Lagevrio Significantly Reduces COVID-19 Hospitalization and Death

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Key Findings:

- In this unadjusted analysis, patients 65 years of age and older with one or more comorbidities and treated with Lagevrio (molnupiravir) have significant decreases in rates of hospitalization (1.86% vs. 3.00%) and death (0.20% vs. 0.42%) compared to those not treated with Lagevrio or Paxlovid.

Recommended Actions

- In line with the FDA's Emergency Use Authorization,[1] clinicians should consider Lagevrio as an alternative treatment to Paxlovid for older patients when Paxlovid and Remdesivir are unavailable or clinically inappropriate.
- Patients diagnosed with COVID-19 should follow up with their healthcare provider to access antiviral treatments, including Lagevrio, if they are not eligible for Paxlovid.

In December 2021, the FDA issued an emergency use authorization for the antiviral drug Lagevrio (molnupiravir) to reduce the severity of symptoms and hospitalization in adults with mild to moderate cases of COVID-19 for whom other FDA-approved treatment options (Paxlovid or remdesivir) are not accessible or clinically appropriate. We studied 1,666,083 cases of COVID-19 in adults between December 23, 2021, and July 31, 2022. Of these cases, Lagevrio was prescribed nearly nine times less frequently than Paxlovid (21,615 Lagevrio treatments vs. 191,848 Paxlovid treatments). We also found that the population treated with Lagevrio was older on average compared to the population prescribed Paxlovid (Figure 1).

Age Distribution of Treatment Groups

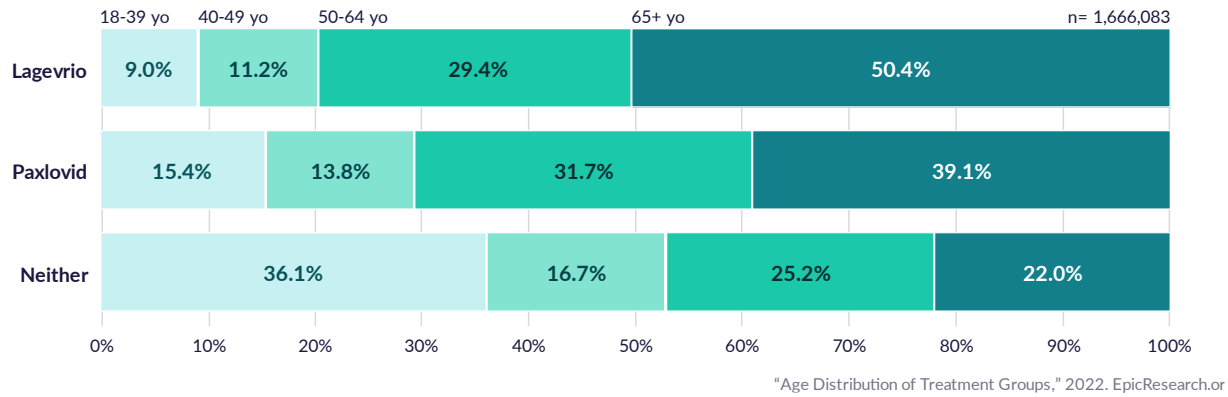

Figure 1. The age distribution for patients prescribed Lagevrio, Paxlovid, or neither.

To identify how Lagevrio has affected hospital admissions and deaths in COVID-19 patients, we looked at cases involving patients who were 18 and older and had at least one comorbidity and whether they were hospitalized two or more days after their initial COVID-19 diagnosis. When comparing the population that received Lagevrio to the patients who received neither Lagevrio nor Paxlovid, we found decreases in hospital admissions and deaths for the Lagevrio population within each age group (Figure 2). The largest differences were found in the 65+ age group where we found a 38.12% reduced admission rate and a 51.96% reduced death rate compared to those who took neither Lagevrio nor Paxlovid. Patients who were hospitalized less than two days after their COVID-19 diagnosis were excluded because they may not have had time to initiate treatment to prevent hospitalization.

