NON-INTERVENTIONAL (NI)/LOW-INTERVENTIONAL STUDY TYPE 1 (LIS1) STUDY REPORT

PASS information

Title	A standing cohort to understand the characteristics of patients with COVID-19 and contextualize the COVID-19 complication and safety events of interests using US OPTUM® EHR data
Protocol number	C4671040
Version identifier of the study report	1.0
Date	18 February 2026
EU Post Authorization Study (PAS) register number	EUPAS48654
Active substance	Nirmatrelvir/Ritonavir (ATC code J05AE30)
Medicinal product	Paxlovid
Product reference	150 mg pink film-coated tablet of Nirmatrelvir 100 mg white film-coated tablet of Ritonavir
Procedure number	PF-07321332
Marketing Authorization Holder (MAH)	Pfizer Limited
Joint Post-Authorization Safety Study (PASS)	No
Research question and objectives	**Research Questions:** 1. What are the demographic and clinical characteristics and healthcare utilization of all COVID-19 patients (Overall Source Cohort); and multiple sub-cohorts including COVID-19 patients with characteristics similar to the

	Paxlovid clinical trial programs (Trial Similar Cohorts) and COVID-19 patients treated with Paxlovid (Paxlovid Cohort)? 2. What is background incidence of clinical manifestations of COVID-19 among COVID-19 patients including subpopulation of interests (e.g., hospitalized patients, trial similar patients)? 3. What are the background rates of events that may be potential Paxlovid safety concerns among COVID-19 patients? 4. What are the incidences of long COVID-19 or post-acute sequalae SARS CoV-2 (PASC) characteristics of patients with long COVID? 5. What is the feasibility to assess the Real-world effectiveness of Paxlovid? The following are the research objectives that will be addressed in this study: **Primary Objectives:** Objective 1: Describe the distribution of demographics, co-morbid conditions, medical history, selected biomarkers, and healthcare utilization at baseline for COVID-19 patients (including subpopulation with long COVID) Objective 2: Describe the time to clinical events (e.g. hospitalization, ICU admission, death) Objective 3: Estimate background incidence of COVID-19 manifestations/complications and safety outcome of interests following COVID-19 infection or Paxlovid exposure Objective 4: Estimate incidence of long COVID-19 or post-acute sequalae SARS CoV-2 (PASC) and assess health effects of Long COVID. Objective 5: Describe the health equity and demographic and clinical characteristics (e.g. co-morbid conditions, outcomes, treatment patterns, healthcare utilization) among patients treated with Paxlovid

	Secondary Objectives: Objective 1: Estimate the incidence of oxygen supplementation among COVID-19 patients hospitalized with mechanical ventilation/ECMO **Exploratory Objectives:** Objective 1: Identify predictors of COVID-19 severe outcomes/manifestations and Long COVID with machine learning (ML) methods Objective 2: Predict risk of developing severe outcomes/manifestation and Long COVID at the patient level with machine learning (ML) methods Objective 3: Assess the feasibility of Real-world effectiveness of Paxlovid in reducing the COVID-19 related outcomes (e.g. hospitalization).
Country(-ies) of study	United States
Co-Authors	[redacted] [redacted]

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Not Applicable

Appendix 3.1. List of Investigators by Country

Not Applicable

Appendix 3.2. List of Independent Ethics Committee (IEC) or Institutional Review Board (IRB) and Corresponding Protocol Approval Dates

Not Applicable

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Not Applicable

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Not Applicable

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Not Applicable

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Not Applicable

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Not Applicable

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Not Applicable

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Not Applicable

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Not Applicable

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Not Applicable

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Not Applicable

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Not Applicable

Appendix 8. ADDITIONAL DOCUMENTS

Not Applicable

1. ABSTRACT (STAND-ALONE DOCUMENT)

2. LIST OF ABBREVIATIONS

Abbreviation	Definition
AE	Adverse event
ARDS	Acute (or adult) respiratory distress syndrome
AUC	Area Under the Curve
BMI	Body mass index
CABG	Coronary artery bypass graft
CI	Confidence interval
COPD	Chronic obstructive pulmonary disease
COVID-19	Coronavirus disease 2019
CRP	C-reactive protein
CVD	Cardiovascular disease
ER	Emergency room
EU	European Union
FDA	Food and Drug Administration
GPP	Good Pharmacoepidemiology Practice
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HF	Heart Failure
HIPAA	Health Insurance Portability and Accountability Act
HIV	Human immunodeficiency virus
HMG-CoA	3-hydroxy-3-methylglutaryl co-enzyme A
ICD	International classification of diseases
IDN	Integrated Delivery Network
IEC	Independent Ethics Committee
ILD	Interstitial lung disease
IQR	Interquartile range
IRB	Institutional Review Board

LASSO	Least Absolute Shrinkage and Selection Operator
LDH	Lactate dehydrogenase
NA	Not Applicable
NI	Non-interventional
NIH	National Institutes of Health
NMSC	Non-melanoma skin cancer
PAH	Pulmonary arterial hypertension
PAS	Post-Authorization study
PASS	Post-Authorization Safety Study
PCC	Post-COVID conditions
PCR	Polymerase chain reaction
PSM	Propensity score matching
RWD	Real-world data
SAP	Statistical Analysis Plan
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
SES	Socio-economic status
SVM	Support Vector Machine
TSC	Trial Similar Cohort
US	United States
XGBoost	Extreme Gradient Boosting

3. INVESTIGATORS

Principal Investigator(s) of the Protocol

Name, degree(s)	Title	Affiliation
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

Lead Country Investigator(s) of the Protocol

Not applicable

4. OTHER RESPONSIBLE PARTIES

Not applicable

5. MILESTONES

Milestone	Planned date	Actual date	Comments
Start of data collection	01 May 2022	01 May 2022	
Registration in the European Union (EU) PAS register	19 August 2022	10 October 2022	The protocol was originally designated as non-PASS. Following changes to the subgroup analyses, it was designated as PASS, as recorded in Amendment 1.
End of data collection	28 February 2025	29 August 2025	Original planned milestone not reached as more data and time was needed for the exploratory machine learning Long COVID objective.
Final report of study results	27 February 2026	27 February 2026	

6. RATIONALE AND BACKGROUND

A novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was first identified in December 2019 as the cause of a respiratory illness designated coronavirus disease 2019, or COVID-19[1]. The infection may be asymptomatic but symptomatic cases may present with cough, fever, dyspnea, headache, diarrhea, altered mental status, myalgia etc. Serious disease may manifest as acute respiratory distress syndrome, septic shock, and multi-organ dysfunction. As of January 2022, at least 324,196,758 cases have been confirmed worldwide, and at least 5,531,843 deaths have occurred. [2]

A number of different classes of drugs are being evaluated or newly developed for treatment or post-exposure prophylaxis of COVID-19. As of the date of issuance of clinical trial of Paxlovid (PF-07321332/ritonavir), only 1 anti-viral drug with activity against SARS CoV-2, remdesivir, an RNA polymerase inhibitor, has received approval in hospitalized patients with COVID-19. [3] Monoclonal antibodies (containing casirivimab and imdevimab or bamlanivimab and estesevimab) received emergency use authorization for mild to moderate COVID-19 in recently diagnosed high risk nonhospitalized patients. Both of these options are administered intravenously and require administration by healthcare professionals. As of October 2021, there were no approved oral alternatives to PF-07321332/ritonavir for the treatment of mild-to-moderate COVID-19 in adult patients with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death. [4-6]

There is an urgent and unmet need for antiviral agents that could be used for the treatment of non-hospitalized persons with COVID-19. Nirmatrelvir/ritonavir (Paxlovid), a potent and selective inhibitor of the SARS-CoV-2 3CL protease, was developed by Pfizer Inc. as an oral treatment in patients with COVID-19 in outpatient setting. The coronavirus 3CL protease is a virally encoded enzyme that is critical to the SARS-CoV-2 replication cycle, analogous to other obligatory virally encoded proteases (e.g., HIV Protease, HCV Protease).[7] In December 2021, Food and Drug Administration FDA has authorized the emergency use of Paxlovid in adult and pediatric patients 12 years of age and older (weighing at least 88 pounds (40 kg)]) with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death. [8]

There is limited information about the safety and effectiveness of using Paxlovid, to treat people with mild-to-moderate COVID-19 in real-world settings. [8] Understanding the epidemiology and clinical manifestations of COVID-19, as well as the background rates of potential Paxlovid related adverse events (AEs) among COVID-19 patients who are at high and standard risk of progression to severe illness in real-world setting can provide critical context for interpreting potential safety events and clinical manifestations in on-going clinical trials post-marketing, with broaden patient population. This population-based cohort study using US OPTUM® COVID-19 EHR data will provide background rates of safety events of interest to support Paxlovid program. The Phase 3 clinical trial inclusion and exclusion criteria will be applied to a subgroup of the population to create a trial-similar cohort. This study is being conducted in anticipation of the need to address possible questions about safety emanating from reports of AEs associated with Paxlovid. The timeframes for this study will consider the health impacts as well as changes in healthcare utilization that COVID-19 may have in interpreting our understanding of potential safety events. Additional outcome events and subgroups may be incorporated in this study over time. Given the global scale of COVID-19 pandemic, there is an increasing need to better understand and characterize the post-acute sequalae SARS CoV-2 (PASC) or long COVID. [9,10] This study will also aim at describing the characteristics COVID-19 outcome/long COVID including those exposed to Paxlovid in real-world setting. Such information may inform clinical trial design and disease management for the long-term health effects of the

COVID patients. Moreover, this study provides insights into understanding of potential racial disparities among patients using Paxlovid. The exploratory analyses may help identify predictors of severe COVID-19 outcomes/ manifestations and long Covid and predict the risk developing the severe outcomes/ manifestations and long Covid at individual level in real-world setting.

