosentan
- Herbals
 - St John's Wort
- Psychotropics
 - Clozapine
 - Lurasidone
 - Pimozide
- Cancer Agents
 - Apalutamide (Erleada)
 - Enzalutamide
 - Neratinib (Nerlynx)
 - Venetoclax (Venclexta)
- Anti-infectives for TB
 - Rifampin
 - Rifapentin
- Calcineurin inhibitors
 - Cyclosporine, Tacrolimus
- mTOR kinase inhibitors
 - Sirolimus, Everolimus

Contraindicated: Do not use Paxlovid® UNLESS drug can be safely held/replaced

- Alpha blocker
 - Alfluzozin
- Gastropromkinetic
 - Cisapride
- Anti-gout
 - Colchicine
- Ergot derivatives
 - Dihydroergotamine
 - Ergotamine
 - Methylergonovine
- Lipid Lowering Drugs
 - Lomitapide
 - Lovastatin
 - Simvastatin
- Benzodiazepines
 - Midazolam
 - Triazolam
- Anticoagulants
 - Rivaroxaban
 - Ticagrelor

Paxlovid® Summary

- Pharmacology: SARS-Cov-2 protease inhibitor + ‘booster’
- Indication: Mild patients, within 5 days of symptom onset
- Dosing reduction for moderate renal impairment
- Avoid in severe renal or hepatic impairment
- Obtain a ‘Best Possible Medication History’ (include OTC meds, herbals)
 - Screen for the ‘high risk contraindicated’ drugs

Molnupiravir Comparison

	Nirmatrelvir/Ritonavir	Molnupiravir
Mechanism	Protease inhibitor + 'booster'	Nucleoside Analogue
Indication	Adults, Mild-moderate COVID-19, wt > 40kg	Adults, Mild-moderate COVID-19, no wt
When to start	Within 5 days of symptom onset	Within 5 days of symptom onset
Dose	300mg/100 mg every 12 hour x 5 days (3 tabs per dose)	800 mg every 12 hours x 5 days (4 tabs per dose)
Renal Dose	Adjust eGFR 30-59mL/min Avoid eGFR <30ml/min	N/A
Hepatic	Avoid Child-Pugh Class C	N/A
Warnings	Beware drug interactions Hepatotoxicity HIV-1 drug resistance in patients with HIV-1 infection	Embryo-fetal toxicity Bone and cartilage toxicity
Adverse Reactions	Dysguesia, diarrhea, hypertension, myalgia	Diarrhea, nausea, dizziness
Pregnancy	No human data	Not recommended
Clinical Data	EPIC-HR	MOVE-OUT

Molnupiravir FDA EUA. <https://www.fda.gov/media/155054/download>

Bernal AJ. et al. N Engl J Med 2022; 386:509-520. February 10, 2022 (e-pub Dec 2021), DOI: 10.1056/NEJMoa2116044

Who should receive COVID
specific treatment?

Mildly Ill Patients

Patients who do not require new or additional supplemental oxygen from their baseline status

This guidance applies to mildly ill patients in any setting, including the community, hospital (including nosocomial cases), and congregate care settings.

It is recommended that eligibility for outpatient therapies include patients who test positive for SARS-CoV-2 on either PCR or a healthcare-professional administered RAT or ID now.

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	<ul style="list-style-type: none">• 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, antineoplastic, 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.

STEP 2 ► Based on the risk level, refer to the corresponding recommendation statements below.

RISK LEVEL	RECOMMENDATIONS
HIGHER RISK OF SEVERE DISEASE <i>Individuals who have a ≥5% risk of hospitalization or are immunocompromised</i>	<ul style="list-style-type: none">► It is recommended that higher risk patients receive one of nirmatrelvir/ritonavir (Paxlovid), sotrovimab, or remdesivir. The choice of drug depends on availability, contraindications, and ease of administration. These individuals should have a reasonable expectation for 1-year survival prior to SARS-CoV-2 infection.● Nirmatrelvir/ritonavir (Paxlovid) at a dose of 300 mg nirmatrelvir (two 150 mg tablets) with 100 mg ritonavir (one 100 mg tablet), with all three tablets taken together orally twice daily for 5 days, is recommended for these patients if they present within 5 days of symptom onset.<ul style="list-style-type: none">• In patients with moderate renal impairment (eGFR ≥30 to <60 mL/min), the dose should be reduced to 150 mg nirmatrelvir (one 150 mg tablet) and 100 mg ritonavir (one 100 mg tablet) taken together twice daily for 5 days. Paxlovid is not recommended in patients with severe renal impairment (eGFR <30 mL/min).• Specialized pharmacist consultation is important to mitigate any significant drug-drug interactions with other drugs.• Paxlovid should be preferentially deployed in regions and to populations where administration is a barrier to intravenous medication.● Sotrovimab 500 mg IV x 1 dose is recommended for these patients if they present within 7 days of symptom onset.<ul style="list-style-type: none">• Previous SARS-CoV-2 infection and vaccination status do not need to be considered. Serologic testing is not recommended.● Remdesivir 200 mg IV on day 1, then 100 mg IV daily for 2 days is recommended for these patients if they present within 7 days of symptom onset.► If the above drugs are unavailable or contraindicated:<ul style="list-style-type: none">▲ Fluvoxamine may be considered for patients with mild COVID-19 illness presenting within 7 days of symptom onset. The recommended starting dose is 50 mg PO daily, titrated up to 100 mg PO twice daily for a total of 15 days. Pharmacist consultation and outpatient provider follow-up is important to avoid any significant adverse drug interactions with fluvoxamine. This recommendation balances the very low certainty evidence of benefit for preventing hospitalization with the need for management options for mild illness with a reasonable safety profile during a surge in COVID-19 cases due to the Omicron variant.▲ Budesonide 800 mcg inhaled twice daily for 14 days may be considered for these patients. This recommendation is based on very low certainty evidence of reduction in duration of symptoms, and the need for outpatient treatment options with a reasonable safety profile during an anticipated spike in COVID-19 cases due to the Omicron variant. Budesonide may have a role as an additional therapy in patients already on other therapies who have respiratory symptoms.
STANDARD RISK <i>Individuals with <5% risk of hospitalization</i>	<ul style="list-style-type: none">● Reassurance and information for self-monitoring of symptoms (including self-monitoring of oxygen saturation) are recommended.▲ Fluvoxamine 50 mg PO daily titrated up to 100 mg PO twice daily for a total of 15 days may be considered for these patients if they present within 7 days of symptom onset. See fluvoxamine recommendation statement for higher risk mildly ill patients.▲ Budesonide 800 mcg inhaled twice daily for 14 days may be considered for these patients. See budesonide recommendation statement for higher risk mildly ill patients.■ The following therapies are not recommended for these patients: sotrovimab, nirmatrelvir/ritonavir (Paxlovid), and remdesivir.