Hospitalization and Death Rates Among Patients with Lagevrio vs. Without Lagevrio or Paxlovid

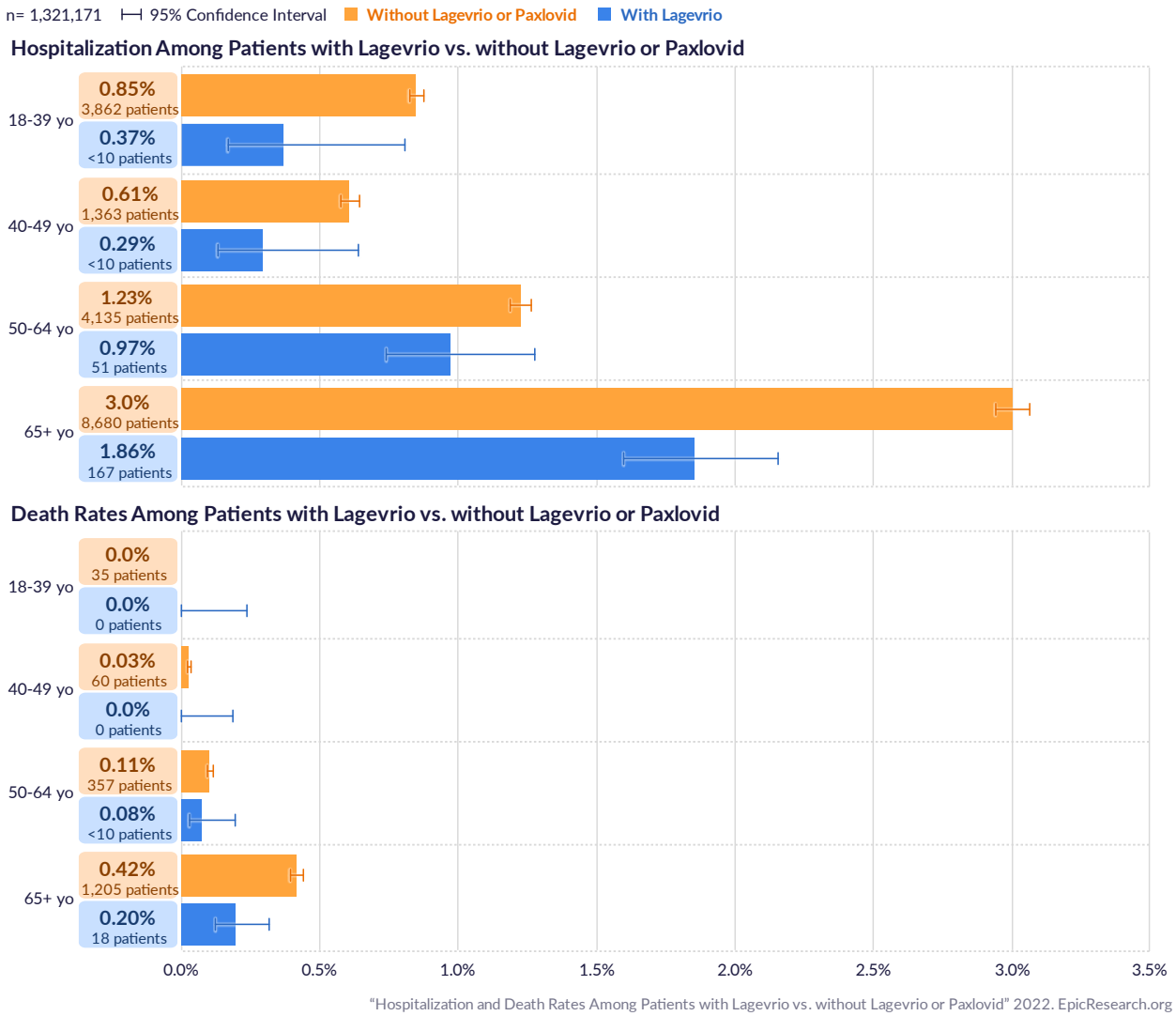

Figure 2: Hospital admission and death rates for patients with at least one comorbidity treated with Lagevrio or with neither Lagevrio nor Paxlovid broken out by age group. Significant differences exist in the 65+ age group for both measures.

This study did not evaluate or adjust for vaccination status, comorbidity type, or socioeconomic status, which might also affect a patient's likelihood of hospitalization or death from COVID-19.[2,3]

Paxlovid remains the most widely used and efficacious antiviral drug when treating COVID-19.[4,5] However, this analysis suggests Lagevrio may be a good alternative to reduce the risk of COVID-19 hospitalization or death for patients 65 and older who have comorbidities but are not eligible for Paxlovid.

These data come from Cosmos, a HIPAA-defined Limited Data Set of more than 167 million patients from 181 Epic organizations including 1,063 hospitals and more than 22,500 clinics, serving patients in all 50 states and Lebanon. This study was completed by two teams that worked independently, each composed of a clinician and research scientists. The two teams came to similar conclusions.

