

Paxlovid Significantly Reduces COVID-19 Hospitalizations and Deaths

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Key Findings:

- In an unadjusted analysis, patients who are prescribed Paxlovid are about 2 times less likely to be hospitalized for COVID-19 and about four times less likely to die from COVID-19 than those who might be eligible for Paxlovid but did not receive a Paxlovid prescription.
- Fully vaccinated patients over age 50 who were treated with Paxlovid are about three times less likely to be hospitalized than those not treated with Paxlovid.
- Patients aged 40-49 are about two times less likely to be hospitalized when treated with Paxlovid, although results vary depending on vaccination status.

The anti-viral treatment Paxlovid received FDA emergency use approval in December 2021 to reduce the likelihood of severe COVID-19 disease. In the U.S., patients are eligible for Paxlovid if they are determined to be high risk for complications from COVID-19.¹ We studied 567,560 patients who could have received Paxlovid treatment between March 1, 2022, and August 1, 2022. Of these, 146,256 received Paxlovid and 421,304 did not. In an unadjusted analysis, patients who did not receive Paxlovid were two times more likely to be hospitalized and four times more likely to die compared to those who did receive Paxlovid (Figure 1).

Lower Admission Rate and Death Rate with Paxlovid Treatment

Mar 1 – Aug 1, 2022 n=567,560

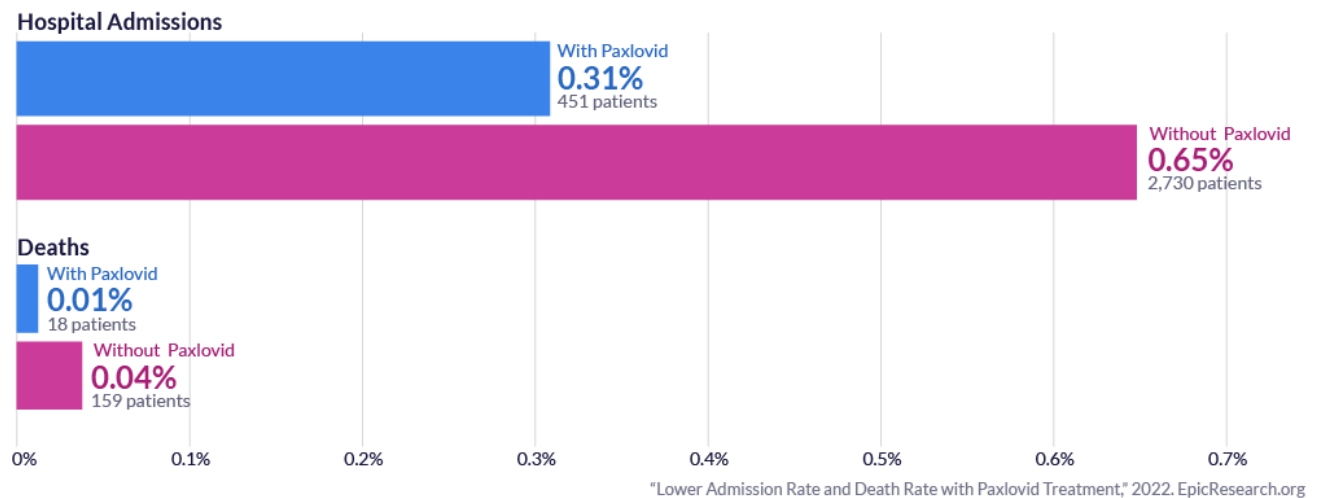


Figure 1. Overall unadjusted COVID-19 hospitalization and death rates by Paxlovid use from March 1, 2022, through August 1, 2022.

When stratified by age, patients aged 65+ are 2.5 times more likely to be hospitalized if not treated with Paxlovid (Figure 2).

