Therapeutics Initiative
Better prescribing. Better health.

THERAPEUTICS LETTER 149
May - June 2024

Plain Language Summary

Should I take Paxlovid™ for COVID-19?

BOTTOM LINE:

For most people with COVID-19, Paxlovid™ will:

- **NOT make you feel better faster**
- **NOT lower your chance of dying or going to the hospital**

What is Paxlovid™?

Paxlovid™ (nirmatrelvir-ritonavir) is a medication for some people who have COVID-19. It is meant to lower the chance of dying or going to the hospital because of COVID-19. Paxlovid™ is for people who:

- have tested positive for COVID-19 within the last 5 days, and
- are at high risk of dying or going to the hospital because of COVID-19.

What does "high risk" mean?

Only people at high risk should be offered Paxlovid™. This includes those who are:

- severely immunocompromised (for example, those who have received an organ transplant, or are being treated for blood cancer), or
- moderately immunocompromised (for example, those being treated for cancer, taking immunosuppressants, some people with HIV)

For such people, Paxlovid™ may lower the chance of dying or going to the hospital. Ask your doctor or nurse practitioner if you think you might be at high risk.

What if I am not "high risk"?

If you are not in the high-risk categories above, Paxlovid™ is unlikely to make you feel better faster, or lower your chance of dying or going to the hospital because of COVID-19. You could also experience side effects from taking Paxlovid™. The chance of hospitalization or death from COVID-19 in BC is now very low.

Has the definition of "high risk" changed?

Yes. Early in the COVID-19 pandemic, certain things were thought to make people much more likely to get very sick from COVID-19. This included older age and conditions like stroke, diabetes, or heart disease. Now, most people are vaccinated or have already had COVID-19. The current circulating strains of the virus are less likely to make someone very sick compared to early in the pandemic.

Does Paxlovid™ have side effects?

People taking Paxlovid™ are more likely to notice side effects compared with those who don't. Side effects can include altered taste, diarrhea, muscle aches, or nausea. Your prescriber and pharmacist will need to check if your other medications are safe to take with Paxlovid™. You may have to stop some of your usual medications when taking Paxlovid™.

Abstract

Background: In 2024 the risk of hospitalization or death due to COVID-19 is low for most people under age 80 in British Columbia (BC). However, for those at high risk of complications, the antiviral drug combination nirmatrelvir-ritonavir (NMV-r, marketed as Paxlovid™) has shown promise in reducing the composite risk of hospitalization and death from COVID-19.

Methods: We evaluated the effectiveness of NMV-r based on data from 3 randomized controlled trials conducted by Pfizer and an observational study conducted by the Therapeutics Initiative in British Columbia. In addition to the impact of NMV-r on COVID-19-related hospitalization or death, we considered the impact of vaccination status on the drug's effectiveness.

Results: The EPIC-HR trial showed a significant reduction in hospitalization and death in high-risk, unvaccinated patients during 2021. In contrast, the 2021-2022 EPIC-SR trial found no benefit for lower-risk, vaccinated patients. The BC observational study found statistically significant risk reductions in high-risk groups, but not in an expanded eligibility group. NMV-r does not affect symptom duration or prevent transmission and is not known to prevent long-COVID.

Conclusions: NMV-r may benefit high-risk COVID-19 patients, but it offers little advantage for lower-risk, vaccinated individuals. As Paxlovid™ will cost Canadians about $1,400 per treatment, cost-effectiveness is a significant consideration. The ongoing *PANORAMIC* and *CanTreatCOVID* clinical trials may provide further insights into NMV-r's long-term effects on COVID-19 and on healthcare utilization.

Keywords: Antiviral Agents, Cost-Benefit Analysis, COVID-19, Combination Drug Therapy, Nirmatrelvir, Paxlovid, Randomized Controlled Trials as Topic, Risk Factors, Ritonavir.

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For most people, Paxlovid™

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Won't make you feel better faster if you have COVID-19

Won't lower your chance of dying or going to the hospital because of COVID-19

For people who are immunocompromised, Paxlovid™ may lower their chance of dying or going to the hospital from COVID-19

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How useful is Paxlovid™ in 2024?