◆ There is currently insufficient evidence to make a recommendation around aspirin or anticoagulation for mildly ill patients.

■ The following therapies are not recommended for mildly ill patients: dexamethasone, tocilizumab, sarilumab, and baricitinib.

Ontario Science Table. Updated.
Feb.23, 2022

Question 1:

- Is my patient at high risk of ending up in hospital?
 - High = >5% Risk
 - **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.

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	<ul style="list-style-type: none">• 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	

Significant Immunodeficiency

- **Malignancy** - with receipt of treatment for solid tumors and hematologic malignancies (including individuals with lymphoid malignancies who are being monitored without active treatment),
- **Solid-organ transplant** and taking immunosuppressive therapy,
- 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.

STEP 2 ► Based on the risk level, refer to the corresponding recommendation statements below.

RISK LEVEL	RECOMMENDATIONS
<div>HIGHER RISK OF SEVERE DISEASE</div> <div>Individuals who have a ≥5% risk of hospitalization or are immunocompromised</div> <div>5 Days</div> <div>7 Days</div>	<p>► <i>It is recommended that higher risk patients receive one of nirmatrelvir/ritonavir (Paxlovid), sotrovimab, or remdesivir. The choice of drug depends on availability, contraindications, and ease of administration. These individuals should have a reasonable expectation for 1-year survival prior to SARS-CoV-2 infection.</i></p> <ul style="list-style-type: none">● Nirmatrelvir/ritonavir (Paxlovid) at a dose of 300 mg nirmatrelvir (two 150 mg tablets) with 100 mg ritonavir (one 100 mg tablet), with all three tablets taken together orally twice daily for 5 days, is recommended for these patients if they present within 5 days of symptom onset.<ul style="list-style-type: none">• In patients with moderate renal impairment (eGFR ≥30 to <60 mL/min), the dose should be reduced to 150 mg nirmatrelvir (one 150 mg tablet) and 100 mg ritonavir (one 100 mg tablet) taken together twice daily for 5 days. Paxlovid is not recommended in patients with severe renal impairment (eGFR <30 mL/min).• Specialized pharmacist consultation is important to mitigate any significant drug-drug interactions with other drugs.• Paxlovid should be preferentially deployed in regions and to populations where administration is a barrier to intravenous medication.● Sotrovimab 500 mg IV x 1 dose is recommended for these patients if they present within 7 days of symptom onset.<ul style="list-style-type: none">• Previous SARS-CoV-2 infection and vaccination status do not need to be considered. Serologic testing is not recommended.● Remdesivir 200 mg IV on day 1, then 100 mg IV daily for 2 days is recommended for these patients if they present within 7 days of symptom onset. <p>► <i>If the above drugs are unavailable or contraindicated:</i></p> <ul style="list-style-type: none">▲ Fluvoxamine may be considered for patients with mild COVID-19 illness presenting within 7 days of symptom onset. The recommended starting dose is 50 mg PO daily, titrated up to 100 mg PO twice daily for a total of 15 days. Pharmacist consultation and outpatient provider follow-up is important to avoid any significant adverse drug interactions with fluvoxamine. This recommendation balances the very low certainty evidence of benefit for preventing hospitalization with the need for management options for mild illness with a reasonable safety profile during a surge in COVID-19 cases due to the Omicron variant.▲ Budesonide 800 mcg inhaled twice daily for 14 days may be considered for these patients. This recommendation is based on very low certainty evidence of reduction in duration of symptoms, and the need for outpatient treatment options with a reasonable safety profile during an anticipated spike in COVID-19 cases due to the Omicron variant. Budesonide may have a role as an additional therapy in patients already on other therapies who have respiratory symptoms.
<div>STANDARD RISK</div> <div>Individuals with <5% risk of hospitalization</div>	<ul style="list-style-type: none">● Reassurance and information for self-monitoring of symptoms (including self-monitoring of oxygen saturation) are recommended.▲ Fluvoxamine 50 mg PO daily titrated up to 100 mg PO twice daily for a total of 15 days may be considered for these patients if they present within 7 days of symptom onset. See fluvoxamine recommendation statement for higher risk mildly ill patients.▲ Budesonide 800 mcg inhaled twice daily for 14 days may be considered for these patients. See budesonide recommendation statement for higher risk mildly ill patients.■ The following therapies are not recommended for these patients: sotrovimab, nirmatrelvir/ritonavir (Paxlovid), and remdesivir.