References

1. Fact Sheet for Patients and Caregivers Emergency Use Authorization (EUA) Of LAGEVRIO™ (molnupiravir) capsules For Coronavirus Disease 2019 (COVID-19). (n.d.). Retrieved October 20, 2022, from https://www.fda.gov
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3. Lily Rubin-Miller MPH, Christopher Alban MD, Sean Sullivan MS, Samantha Artiga MHSA. Covid-19 racial disparities in testing, infection, hospitalization, and death: Analysis of Epic Patient Data. Epic Research. https://epicresearch.org/articles/covid-19-racial-disparities-in-testing-infection-hospitalization-death. Accessed November 11, 2022.
4. Gottlieb RL, Vaca CE, Paredes R, et al. Early Remdesivir to Prevent Progression to Severe Covid-19 in Outpatients. *N Engl J Med*. 2022;386(4):305-315. doi:10.1056/NEJMoa2116846
5. Jayk Bernal A, Gomes da Silva MM, Musungaie DB, et al. Molnupiravir for Oral Treatment of Covid-19 in Nonhospitalized Patients. *N Engl J Med*. 2022;386(6):509-520. doi:10.1056/NEJMoa2116044

Data Definitions

Term	Definition
Paxlovid Treatment	A medication order with RxNorm code of 2587898 or 2587899
Lagevrio Treatment	A medication order with RxNorm code of 2587901
Lagevrio Population	Patients who contracted COVID, were not admitted on the initial or second day of COVID infection (from the Adjusted COVID Start Date) and received a prescription for Lagevrio. Patients who received a Lagevrio or Paxlovid prescription outside of the first five days of the COVID infection were excluded. Patients who received a Lagevrio prescription the day prior to a COVID admission or later are not in this population.
No Anti-Viral Population	Patients who contracted COVID, were not admitted on the Adjusted COVID Start Date or the following day and were not treated with Lagevrio or Paxlovid. Patients who received a Lagevrio or Paxlovid prescription outside of the first five days of the COVID infection were

	excluded. Patients who received a Lagevrio prescription the day prior to a COVID admission or later are included in this population.
Adjusted COVID Start Date	The earlier date of either the initial COVID diagnosis, a Paxlovid prescription, or a Lagevrio prescription that indicates the start of a COVID infection.
Outcome: COVID-19 Hospital Admission	Hospital admission within 14 days of the Adjusted COVID Start Date, with an encounter diagnosis mapped to ICD-10-CM code U07.1 or SNOMED CT code 840539006 (COVID-19). Patients already hospitalized on the Adjusted COVID Start Date or admitted on the initial or subsequent day of the infection are excluded.
Outcome: Death	Death within 30 days of the Adjusted COVID Start Date after being admitted to the hospital for COVID-19, or a discharge disposition containing "Expired." Deaths after 30 days are assumed to be unrelated and not counted toward the outcome.
Comorbidity: ADHD	A problem list problem mapped to ICD-10-CM code F90* prior to the Adjusted COVID Start Date and either added within the year prior to the Adjusted COVID Start Date or resolved after the Adjusted COVID Start Date or currently active.
Comorbidity: Alcoholic Liver Disease	A problem list problem mapped to ICD-10-CM code K70* prior to the Adjusted COVID Start Date and either added within the year prior to the Adjusted COVID Start Date or resolved after the Adjusted COVID Start Date or currently active.
Comorbidity: Asthma	A problem list problem mapped to ICD-10-CM code J45* prior to the Adjusted COVID Start Date and either added within the year prior to the Adjusted COVID Start Date or resolved after the Adjusted COVID Start Date or currently active.
Comorbidity: Autoimmune Hepatitis	A problem list problem mapped to ICD-10-CM code K75.4 or SNOMED-CT code 408335007 prior to the Adjusted COVID Start Date and either added within the year prior to the Adjusted COVID Start Date or resolved after the Adjusted COVID Start Date or currently active.
Comorbidity: Bronchiectasis	A problem list problem mapped to ICD-10-CM code J47, J47.0, J47.1, J47.9, Q33.3, or Q89.3 or SNOMED-CT code 12295008 prior to the Adjusted COVID Start Date and either added within the year prior to the Adjusted COVID Start Date or resolved after the Adjusted COVID Start Date or currently active.
Comorbidity: CAD	A problem list problem mapped to ICD-10-CM code I25.1*, I25.7*, I25.81*, I25.82, or I25.83 or SNOMED-CT code 63739005, 429673002, 445512009, 67682002, or 53741008 prior to the Adjusted COVID Start Date and either added within the year prior to the Adjusted COVID Start Date or resolved after the Adjusted COVID Start Date or currently active.
Comorbidity: Cancer	A problem list problem mapped to ICD-10-CM code C00-C96 or D00-D09 or D37-D49 prior to the Adjusted COVID Start Date and either added within the year prior to the Adjusted COVID Start Date or resolved after the Adjusted COVID Start Date or currently active.

