# MOLNUPAVIR IN PREVIOUSLY UNINFECTED NON-HOSPITALIZED PERSONS WITH COVID-19

*Adeel A. Butt, MBBS, MS;[1,2,3,4] Peng Yan, MS;[1] Obaid S. Shaikh, MD;[1,5] Saad B. Omer, MD, MPH, PhD;[6] Florian B. Mayr, MD, MS[7,8], Victor B. Talisa, PhD;[7,8]*

[1] VA Pittsburgh Healthcare System, Pittsburgh, PA, USA; [2] Department of Medicine, Weill Cornell Medicine, New York, NY and Doha, Qatar; [3] Department of Population Health Sciences, Weill Cornell Medicine, New York, NY and Doha, Qatar; [4] Hamad Medical Corporation, Doha, Qatar' [5] Department of Medicine, Division of Gastroenterology, University of Pittsburgh, PA, USA; [6] Institute for Global Health, Yale University, New Haven, CT, USA; [7]CRISMA Center, Department of Critical Care Medicine, University of Pittsburgh, PA, USA; [8] University of Pittsburgh School of Medicine, Pittsburgh, USA;

**Contact information:**
**Adeel Ajwad Butt, MBBS, MS, FACP, FIDSA**
**Mailstop 151, University Drive C**
**Pittsburgh, PA 15240**
**Email: aab2005@med.cornell.edu**

## BACKGROUND

- In December 2021, two novel oral antiviral agents, Nirmatrelvir/ritonavir (NMV/r) and Molnupiravir (MPV), were granted Emergency Use Authorization (EUA) by the Food and Drug Administration (FDA) for treatment of early symptomatic patients with mild to moderate COVID-19 at high risk of progression to severe disease.
- In a phase 3 double-blind, randomized, placebo controlled trial in symptomatic, unvaccinated, non-hospitalized adults with mild to moderate disease who had at least one risk factor for disease progression, MPV was associated a significant reduction in hospitalization or death by day 29.
- However, observational and real-world studies have reported mixed results, with some studies demonstrating reduction in the risk of severe disease or death, while others have not demonstrated a clear benefit.
- In a large observational study including 2,661 patients and 2,661 propensity score-matched controls, MPV was not associated with a significant reduction in the risk of the severe COVID-19 or COVID-19 specific mortality (HR, 0.83; 95% CI, 0.57-1.21).

## OBJECTIVES

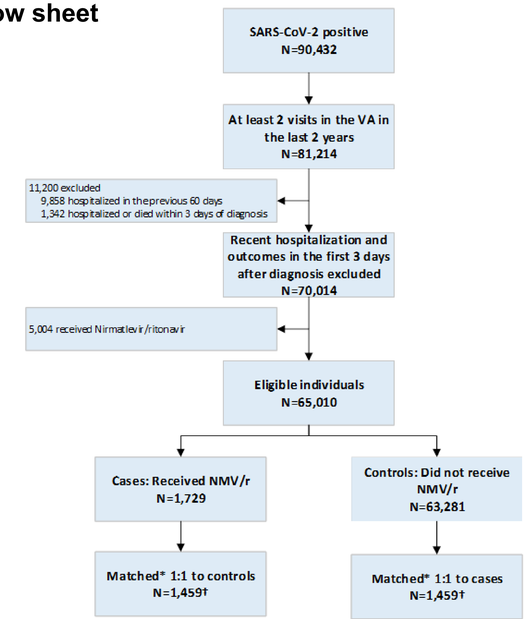
- To determine the effect of MPV treatment upon hospitalization and death in a previously uninfected, non-hospitalized, high-risk population.

## METHODS

- We used a matched cohort design to emulate a target trial.
- Eligible individuals were those in the VA COVID-19 Shared Data Resource who had a first confirmed SARS-CoV-2 infection between January 1 and August 31, 2022, and were free of an outcome event (hospitalization or death) within 3 days of testing positive.
- Those who were hospitalized in the 60-days period prior to the index COVID-19 test date were ineligible.
- Among the eligible individuals, we matched those who were prescribed NMV/r with those who did not receive NMV/r within 3 days of COVID-19 diagnosis date.
- Controls were matched 1:1 on age (5-year blocks), race, sex, body mass index, Charlson Comorbidity Index, VA facility where MPVwas prescribed, and vaccination status.
- Absolute risk difference (ARD) between the two groups along with 95% confidence intervals were estimated using logistic regression models fit using generalized estimating equations to account for correlated outcomes within each matched pair.
- The overall absolute difference between the groups, as well as for various sub-strata of the population by age, sex, body mass index, presence of various comorbidities, and vaccination status were tabulated and graphed.