In Summary

- High Risk of Hospitalization (Member of a priority community, Age >70 unvaccinated, Immunodeficiency)
 - Within 5 days and High Risk with NO major DI concerns → Nirmatrelvir/r
 - Within 7 days and High Risk, Does not meet Criteria for Nirmatrelvir/r
 - → Sotrovimab
 - Until Mar. 31, 2022 → LUC3 (Via LHSC 4-OPD)
 - If Transplant Patient → Transplant ID (Via LHSC 4-OPD)

Considerations When Prescribing COVID-19 Therapeutics

Need	Nirmatrelvir	Sotrovimab	Remdesivir	Molnupiravir
Efficacy	✓✓✓	✓✓✓	✓✓✓	✓
Ease of delivery	✓✓✓	X	XXX	✓✓✓
Drug Interactions	XXX	✓✓	✓✓	✓✓
Safety during pregnancy	✓	✓	✓✓	XXX
Authorized in children (>12)	✓✓	✓✓	✓✓✓*	XX
Supply/Access				

*Remdesivir approved for children >age 12 years and >40 kg; authorized for children under age of 12 years (3.5 to 40 kg)

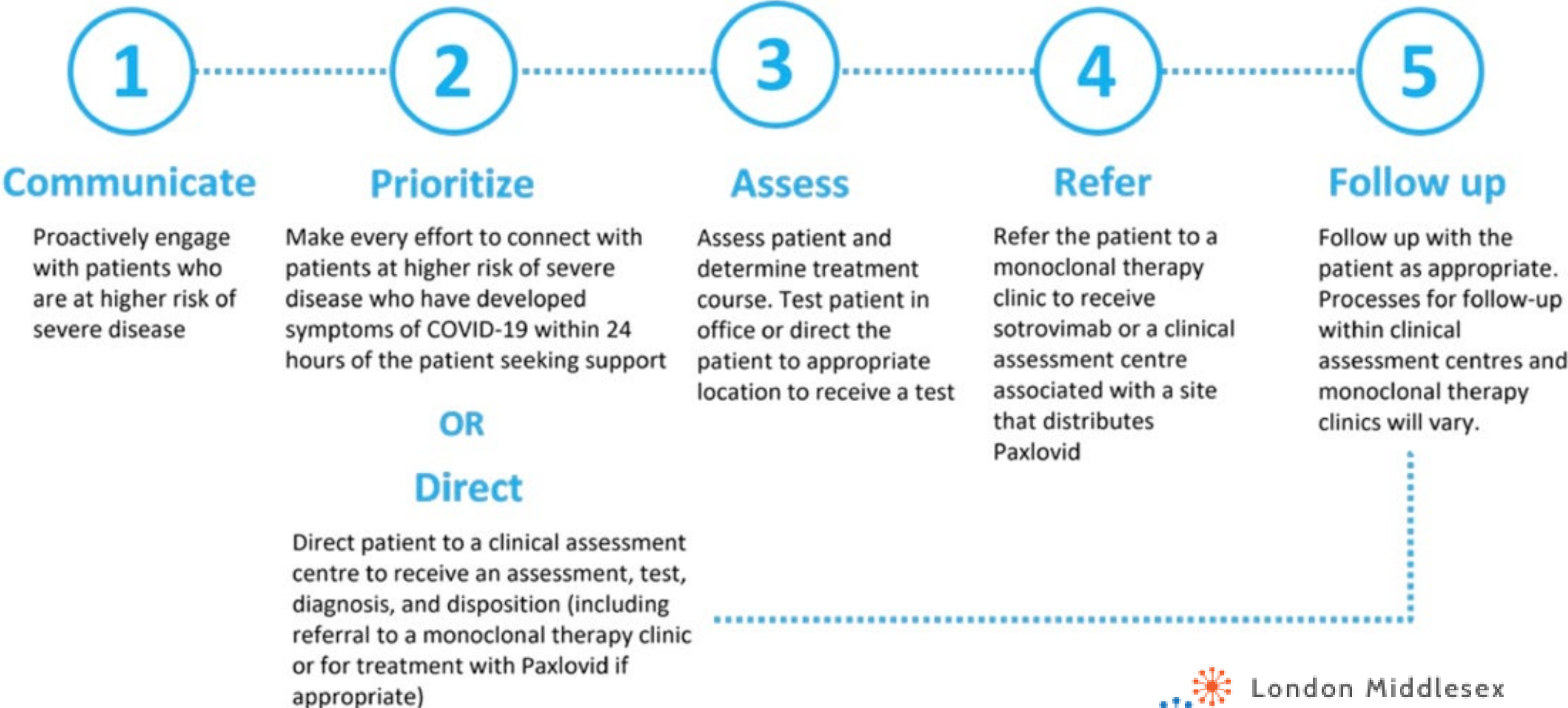
How to get COVID-19 Antiviral Therapy for your Patients

Dr. Gordon Schacter
London Middlesex Pandemic Clinical Lead

March 1, 2022



Pathway for Primary Care Providers – Ontario Health



Step 1: Communicate

- Proactively engage with patients who are considered at higher risk of severe disease.
- Consider engaging with patients:
 - During appointments (both you and your office staff)
 - Patient email blast
 - Via targeted email or telephone (after identifying patients at higher risk for severe disease via EMR search)
 - By updating the practice's website or online booking portal
 - By office Social Media accounts
 - Educational Handouts
- **Tool: I think I have COVID. When should I call my doctor?**
(https://dfcm.utoronto.ca/sites/default/files/assets/files/Q2_When_to_Call_FINAL.pdf)
- This resource from the Department of Community and Family Medicine at the University of Toronto and the Ontario College of Family Physicians provides plain-language instructions on when patients should call their primary care provider, including specific instructions for patients at higher risk.
- Additional resources to help the public make sense of the latest guidance around COVID/Omicron are available at www.ConfusedAboutCovid.ca.