This non-interventional study (NIS) is designated as a Post-Authorization Safety Study (PASS) and is conducted voluntarily by Pfizer.

7. RESEARCH QUESTION AND OBJECTIVES

Research Questions:

1. What are the demographic and clinical characteristics and healthcare utilization of all COVID-19 patients (Overall Source Cohort); and multiple sub-cohorts including COVID-19 patients with characteristics similar to the Paxlovid clinical trial programs (Trial Similar Cohorts) and COVID-19 patients treated with Paxlovid (Paxlovid Cohort)?

2. What is background incidence of clinical manifestations of COVID-19 among COVID-19 patients including subpopulation of interests (e.g., hospitalized patients, trial similar patients)?

3. What are the background rates of events that may be potential Paxlovid safety concerns among COVID-19 patients?

4. What are the incidences of long COVID-19 or post-acute sequalae SARS CoV-2 (PASC) characteristics of patients with long COVID?

5. What is the feasibility to assess the Real-world effectiveness of Paxlovid?

The following are the research objectives that will be addressed in this study:

Primary Objectives:

- Objective 1: Describe the distribution of demographics, co-morbid conditions, medical history, selected biomarkers, and healthcare utilization at baseline for COVID-19 patients (including subpopulation with long COVID)

- Objective 2: Describe the time to clinical events (eg, hospitalization, ICU admission, death)

- Objective 3: Estimate background incidence of COVID-19 manifestations/complications and safety outcome of interests following COVID-19 infection or Paxlovid exposure

- Objective 4: Estimate incidence of long COVID-19 or post-acute sequalae SARS CoV-2 (PASC) and assess health effects of Long COVID.

- Objective 5: Describe the health equity and demographic and clinical characteristics (eg, comorbid conditions, outcomes, treatment patterns, healthcare utilization) among patients treated with Paxlovid

Secondary Objectives:

- Objective 1: Estimate the incidence of oxygen supplementation among COVID-19 patients hospitalized with mechanical ventilation/ECMO

Exploratory Objectives:

- Objective 1: Identify predictors of COVID-19 severe outcomes/manifestations and Long COVID with machine learning (ML) methods

- Objective 2: Predict risk of developing severe outcomes/manifestation and Long COVID with machine learning (ML) methods at the patient level

- Objective 3: Assess the feasibility of Real-world effectiveness of Paxlovid in reducing the COVID-19 related outcomes (e.g., hospitalization).

8. AMENDMENTS AND UPDATES

Table 1. Amendments to the Protocol

Amendment number	Date	Substantial or administrative amendment	Protocol section(s) changed	Summary of amendment	Reason
1	24 May 2022	Administrative	Title Page and section 8	Added research question: What is the feasibility to assess the Real-world effectiveness of Paxlovid? Added Exploratory objective 3: Assess the feasibility of Real-world effectiveness of Paxlovid in reducing the COVID-19 related outcomes (eg, hospitalization).	Understanding Real-world effectiveness of Paxlovid can provide useful data to help expand the leaning from the previous clinical trials and accelerate ongoing or future clinical trials
			Title page	Added PASS information to title page.	Study was evaluated as voluntary PASS study and wording had to be aligned with internal requirements.
			Section 7	Added mandatory PASS wording	Study was evaluated as voluntary PASS.
			Section 9.2.2.3	Added: Method to refine index date per research	To clarify the language of index date and follow up.

				question will be defined in Statistical analysis plan (SAP)	
			Section 9.3	Added: Potential effectiveness of interests* • Hospitalization • All-cause mortality • ICU/Mechanical Ventilation • In Hospital death *The outcomes may be removed or added depending on the data availability for proper analyses.	These 4 outcomes were added, because they are severe COVID-19 outcomes aligned with Paxlovid indication
			Section 9.8	Added: To assess the feasibility of real-world effectiveness of Paxlovid, we will apply propensity score matching (PSM) method to control confounding and prescription time distribution	One of the challenges using real-world data is to deal with confounding and bias. PSM and PTDM were selected to allow us better control confounding and cope with immortal bias

				method (PTDM) to handle immortal bias.	
2	23 Aug 2022	Substantial	Title page	Corrected format and information on title page. Deleted Exploratory objectives.	To align with correct title page for PASS study conducted in USA. Title page should only show primary and secondary objectives.
			Section 3	Added “NIS Lead” to table. Deleted table of Co-Investigators.	To align with requirements, the role of “NIS Lead” was added to the table. This table is for studies with study sites, which is not the case for this study.
			Section 4	Added section for abstract.	Since this is a PASS the protocol abstract is required.
			Section 5	Added new table for amendments and updates.	The correct table has been added to list all the amendments and updates.
			Section 6	Milestones were updated.	Update of milestones was done to align with current status.
			Section 9.1	Added that this is a secondary structured data collection.	For clarification the study type was added to this section.
			Section 9.2.1	Added a sentence describing what a	This sentence was added for clarification.

				validation substudy is.	
			Section 9.3.1 and section 9.3.2	Rearranged inclusion and exclusion criteria	Change was done to be aligned with template and facilitate understanding
			Section 9.4	Added clarification of COVID-19 Reinfection and Rebound	This sentence was added for clarification.
			Section 9.6	Added 2 sentences at the end of the section.	Text was added to describe new data source starting at the end of 2022.
			Section 10.1	Deletion of second sentence in this section.	The deleted sentence was in the wrong section, it is part of section 11.
			Section 11	Changed text to align with correct safety wording.	This study does not have any unstructured data, safety wording was aligned.
			Section 12	Clarified that there will be one final study report and multiple publications.	There will be no interim report. Interim data analysis will be published as scientific manuscript.
			Section 14	Added section 14.	Section 14 was added to list the figures.
			Annex 1	Added table in annex 1.	Table in annex 1 was added because the stand alone abstract is required.
			Throughout the protocol	Minor editorial edits and correction	NA

				of spelling mistakes.	

9. RESEARCH METHODS

9.1. Study design

This is a non-interventional (NI), observational, retrospective cohort study using structured data and population-based with ongoing retrospective and prospective data collection from electronic healthcare data in the US. This study included adults (≥18 years of age) and pediatric patients (<18 years of age) with COVID-19 diagnosis (i.e. positive PCR or antigen results of direct SARS-CoV-2 viral testing or have confirmed COVID-19 diagnosis codes). Within the population-based general cohort (COVID-19 Cohort), a sub-cohort was created based on similar eligibility criteria as those used in select Paxlovid clinical trials (e.g. C4671005 [NCT04960202], C4671002 [NCT05011513]) to attempt to emulate the characteristics of select clinical trial program populations (Paxlovid Trial Similar COVID-19 Sub-cohorts). Patients with Paxlovid prescription were included in a subgroup analysis. All Paxlovid users were included in the study. The study population was followed from the COVID-19 diagnosis or Paxlovid prescription to identify outcomes of interests (heath outcomes, COVID-19 complications, and long COVID) complications, and long COVID).

Additional details on index dates, episode definitions, matching criteria, matching methods, and appropriate modeling considerations were provided in the statistical analysis plan (SAP) (Appendix 4).

9.2. Setting

This study was conducted using Optum's COVID-19 Electronic Health Record Data during the period of January 01, 2020, to June 30, 2024. Details about the database are found in Section 9.5 Data sources and measurement. The COVID-era cohorts were refreshed annually to include additional individuals, follow-up time, and events. These refreshes and cohorts are described in the Statistical Analysis Plan (SAP) (Appendix 4).

9.3. Subjects

The study population consisted of patients who tested positive or were diagnosed with COVID-19 (i.e. positive PCR or antigen results of direct SARS-CoV-2 viral testing or have confirmed COVID-19 diagnosis codes). All Paxlovid users were included in the study.

Within the study population, three Source Cohorts of general population with COVID-19 were formed (Figure 1):

- 1a: Overall COVID-19 patients.
- 1b: Hospitalized patients (i.e. hospitalized within 30 days of index date) for COVID-19.
- 1c: Non-hospitalized patients (i.e. not hospitalized within 30 days of index date) with COVID-19.

Within Source Cohort of 1a, 1b, and 1c, the following Trial Similar Cohorts, were formed:

Patients at high risk of progression to severe illness (Figure 1)

- 2a: Subgroup of the general population cohort 1a who meet relevant inclusion/exclusion criteria of the Paxlovid clinical trial (C4671005) which include age ≥18 years, confirmed

COVID-19 infection diagnosis, high-risk for progression to severe COVID-19 and absence of prior hospitalization for COVID-19 (other than for incident event), liver / renal disease, HIV, recent (≤7 days) hospitalizations or surgeries and prohibited medications (CYP3A4 inducers).

- 2b: Subgroup of the hospitalized patient cohort 1b who meet relevant inclusion/exclusion criteria of the Paxlovid clinical trial (C4671005), as noted above in 2a.