Vignette: *During a possible future resurgence of the COVID-19 pandemic, two patients test positive and ask you to prescribe antiviral therapy. One is 47 years old, up to date on his COVID vaccinations, but overweight and worried about his lungs because he smokes. Having paid taxes for years, he feels that he deserves access to treatment. Your second patient is 78 and also fully immunized; but she has diabetes, heart failure and is undergoing treatment for breast cancer.* ***Should you prescribe Paxlovid™ for both, or only for one?***

Summary and Conclusions

- **The risk of hospitalization or death resulting from COVID-19 in 2024 is low in British Columbia for most people under 80 years of age.**
- **For people at high risk of complications from COVID-19, results of the EPIC-HR trial and BC observational data are congruent. The antiviral drug combination nirmatrelvir-ritonavir (NMV-r) also known by its brand name Paxlovid™ reduces the composite risk of hospitalization with COVID-19, and death from any cause.**
- **In contrast, people who are vaccinated are at lower risk and are unlikely to benefit.**
- **NMV-r does not shorten symptoms or prevent transmission, and is not known to prevent long-COVID.**
- **A large ongoing trial in the United Kingdom and the similar *CanTreatCOVID* trial in Canada may provide further information within 1-2 years.**
- **Paxlovid™ is expected to cost Canadians about $1,400 for a 5-day course of therapy. Before prescribing it, consider the cost of treating what may be hundreds of patients to prevent one event.**

Evidence has emerged gradually as to who is most likely to benefit from NMV-r for COVID-19

In January 2022 Health Canada approved the antiviral drug combination nirmatrelvir-ritonavir (NMV-r) also known by its brand name Paxlovid™. A year later, Therapeutics Letter 141 provided an interim analysis of the effects of NMV-r on COVID-19–related hospitalization or death from any cause in British Columbians eligible for treatment.[1]

By then, Pfizer Inc. had completed 3 double-blind randomized clinical trials (RCTs) of NMV-r as part of a program entitled Evaluation of Protease Inhibition for COVID-19 (EPIC). Reported numbers of participants differ between a March 16, 2023 US FDA Briefing Document[2] and the sponsor's published reports. Numbers shown below are from the references cited:

- **EPIC-HR:** 5 days of NMV-r vs placebo for 2,246 **unvaccinated** people with confirmed infection deemed at "high risk" from COVID-19 who were enrolled between July 16 and December 9, 2021 and predominantly infected with the Delta variant. Results published online on February 16, 2022 demonstrated a clinically and statistically significant reduced risk of hospitalization and death in this **early pandemic high-risk population.**[3] Therapeutics Letter 141 summarized these results.[1]
- **EPIC-SR:** 5 days of NMV-r vs placebo for 1,296 people with confirmed infection deemed at "standard risk" who were fully vaccinated with risk factors for progression or unvaccinated, enrolled between August 25, 2021 and July 25, 2022 and infected with either Delta or Omicron variants. Pfizer announced by media release on June 14, 2022 that EPIC-SR **did not achieve its primary endpoint of shortening symptom duration.**[4] On August 14, 2023 it posted results at clinicaltrials.gov[5] and published formal results on April 4, 2024.[6] Below, we discuss these results further.
- **EPIC-PEP:** 5 or 10 days of NMV-r vs placebo for post-exposure prophylaxis in 2,954 people with **infected household contacts**, enrolled between September 9, 2021 and April 12, 2022. Pfizer announced by media release on April 29, 2022 that **numerical reductions of infections were not statistically significant.**[7] It posted results to clinicaltrials.gov on May 6, 2023[8] but has yet to publish EPIC-PEP.

This Therapeutics Letter highlights the final results of our BC observational study, and contextualizes our findings with results from the newly published EPIC-SR trial.

What can we learn from the EPIC trials?

The 3 EPIC trials were double-blinded, randomized, placebo-controlled trials (DBRCT) designed, sponsored, and conducted by Pfizer.