## RESULTS

### Study flow sheet




### Baseline characteristics

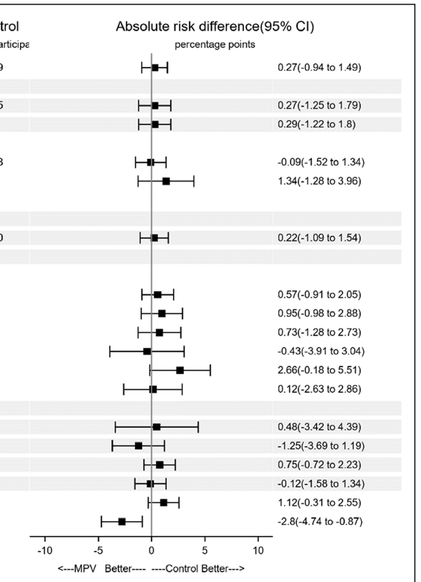
| | Before matching | | | Matched cohort | | |
|---|---|---|---|---|---|---|
| | (MPV) group | Controls | | (MPV) group | Controls | |
| | *N=1729* | *N=63281* | P-value | *N=1459* | *N=1459* | SMD* |
| Median age (IQR) years | 69.4 (60.6,75.5) | 57.1 (43.8,68.9) | <.0001 | 69.4 (60.7,75.3) | 69.6 (60.6,75.1) | -0.0014 |
| Male sex, % | 89.71% | 73.01% | <.0001 | 91.84% | 91.84% | 0 |
| Race, % | | | <.0001 | | | 0 |
| White | 71.14% | 54.45% | | 75.94% | 75.94% | |
| Black | 21.57% | 19.90% | | 20.49% | 20.49% | |
| Other/unknown | 7.29% | 25.64% | | 3.56% | 3.56% | |
| Mean Body mass index, kg/m2 | 30.6 (6.3) | 30.7 (6.6) | 0.79 | 31.1 (6.3) | 30.9 (6.1) | -0.0333 |
| Median (IQR) Charlson Comorbidity Index score | 2 (1,4) | 1 (0,2) | <.0001 | 2 (1,4) | 2 (1,4) | 0 |
| Comorbidities at or before baseline, % | | | | | | |
| Diabetes | 47.95% | 25.21% | <.0001 | 46.06% | 44.69% | -0.0275 |
| Cardiovascular disease | 58.42% | 28.76% | <.0001 | 57.23% | 50.17% | -0.1419 |
| Chronic kidney disease | 26.32% | 10.69% | <.0001 | 23.99% | 21.18% | -0.0672 |
| Chronic lung disease | 27.18% | 13.44% | <.0001 | 26.53% | 24.81% | -0.0392 |
| Cancer diagnosis | 25.04% | 13.48% | <.0001 | 23.92% | 26.39% | 0.0569 |
| Vaccination status at baseline | | | <.0001 | | | 0 |
| Unvaccinated or primary series incomplete | 14.75% | 42.75% | | 14.19% | 14.19% | |
| Primary series completed | 22.79% | 24.75% | | 22.00% | 22.00% | |
| Primary series PLUS booster | 62.46% | 32.50% | | 63.81% | 63.81% | |
| Geographical location, % | | | <.0001 | | | 0.0921 |
| City/Town | 6.48% | 5.17% | | 6.72% | 6.58% | |
| Small Town/Rural | 5.03% | 3.36% | | 5.28% | 3.56% | |
| Urban | 74.09% | 69.37% | | 74.23% | 73.41% | |
| Unknown | 14.40% | 22.10% | | 13.78% | 16.45% | |
| Median number of days (IQR) to first prescription | 0 (0,1) | | | 0 (0,1) | | 0 |
| Symptomatic at baseline, % | 82.07% | 55.32% | <.0001 | 82.04% | 65.39% | -0.3853 |
| Asymptomatic at baseline, % | 17.93% | 44.68% | <.0001 | 17.96% | 34.61% | 0.3853 |

**Acknowledgments:** This study used data created by the VA COVID-19 Shared Data Resource and resources and facilities of the VA Informatics and Computing Infrastructure. It is also supported by resources and the use of facilities at the VA Pittsburgh Healthcare System and the central data repositories maintained by the VA Information Resource Center. The views expressed in this article are those of the authors and do not necessarily reflect the position or policy of the U.S. Department of Veterans Affairs or the funding agencies.