- 2c: Subgroup of the non-hospitalized patient cohort 1c who meet relevant inclusion/exclusion criteria of the Paxlovid clinical trial (C4671005), as noted above in 2a.

*Patients at standard risk of progression to severe illness (*Figure 1*)*

- 3a: Subgroup of the general population cohort 1a who meet relevant inclusion/exclusion criteria of the Paxlovid clinical trial (C4671002) which include age ≥18 years, confirmed COVID-19 infection diagnosis, Non-hospitalized at diagnosis, low or standard-risk for progression to severe COVID-19 and absence of high-risk medical conditions for severe COVID-19, evidence of immunosuppression.

- 3b: Subgroup of the hospitalized patient cohort 1b who meet relevant inclusion/exclusion criteria of the Paxlovid clinical trial (C4671002), as noted above in 3a.

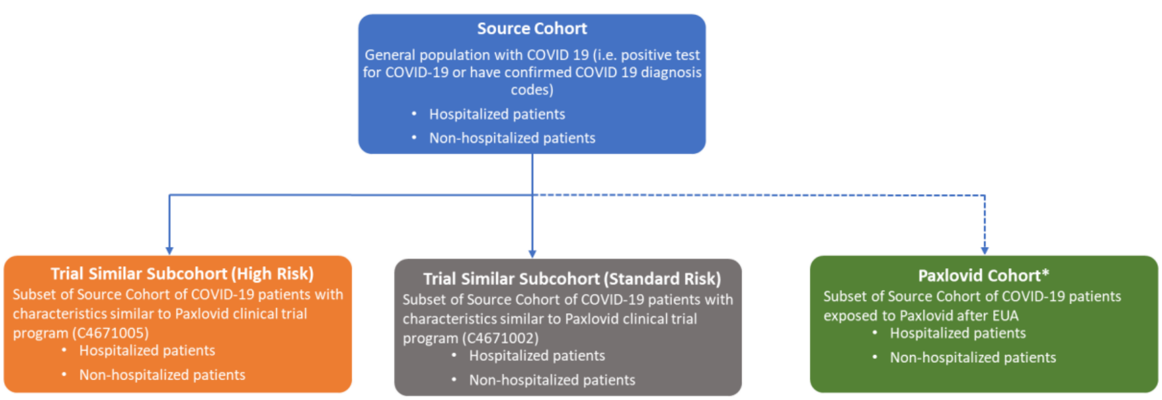
- 3c: Subgroup of the non-hospitalized patient cohort 1b who meet relevant inclusion/exclusion criteria of the Paxlovid clinical trial (C4671002), as noted above in 3a.

A sub-cohort of patients who were exposed to Paxlovid in real-world settings were created.

If a patient had an exposure to Paxlovid without COVID PCR/antigen testing/diagnosis data, this patient can be captured in the Paxlovid cohort.

Additional special populations (e.g. pediatric population) are added as a subset.

Figure 1. Flowchart outlining the study cohort and sub-cohorts



Note: Any addition of a special population (e.g. immunocompromised patients, pediatric population, severe renal cohort etc.) as well as patients with multiple infections of COVID-19 or patients received

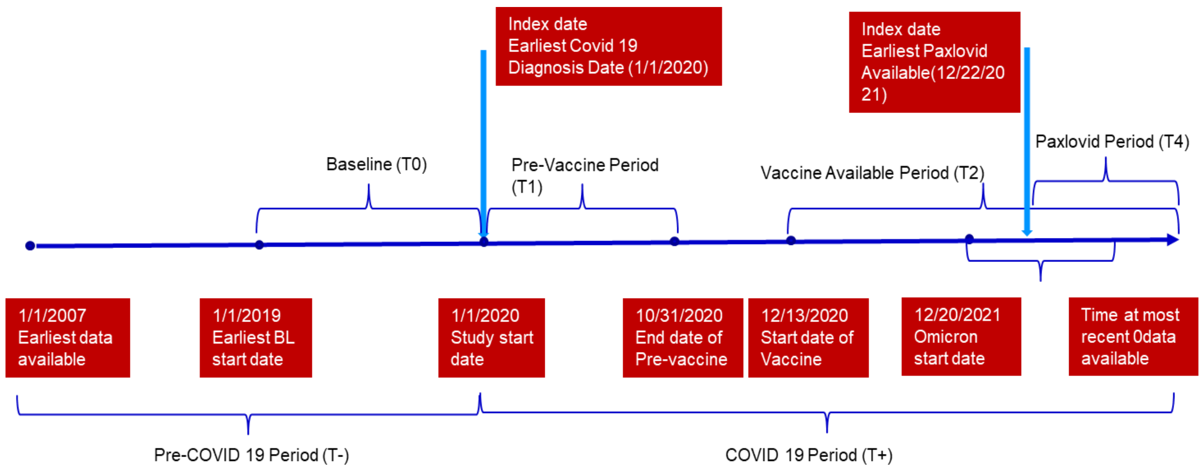
COVID-19 vaccines can be a subset of either Source Cohort or high/standard risk cohort. For Paxlovid cohort, if a patient had an exposure to Paxlovid without COVID PCR/ antigen testing/diagnosis data, this patient can be captured in the Paxlovid cohort.

9.3.1. Time periods

9.3.1.1. Study period

The study included an overall study period and four sub-periods for each Source Cohort and sub-cohort Figure 2):

Figure 2. Flowchart outlining the study periods



Study period: COVID-19-era (T+) included Jan 1, 2020 – most recent data available at the time of analytic dataset creation. The study period will be further stratified as follows:

- Study period i (T1): Active COVID-19-era (Pre-Vaccine Period) included January 1, 2020 – October 31, 2020.
- Study period ii (T2): Active COVID-19-era (Vaccine Available Period) included Dec 13, 2020 – most recent data available at the time of analytic dataset creation.
- Study period iii (T3): Omicron Period (Approximate time period when Omicron is dominated) included December 15, 2021 – July 20, 2022.
- Study period iv (T4): Paxlovid Period (Paxlovid Available after EUA) included December 22, 2021 (i.e. EUA approval) to most recent data available at the time of analytic dataset creation.

9.3.1.2. Baseline period

The 365 days before index date (see Section 9.3.1.1) was defined as the baseline period (T0, Figure 2).

9.3.1.3. Index date

The index date for the COVID-19 Source and the Trial Similar Sub-cohort were defined as the date of first date tested positive or diagnosed for COVID-19 (i.e. positive PCR or antigen results of direct SARS-CoV-2 viral testing or have confirmed COVID-19 diagnosis codes) during the study period.

Method to refine index date per research question was defined in SAP.

The index date for the Paxlovid cohort was defined as the date of first prescription of Paxlovid during the study period.

9.3.1.4. Follow-up

The follow-up period starts at index date and participants were followed until the date of the first occurring of the following events:

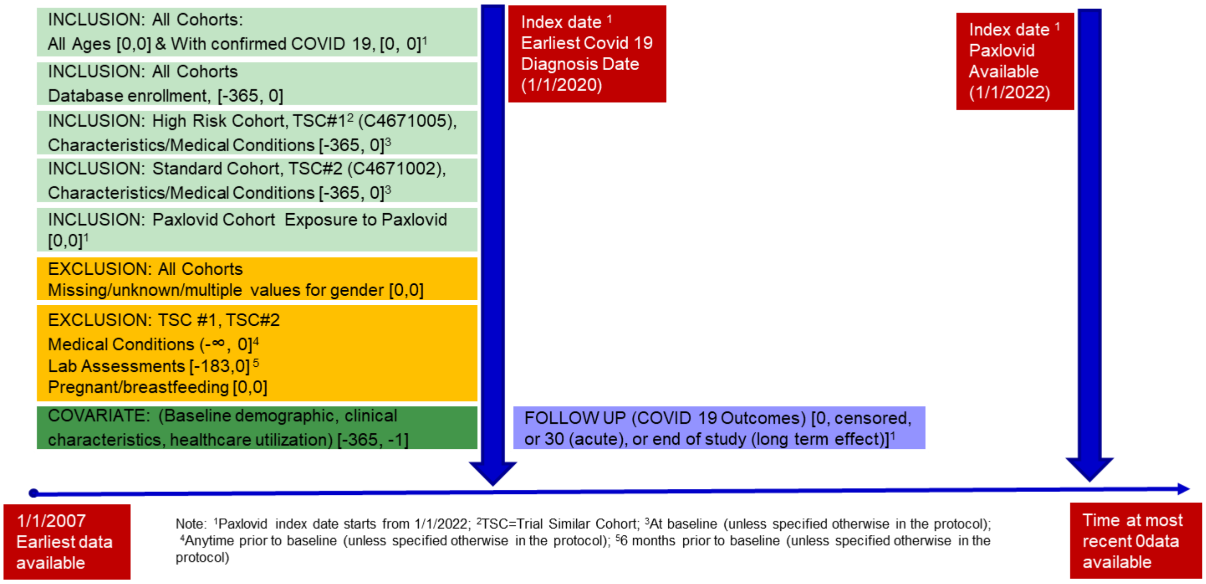
- Death
- At the end of their database disenrollment from the database
- At the end of study period (Section 9.3.1.1)
- Occurrence of the outcome of interest

Follow-up time for hospitalized patients met the criterion in Section 9.3.1 (i.e. hospitalized within 30 days of COVID-19 diagnosis or index date). Details as well as follow-up windows for long COVID were defined in SAP.