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EPIC-HR (**"High-Risk"**) included unvaccinated patients who were expected to be at high risk for complications from COVID-19, including from immunosuppression, smoking, cardiovascular disease, and cancer.[3] The median age was 46 and 13% of participants were 65 or older. Its primary endpoint was the composite of hospitalization with COVID-19 or death from any cause by day 28 post-enrolment. NMV-r reduced this endpoint by an absolute risk reduction of 5.6%, 95% confidence interval 4.0% to 7.2%, number needed to treat (NNT) = 18 to prevent 1 hospitalization or death. (Table)

In contrast, **EPIC-SR** (**"Standard-Risk"**) included patients without the high-risk factors of participants in EPIC-HR. In this trial, 57% were fully vaccinated against COVID-19, the median age was 42, and only 5% were 65 or older.[6] The primary endpoint was time to sustained alleviation of symptoms. COVID-19–related hospitalization or death from any cause was a secondary endpoint. No difference was observed in any of these endpoints. (Table)

It is important to appreciate that EPIC-HR was conducted in unvaccinated people during the Delta wave of the COVID-19 pandemic. EPIC-SR also included 43% unvaccinated participants and overlapped the Delta and Omicron waves. Thus the generalizability of the EPIC findings is unknown for treatment of vaccinated patients in 2024 or subsequently, and for people infected with an Omicron variant.

The EPIC-PEP trial also spanned the period of Delta and then Omicron variant prevalence.[8] While these results remain unpublished, the US FDA concluded that the difference between a 2.4% to 2.6% short-term infection rate amongst NMV-r treated household contacts of an infected patient vs. 3.9% amongst placebo recipients was neither clinically meaningful nor statistically significant.[2]

One challenge to understanding the EPIC trial results is whether **advanced age, of itself,** increases serious outcomes from COVID-19 that can be mitigated by NMV-r treatment. EPIC-HR defined as "high risk" anyone over age 60, but **participants were unvaccinated** (during the second year of the pandemic).[9] The trial report refers to only 268 people age ≥65.[3] In EPIC-SR, anyone age ≥18 without high-risk comorbidities was eligible and considered as having "standard risk" for COVID-19 complications.[10] This included 65 people age ≥65 who were fully vaccinated, the oldest was 87. Thus, **age alone is at best an arbitrary marker for risks from COVID-19,** and needs to be contextualized among other risk factors such as vaccination status and comorbidities.

Observational study of NMV-r in BC: final results

Therapeutics Initiative researchers used BC Ministry of Health datasets to analyze the 28-day risk of COVID-19-related hospitalization or death from any cause in the groups eligible for treatment.[11] This mimics the outcomes studied in EPIC-HR. To minimize confounding bias, we limited our analysis to the subset of British Columbia residents to whom NMV-r was dispensed ("index cases"), and for whom we could match a person (control) of the same age (±2 years), sex, and who was infected with laboratory-confirmed COVID-19 infection within a month of the paired index case. We also matched for propensity scores, a common pharmacoepidemiologic method to control for imbalances in comorbidities between groups.

We studied 4 groups of patients, of which 3 included people considered **"clinically extremely vulnerable"** (CEV) by virtue of medical conditions previously designated in early 2021 to prioritize COVID-19 vaccinations. The first 2 groups included people age ≥18 who were severely (CEV1) or moderately (CEV2) immunocompromised. A third (CEV3) comprised people who were not immunocompromised, but with medical conditions that engender a high risk for complications from COVID-19. A fourth "Expanded Eligibility" group allowed wider access to NMV-r.

The BC eligibility criteria for NMV-r treatment, updated in November 2023 are available online.[12] However, they may change due to efficacy and effectiveness evidence accumulated since 2021, as suggested by the Canadian Drug Expert Committee in January 2024.[13]

The Table juxtaposes results from the EPIC-HR and EPIC-SR DBRCTs with observational findings from BC patients with a positive polymerase chain reaction (PCR) test who were eligible for and received NMV-r, and from matched controls between February 1, 2022, and February 3, 2023, when most British Columbians were fully vaccinated. The median age of these BC patients and controls was 70.

Compared with controls who did not receive NMV-r, treatment was associated with statistically significant absolute risk reductions in the composite outcome of 2.5% in the CEV1 group, and 1.7% in the CEV2 group. There was a non-statistically significant absolute risk reduction of 1.3% in the CEV3 group, but a non-statistically significant absolute risk increase in the Expanded Eligibility group. In this group, the BC cohort most similar to people studied in the EPIC-SR trial, our results also did not identify a benefit from NMV-r (Paxlovid™).