Rates of Hospitalization and Death by Age Group – All Vaccination Statuses

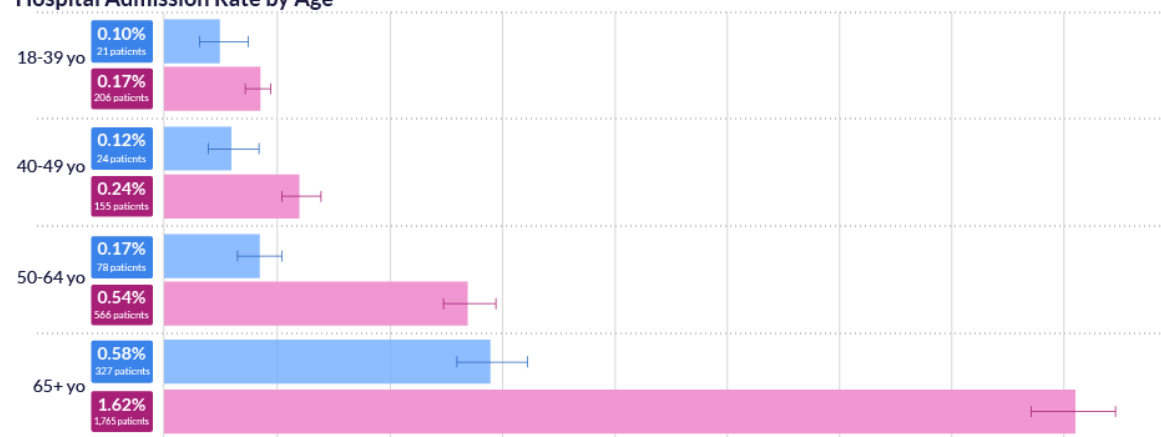
Mar 1 – Aug 1, 2022 n=547,501

95% Confidence Interval

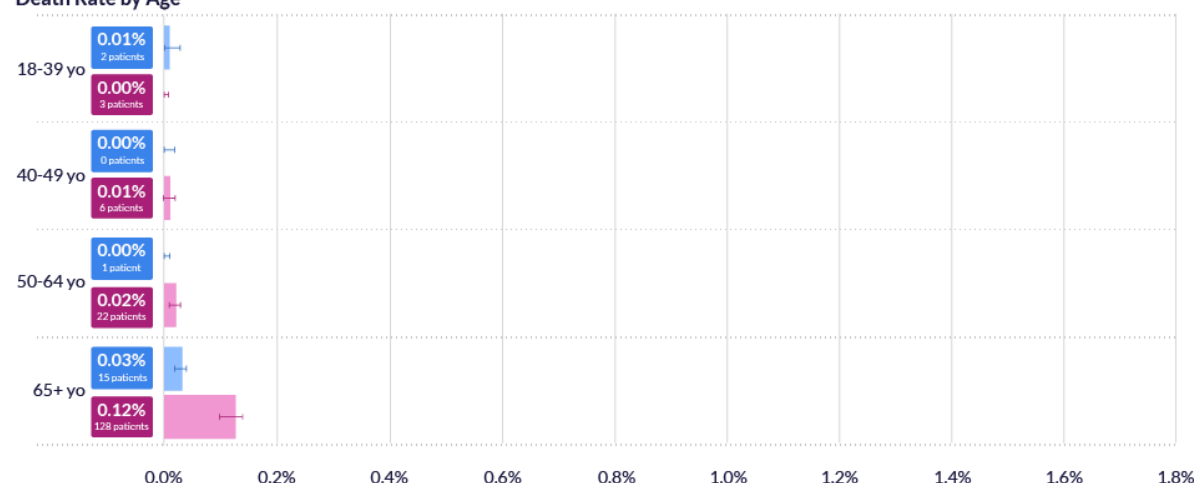
With Paxlovid

Without Paxlovid

Hospital Admission Rate by Age



Death Rate by Age



"Rates of Hospitalization and Death by Age Group – All Vaccination Statuses," 2022. EpicResearch.org