9.3.2. Inclusion and Exclusion Criteria

The inclusion and exclusion criteria for the Source Cohort, Trial Similar Cohorts (TSC), and Paxlovid cohort are described respectively in this section. Figure 3 shows the inclusion and exclusion assessment windows.

Figure 3. Inclusion & Exclusion Assessment Window (Days)



9.3.2.1. COVID-19 Source Cohort

The inclusion and exclusion criteria to ascertain the Source Cohort (Section 9.3) are listed as follows:

Inclusion Criteria

1. Tested positive or diagnosed for COVID-19 (i.e. positive PCR or antigen results of direct SARS-CoV-2 viral testing or have confirmed COVID-19 diagnosis codes: SARS-CoV-2L severe acute respiratory syndrome coronavirus 2; PCR: polymerase chain reaction) during the study period.

2. At least 12 months of ≥1 healthcare activity prior to index date (Section 9.3.1.3).

3. Integrated delivery network information to allow linkage of outpatient and inpatient records.

Additionally, the Source Cohort is further stratified into two subpopulations: hospitalized - those who were hospitalized within 30 days after the index date (Section 9.3.1.3); and non-hospitalized - those without hospitalization within 30 days after the index date (Section 8.2.1).

Exclusion criteria

1. Missing, unknown, or multiple values for gender

9.3.2.2. Trial Similar Cohort (TSC)

In addition to inclusion criteria in Section 9.3.2.1, patients in the Paxlovid Trial Similar Cohorts must meet the following inclusion and exclusion criteria. Although not an exact match, the listed criteria provide a sub-cohort with patient characteristics that are as similar as possible to the patients in the Paxlovid clinical trial programs.

9.3.2.2.1. High Risk Cohort (TSC to C4671005)

Inclusion Criteria

1. Has at least 1 characteristic or underlying medical condition associated with an increased risk of developing severe illness from COVID-19 at baseline (unless specified otherwise) including:

    a. ≥60 years of age at the index date

    b. Body mass index (BMI) >25 kg/m2

    c. Current smoker (cigarettes smoking at baseline)

    d. Immunosuppressive disease (e.g., bone marrow or organ transplantation or primary immune deficiencies) OR prolonged use of immune-weakening medications:

        i. Has received treatment with biologics (eg, infliximab, ustekinumab), immunomodulators (eg, methotrexate, 6MP, azathioprine) or cancer chemotherapy within 90 days prior to index date.

        ii. HIV infection

    e. Chronic lung disease (i.e. Asthma, chronic obstructive pulmonary disease [COPD], interstitial lung disease [ILD])

    f. Known diagnosis of hypertension

    g. Cardiovascular disease (CVD), defined as history of any of the following: myocardial infarction, stroke, transient ischemic attack (TIA), heart failure (HF), angina with prescribed nitroglycerin, coronary artery bypass graft surgery (CABG), percutaneous coronary intervention (PCI), carotid endarterectomy, and aortic bypass

    h. Type 1 or Type 2 diabetes mellitus

    i. Chronic kidney disease (CKD) (excluding dialysis or end stage of renal disease)

    j. Sickle cell disease

    k. Neurodevelopmental disorders or other conditions that confer medical complexity

    l. Any cancer diagnoses, other than localized skin cancer (i.e. NMSC) at baseline, within one year prior to index date

Exclusion Criteria

Participants are excluded from the study if any of the following criteria apply:

Medical Conditions (any time prior to index date, unless specified otherwise)

1. History of hospitalization within 30 days prior to Index date

2. Known medical history of active liver disease (other than nonalcoholic hepatic steatosis), including chronic or active hepatitis B or C infection, primary biliary cirrhosis, or acute liver failure.

3. Receiving dialysis or end stage of renal disease

Other Exclusions:

4. Females who are pregnant or breastfeeding within 9 months prior to index date.

9.3.2.2.2. Standard Risk Cohort

Inclusion Criteria

See Source Cohort inclusion criteria in Section 9.3.2.1

Exclusion Criteria

Has at least 1 characteristic or underlying medical condition associated with an increased risk of developing severe illness from COVID-19, including:

- ≥65 years of age at the index date
- BMI ≥30 kg/m^2
- "High Risk Cohort – Inclusion Criteria 1.c – 1.l " (Section 9.3.2.2.1)
- "High Risk Cohort – Exclusion Criteria #1 - #4" (Section 9.3.2.2.1)

9.3.2.3. Paxlovid Cohort

Inclusion/exclusion criteria:

Patients who met the inclusion and exclusion criteria in Source Cohort and exposed to Paxlovid after EUA approval on December 22, 2021. If a patient had an exposure to Paxlovid without COVID PCR testing/diagnosis data, this patient can be captured in the Paxlovid cohort.

9.4. Variables

9.4.1. Covariates

Baseline covariates for the Source Cohort included demographics, comorbidities, and health utilization. For the Paxlovid cohort and non-Paxlovid cohort, treatments contraindicated with Paxlovid, treatments for COVID, COVID-19 vaccines, past COVID-19 infection, top 50 diagnoses, top 50 procedures, top 50 prescriptions, and Paxlovid provider/specialty were included. The list of covariates and operational definitions are provided in Table 2.

Table 2. Operational Definition of Baseline Covariates

Variable	Values	Operational definition	Time Window	Role
Demographics				
Calendar year at index date	Calendar year for the Source Cohort; calendar month for Paxlovid	Calendar year for the Source Cohort; calendar month for Paxlovid	at index date	Covariate description
Age	categorical: 1=<12; 2=12-17; 3=18-29; 4=30-39; 5=40-49; 6=50-59; 7=60-64; 8=65-74; 9=75-84; 10=85+; continuous; <65 vs >=65; 60-74; 75+; 0-4; 5-11; 12-17	Use birth year and index year for age calculation	at index date	Covariate description; Stratified analysis; Trial-similar criteria
Sex	1=Male; 2=Female	Patients with unknown or missing gender were excluded	at index date or the closest date from index	Covariate description; Stratified analysis
Race	1=White, 2=Black or African American, 3=Asian, 4=Other, Unknown		at index date or the closest date from index	Covariate description; Stratified analysis
Ethnicity	1=Hispanic; 2=non-Hispanic; 3=Others or unknown		at index date or the closest date from index	Covariate description; Stratified analysis
U.S. Geographic Region	1=Northeast, 2=Midwest, 3=South, 4=West, 5=Other/Unknown,		at index date or the closest date from index	Covariate description; Stratified analysis
Insurance Type	1=Commercial, 2=Medicaid, 3=Medicare, 4=Other Payor Type, 5=Uninsured, 6=Unknown;	Other insurance type and unknown can be combined; for multiple insurances, choose the one closest to index date; if	at index date or the closest date from index	Covariate description

		on the same date has multiple insurance, give priority to this order: Commercial, Medicare, Medicare, other type , and uninsurance.		
Comorbidities and Medical History				
Autoimmune diseases				
Multiple Sclerosis	1="Yes", 0="No"	See dx code list	during 12 months baseline period;	Covariate description
Sjogren's syndrome	1="Yes", 0="No"	See dx code list	during 12 months baseline period;	Covariate description
Guillain-Barré syndrome	1="Yes", 0="No"	See dx code list	during 12 months baseline period;	Covariate description
Idiopathic thrombocytopenia purpura	1="Yes", 0="No"	See dx code list	during 12 months baseline period;	Covariate description
Autoimmune thyroiditis	1="Yes", 0="No"	See dx code list	during 12 months baseline period;	Covariate description
Giant cell arteritis	1="Yes", 0="No"	See dx code list	during 12 months baseline period;	Covariate description
Psoriasis	1="Yes", 0="No"	See dx code list	during 12 months baseline period;	Covariate description
Systemic or cutaneous lupus erythematosus	1="Yes", 0="No"	See dx code list	during 12 months baseline period;	Covariate description
Autoimmune arthritis/rheumatoid arthritis	1="Yes", 0="No"	See dx code list	during 12 months	Covariate description

			baseline period;	
Respiratory conditions				
Asthma	1="Yes", 0="No"	See dx code list	during 12 months baseline period;	Covariate description; Trial-similar criteria
COPD	1="Yes", 0="No"	See dx code list	during 12 months baseline period;	Covariate description; Trial-similar criteria
ILD	1="Yes", 0="No"	See dx code list	during 12 months baseline period;	Cohort creation; Trial-similar criteria
Cardiovascular or cerebrovascular conditions				
Coronary Heart Disease	1="Yes", 0="No"	See dx code list	during 12 months baseline period;	Covariate description
Cardiomyopathies	1="Yes", 0="No"	See dx code list	during 12 months baseline period;	Covariate description
Cerebrovascular disease or stroke (including Transient Ischemic Attack)	1="Yes", 0="No"	See dx code list	during 12 months baseline period;	Covariate description; Trial-similar criteria
Hypertension	1="Yes", 0="No"	See dx code list	during 12 months baseline period;	Covariate description; Trial-similar criteria
Liver or renal conditions				
Chronic Kidney Disease	1="Yes", 0="No"	See dx code list	during 12 months baseline period;	Covariate description; Trial-similar criteria
Liver Disease	1="Yes", 0="No"	See dx code list	during 12 months baseline period;	Covariate description
Infections				