Step 2: Prioritize

- Awareness of the prioritization matrix
 - You and your office staff
- Timely access to care vital (≤ 24 hours)
 - **Tool: Script to support staff in identifying patients who may be eligible for outpatient treatment**
 - A script to support staff in identifying patients who may be eligible for outpatient treatment is available at the link below. Patients flagged as potentially eligible should be seen by their Family Physician/NP or other PCP within 24 hours or directed to a COVID-19 clinical assessment centre.
 - <https://quorum.hqontario.ca/Portals/0/Project%20Resources/Script%20for%20primary%20care%20practice%20staff%20-%202022-01-31.pdf>



Step 3: Assess

- Virtual or In Person Assessment (within 24 hours)
- Severe symptoms? → Emergency Department
- Patient eligibility and contraindications
 - Renal and Hepatic Status assessment
- Positive COVID-19 Test
- The preferred order of COVID-19 testing options to ensure test results are available as quickly as possible is as follows:
 - ID NOW or other rapid molecular test administered by a health care professional
 - A rapid antigen test **administered by a health care professional**, with concurrent lab-based PCR if the rapid antigen test is negative *
 - A lab-based PCR test

* Rapid Antigen Tests can be ordered for free for your office by going to the Ontario Health West / HMMS order site. <https://hmmscovid19.ca>