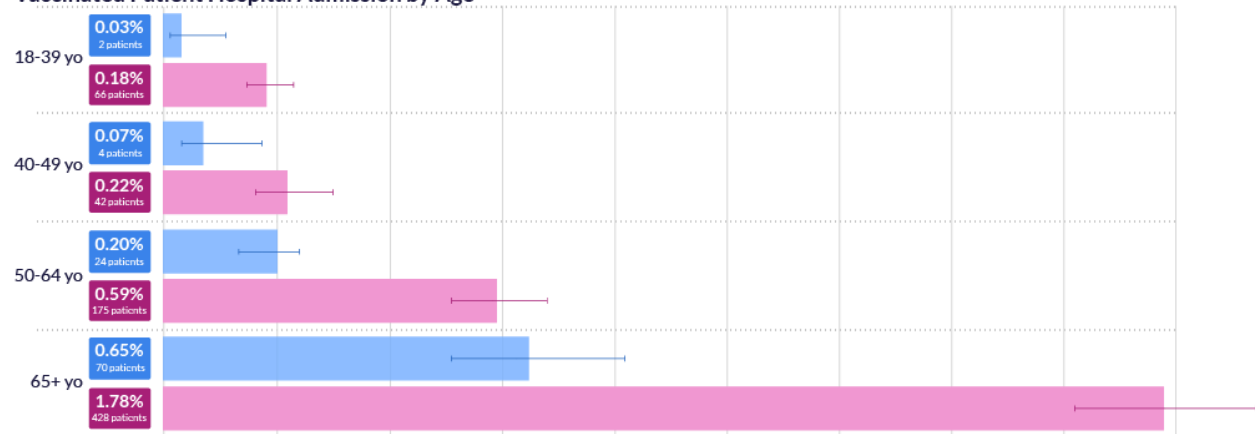
Figure 2. Unadjusted age distribution of COVID-19 hospitalization and death rates by Paxlovid use from March 1, 2022, through August 1, 2022. All vaccinated, boosted, and unvaccinated patients are included. No adjustment for vaccination or comorbidity is included.

As previously published, having a full series of COVID-19 vaccination and a booster decreases risk of hospitalization and death from COVID-19. Figures 3 and 4 evaluate whether being treated with Paxlovid adds benefit to patients already vaccinated with a primary series and/or boosted. Figure 3 includes patients with a complete COVID-19 series without booster and Figure 4 includes patients with the complete series and a single booster. At the time of this study, the EUA allowed only immunocompromised patients to be eligible for two boosters. There were too few patients with two boosters to meaningfully study a difference in outcomes for that group.

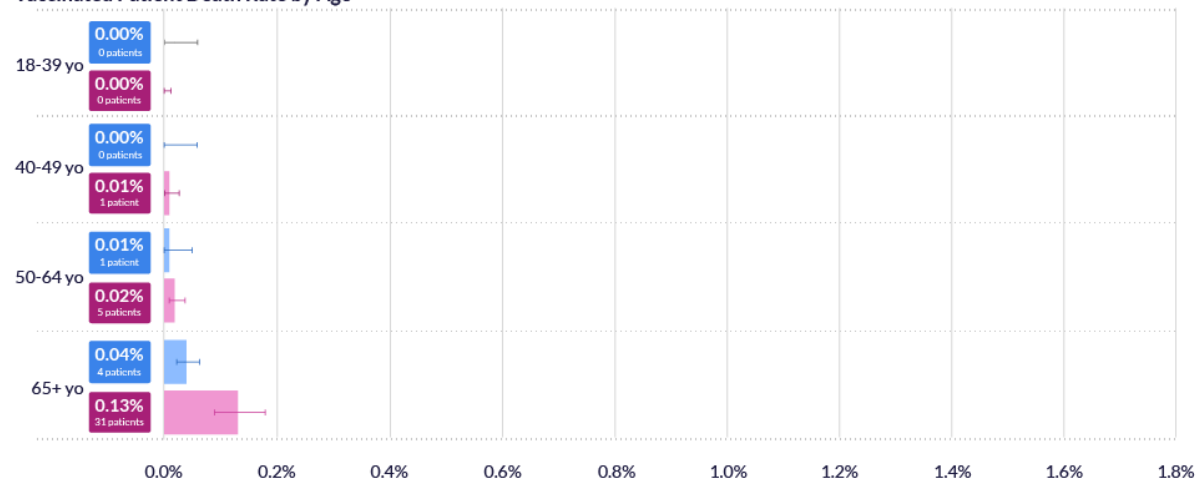
Rates of Hospitalization and Death Among Patients with and Without Paxlovid Treatment – Fully Vaccinated Patients

Mar 1 – Aug 1, 2022 n=144,644 95% Confidence Interval With Paxlovid Without Paxlovid

Vaccinated Patient Hospital Admission by Age



Vaccinated Patient Death Rate by Age



"Rates of Hospitalization and Death Among Patients With and Without Paxlovid Treatment – Fully Vaccinated Patients," 2022. EpicResearch.org

Figure 3. Unadjusted age distribution of COVID-19 hospitalization and death rates by Paxlovid use from March 1, 2022, through August 1, 2022, for patients with a complete primary series of COVID-19 vaccination but no documented booster vaccination.