HBV	1="Yes", 0="No"	See dx code list	during 12 months baseline period;	Covariate description; Trial-similar criteria
HCV	1="Yes", 0="No"	See dx code list	during 12 months baseline period;	Covariate description; Trial-similar criteria
HIV infection	1="Yes", 0="No"	See dx code list	during 12 months baseline period;	Covariate description; Trial-similar criteria
Other				
Smoking	1=Current; 0=Former/Never	Identified from diagnosis or observation table	during 12 months baseline period;	Covariate description; Trial-similar criteria
BMI>=30 or obesity	1="Yes", 0="No"	Weight and height, and BMI used where possible, obesity diagnosis code used when BMI components not available. BMI= weight (kg) / [height (m)]2; or 703 x weight (lbs) / [height (in)]2	during 12 months baseline period;	Covariate description; Trial-similar criteria
Hyperlipidemia	1="Yes", 0="No"	See dx code list	during 12 months baseline period;	Covariate description
Diabetes Mellitus	1="Yes", 0="No"	See dx code list	during 12 months baseline period;	Covariate description; Trial-similar criteria
Cancer	1="Yes", 0="No"	See dx code list	during 12 months	Covariate description: Trial-

			baseline period;	similar criteria
Sickle cell disease	1="Yes", 0="No"	See dx code list	during 12 months baseline period;	Covariate description; Trial-similar criteria
Deyo-Charlson Comorbidity Index Score	Continuous; mean/SD	See dx code list and CCI program	during 12 months baseline period;	Covariate description
CRP	1=>0.0082 mg/Liter; 0=otherwise; 9=missing	Identified from lab table via LOINC codes or test description; among hospitalized patients only	Within 10 days prior to the index date	Covariate description
LDH	1=>245 U/Liter; 0=otherwise; 9=missing	Identified from lab table via LOINC codes or test description; among hospitalized patients only	Within 10 days prior to the index date	Covariate description
Ferritin	1=>300ng/ml; 0=otherwise; 9=missing	Identified from lab table via LOINC codes or test description; among hospitalized patients only	Within 10 days prior to the index date	Covariate description
D-dimer	1=>1mcg/ml; 0=otherwise; 9=missing	Identified from lab table via LOINC codes or test description; among hospitalized patients only	Within 10 days prior to the index date	Covariate description
Healthcare utilization				
Hospitalization	Categorical: 0, 1, 2+; Continuous; mean/SD; median, IQR	From encounter table	30 days before and after the index date	Covariate description

Length of Stay	Continuous; mean/SD; median, IQR	From encounter table	30 days before and after the index date	Covariate description
Emergency Room Visits	Categorical: 0, 1, 2+; Continuous; mean/SD; median, IQR	From encounter table	30 days before and after the index date	Covariate description
Physician Office Visits	Categorical: 0, 1, 2+; Continuous; mean/SD; median, IQR	From encounter table	30 days before and after the index date	Covariate description
Telemedicine Visits	Categorical: 0, 1, 2+; Continuous; mean/SD; median, IQR	From encounter table	30 days before and after the index date	Covariate description
Urgent Care Visits	Categorical: 0, 1, 2+; Continuous; mean/SD; median, IQR	From encounter table	30 days before and after the index date	Covariate description
Treatment Contraindicated with Paxlovid (Exclusion criteria for effectiveness study, 28 days prior to the index date)				
Alpha1-adrenoreceptor antagonist				
Alfuzosin	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
Analgesics				
Pethidine	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
Propoxyphene	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
Antianginal				
Ranolazine	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description

Antiarrhythmic				
Amiodarone	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
Dronedarone	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
Flecainide	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
Propafenone	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
Quinidine	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
Anti-gout				
Colchicine	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
Antipsychotics	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
Clozapine	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description

Pimozide	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
Lurasidone	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
Ergot derivatives				
Ergotamine	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
Methylergonovine	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
Dihydroergotamine	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
HMG-CoA reductase inhibitors				
Lovastatin	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
Simvastatin	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
PDE5 inhibitor				
Sildenafil (Revatio®)	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from	Covariate description

			index date to 14 days	
Sedative/hypnotics				
Triazolam	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
Oral midazolam	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
Anticancer drugs				
Apalutamide	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
Anticonvulsant				
Carbamazepine	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
Phenobarbital	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
Phenytoin	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
Antimycobacterial				
Rifampin	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
Herbal products				

St. John's Wort	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
Treatments for COVID [11, 12] (Exclusion criteria for effectiveness study, 28 days prior to the index date)				
Anti-SARS-CoV-2 Antibody Products				
Bamlanivimab/Etesevimab	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
Casirivimab/Imdevimab	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
Sotrovimab	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
Tixagevimab/Cilgavimab	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
Bebtelovimab	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
Convalescent plasma	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
Antiviral therapy				

Remdesivir	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
Molnupiravir	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
Chloroquine/hydroxychloroquine	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
Azithromycin	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
Lopinavir/ritonavir	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
Ivermectin	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
Nitazoxanide	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
Ribavirin	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description

Interferon-beta	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
Immunomodulators				
Systemic Corticosteroids				
Dexamethasone	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
Methylprednisolone	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
Fluvoxamine	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
Interleukin inhibitors				
Tocilizumab	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
Sarilumab	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
Antithrombotic Therapy				
Heparin	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	from -28 days to index-1 and from index date to 14 days	Covariate description
COVID-19 vaccines	1="Yes", 0="No"	See drug code list; Paxlovid cohort only	Any time prior to	Covariate description

			the index date	
Past COVID infection	counts	A 90 days gap were used to define different episode of COVID infection	Any time prior to the index date	Covariate description
Top 50 diagnoses		Rank based on the frequency and proportion	12 months prior to the index date	
Top 50 procedures		Rank based on the frequency and proportion	12 months prior to the index date	
Top 50 medications	1="Yes", 0="No"	Rank based on the frequency and proportion	12 months prior to the index date	Covariate description
Medical specialty of the prescribers	1="Yes", 0="No"	Paxlovid cohort only	at index date	Covariate description

9.4.2. Outcomes

Outcome events were pre-specified health outcomes, including those that were part of Paxlovid or identified after the EUA post marketing. [8] The list of events of interest is provided below. This list of outcome events was chosen based on clinician's expert opinion, biologic plausibility, and feasibility of identification in EHR or claims data. The list of events of interest is provided in Table 3.

COVID-19 Re-infection:

A 90-day gap was used to define the episodes of COVID re-infection identified with either a positive lab test or the diagnosis codes. This is defined in the SAP (Appendix 4).

Table 3. Operational Definitions of Outcomes of Interest

Variable name	**Values**	**Operational definition**	**Time Window**
COVID-19 Complications/interventions			
Pneumonia	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	Index date+29 days

Table 3. Operational Definitions of Outcomes of Interest

Variable name	**Values**	**Operational definition**	**Time Window**
Kidney failure	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	Index date+29 days
Thrombotic event	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	Index date+29 days
ARDS	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	Index date+29 days
Heart failure	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	Index date+29 days
Sepsis/septic shock	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	Index date+29 days
Mechanical ventilation/ECMO	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	Index date+29 days
Hospitalization	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	Index date+29 days
All-cause mortality	1="Yes", 0="No"	Use death algorithm to define the death date	Index date+29 days
In hospital death	1="Yes", 0="No"	Use death algorithm to define the death date	Index date+29 days
Multi-organ dysfunction/failure	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	Index date+29 days

Table 3. Operational Definitions of Outcomes of Interest

Variable name	**Values**	**Operational definition**	**Time Window**
Vasopressor use	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	Index date+29 days
Health Outcomes			
Renal impairment	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period
Hepatic impairment	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period
Dysgeusia	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period
Diarrhea	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period
Hypersensitivity/Serious allergic reactions	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period
Potential effectiveness of interest			
Hospitalization	1="Yes", 0="No"	Remove hospitalization within 30 days prior to the index date	Index date+29 days
All-cause mortality	1="Yes", 0="No"	Remove hospitalization within 30 days prior to the index date	Index date+29 days
ICU/Mechanical ventilation	1="Yes", 0="No"	Remove hospitalization within 30 days prior to the index date	Index date+29 days

Table 3. Operational Definitions of Outcomes of Interest			
Variable name	**Values**	**Operational definition**	**Time Window**
In-hospital death	1="Yes", 0="No"	Remove hospitalization within 30 days prior to the index date	Index date+29 days
Time from Index Date to Clinical Events			
Pneumonia	Mean/SD; Median/IQR	Event date-Index date+1	Index date+29 days
Kidney failure	Mean/SD; Median/IQR	Event date-Index date+1	Index date+29 days
Thrombotic event	Mean/SD; Median/IQR	Event date-Index date+1	Index date+29 days
ARDS	Mean/SD; Median/IQR	Event date-Index date+1	Index date+29 days
Heart failure	Mean/SD; Median/IQR	Event date-Index date+1	Index date+29 days
Sepsis/septic shock	Mean/SD; Median/IQR	Event date-Index date+1	Index date+29 days
Mechanical ventilation/ECMO	Mean/SD; Median/IQR	Event date-Index date+1	Index date+29 days s
Hospitalization	Mean/SD; Median/IQR	Event date-Index date+1	Index date+29 days
All-cause mortality	Mean/SD; Median/IQR	Event date-Index date+1	Index date+29 days
In hospital death	Mean/SD; Median/IQR	Event date-Index date+1	COVID diagnosis+30 days
Multi-organ dysfunction/failure	Mean/SD; Median/IQR	Event date-Index date+1	Index date+29 days
Vasopressor use	Mean/SD; Median/IQR	Event date-Index date+1	Index date+29 days
Renal impairment	Mean/SD; Median/IQR	Event date-Index date+1	During follow-up period
Hepatic impairment	Mean/SD; Median/IQR	Event date-Index date+1	During follow-up period
Dysgeusia	Mean/SD; Median/IQR	Event date-Index date+1	During follow-up period
Diarrhea	Mean/SD; Median/IQR	Event date-Index date+1	During follow-up period
Hypersensitivity/Serious allergic reactions	Mean/SD; Median/IQR	Event date-Index date+1	During follow-up period
Long COVID			
Any below medical condition	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4