COVID-19-related emergency hospitalization or death: treatment effects in EPIC RCTs and BC real world population, by eligibility group

Variable	DBRCT EPIC-HR	DBRCT EPIC-SR[b]	Observational CEV1	Observational CEV2	Observational CEV3	Observational Expanded Eligibility[d]
NMV-r treated	N = 1,039	N = 654	280	1,314	1,050	789
Events[a] (%)	8 (0.8)	5 (0.8)	NA[c]	23	25	35
Control	N = 1,046	N = 634	280	1,314	1,050	789
Events (%)	66 (6.3)	10 (1.6)	NA[c]	45	39	27
Risk difference (95% CI)	**-5.6% (-7.2 to -4.0)**	-0.8% (-2.0 to +0.4)	**-2.5% (-4.8 to -0.2)**	**-1.7% (-2.9 to -0.5)**	-1.3% (-2.8 to +0.1)	+1.0% (-0.9 to +2.9)
Relative risk	0.12	0.49	0.22	0.51	0.64	1.30

Notes: statistically significant results are **bolded.**

a) Events = {COVID-19 related hospitalizations + all cause deaths}

b) Time to sustained alleviation of symptoms averaged 13.8 days for NMV-r, and 14.1 days for placebo (NS)

c) NA: small numbers masked to preserve privacy under BC Protection of Privacy law

d) For BC's original definition of "clinically extremely vulnerable" (CEV) patients, see reference 12. The more recent CDEC/CADTH definition is more restrictive.[13]

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What can we tell patients who contract COVID-19?

For most people in British Columbia, the risk of hospitalization with COVID-19 or death from COVID-19 is now very low. In October 2023, scientists at the BC Centre for Disease Control published their analysis of severe outcome risks due to **first infections** among residents of BC's Lower Mainland.[14] The most recent interval studied was July 31 to December 3, 2022.

For the latter part of 2022 they estimated the following risks for people newly infected with COVID-19:

Ages 60 to 69:

- death: about 3 per 10,000 infected (18 events among 69,830 people);
- hospitalization for COVID-19: about 16 per 10,000 (112 events).

Ages 70 to 79:

- death: about 11 per 10,000 (35 events among 31,440 people);
- hospitalization for COVID-19: about 73 per 10,000 (228 events).

Given these estimates, even if NMV-r could hypothetically have reduced the risk of death or hospitalization by 50% in people aged 70 to 79 (for which no evidence exists), the number needed to treat (NNT) to prevent one death during the second half of 2022 would have been about 1,800. To prevent one hospitalization, the NNT would have been about 275. The BCCDC authors emphasize that their estimates refer to people infected for the first time.[14] However, severe outcome risks may be even lower - and the corresponding NNTs even higher - among people who are fully vaccinated and have also acquired natural immunity from a COVID-19 infection.

The EPIC-SR and EPIC-PEP randomized clinical trials did not show that NMV-r can reduce symptom duration, or prevent COVID-19 after exposure. Currently, there is also no evidence that early treatment with NMV-r for acute COVID-19 infection can prevent long-COVID.[13] We also do not know whether NMV-r can prevent hospitalization of typical residents in long-term care.

NMV-r relies on ritonavir to prolong the half-life of nirmatrelvir by potent inhibition of CYP3A, an important drug-metabolizing enzyme in the liver and the small intestine.[15] Because CYP3A metabolizes about half of commonly used drugs, using NMV-r requires special attention to potential toxicity from other medications. The most common adverse effects are taste alteration and diarrhea, but patients need to understand that NMV-r is also potentially dangerous to some.

Will more information from RCTs be forthcoming?