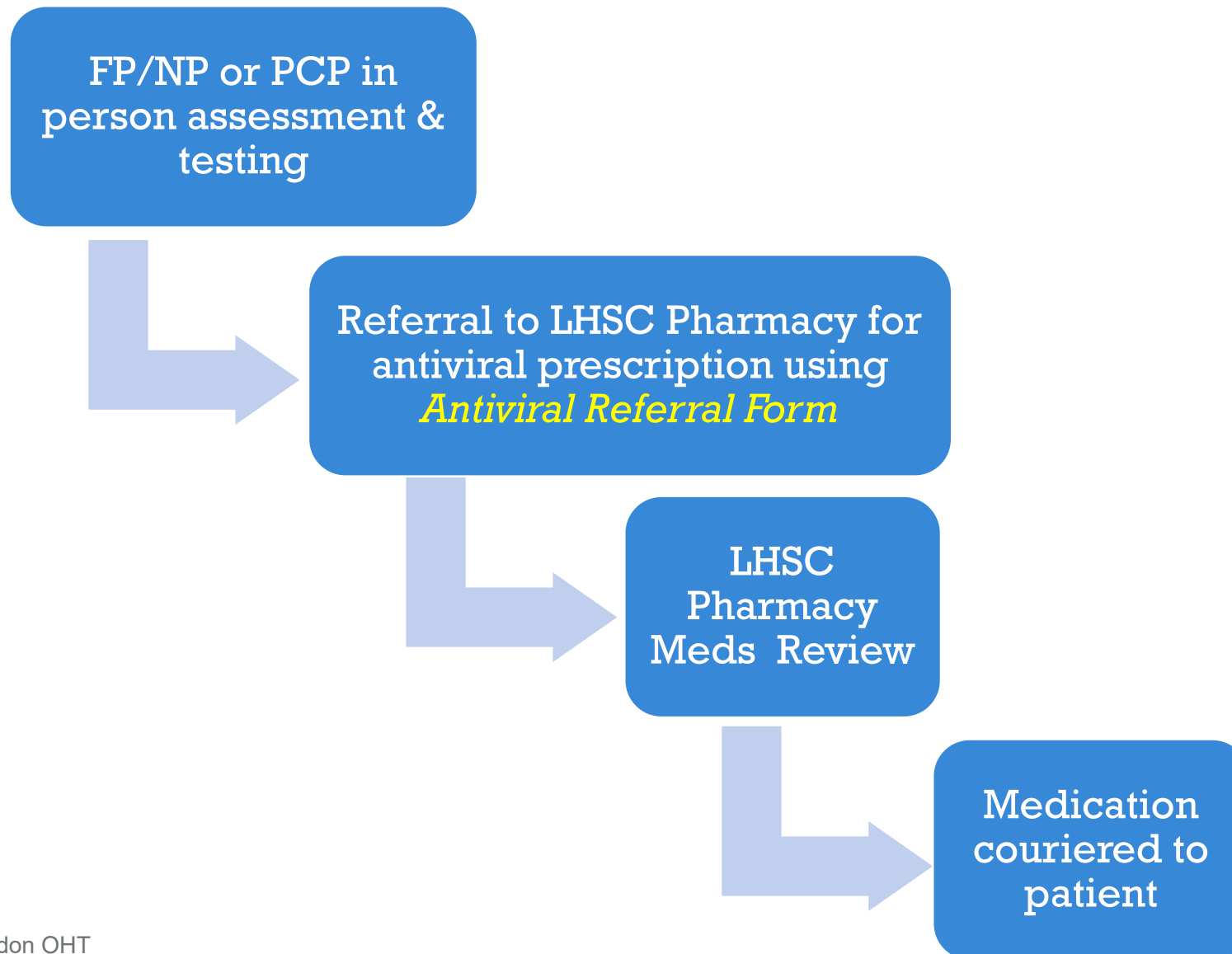


Step 4: Refer

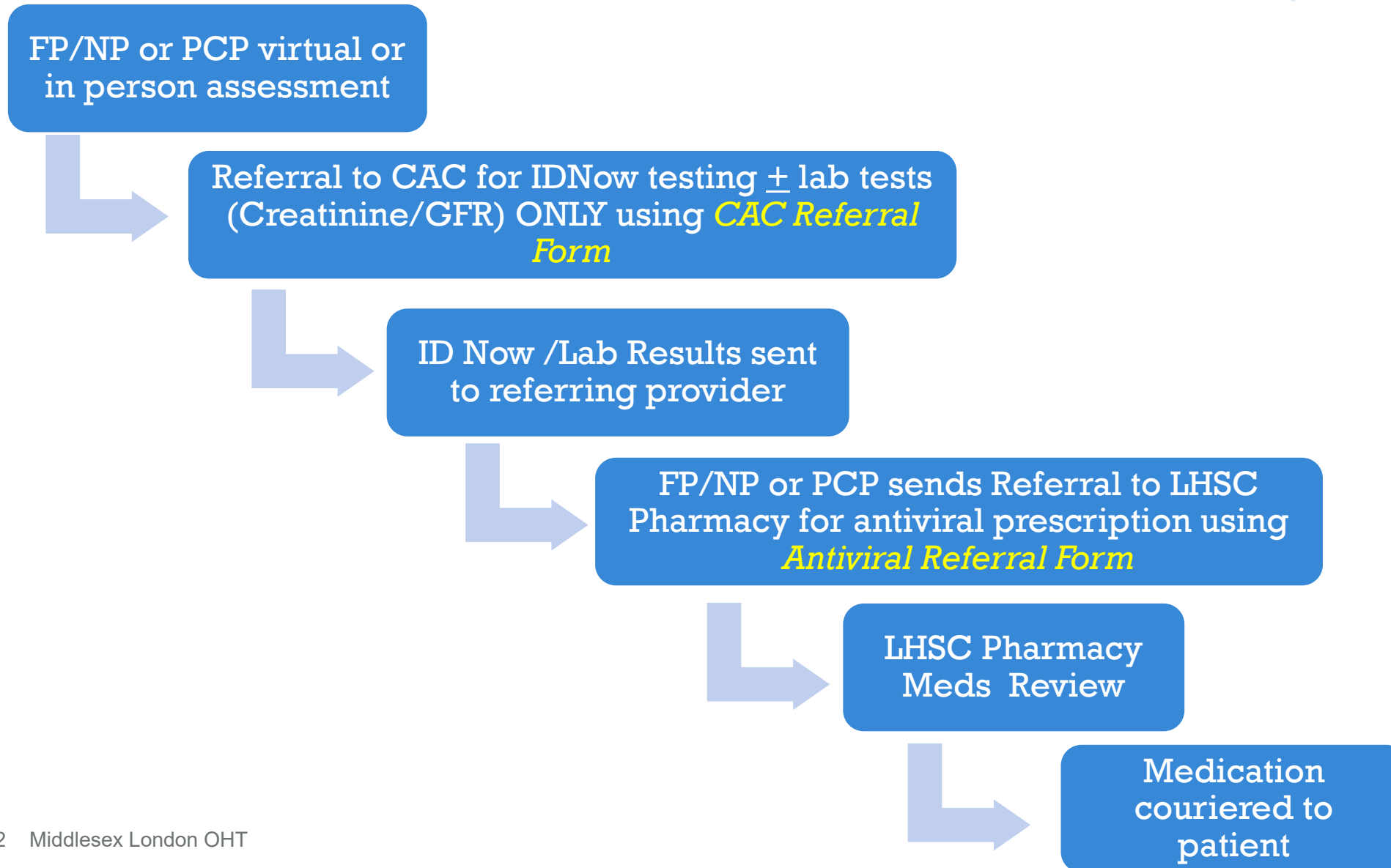
- 3 Clinical Pathways for referral



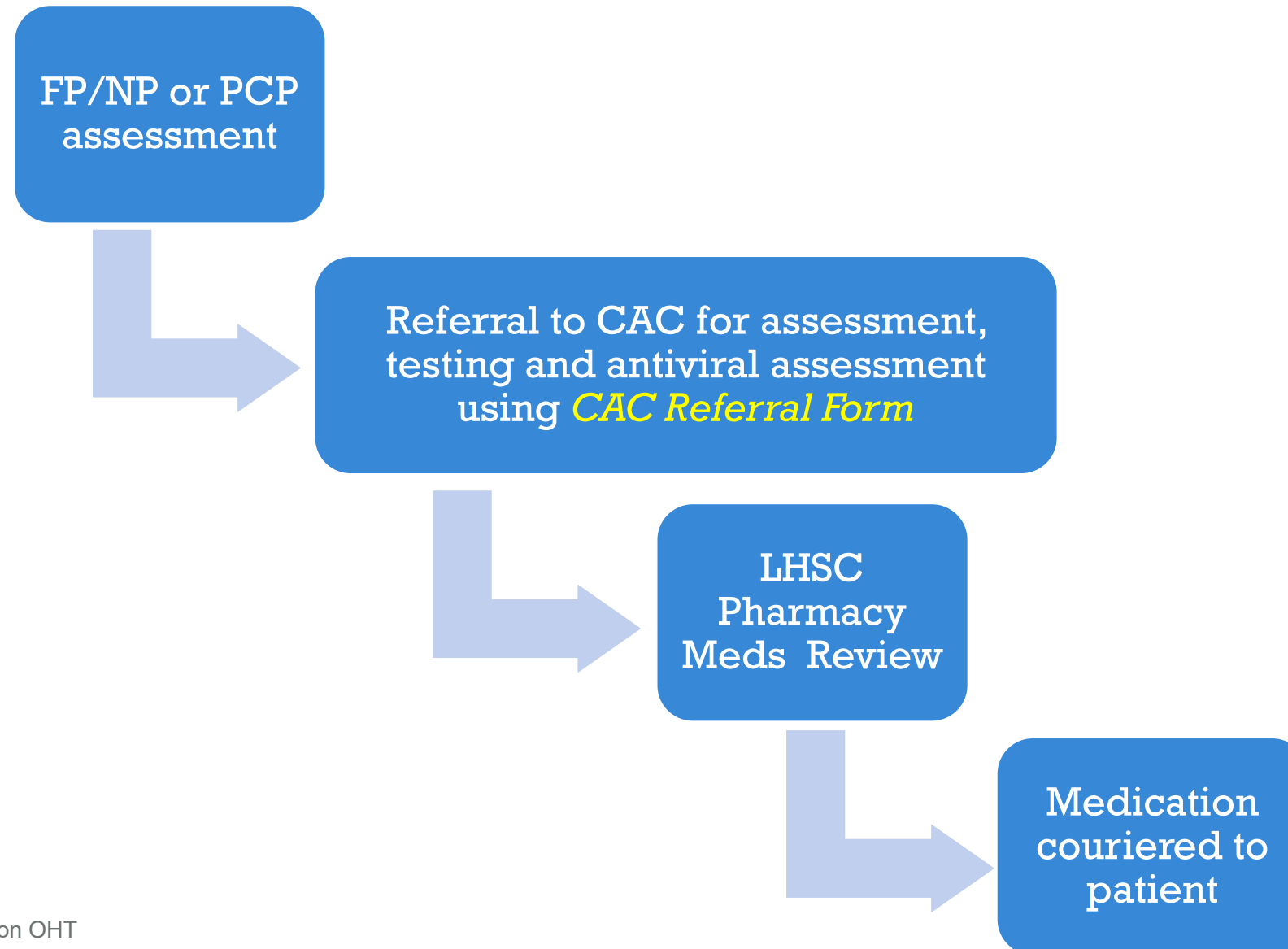
Clinical Pathway #1:



Clinical Pathway #2:



Clinical Pathway #3:



Paxlovid Prescription Form



London Middlesex
Primary Care Alliance

Paxlovid™ Prescription

Please fax completed form to: North Tower Prescription Centre (Fax: (519)685-8135)

Prescriber Information		Patient Information			
First Name	Last Name	First Name	Last Name	Sex (at birth) <input type="checkbox"/> Male <input type="checkbox"/> Female	DOB
Address		Address		Health Card No.	Version
City	Postal Code	City	Postal Code		
Telephone	Fax	Telephone	Preferred Language <input type="checkbox"/> EN <input type="checkbox"/> Other		

Inclusion criteria: must meet criteria to proceed with treatment

Date of positive COVID test: _____ Date of symptom onset (must be ≤5 days): _____

Higher Risk of Severe Disease
☐ Immunocompromised or immunosuppressed (see below)
☐ Unvaccinated:

☐ Age 39 or below and at least 3 risk factors
☐ Age 40-69 and at least 1 risk factor
☐ Age 70 or greater

☐ Vaccinated with 1 or 2 doses

☐ Age 20-69 and at least 3 risk factors
☐ Age 70 or greater and at least 1 risk factor

☐ Vaccinated with 3 doses

☐ Age 70 or greater with at least 3 risk factors

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 applies)

☐ 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)

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

Immunocompromise Factors: (Check all that applies)

☐ 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 > 2 weeks)

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

(*) Depending on absolute contraindications

Paxlovid™ Assessment:

☐ Attach current medication, herbal, OTC list
☐ Patient's home pharmacy
☐ Home pharmacy phone number
☐ Allergies ☐ NKA
Existing liver impairment: ☐ YES ☐ NO ☐ UNKNOWN
If known, what is the Child-Pugh class?
Existing renal impairment: ☐ YES ☐ NO ☐ UNKNOWN
Is the patient pregnant? ☐ YES ☐ NO ☐ N/A
*Please refer to science table for more information: <https://covid19-sciencestable.ca/sciencebrief/nirmatrelvir-ritonavir-paxlovid-what-prescribers-and-pharmacists-need-to-know/>

Patient Stats & Laboratory Values (Refer to CAC if more than 3 months)

Height (cm)	Weight (Kg)
SCr (µmol/L)	eGFR (ml/min)
Albumin (g/L) (optional)	Bilirubin (µmol/L) (optional)
INR (optional)	Ascites severity

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 >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 >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 provider assumes responsibility for all follow up.

Physician/NP Registration Number

Signature

Date



Paxlovid Prescription Form



Paxlovid™ Prescription

Please fax completed form to: North Tower Prescription Centre (Fax: (519)685-8135)

Prescriber Information		Patient Information			
First Name	Last Name	First Name	Last Name	Sex (at birth) <input type="checkbox"/> Male <input type="checkbox"/> Female	DOB
Address		Address		Health Card No.	Version
City	Postal Code	City	Postal Code		
Telephone	Fax	Telephone	Preferred Language <input type="checkbox"/> EN <input type="checkbox"/> Other		

Inclusion criteria: must meet criteria to proceed with treatment

Date of positive COVID test:

Date of symptom onset (must be ≤5 days):

Higher Risk of Severe Disease

- ☐ Immunocompromised or immunosuppressed (see below)
- ☐ Unvaccinated:
 - ☐ Age 39 or below and at least 3 risk factors
 - ☐ Age 40-69 and at least 1 risk factor
 - ☐ Age 70 or greater
- ☐ Vaccinated with 1 or 2 doses
 - ☐ Age 20-69 and at least 3 risk factors
 - ☐ Age 70 or greater and at least 1 risk factor
- ☐ Vaccinated with 3 doses
 - ☐ Age 70 or greater with at least 3 risk factors

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 applies)

- ☐ 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)

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

Immunocompromise Factors: (Check all that applies)

- ☐ 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 > 2 weeks)

(*) Depending on absolute contraindications

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



Paxlovid Prescription Form

Paxlovid™ Assessment:		
<input type="checkbox"/> Attach current medication, herbal, OTC list	Patient Stats & Laboratory Values (Refer to CAC if more than 3 months)	
<input type="checkbox"/> Patient's home pharmacy		
<input type="checkbox"/> Home pharmacy phone number		
<input type="checkbox"/> Allergies <input type="checkbox"/> NKA		
Existing liver impairment: <input type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> UNKNOWN		
If known, what is the Child-Pugh class?	Height (cm)	Weight (Kg)
Existing renal impairment: <input type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> UNKNOWN	SCr (μmol/L)	eGFR (ml/min)
Is the patient pregnant? <input type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> N/A	Albumin (g/L) (optional)	Bilirubin (μmol/L) (optional)
*Please refer to science table for more information: https://covid19-sciencetable.ca/sciencebrief/nirmatrelvir-ritonavir-paxlovid-what-prescribers-and-pharmacists-need-to-know/	INR (optional)	Ascites severity
<i>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.</i>		

Medication Order
Standard Dose (eGFR >60ml/min)
<input type="checkbox"/> 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 >30-59ml/min)
<input type="checkbox"/> 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 provider assumes responsibility for all follow up.