Table 3. Operational Definitions of Outcomes of Interest

Variable name	Values	Operational definition	Time Window
			weeks, >=12 weeks; >=6 months
Post-COVID syndrome	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
General symptoms			
Fatigue	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Intermittent fever	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Post-exertional malaise	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Multisystem inflammatory syndrome (MIS)	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Respiratory symptoms			
Dyspnea or Shortness of breath	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Cough	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4

Table 3. Operational Definitions of Outcomes of Interest

Variable name	Values	Operational definition	Time Window
			weeks, >=12 weeks; >=6 months
Nasal Congestion	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Lung function abnormalities (Acute bronchiolitis, Lung fibrosis , ILD)	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Hypoxaemia	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Cardiovascular and cerebrovascular symptoms			
Chest pain	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Palpitations or Fast-beating or pounding heart	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Myocarditis	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Pericarditis	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months

Table 3. Operational Definitions of Outcomes of Interest

Variable name	Values	Operational definition	Time Window
Myocardial infarction	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Angina	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Atrial fibrillation	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Atrial flutter	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Sinus tachycardia	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Sinus bradycardia	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Heart failure	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Stroke	1="Yes", 0="No"	See code list; incidence case: no corresponding event	During follow-up period; overall and by follow-up intervals: >=4

Table 3. Operational Definitions of Outcomes of Interest

Variable name	Values	Operational definition	Time Window
		from -183 to -15 days prior to the index date	weeks, >=12 weeks; >=6 months
TIA	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Neurological symptoms			
Headache	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Insomnia	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Cognitive impairment	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Confusion	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Anosmia or Loss of smell	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Ageusia or Loss of taste	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months

Table 3. Operational Definitions of Outcomes of Interest			
Variable name	**Values**	**Operational definition**	**Time Window**
Depression	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Anxiety Disorders	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Post-traumatic Stress Disorder	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Substance Use Disorders	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Suicidal behavior and suicide ideation	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Dizziness on standing (light-headedness)	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Pins-and-needles feelings	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Dysautonomia	1="Yes", 0="No"	See code list; incidence case: no corresponding event	During follow-up period; overall and by follow-up intervals: >=4

Table 3. Operational Definitions of Outcomes of Interest

Variable name	Values	Operational definition	Time Window
		from -183 to -15 days prior to the index date	weeks, >=12 weeks; >=6 months
Digestive symptoms			
Abdominal pain	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Diarrhea	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Nausea	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Constipation	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Musculoskeletal and Skin			
Arthralgia or joint pain	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Myalgia or muscle pain	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Body aches	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4

Table 3. Operational Definitions of Outcomes of Interest

Variable name	Values	Operational definition	Time Window
			weeks, >=12 weeks; >=6 months
Rash	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Alopecia	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Hair loss	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Endocrine symptoms			
Diabetes mellitus (Type I & II)	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Diabetic ketoacidosis	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Thyroiditis	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Hypothyroidism	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months

Table 3. Operational Definitions of Outcomes of Interest

Variable name	**Values**	**Operational definition**	**Time Window**
Hyperthyroidism	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Menstrual/period issues	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Hematologic symptoms			
DVT	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
PE	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Renal symptoms			
Acute kidney injury	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Chronic kidney disease	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months
Renal Replacement Therapy (Hemodialysis, Peritoneal Dialysis)	1="Yes", 0="No"	See code list; incidence case: no corresponding event from -183 to -15 days prior to the index date	During follow-up period; overall and by follow-up intervals: >=4 weeks, >=12 weeks; >=6 months

9.5. Data sources and measurement

Given the urgent need to clinically understand the novel virus of COVID-19, Optum® developed a low latency data pipeline that enables minimal data lag, while preserving as much clinical data as possible. The data are sourced from Optum's® longitudinal electronic health record (EHR) repository, which is derived from dozens of healthcare provider organizations in the US, including more than 700 hospitals and 7,000 clinics, which was used for this study. The data are certified as deidentified by an independent statistical expert following the Health Insurance Portability and Accountability Act of 1996 (HIPAA) statistical deidentification rules and managed according to Optum® customer data use agreements. Information is processed, normalized, and standardized across the continuum of care from both acute inpatient stays and outpatient visits. By normalizing, validating, and aggregating the de-identified data, Optum generates a longitudinal view of patient care. Optum® data elements include demographics, medications prescribed and administered, immunizations, allergies, lab results (including microbiology), vital signs and other observable measurements, clinical and inpatient stay administrative data and coded diagnoses and procedures. In addition, Optum® uses natural language processing (NLP) computing technology to transform critical facts from physician notes into usable datasets. The NLP data provides detailed information regarding signs and symptoms, family history, disease related scores (i.e. Routine assessment of patient index data 3 (RAPID3) for rheumatoid arthritis, or CHADS2 for stroke risk), genetic testing, medication changes, and physician rationale behind prescribing decisions that might never be recorded in the HER. The COVID-19 dataset incorporates a wide swathe of raw clinical data, including new, unmapped COVID-19 specific clinical data points from both inpatient and ambulatory electronic medical records, practice management systems, and numerous other internal systems. Information is processed from across the continuum of care, including acute inpatient stays and outpatient visits. The COVID-19 data capture point-of-care diagnostics specific to the COVID-19 patient during initial presentation, acute illness, and convalescence, with over 500 mapped labs and bedside observations, including COVID-19-specific testing.

The Optum® COVID-19 EHR dataset elements included patient-level information: demographics, mortality (captured from Social Security Administration Death Master File, electronic medical records and Centers for Medicare and Medicaid Services), as well as clinical interventions, such as medications prescribed and administered, laboratory results, and vital signs and other biometric measures. The data are comprised of multiple tables that can be linked by a common patient identifier (an anonymous, randomized string of characters). The COVID-19 patient data included patients in the EHR database who had documented clinical care from January 2007 through to the most current monthly data release with a documented exposure to, or had been tested for, SARS-CoV-2 (positive or negative result), and/or had a diagnosis of COVID-19, or acute respiratory illness, after February 1, 2020. Thus, not all patients within the Optum® COVID-19 EHR dataset had received a diagnosis of COVID-19. Patients with COVID-19 were identified via a diagnosis code for SARS-CoV-2, a positive test for SARS-CoV-2 active infection (antigen and/or polymerase chain reaction), and/or a positive antibody test. The Optum® COVID-19 EHR dataset included medical records from 2007, allowing for the utilization of patients' medical history in the analysis.

Diagnosis data, laboratory data, and surgical procedure data for the study period of interest was first obtained from structured data (via International Classification of Diseases, Ninth Revision/Tenth Revision, Clinical Modification [ICD-9-CM/ICD-10-CM], International Classification of Diseases, Ninth Revision/Tenth Revision, Procedure Classification System [ICD-9-PCS/ICD-10-PCS], or Current Procedure Terminology (CPT) codes where applicable. Drug treatment data may also have been pulled from prescription written, medication administration, and procedure tables when appropriate (via ICD-9-CM/ICD-10-CM, National Drug Center [NDC], CPT, and Healthcare Common Procedure Coding System [HCPCS] codes where applicable).

Optum's COVID-19 EHR Database has been formally de-identified by an independent statistical expert following HIPAA statistical de-identification rules and managed according to Optum® customer data use agreements. In addition to these structured data, Optum has clinical notes available from some EHR systems and is able to use technology to search the verbatim text for phrases of interest and extract a small portion of those notes for review and clinical assessment. All data elements from this source are stored on Optum's firewalled, password protected database. These data can only be extracted by approved Optum study personnel using standard and commercially available software (e.g., SAS, SQL, Python).

The Optum database is regularly updated. The date and version of the database were specified in the report of the cohort, and any intermediate datasets archived as necessary for these results if requested to be submitted to a regulatory agency or published.

All analyses for this study were conducted in SAS (version 9.4 or higher, SAS Institute, Cary, North Carolina, US) unless specified otherwise.

9.6. Bias

Outcome misclassification was a possibility, as delayed and misdiagnosis of COVID-19 is possible. Laboratory results and vital signs/other biometric measures may have been incomplete and therefore only available for a subset of the patients. Another limitation inherent to EHR databases is that information on prescriptions recorded for outpatients in this database does not necessarily indicate that the medication was consumed or taken as prescribed; similarly, medications filled over the counter or provided as samples by the physician may not have been recorded in the database. Due to the nature of EHR data, conditions not requiring treatment or office visits tend to be systematically under-recorded; therefore, it is possible that this study may only capture severe conditions that were considered in the risk factor models. Patients may have received health care outside of the network of providers and healthcare organizations that contributed to the Optum databases, or prior to having the index diagnosis and we may not be able to exclude the possibility that a patient was diagnosed with COVID-19, as well as other risk factors, prior to entry into a healthcare system where Optum has EHR access.