Rates of Hospitalization and Death Among Patients with and Without Paxlovid Treatment – Vaccinated & Boosted Patients

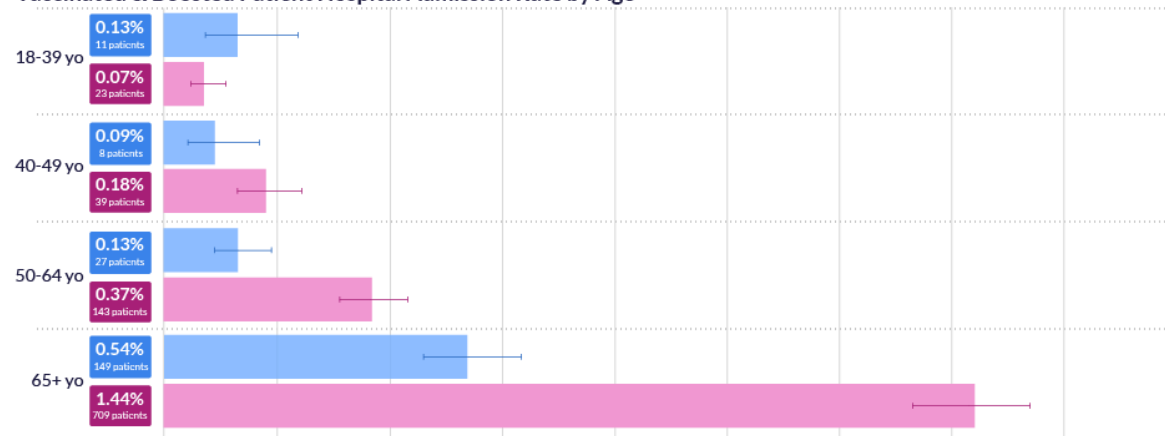
Mar 1 – Aug 1, 2022 n=206,189

95% Confidence Interval

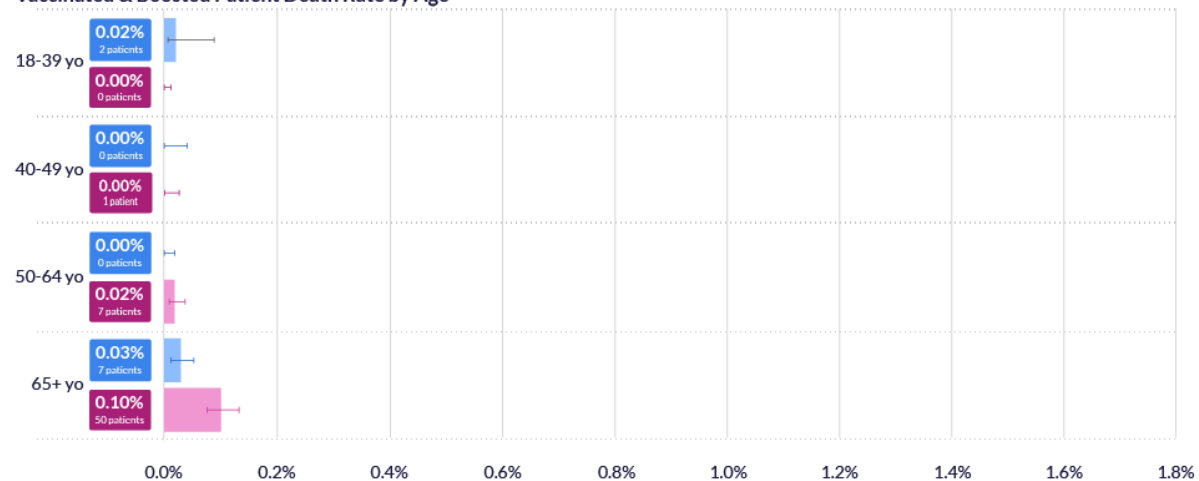
With Paxlovid

Without Paxlovid

Vaccinated & Boosted Patient Hospital Admission Rate by Age



Vaccinated & Boosted Patient Death Rate by Age



"Rates of Hospitalization and Death Among Patients With and Without Paxlovid Treatment – Vaccinated & Boosted Patients," 2022. EpicResearch.org