PANORAMIC is a large publicly funded open label trial in the United Kingdom (UK), designed and run from Oxford University.[16] It began by evaluating treatment of early COVID-19 with molnupiravir, a different antiviral drug licensed in the UK, from December 2021 to late April 2022. In 25,708 people (mean age 57 years, 94% having received at least 3 vaccine doses) molnupiravir did not prevent hospitalization or death, compared with usual care alone.[17] It was also not cost-effective for overall health utilization.[18] Molnupiravir is not approved in Canada except for use in clinical trials.[19]

Between April 2022 and the end of recruitment on March 28, 2024, the PANORAMIC trialists also randomized 3,516 participants to open-label NMV-r versus usual care.[20] This part of the PANORAMIC trial will eventually provide additional information about NMV-r, including whether it can reduce long-term persistence of symptoms and healthcare utilization at 3 and 6 months after treatment.[16,21]

The Canadian Institutes of Health Research (CIHR), Health Canada, and the Public Health Agency of Canada sponsored a similar trial, CanTreatCOVID, which began to randomize Canadian patients to NMV-r or usual care in January 2023.[22] The trial protocol mirrors PANORAMIC's practical approach to self-enrolment through a website or referral by clinicians. Anyone age 50 years or older who tests positive for COVID-19 is eligible to participate, as well as younger adults with chronic conditions. Patients can self-refer at www.cantreatcovid.org, and preliminary results are expected in 2025. The study website shows 454 Canadians had enrolled as of April 17, 2024.

Is NMV-r therapy worth the cost?

This is an important question for an expensive drug. In Canada, a 5-day course of Paxlovid™ has a retail cost of about $1,400 (including dispensing).[13] Roughly 300 people currently take NMV-r each week in BC. Similar utilization could total nearly $22 million/year. Healthcare resources are always in high demand, and money devoted to drugs is not available for other parts of the healthcare system. For perspective, $1,400 approximates the hospital cost of a surgical procedure such as cholecystectomy or hernia repair, can vaccinate about 75 people against COVID-19, or cover about 40 routine patient visits with a family doctor.

Vignette resolution: *Your 47 year-old patient is unlikely to benefit from NMV-r, so you review his COVID-19 vaccination history and advise him about current booster options and recommendations. But your 78 year-old may have a substantially higher risk for complications from COVID-19 due to her pre-existing chronic conditions, and meets criteria recently proposed by the Canadian Drug Expert Committee.[13] Again, you review vaccination status, but as her symptoms began yesterday and she tested positive, you prescribe NMV-r after checking for interactions with her usual drug therapy.*

References

1. Therapeutics Initiative. *Paxlovid in British Columbia: Interim real-world analysis.* Therapeutics Letter 141, January-February 2023. https://ti.ubc.ca/letter141
2. Food and Drug Administration. *FDA briefing document: Antimicrobial Drugs Advisory Committee meeting, March 16, 2023.* https://www.fda.gov/media/166197/download Errata: https://www.fda.gov/media/166198/download
3. Hammond J, Leister-Tebbe H, Gardner A, et al. *Oral Nirmatrelvir for High-Risk, Nonhospitalized Adults with Covid-19.* New England Journal of Medicine. 2022; 386(15):1397-1408. DOI: 10.1056/NEJMoa2118542
4. Pfizer. *Pfizer Reports Additional Data on PAXLOVID™ Supporting Upcoming New Drug Application Submission to US FDA.* June 14, 2022. https://www.pfizer.com/news/press-release/press-release-detail/pfizer-reports-additional-data-paxlovidtm-supporting
5. US National Library of Medicine. *Evaluation of Protease Inhibition for COVID-19 in Standard-Risk Patients (EPIC-SR).* https://classic.clinicaltrials.gov/ct2/show/results/NCT05011513
6. Hammond J, Fountaine RJ, Yunis C, et al. *Nirmatrelvir for Vaccinated or Unvaccinated Adult Outpatients with Covid-19.* New England Journal of Medicine. 2024; 390(13):1186-1195. DOI: 10.1056/NEJMoa2309003
7. Pfizer. *Pfizer Shares Top-Line Results from Phase 2/3 EPIC-PEP Study of PAXLOVID™ for Post-Exposure Prophylactic Use.* https://www.pfizer.com/news/press-release/press-release-detail/pfizer-shares-top-line-results-phase-23-epic-pep-study
8. US National Library of Medicine. *A Study of a Potential Oral Treatment to Prevent COVID-19 in Adults Who Are Exposed to Household Member(s) With a Confirmed Symptomatic COVID-19 Infection.* https://classic.clinicaltrials.gov/ct2/show/results/NCT05047601
9. Pfizer. *EPIC-HR Protocol C4671005: Oral Nirmatrelvir for High-Risk, Nonhospitalized Adults with Covid-19.* New England Journal of Medicine. 2022; 386(15) https://nejm.org/doi/suppl/10.1056/NEJMoa2118542/suppl_file/nejmoa2118542_protocol.pdf