Physician/NP Registration Number

Signature

Date



CAC Referral Form



London Health Sciences Centre **Carling Heights Covid-19 Clinical Assessment Centre Paxlovid™ Referral Form**

Please Fax Completed Form to: North Tower Prescription Centre (Fax: 519-685-8135)

Prescriber Information		Patient Information			
First Name <i>Enter Name</i>	Last Name <i>Enter Name</i>	First Name <i>Enter Name</i>	Last Name <i>Enter Name</i>	Sex (at birth) <input type="checkbox"/> Male <input type="checkbox"/> Female	DOB <i>Enter DOB</i>
Address <i>Enter Address</i>		Address <i>Enter Address</i>		Health Card No. <i>Enter HC No.</i>	Version <i>Enter Version</i>
City <i>Enter City</i>	Postal Code <i>Enter Postal Code</i>	City <i>Enter City</i>	Postal Code <i>Enter Postal Code</i>	PIN # <i>Enter PIN #</i>	
Telephone <i>Enter Telephone</i>	Fax <i>Enter Fax</i>	Telephone <i>Enter Telephone</i>	Preferred Language <input type="checkbox"/> EN <input type="checkbox"/> Other <i>Please specify</i>		

Inclusion criteria: must meet criteria to proceed with treatment

Date of positive COVID test: *Click or tap to enter a date.* Type of Test: ☐ Provider Administered RAT ☐ PCR ☐ ID NOW ☐ Pending ☐ Not done

Date of symptom onset (must be ≤5 days): *Click or tap to enter a date.* Note: Standard risk patients do not qualify for Paxlovid™

Higher Risk of Severe Disease

☐ Immunocompromised or immunosuppressed (see below)

☐ Unvaccinated:

☐ Age 39 or below and at least 3 risk factors

☐ Age 40-69 and at least 1 risk factor

☐ Age 70 or greater

☐ Vaccinated with 1 or 2 doses

☐ Age 20-69 and at least 3 risk factors

☐ Age 70 or greater and at least 1 risk factor

☐ Vaccinated with 3 doses

☐ Age 70 or greater with at least 3 risk factors

Therapeutics should always be recommended for immunocompromised individuals not expected to mount an adequate response to COVID-19 vaccination or SARS-CoV-2 infection due to their underlying immune status, regardless of age or vaccine status.

Immunocompromised Factors: (check all that applies)	Risk Factors: (check all that applies)
<input type="checkbox"/> Receipt of solid-organ transplant and taking immunosuppressive therapy (*)	<input type="checkbox"/> Obesity (BMI ≥30 kg/m²)
<input type="checkbox"/> Treatment for solid tumors and hematologic malignancies (including individuals with lymphoid malignancies who are being monitored without active treatment)	<input type="checkbox"/> Diabetes
<input type="checkbox"/> Receipt of chimeric antigen receptor (CAR) T-cell or hematopoietic stem cell transplant (within 2 years of transplantation or taking immunosuppression therapy)	<input type="checkbox"/> Heart disease, hypertension, congestive heart failure
<input type="checkbox"/> Alkylating agents, antimetabolites (*)	<input type="checkbox"/> Chronic respiratory disease, including cystic fibrosis
<input type="checkbox"/> Transplant-related immunosuppressive drugs	<input type="checkbox"/> Cerebral palsy
<input type="checkbox"/> Cancer chemotherapeutic agents classified as severely immunosuppressive	<input type="checkbox"/> Intellectual disability of any severity
<input type="checkbox"/> HIV (must be on antiretroviral therapy)	<input type="checkbox"/> Sickle cell disease
<input type="checkbox"/> Moderate or severe primary immunodeficiency (e.g. Common Variable Immunodeficiency, DiGeorge Syndrome, Good's Syndrome, Hyper-IgE Syndrome, Wiskott-Aldrich Syndrome)	<input type="checkbox"/> Moderate or severe kidney disease (eGFR <60 mL/min)
<input type="checkbox"/> Anti-TNF blockers or other biologic agents that are immunosuppressive or immunomodulatory (*)	<input type="checkbox"/> Moderate or severe liver disease (e.g. Child-Pugh Class B or C cirrhosis)
<input type="checkbox"/> Taking chronic oral corticosteroid (≥20 mg prednisone or equivalent per day when administered for ≥2 weeks)	<input type="checkbox"/> Receiving other active cancer treatment not included in immunocompromised list

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

There is a lack of data on nirmatrelvir/ritonavir use in pregnant patients, if you feel your patient would benefit from treatment,

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

this should be managed by a multidisciplinary team with expertise in the management of pregnancy.

***Depending on absolute contraindications**

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. Patients should be advised not to breastfeed for the duration of treatment and four days afterwards, during which time breast milk should be pumped and discarded.