Comorbidity: Cardiomyopathy	A problem list problem mapped to ICD-10-CM code I42*, I43, A36.81, B33.24, or I25.5 or SNOMED-CT 85898001 and not mapped to SNOMED 281666001, 312850006, or 765205004 prior to the Adjusted COVID Start Date and either added within the year prior to the Adjusted COVID Start Date or resolved after the Adjusted COVID Start Date or currently active.
Comorbidity: Cerebral Palsy	A problem list problem mapped to ICD-10-CM code G80* prior to the Adjusted COVID Start Date and either added within the year prior to the Adjusted COVID Start Date or resolved after the Adjusted COVID Start Date or currently active.
Comorbidity: Cerebrovascular Disease	A problem list problem mapped to SNOMED-CT code 62914000 prior to the Adjusted COVID Start Date and either added within the year prior to the Adjusted COVID Start Date or resolved after the Adjusted COVID Start Date or currently active.
Comorbidity: Chronic Kidney Disease	A problem list problem mapped to ICD-10-CM code I12.9, I13.0, I13.10, N18.1, N18.2, N18.3, N18.4, or N18.9 or SNOMED-CT code 431855005, 431856006, 433144002, or 431857002 prior to the Adjusted COVID Start Date and either added within the year prior to the Adjusted COVID Start Date or resolved after the Adjusted COVID Start Date or currently active.
Comorbidity: Chronic Kidney Disease in Pregnancy	A problem list problem mapped to ICD-10-CM code O10.2, O10.21, O10.212, O10.213, O10.219, O10.22, O10.23, O10.3, O10.31, O10.311, O10.312, O10.313, O10.319, O10.32, O10.33 prior to the Adjusted COVID Start Date and either added within the year prior to the Adjusted COVID Start Date or resolved after the Adjusted COVID Start Date or currently active.
Comorbidity: Cirrhosis	A problem list problem mapped to ICD-10-CM code K74* or K70.3 or SNOMED-CT code 19943007 prior to the Adjusted COVID Start Date and either added within the year prior to the Adjusted COVID Start Date or resolved after the Adjusted COVID Start Date or currently active.
Comorbidity: Congenital Malformations	A problem list problem mapped to ICD-10-CM code Q00*-Q89* prior to the Adjusted COVID Start Date and either added within the year prior to the Adjusted COVID Start Date or resolved after the Adjusted COVID Start Date or currently active.
Comorbidity: COPD	A problem list problem mapped to ICD-10-CM code J43* or J44* or SNOMED-CT code 1364500, 45145000, 185086009, 425748003, or 195951007 and “bronchiolitis” not included in the diagnosis name prior to the Adjusted COVID Start Date and either added within the year prior to the Adjusted COVID Start Date or resolved after the Adjusted COVID Start Date or currently active.
Comorbidity: Current or Former Smoker	Patients who have ever reported their smoking status to be “Light Smoker,” “Heavy Tobacco Smoker,” “Every Day,” “Current Every Day Smoker,” “Heavy Smoker,” “Light Tobacco Smoker,” “Current Some Day Smoker,” “Smoker, Current Status Unknown,” “Some Days,” “Former Smoker,” or “Former”.