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10. Pfizer. *EPIC-SR Protocol C4671002: Nirmatrelvir for Vaccinated or Unvaccinated Adult Outpatients with Covid-19.* New England Journal of Medicine 2024; 390(13) https://www.nejm.org/doi/suppl/10.1056/NEJMoa2309003/suppl_file/nejmoa2309003_protocol.pdf
11. Dormuth CR, Kim JD, Fisher A, et al. *Nirmatrelvir-Ritonavir and COVID-19 Mortality and Hospitalization Among Patients With Vulnerability to COVID-19 Complications.* JAMA Network Open 2023; 6(10):e2336678. DOI: 10.1001/jamanetworkopen.2023.36678
12. BC COVID Therapeutics Committee (CTC). *Clinical Practice Guide for the Use of Therapeutics in Mild-Moderate COVID-19.* November 2023 Update. http://www.bccdc.ca/Health-Professionals-Site/Documents/COVID-treatment/ClinicalPracticeGuide_Therapeutics_MildModerateCOVID.pdf
13. Canadian Agency for Drugs, Technology and Health Assessment. *CADTH Reimbursement Recommendation Nirmatrelvir-Ritonavir (Paxlovid™).* January 2024. https://www.cadth.ca/sites/default/files/DRR/2024/SR0808%20Paxlovid%20-%20Draft%20CADTH%20Recommendation.pdf
14. Skowronski DM, Kaweski SE, Irvine MA, et al. *Risk of hospital admission and death from first-ever SARS-CoV-2 infection by age group during the Delta and Omicron periods in British Columbia, Canada.* CMAJ Canadian Medical Association Journal 2023; 195(42):E1427-1439. DOI: 10.1503/cmaj.230721
15. Pfizer Canada. *Paxlovid™ Product Monograph.* Revised January 2, 2024. https://covid-vaccine.canada.ca/info/pdf/paxlovid-pm-en.pdf
16. University of Oxford. *PANORAMIC: Platform Adaptive trial of NOvel antiviRals for eArly treatMent of COVID-19 in the Community.* https://www.panoramictrial.org
17. Butler CC, Hobbs FDR, Gbinigie OA, et al. *Molnupiravir plus usual care versus usual care alone as early treatment for adults with COVID-19 at increased risk of adverse outcomes (PANORAMIC): an open-label, platform-adaptive randomized controlled trial.* Lancet 2023; 401(10373):281-293. DOI: 10.1016/S0140-6736(22)02597-1
18. Png ME, Harris V, Grabey J, et al. *Cost-utility analysis of molnupiravir plus usual care versus usual care alone as early treatment for community-based adults with COVID-19 and increased risk of adverse outcomes in the UK PANORAMIC trial.* British Journal of General Practice 2024. DOI: 10.3399/BJGP.2023.0444
19. Health Canada Drug and Health Product Portal. *Summary of Cancellation for Molnupiravir (*Lagevrio).* April 26, 2023. https://dhpp.hpfb-dgpsa.ca/review-documents/resource/RDS1683828447298
20. Butler C. *A clinical trial investigating novel treatments for COVID-19 in the community.* ISRCTN registry. 2024. DOI: 10.1186/ISRCTN30448031
21. University of Oxford. *PANORAMIC trial documents.* Updated: October 12, 2023. https://panoramictrial.org/for-healthcare-professionals/documents Protocol: https://panoramictrial.org/files/protocols/panoramic_protocol_v8-0_04oct2023.pdf
22. Pinto A, et al. *Canadian Adaptive Platform Trial of Treatments for COVID in Community Settings (CanTreatCOVID).* 2024. https://cantreatcovid.org

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