Nirmatrelvir / Ritonavir Eligibility Assessment:

☐ Attach current medications (from past 14 days), herbal, nutraceuticals, and OTC list

☐ Patient's home pharmacy *Enter Pharmacy name*

☐ Home pharmacy phone number *Enter Pharmacy phone number*

☐ Allergies *Enter Allergies Here* ☐ NKA

Existing liver impairment: ☐ YES ☐ NO ☐ UNKNOWN

If known, Child-Pugh Class? ☐ Class A ☐ Class B ☐ Class C

Existing renal impairment: ☐ YES ☐ NO ☐ UNKNOWN

***Please refer to science table for more information on contraindications: <https://covid19-sciencetable.ca/sciencebrief/nirmatrelvir-ritonavir-paxlovid-what-prescribers-and-pharmacists-need-to-know/>**

Scan the QR code for Nirmatrelvir/Ritonavir product monograph

Patient Stats & Laboratory Values
(Refer to CAC if >6 months or acute illness)

Height (cm) <i>Enter Height</i>	Weight (Kg) <i>Enter Weight</i>
Scr (μmol/L) <i>Enter Scr Value</i>	eGFR (mL/min) <i>Enter eGFR</i>
Albumin (g/L) <i>Enter level (optional)</i>	Bilirubin (μmol/L) <i>Level (optional)</i>
INR <i>Enter INR (optional)</i>	ALT (U/L)
Platelet Count (x10 ⁹ /L)	Beta hCG (if of child-bearing age)
Encephalopathy <i>Choose Grade</i>	Ascites severity <i>Choose Grade</i>

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.

Failure to provide this information will delay timely assessment for therapy.

☐ I acknowledge I have reviewed the Ontario Science Table COVID-19 advisory for Ontario drug interactions

☐ I have attached the most up to date medication record for the above-named patient

Signature of referring provider: _____

Date: *Click or tap to enter a date.*

Purpose for Referral:

Please Select All that Apply:

☐ 1. **Assessment and Management by the Carling Heights Covid-19 Clinical Assessment Centre Nurse Practitioner**

☐ 2. **ID NOW Test**

Referring provider would like to be notified of ID NOW results via:

☐ Fax: _____

☐ Office Phone Number: _____

☐ Alternative Phone Number: _____

☐ 3. **Blood Work Required:**

☐ SCr

☐ eGFR

☐ Albumin

☐ Bilirubin

☐ ALT

☐ INR

☐ CBC

☐ Beta hCG

It is the responsibility of the referring provider to follow up on any and all abnormal blood results

Exclusions
(if any one criterion is met, patient does NOT qualify for therapy. Do not refer for prescription)

☐ On dialysis or eGFR less than 30 mL/min

☐ Requires medications to be crushed or split

☐ Has had a severe hypersensitivity reaction to nirmatrelvir, ritonavir, or excipients

☐ Has an oxygen saturation less than 92% on room air

☐ Greater than 5 days of symptoms

☐ Unwilling to take COVID therapy

☐ Has severe hepatic impairment (Child-Pugh Class C cirrhosis or greater)

☐ Living with HIV and **not** on antiretroviral medication

In order to mitigate the many potential drug interactions, a comprehensive and updated medication list must be provided for review prior to initiating nirmatrelvir/ritonavir. This review will be completed by pharmacy to determine eligibility.

Enter Number *Click to enter a date.*

Physician/NP Name and Registration # _____ Signature _____ Date _____

CAC Referral Form

Purpose for Referral:	
Please Select All the Apply:	
<input type="checkbox"/> 1. Assessment and Management by the Carling Heights Covid-19 Clinical Assessment Centre Nurse Practitioner <ul style="list-style-type: none">By referring this patient and if medication is prescribed, the referring provider assumes responsibility for all follow-up based on any discharge instructions from the Carling Heights COVID-19 Clinical Assessment Centre	
<input type="checkbox"/> 2. ID NOW Test	
Referring provider would like to be notified of ID NOW results via:	
<input type="checkbox"/> Fax: _____	
<input type="checkbox"/> Office Phone Number: _____	
<input type="checkbox"/> Alternative Phone Number: _____	
<input type="checkbox"/> 3. Blood Work Required:	
<input type="checkbox"/> SCr	
<input type="checkbox"/> eGFR	
<input type="checkbox"/> Albumin	
<input type="checkbox"/> Bilirubin	
<input type="checkbox"/> ALT	
<input type="checkbox"/> INR	
<input type="checkbox"/> CBC	
<input type="checkbox"/> Beta hCG	
It is the responsibility of the referring provider to follow up on any and all abnormal blood results	
Exclusions (if any one criterion is met, patient does NOT qualify for therapy. Do not refer for prescription)	
<input type="checkbox"/> On dialysis or eGFR less than 30 mL/min	<input type="checkbox"/> Greater than 5 days of symptoms
<input type="checkbox"/> Requires medications to be crushed or split	<input type="checkbox"/> Unwilling to take COVID therapy
<input type="checkbox"/> Has had a severe hypersensitivity reaction to nirmatrelvir, ritonavir, or excipients	<input type="checkbox"/> Has severe hepatic impairment (Child-Pugh Class C cirrhosis or greater)
<input type="checkbox"/> Has an oxygen saturation less than 92% on room air	<input type="checkbox"/> Living with HIV and not on antiretroviral medication
In order to mitigate the many potential drug interactions, a comprehensive and updated medication list must be provided for review prior to initiating nirmatrelvir/ritonavir. This review will be completed by pharmacy to determine eligibility.	

Enter Number

Physician/NP Name and Registration #

Signature

Click to enter a date.

Date



Step 5: Follow up

- For Antiviral Therapy, patients will need close monitoring for drug interactions and side effects.
- Follow-up may include:
 - Ongoing monitoring (e.g., via COVID@Home, or Home and Community Care Support Services Remote Patient Monitoring)
 - Virtual or in person follow up (<https://hfam.ca/clinical-pathways-and-evidence/covid/assessment-diagnosis-and-management-of-covid/>)



Thank you!

For more information, please contact gschacter@me.com

Q&A