Comorbidity: Cystic Fibrosis	A problem list problem mapped to ICD-10-CM code E84* prior to the Adjusted COVID Start Date and either added within the year prior to the Adjusted COVID Start Date or resolved after the Adjusted COVID Start Date or currently active.
Comorbidity: Dementia	A problem list problem mapped to ICD-10-CM code F01*, F02*, F03*, G30*, or G31.0* prior to the Adjusted COVID Start Date and either added within the year prior to the Adjusted COVID Start Date or resolved after the Adjusted COVID Start Date or currently active.
Comorbidity: Heart Failure	A problem list problem mapped to ICD-10-CM code I50*, I11.0, I13.0, or I13.2 or SNOMED-CT code 56675007 and not mapped to ICD-10-CM I50.21, I50.31, I50.41, or I50.811 and not mapped to SNOMED-CT 84114007 prior to the Adjusted COVID Start Date and either added within the year prior to the Adjusted COVID Start Date or resolved after the Adjusted COVID Start Date or currently active.
Comorbidity: HIV	A problem list problem mapped to ICD-10-CM code B20* prior to the Adjusted COVID Start Date and either added within the year prior to the Adjusted COVID Start Date or resolved after the Adjusted COVID Start Date or currently active.
Comorbidity: Immunosuppressive Medications	Documentation of a prescription or administration of an immunosuppressive medication as identified by mapping to RxNorm codes, pharmaceutical classes or subclasses with route- based exclusions where the medication was initiated prior to the Adjusted COVID Start Date and either started or ended within the three months prior to the Adjusted COVID Start Date.
Comorbidity: Intellectual and Developmental Disabilities	A problem list problem mapped to ICD-10-CM code F70*, F71*, F72*, F73*, F78*, F79*, F80*, F82*, F84*, F88*, or F89* prior to the Adjusted COVID Start Date and either added within the year prior to the Adjusted COVID Start Date or resolved after the Adjusted COVID Start Date or currently active.
Comorbidity: Interstitial Lung Disease	A problem list problem mapped to SNOMED-CT code 233703007 prior to the Adjusted COVID Start Date and either added within the year prior to the Adjusted COVID Start Date or resolved after the Adjusted COVID Start Date or currently active.
Comorbidity: Learning Disabilities	A problem list problem mapped to ICD-10-CM code F81* prior to the Adjusted COVID Start Date and either added within the year prior to the Adjusted COVID Start Date or resolved after the Adjusted COVID Start Date or currently active.
Comorbidity: Limitation of Activities	A problem list problem mapped to ICD-10-CM code Z73.6 prior to the Adjusted COVID Start Date and either added within the year prior to the Adjusted COVID Start Date or resolved after the Adjusted COVID Start Date or currently active.
Comorbidity: Mood Disorders and Depression	A problem list problem mapped to ICD-10-CM code F30*, F31*, F32*, F33*, F34*, F39*, F06.3*, F10.14, F10.24, F10.94, F11.14, F11.24, F11.94, F13.14, F13.24, F13.94, F14.14, F14.24, F14.94, F15.14, F15.24, F15.94, F16.14, F16.24, F16.94, F18.14, F18.24, F18.94, F19.14, F19.24, or F19.94 prior to the Adjusted COVID Start Date and either added

	within the year prior to the Adjusted COVID Start Date or resolved after the Adjusted COVID Start Date or currently active.
Comorbidity: Non-alcoholic Liver Disease	A problem list problem mapped to ICD-10-CM code K76.0* or SNOMED-CT code 197315008 prior to the Adjusted COVID Start Date and either added within the year prior to the Adjusted COVID Start Date or resolved after the Adjusted COVID Start Date or currently active.
Comorbidity: Obesity	A patient whose most recent BMI prior to or on the Adjusted COVID Start Date was 30 or above.
Comorbidity: Pregnancy Active or within Prior 42 Days	Documentation that a patient had an active pregnancy within the 42 days prior to the Adjusted COVID Start Date.
Comorbidity: Primary Immunodeficiencies	A problem list problem mapped to ICD-10-CM code B20, D71, D80.0, D80.1, D80.2, D80.3, D80.4, D80.5, D80.6, D80.7, D80.8, D80.9, D81.0, D81.1, D81.2, D81.3, D81.4, D81.5, D81.6, D81.7, D81.8, D81.81, D81.810, D81.819, D81.89, D82.0, D82.1, D82.2, D82.3, D82.8, D82.9, D83.0, D83.1, D83.2, D83.8, D83.9, D84.0, D84.1, D84.8, or D84.9 prior to the Adjusted COVID Start Date and either added within the year prior to the Adjusted COVID Start Date or resolved after the Adjusted COVID Start Date or currently active.
Comorbidity: Pulmonary Arterial Hypertension	A problem list problem mapped to ICD-10-CM code I27* or SNOMED-CT code 11399002 prior to the Adjusted COVID Start Date and either added within the year prior to the Adjusted COVID Start Date or resolved after the Adjusted COVID Start Date or currently active.
Comorbidity: Pulmonary Embolism	A problem list problem mapped to ICD-10-CM code I26*, I27.27, or Z86.711 prior to the Adjusted COVID Start Date and either added within the year prior to the Adjusted COVID Start Date or resolved after the Adjusted COVID Start Date or currently active.
Comorbidity: Schizophrenia Spectrum	A problem list problem mapped to ICD-10-CM code F20*, F21*, F22*, F23*, F24*, F25*, F28* or F29* prior to the Adjusted COVID Start Date and either added within the year prior to the Adjusted COVID Start Date or resolved after the Adjusted COVID Start Date or currently active.
Comorbidity: Sickle Cell Disease	A problem list problem mapped to ICD-10-CM code D57* prior to the Adjusted COVID Start Date and either added within the year prior to the Adjusted COVID Start Date or resolved after the Adjusted COVID Start Date or currently active.
Comorbidity: Spinal Cord Injuries	A problem list problem mapped to ICD-10-CM code S14*, S24*, or S34* prior to the Adjusted COVID Start Date and either added within the year prior to the Adjusted COVID Start Date or resolved after the Adjusted COVID Start Date or currently active.
Comorbidity: Substance Use Disorders	A problem list problem mapped to ICD-10-CM code F10*, F11*, F12*, F13*, F14*, F15*, F16*, F17*, F18*, or F19* prior to the Adjusted COVID Start Date and either added within the year prior to the Adjusted COVID Start Date or resolved after the Adjusted COVID Start Date or currently active.