Figure 4. Unadjusted age distribution of COVID-19 hospitalization and death rates by Paxlovid use from March 1, 2022, through August 1, 2022, for patients with a complete primary series and one COVID-19 vaccination booster.

In our unadjusted analysis, for patients aged 50+ who have received a complete primary series of a COVID-19 vaccination with or without a booster, there is a statistically significant difference in the hospitalization rate for those who received Paxlovid and those who didn't. This remains true regardless of vaccination status. We did not evaluate the effect of race and ethnicity or other potential confounders in this analysis. Patients aged 40-49 show reduced hospitalization rates, but when broken down by vaccination status, the difference in rates is not statistically significant.

This initial analysis did not control for specific comorbidities other than stratifying by age and vaccination status. Patients who were hospitalized within one day of their COVID-19 diagnoses were excluded because they might not have had time to initiate Paxlovid treatment to prevent hospitalization. Patients on other antiviral medications or who took Paxlovid in the 90 days prior to their relevant COVID diagnosis infection or six or more days after their COVID diagnosis were also excluded.

An individual's likelihood of contracting COVID-19 and the severity of the individual's illness is dependent on many factors including COVID-19 variant and whether the individual has had COVID-19 in the past. Additional analysis is planned to adjust for risk factors, such as underlying conditions and race/ethnicity, and will be made available on Epic Research when published. This further analysis is in collaboration with the CDC.

These data come from Cosmos, a HIPAA-defined Limited Data Set of more than 163 million patients from 173 Epic organizations including over 1,000 hospitals and over 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. To view the full data definitions and tables used in this study, please download the PDF version on EpicResearch.org.

References

1. National Institutes of Health. COVID-19 Treatment Guidelines: Ritonavir-Boosted Nirmatrelvir (Paxlovid). <https://www.covid19treatmentguidelines.nih.gov/therapies/antiviral-therapy/ritonavir-boosted-nirmatrelvir--paxlovid-/>. Accessed September 15, 2022.

Data Definitions

Term	Definition
Patients Eligible for Paxlovid	Patients who meet the following criteria: - First COVID admission must be 2 or more days after the Index Event - Patient must be 12+ years old - Patient lives in a US state/territory with 50+ COVID hospitalizations in the dataset - Index Event occurs in a valid encounter type - Patient has had at least 3 face-to-face encounters in the 5 years before the index event Patients were excluded if they met any of the following criteria: - Prescribed Bebtelovimab, Lagevrio, or remdesiveir within 30 days of the Index Event - Prescribed Evusheld 0 to 30 days after the Index Event - Prescribed Paxlovid up to 90 days before or 6 to 30 days after the Index Event - Pregnant or has a documented pregnancy up to 40 days before the Index Event
Index Event / COVID Incidence	Earliest date of documentation of a patient's distinct COVID-19 infection. If this is the patient's first COVID infection that could be a COVID diagnoses or a