9.7. Study Size

This is a NI study with no minimum sample size. Primary and secondary objectives are all descriptive. Based on initial feasibility assessment for exploratory objectives, the Optum EHR database had over 100,000 COVID-19 diagnoses and over 1,000 Paxlovid prescriptions, as well as over 2,500 Long COVID as defined by PCC criteria. In addition, the large size of the database would have allowed for propensity score matching to balance the covariate of the Paxlovid users and non-Paxlovid users. Lastly, machine learning methods, especially those using tree branching methodology, are not as prone to small sample size limitations as regular regression methods.

9.8. Data Transformation

All study data exist as structured data by the time of study for primary and secondary objectives. Analyses were conducted using SAS (version 9.4 or later, SAS Institute, Cary, NC, USA). The study were conducted by Quantitative Epidemiology and Analytic Team, Global Medical Epidemiology, Pfizer. The analytic datasets and programs were stored according to Pfizer's procedures. Detailed methodology for data transformations, particularly complex transformations (e.g., many raw variables used to derive an analytic variable), were documented in the statistical analysis plan (SAP), which is dated, filed and maintained by the sponsor (Appendix 4).

9.9. Statistical methods

Detailed statistics methods are described in the SAP (Appendix 4) and summarized below.

9.9.1. Main summary measures

Baseline characteristics were summarized for Source Cohort, Trial Similar Cohorts, and Paxlovid cohort. Means with standard deviations, medians with interquartile were provided for continuous variables. Numbers and percentages were provided for dichotomous variables or categorical variables.

9.9.2. Main statistical methods

For Primary Objective 1, the number of patients who met the study eligibility criteria of the Source Cohort were tabulated in a attrition table. The number of patients who met the inclusion and exclusion criteria for the trial-similar sub-cohorts were tabulated. Baseline characteristics such as demographics, comorbidities and medical histories, and health care utilization were summarized for the Source Cohort and trial-similar sub-cohorts. The tabulations were reported overall and by hospitalization status. In the overall Source Cohort, the tabulations were further stratified by long-COVID time windows since COVID-19 infection (i.e., >=4 weeks, >=12 weeks, and >=6 months) among patients with at least one symptom of long COVID. In the Paxlovid cohort, patients who meet the Source Cohort eligibility criteria were reported in the attrition table or a flow chart. These baseline characteristics such as demographics, comorbidities and medical histories, health care utilization, treatment patterns (treatments contraindicated with Paxlovid and treatments for COVID, vaccination status), the most frequent 50 prescriptions, and medical specialty of the prescribers were summarized. For all cohorts, means with standard deviations and medians with interquartile ranges were provided for continuous variables. Numbers and percentages were presented for dichotomous variables or categorical variables. Demographics were assessed at the index date (i.e., COVID-19 confirmation for the Source Cohort and first Paxlovid prescription for the Paxlovid cohort) or from the closest record prior to the index date. Comorbidities and medical histories were determined within a one-year baseline period prior to the index date. Health care utilization was ascertained within 30 days before and after the index date. Treatment patterns were described overall and by time windows (i.e., -28 days to index-1 and index to +14 days).

For Primary Objective 2, among patients in the Source Cohort who developed the events of interest during the follow-up period, the time from the index date to the event occurrence were calculated. Median/mean time to each event of interest and interquartile ranges/standard deviation were summarized, overall and by hospitalization status and COVID period.

For Primary Objective 3, patients from the Source Cohort were followed from the first COVID-19 infection (index date) to identify the COVID-19 manifestations/complications and health outcomes. Follow-up time was calculated from the index date to the earliest date of the first occurrence of an outcome, death, end of observation in the database, end of risk window (e.g. 30 days), next COVID-19 infection, and end of the study period or most recent data available. The incidence rate of each study outcome was calculated in the Source Cohort and trial-similar sub-cohorts, overall and by hospitalization status and COVID time periods (i.e., pre-vaccine period, vaccine period, Omicron period, and Paxlovid period). Cumulative incidence and its 95% CI were estimated and illustrated using 1-Kaplan-Meier curves The follow-up started on the index date and ended on the first occurrence of an endpoint, disenrollment, study end date, or death, whichever comes first. The incidence rate was calculated as the number of patients who had evidence of the event divided by the total person time at risk, along with the 95% CI. Only the first event occurring in the risk window was included in the numerator. A wash-out period of 6 months with a buffer period of 14 days prior to the index date was applied to remove potential prevalent cases. Cumulative risks of select outcomes and their 95% CIs were estimated and illustrated using 1-Kaplan-Meier curves in the Source Cohort and Trial Similar Cohort, overall and by hospitalization status and COVID time periods (i.e., pre-vaccine period, vaccine period, Omicron period, and Paxlovid period). Subpopulation analyses were performed among immunocompromised patients, pediatric patients (age >18), and those with severe renal disease (e.g. dialysis or end stage renal disease) if sample size allows. Patients from the Paxlovid cohort were followed from the first Paxlovid prescription (index date of the Paxlovid cohort) to identify the potential health outcomes. Follow-up time was calculated from the first Paxlovid prescription to the earliest date of the first occurrence of an outcome, death, end of observation in the database, end of risk window, and end of the study period or the most recent data available. Incidence rate and cumulative risk of each study outcome were calculated overall and by hospitalization status. Stratified analyses were conducted among Paxlovid users with contraindication medications (yes/no), patients with multiple infections of COVID-19 (0, 1, 2+), or patients who received COVID-19 vaccines (yes/no) using Kaplan-Meier curves. To define the episode of COVID-19 infection, a positive test result of SARS-CoV-2 or a diagnosis of COVID-19, or a history of COVID-19 (ICD 10 Z86.16) were flagged. A gap of 3 months was used to define the multiple infections.

For Primary Objective 4, patients with long COVID symptoms were identified during the follow-up period. Incidence of long COVID were analyzed overall and by follow-up intervals (i.e. after 4 weeks, after 12 weeks, and after 6 months up to 365 days). To estimate the incidence of long COVID, a buffer period of 14 days was used to allow the inclusion of COVID-related events before COVID confirmation. Conditions identified between -183 days to -15 days were considered prevalent and existing events and were removed for incidence estimates. These estimates were performed in the Source Cohort and trial similar sub-cohorts, overall and by hospitalization status and COVID time periods (i.e., pre-vaccine period, vaccine period, Omicron period, and Paxlovid period). Subpopulation analyses were performed among immunocompromised patients, pediatric patients (age >18), and those with severe renal disease. Similar analyses of long COVID were implemented in the Paxlovid cohort except that the index date was the first Paxlovid prescription. Stratified analyses were conducted among Paxlovid users with contraindication medications (yes/no), patients with multiple infections of COVID-19 (0, 1, 2+), or patients who received COVID-19 vaccines (yes/no).

For Primary Objective 5, the analyses for Primary Objectives 1-4 in the Paxlovid cohort were tabulated by age group (<18, 18-64, 65+), gender, race, ethnicity, and region. The number of patients and proportions were summarized.

For Secondary Analysis 1, among patients hospitalized with COVID-19, those who received Mechanical Ventilation/ECMO were identified and oxygen supplementation was extracted from the data if recorded and summarized descriptively as analyses outlined previously.

In Exploratory Objective 1 and 2, machine learning was applied to identify predictors associated with severe COVID manifestations/complications and long COVID and to predict the patient-level risk of these events. The least absolute shrinkage and selection operator (LASSO) regression, random survival forest (RSF), and XGBoosting (XGB) models were fitted for each outcome to rank the importance of the pre-specified predictors. The endpoints were newly developed, incident primary PCC, identified through ICD codes for cardiovascular conditions, including dysrhythmia and ischemic heart disease, or pulmonary conditions, including shortness of breath and cough, as well as secondary PCC identified through ICD codes for selected metabolic, hematologic, musculoskeletal, gastrointestinal, renal, or neurologic conditions and fatigue/malaise. These ICD codes were determined based on collective prior evidence. [13] The look-up time window for all endpoints was between 31 and 120 days after the initial COVID-19 infections. Given the potential bias resulting from a single feature selection method, an ensemble method using weighted average ranking were applied to incorporate the results across the three models and to quantify the ensemble importance in an overall ranking of the important predictors for each outcome. The top resulting predictors from the ensemble selection for each outcome were reviewed by clinical experts for biological plausibility. The final predictors (considered to be statistically and clinically meaningful) were used for patient-level progression prediction. The ranking of important predictors from each model and the ensemble method were illustrated in the figures. The final predictors selected were described in terms of the severe COVID manifestations/complications and long COVID. Time-to-event survival analysis was leveraged to predict the individual risk of developing an outcome of interest over time (e.g. for long COVID at 4 weeks, 12 weeks, and 6 months, time windows varied depending on the outcome of interest). A random sample of 70% of the study cohort were selected for training the model and the 30% holdout set was used for internal validation. The same holdout set was used for testing across all resulting models. Model hyperparameters were tuned using cross-validation. Concordance index (C-index) and area under the receiver operating characteristics curve (AUC) was used to evaluate the model performance. The model with the best performance was applied for the final patient-level risk prediction using the ensemble predictors.