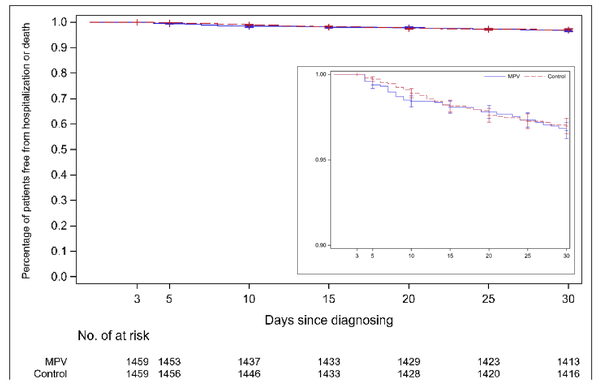
## RESULTS (contd.)

Incidence of hospitalization or death within 30 days and absolute risk difference among patients who received Molnupiravir and controls.

| Subgroup | MPV no. of events | Control no. of participe | Absolute risk difference(95% CI) percentage points |
|---|---|---|---|
| **Total** | 48/1459 | 44/1459 | 0.27(-0.94 to 1.49) |
| **Age** | | | |
| >60 years | 44/1115 | 41/1115 | 0.27(-1.25 to 1.79) |
| <=60 years | 4/344 | 3/344 | 0.29(-1.22 to 1.8) |
| **Race** | | | |
| White | 36/1108 | 37/1108 | -0.09(-1.52 to 1.34) |
| Black | 11/299 | 7/299 | 1.34(-1.28 to 3.96) |
| Others/unknown | 1/52 | 0/52 | |
| **Sex** | | | |
| Male | 47/1340 | 44/1340 | 0.22(-1.09 to 1.54) |
| Female | 1/119 | 0/119 | |
| **Risk factors** | | | |
| Obese(BMI>30) | 18/700 | 14/700 | 0.57(-0.91 to 2.05) |
| Diabetes | 27/672 | 20/652 | 0.95(-0.98 to 2.88) |
| Cardiovascular disease | 38/835 | 28/732 | 0.73(-1.28 to 2.73) |
| Chronic kidney disease | 20/350 | 19/309 | -0.43(-3.91 to 3.04) |
| Chronic lung disease(COPD) | 21/387 | 10/362 | 2.66(-0.18 to 5.51) |
| Cancer diagnosis | 14/349 | 15/385 | 0.12(-2.63 to 2.86) |
| **Vaccination status(no prior infection)** | | | |
| Unvaccinated or primary series incomplete | 10/207 | 9/207 | 0.48(-3.42 to 4.39) |
| Primary series complete, no booster | 7/321 | 11/321 | -1.25(-3.69 to 1.19) |
| Primary series complete, booster | 31/931 | 24/931 | 0.75(-0.72 to 2.23) |
| Primary +/- booster, last dose >3 months ago | 35/1148 | 29/915 | -0.12(-1.58 to 1.34) |
| **Symptomatic at baseline** | 46/1197 | 26/954 | 1.12(-0.31 to 2.55) |
| **Asymptomatic at baseline** | 2/262 | 18/505 | -2.8(-4.74 to -0.87) |




Kaplan-Meier curves depicting percentage of patients without hospitalization or death among those treated with Molnupiravir and untreated controls. P=0.67.




## CONCLUSIONS

- MPV was not associated with a significant reduction in hospitalization or death within 30 days of COVID-19 diagnosis overall.
- A subgroup of patients presenting without symptoms experienced a benefit.

RESEARCH POSTER PRESENTATION DESIGN © 2015
www.PosterPresentations.com