Comorbidity: Thalassemia	A problem list problem mapped to ICD-10-CM code D56* prior to the Adjusted COVID Start Date and either added within the year prior to the Adjusted COVID Start Date or resolved after the Adjusted COVID Start Date or currently active.
Comorbidity: Tuberculosis	A problem list problem mapped to ICD-10-CM code A15*, A17*, A18*, or A19* prior to the Adjusted COVID Start Date and either added within the year prior to the Adjusted COVID Start Date or resolved after the Adjusted COVID Start Date or currently active.
Comorbidity: Type 1 Diabetes	A problem list problem mapped to ICD-10-CM code E10* or SNOMED-CT code 420868002 or 46635009 and not also mapped to ICD-10-CM code O24.4* or SNOMED-CT code 11687002 prior to the Adjusted COVID Start Date and either added within the year prior to the Adjusted COVID Start Date or resolved after the Adjusted COVID Start Date or currently active.
Comorbidity: Type 2 Diabetes	A problem list problem mapped to ICD-10-CM code E11* or SNOMED-CT code 422014003 or 44054006 and not also mapped to ICD-10-CM code O24.4* or E10* or SNOMED-CT code 11687002, 420868002, or 46635009 prior to the Adjusted COVID Start Date and either added within the year prior to the Adjusted COVID Start Date or resolved after the Adjusted COVID Start Date or currently active.

Table 1: Age Distribution of Treatment Groups

Treatment	Total cases	18-39	40-49	50-64	65+
Neither	1452620	524586	242990	365684	319360
Paxlovid	191848	29592	26531	60788	74937
Lagevrio	21615	1955	2420	6350	10890

Table 2: Hospitalization and Death Rates Among Patients with and without Lagevrio Treatment

Summary Category	Medication	Percent admitted to hospital (95% confidence interval)	Percent who died (95% confidence interval)
18-39 Covid Adults 1+ Comorbidities	Lagevrio (n=1611)	0.37% (0.17% - 0.81%)	0.00% (0.00% - 0.24%)
18-39 Covid Adults 1+ Comorbidities	Neither (n=454054)	0.85% (0.82% - 0.88%)	0.01% (0.01% - 0.01%)
40-49 Covid Adults 1+ Comorbidities	Lagevrio (n=2035)	0.29% (0.14% - 0.64%)	0.00% (0.00% - 0.19%)
40-49 Covid Adults 1+ Comorbidities	Neither (n=223163)	0.61% (0.58% - 0.64%)	0.03% (0.02% - 0.03%)
50-64 Covid Adults 1+ Comorbidities	Lagevrio (n=5241)	0.97% (0.74% - 1.28%)	0.08% (0.03% - 0.20%)

50-64 Covid Adults 1+ Comorbidities	Neither (n=336870)	1.23% (1.19% - 1.27%)	0.11% (0.10% - 0.12%)
65+ Covid Adults 1+ Comorbidities	Lagevrio (n=8992)	1.86% (1.60% - 2.16%)	0.20% (0.13% - 0.32%)
65+ Covid Adults 1+ Comorbidities	Neither (n=289205)	3.00% (2.94% - 3.06%)	0.42% (0.39% - 0.44%)