	positive test (antigen or PCR). If it is a reinfection then a positive test is required (antigen or PCR).
COVID-19 Admissions	An inpatient admission that occurs 0 to 28 days after the patient's Index Event and has a COVID-19 diagnosis (ICD-CM: U07.1; SNOMED CT: 840539006)
Paxlovid Prescription	Valid Paxlovid prescriptions must meet the following: Occur 0 to 5 days after the Index Event Occur at least 2 days prior to a COVID admission Occur during a valid encounter type
Primary COVID-19 Vaccination Series Complete	All of the following: Received an mRNA shot at least 3 weeks after their initial dose At least 14 days have passed since booster
COVID-19 Vaccinated & Boosted Patients	Primary series complete and all of the following: Received an mRNA shot 4+ months after final primary series shot Booster occurred after Aug 23, 2021 At least 7 days have passed since booster Only received one booster
Valid Encounter Type	Encounters with one of the following types: Abstract, Allied Health, Ancillary Orders, Ancillary Procedure, Appointment, Clinical Documentation Only, Clinical Support, Documentation, E-Consult, Epic-On-Hand Encounter, E-Visit, External Contact, Follow-Up, Home Care Visit, Hospital Encounter, Hospital Outpatient Visit, Immunization, Infusion, Lab, Lab Requisition, Mobile Order Only, MyChart, Nurse Only, Nurse Triage, Nursing Home, Office Visit, Orders Only, Patient Message, Patient Outreach, Pharmacy Visit, Pre-Evaluation, Pre-Evaluation, Procedure Visit, Procedure Visit, Radiology Appointment, Refill, Telemedicine, Telephone, Transcribe Orders, Treatment, Urgent Care, Walk-In

Data Tables

Table 1: Lower Admission Rate and Death Rate with Paxlovid Treatment

	Total Patients	Hospitalizations	Hospitalization Rate (95% CI)	Deaths	Death Rate (95% CI)
With Paxlovid	146,256	451	0.31% (0.28% to 0.34%)	18	0.01% (0.01% to 0.02%)
Without Paxlovid	421,304	2730	0.65% (0.62% to 0.67%)	159	0.04% (0.03% to 0.04%)

Table 2: Rates of Hospitalization and Death by Age Group – All Vaccination Statuses

	Age	With Paxlovid			Without Paxlovid		
		Total	Hospitalizations	Hospitalization Rate (95% CI)	Total	Hospitalizations	Hospitalization Rate (95% CI)
Hospitalizations	12-17	951	1	0.11% (0.02% to 0.59%)	19,108	38	0.20% (0.14% to 0.27%)
	18-39	22,026	21	0.10% (0.06% to 0.15%)	124,368	206	0.17% (0.14% to 0.19%)
	40-49	20,614	24	0.12% (0.08% to 0.17%)	63,949	155	0.24% (0.21% to 0.28%)
	50-64	46,376	78	0.17% (0.13% to 0.21%)	104,789	566	0.54% (0.50% to 0.59%)
	65+	56,289	327	0.58% (0.52% to 0.65%)	109,090	1,765	1.62% (1.54% to 1.69%)
Deaths	Age	Total	Deaths	Death Rate (95% CI)	Total	Deaths	Death Rate (95% CI)
Deaths	12-17	951	0	0.00% (0.00% to 0.40%)	19,108	0	0.00% (0.00% to 0.02%)
	18-39	22,026	2	0.01% (0.00% to 0.03%)	124,368	3	0.00% (0.00% to 0.01%)
	40-49	20,614	0	0.00% (0.00% to 0.02%)	63,949	6	0.01% (0.00% to 0.02%)
	50-64	46,376	1	0.00% (0.00% to 0.01%)	104,789	22	0.02% (0.01% to 0.03%)
	65+	56,289	15	0.03% (0.02% to 0.04%)	109,090	128	0.12% (0.10% to 0.14%)

Table 3: Rates of Hospitalization and Death Among Patients With and Without Paxlovid Treatment – Fully Vaccinated Patients

	Age	With Paxlovid			Without Paxlovid		
		Total	Hospitalizations	Hospitalization Rate (95% CI)	Total	Hospitalizations	Hospitalization Rate (95% CI)
Hospitalizations	12-17	340	0	0.00% (0.00% to 1.12%)	6,382	11	0.17% (0.10% to 0.31%)
	18-39	6,353	2	0.03% (0.01% to 0.11%)	36,249	66	0.18% (0.14% to 0.23%)
	40-49	6,018	4	0.07% (0.03% to 0.17%)	19,188	42	0.22% (0.16% to 0.30%)
	50-64	12,250	24	0.20% (0.13% to 0.29%)	29,685	175	0.59% (0.51% to 0.68%)
	65+	10,814	70	0.65% (0.51% to 0.82%)	24,087	428	1.78% (1.62% to 1.95%)
	Age	Total	Deaths	Death Rate (95% CI)	Total	Deaths	Death Rate (95% CI)
Deaths	12-17	340	0	0.00% (0.00% to 1.12%)	6,382	0	0.00% (0.00% to 0.06%)
	18-39	6,353	0	0.00% (0.00% to 0.06%)	36,249	0	0.00% (0.00% to 0.01%)
	40-49	6,018	0	0.00% (0.00% to 0.06%)	19,188	1	0.01% (0.00% to 0.03%)
	50-64	12,250	1	0.01% (0.00% to 0.05%)	29,685	5	0.02% (0.01% to 0.04%)
	65+	10,814	4	0.04% (0.01% to 0.10%)	24,087	31	0.13% (0.09% to 0.18%)

Table 4: Rates of Hospitalization and Death Among Patients With and Without Paxlovid Treatment – Vaccinated & Boosted Patients

	Age	With Paxlovid			Without Paxlovid		
		Total	Hospitalizations	Hospitalization Rate (95% CI)	Total	Hospitalizations	Hospitalization Rate (95% CI)
Hospitalizations	12-17	245	1	0.41% (0.07% to 2.28%)	2,864	4	0.14% (0.05% to 0.36%)
	18-39	8,226	11	0.13% (0.07% to 0.24%)	31,090	23	0.07% (0.05% to 0.11%)
	40-49	9,256	8	0.09% (0.04% to 0.17%)	21,655	39	0.18% (0.13% to 0.25%)
	50-64	20,407	27	0.13% (0.09% to 0.19%)	38,689	143	0.37% (0.31% to 0.44%)
	65+	27,474	149	0.54% (0.46% to 0.64%)	49,392	709	1.44% (1.33% to 1.54%)
	Age	Total	Deaths	Death Rate (95% CI)	Total	Deaths	Death Rate (95% CI)
Deaths	12-17	245	0	0.00% (0.00% to 1.54%)	2,864	0	0.00% (0.00% to 0.13%)
	18-39	8,226	2	0.02% (0.01% to 0.09%)	31,090	0	0.00% (0.00% to 0.01%)
	40-49	9,256	0	0.00% (0.00% to 0.04%)	21,655	1	0.00% (0.00% to 0.03%)
	50-64	20,407	0	0.00% (0.00% to 0.02%)	38,689	7	0.02% (0.01% to 0.04%)
	65+	27,474	7	0.03% (0.01% to 0.05%)	49,392	50	0.10% (0.08% to 0.13%)

Table 5: Rates of Hospitalization and Death Among Patients With and Without Paxlovid Treatment – Vaccinated & Twice Boosted Patients

	Age	With Paxlovid			Without Paxlovid		
		Total	Hospitalizations	Hospitalization Rate (95% CI)	Total	Hospitalizations	Hospitalization Rate (95% CI)
Hospitalizations	12-17	2	0	0.00% (0.00% to 65.76%)	10	0	0.00% (0.00% to 27.75%)
	18-39	183	0	0.00% (0.00% to 2.06%)	232	3	1.29% (0.44% to 3.73%)
	40-49	252	0	0.00% (0.00% to 1.50%)	303	2	0.66% (0.18% to 2.37%)
	50-64	4,001	6	0.15% (0.07% to 0.33%)	4,990	15	0.30% (0.18% to 0.50%)
	65+	10,559	33	0.31% (0.22% to 0.44%)	12,836	150	1.17% (1.00% to 1.37%)
	Age	Total	Deaths	Death Rate (95% CI)	Total	Deaths	Death Rate (95% CI)
Deaths	12-17	2	0	0.00% (0.00% to 65.76%)	10	0	0.00% (0.00% to 27.75%)
	18-39	183	0	0.00% (0.00% to 2.06%)	232	0	0.00% (0.00% to 1.63%)
	40-49	252	0	0.00% (0.00% to 1.50%)	303	0	0.00% (0.00% to 1.25%)
	50-64	4,001	0	0.00% (0.00% to 0.10%)	4,990	1	0.02% (0.00% to 0.11%)
	65+	10,559	1	0.01% (0.00% to 0.05%)	12,836	7	0.05% (0.03% to 0.11%)