In Exploratory Objective 3, when evaluating the effectiveness of Paxlovid in the real-world setting, baseline covariates including demographics, comorbidities and medical histories, healthcare utilization, along with the most frequently recorded 50 diagnosed, procedures, and prescriptions were tabulated between Paxlovid and non-Paxlovid cohorts. To create comparable groups, propensity score matching was applied to match each Paxlovid user to up to 4 non-Paxlovid patients. A propensity score model was fit to include demographics, healthcare utilization, baseline characteristics with absolute standardized difference (SD)>0.1, plus top 50 diagnoses, procedures, prescription retained via a stepwise selection. A logistic regression model was used to estimate the logit of the propensity score. Nearest neighbor matching was applied with a caliper of 0.25 times the standard deviation of the logit of the propensity score. A variable ratio, parallel, balanced 1: n, nearest neighbor approach has been demonstrated to increase precision over the fixed ratio matching. After matching, weighted SDs were computed between Paxlovid and non-Paxlovid groups. SD were calculated using the formula provided in this study. Weighting was computed based on the number of matches. The weight was 1 for the Paxlovid group and 1/n for the non-Paxlovid group with given matches. A variable with weighted SD>0.1 was considered imbalanced and further adjusted in the final model. Propensity score matching and balance evaluation was performed separately in the overall cohorts and in the patients who meet the trial-similar criteria. Incidence rates and incidence proportions and their 95% CIs were calculated for each outcome (30 days risk window and 15 days risk window, respectively) in the pre-matched and after-matched cohorts, overall and within high-risk trial-similar cohorts. Follow-up started at the index date and extended to the first occurrence of each endpoint, death, end of risk window, loss to follow-up, or end of the study period (June 8, 2022), whichever occurred first. Hazard ratios (HRs) and 95% CIs were computed using conditional Cox proportional hazards regression model to account for the variable matching set. Variables that were out of balance after matching were adjusted in the Cox model. Stratified analyses were conducted by these subgroups in overall matched cohorts and high risk matched cohorts for age group (>=65 and <65), race (white and black) and patients vaccinated. Within each level of subgroups, balance of baseline covariates was evaluated in the overall matched cohorts and high risk matched cohorts, respectively. Additional imbalanced covariates were included in the Cox model. Healthcare utilization within 30 days following the index date were described in the matched overall and high-risk cohorts. An algorithm for Assigning Date of Death and Deaths During the Study was used. In the Optum database, deaths are recorded by month and year and not by exact date. The following algorithm was applied to assign a death date to each patient who died during follow-up: 1) Assign 15th day of the month as the death date; 2) If death occurred before the index date but on the same month, assign a death date of the last day of the month of death; 3) If death occurred after the end of follow-up but on the same month, assign the death date to be the same as the follow-up end date and consider this patient to have died in the study.

9.9.3. Missing Values

No imputation for missing values was performed. Missing data were assumed missing completely at random and were removed from the analyses.

9.9.4. Sensitivity analyses

None

9.9.5. Amendments to the statistical analysis plan

None

9.10. Quality control

Analyses are programmed according to the specifications in the protocol, and the SAP, and documented in a programming plan as appropriate. Final deliverables are reviewed and verified by a second, independent programmer who may also perform double programming. All quality checks are documented in the programming plan. The ICD-9-CM and ICD-10-CM codes used in the study were reviewed against relevant codes used in the Food and Drug Administration (FDA) Sentinel program whenever applicable; if there were any discrepancies, the Sentinel codes were used unless there was a strong rationale to use internally developed ICD codes and/or ICD algorithms instead. Additional validation of the code lists was performed by the protocol authors, including the safety risk lead and clinical development scientist. All efforts were made to ensure quality and safe storing of data and reports. Quality control (QC) checks were performed on all SAS programming, data tables, and reports generated in the course of this research. QC findings and documentation of remedial action were maintained. Storage of programming, data, and reports were carried out per standard procedures, and as specified in Section 9.5. For validation of the same day hospitalization patients in Exploratory Objective 3, after the Optum NLP team created key term tags for use in the snippet review for the two Optum clinicians who reviewed patient notes with these key terms mentioned, the two clinicians recorded their findings from the notes regarding whether the notes supported a determination of the reason for the same day hospitalization.

9.11. Protection of human subjects

<u>Subject information and consent</u>

Not Applicable

<u>Independent Ethics Committee (IEC)/Institutional Review Board (IRB)</u>

Independent Ethics Committee (IEC)/ Institutional Review Board (IRB) review was not required.

<u>Ethical conduct of the study</u>

The study was conducted in accordance with legal and regulatory requirements, as well as with scientific purpose, value and rigor and followed generally accepted research practices described in Guidelines for Good Pharmacoepidemiology Practices (GPP) [14], European Medicines Agency (EMA) European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) Guide on Methodological Standards in Pharmacoepidemiology[15], FDA Guidance for Industry and FDA Staff: Best Practices for Conducting and Reporting Pharmacoepidemiologic Safety Studies Using Electronic Healthcare Data[16], and Good practices for real-world data studies of treatment and/or comparative effectiveness: Recommendations from the joint International Society for Pharmacoeconomics and Outcomes Research (ISPOR)–International Society for Pharmacoepidemiology (ISPE) Special Task Force on real-world evidence in health care decision making [17].

10. RESULTS

10.1. Participants

10.1.1. Primary Objectives & Secondary Objectives

Source Cohort (as described in Section 9.3.2.1)

Table 4 summarizes the derivation of the COVID-19 Source Cohort from the Optum® COVID-19 EHR data release. Among all patients in the data release, those with evidence of SARS-CoV-2 infection based on a positive PCR or antigen test and/or a COVID-19 diagnosis code were identified. Application of the index date requirement (on or after 1 January 2020), a minimum of 12 months of prior healthcare activity, and availability of integrated delivery network information further refined the cohort. Exclusion of patients with missing, unknown, or multiple values for sex resulted in the final Source Cohort used for subsequent analyses.

Table 4. Attrition table for Source Cohort

Step	N
0. Total individuals in this data release (covid19_optum_ehr_202209)	12,098,922
0.1 Have a positive PCR or antigen result of direct SARS-CoV-2	1,155,292
0.2 have a diagnosis code of ICD 10 U07.1	1,751,353
1. Have a positive PCR or antigen result of direct SARS-CoV-2 or have a diagnosis code of ICD 10 U07.1	2,200,127
1.1 + index_date >= 2020-01-01	2,197,942
2. Have at least 12 months of >=1 healthcare activity prior to the index date	1,926,090
3. Have integrated delivery network (IDN) information to allow linkage of outpatient and inpatient records	1,669,952
4. exclude Missing, unknown, or multiple values for gender **(final count)**	1,663,017

Trial Similar Cohort High Risk (as described in Section 9.3.2.2.1)

Table 5 presents the derivation of the high-risk Trial Similar Cohort through the sequential application of inclusion and exclusion criteria. Among patients in the eligible high-risk trial-similar cohort Source Cohort, high-risk characteristics were identified during the prespecified baseline assessment windows. These characteristics included advanced age (≥60 years), elevated body mass index (>25 kg/m²), current smoking status, hypertension, chronic lung disease, cardiovascular disease, diabetes mellitus, chronic kidney disease, neurodevelopmental disorders, recent cancer diagnoses, and selected immunocompromising conditions. Exposure to immunomodulatory agents or cancer chemotherapy within defined pre-index windows and documented HIV infection or sickle cell disease were also captured, though less frequently.

Table 5. Attrition table for Trial Similar Cohort High Risk

	Time Window	N	%
Inclusion Criteria			
≥60 years	at index date	426,487	25.65
BMI >25 kg/m2	at index date or closest to index date	786,023	47.26
Current smoker	during one year baseline period	440,235	26.47
Immunosuppressive disease			

Table 5. Attrition table for Trial Similar Cohort High Risk

	Time Window	N	%
Bone marrow or organ transplantation	during one year baseline period	1,899	0.11
Primary immune deficiencies	during one year baseline period		
Treatment with biologics (eg, infliximab, ustekinumab)	90 days prior to index date	10,674	0.64
Immunomodulators with methotrexate, 6MP, azathioprine	90 days prior to index date	17,103	1.03
cancer chemotherapy	90 days prior to index date	9,519	0.57
HIV infection	during one year baseline period	4,089	0.25
Chronic lung disease with asthma, COPD, ILD	during one year baseline period	201,796	12.13
Hypertension	during one year baseline period	407,813	24.52
Cardiovascular disease			
Myocardial infarction	during one year baseline period	15,727	0.95
Stroke	during one year baseline period	16,901	1.02
Transient ischemic attack (TIA)	during one year baseline period	7,746	0.47
Heart failure (HF)	during one year baseline period	68,166	4.10
Angina with prescribed nitroglycerin	during one year baseline period	23,238	1.40
Coronary artery bypass graft surgery (CABG)	during one year baseline period	14,831	0.89
Percutaneous coronary intervention (PCI)	during one year baseline period	25,139	1.51
Carotid endarterectomy	during one year baseline period	287	0.02
Aortic bypass	during one year baseline period	36	0.00
Type 1 or Type 2 diabetes mellitus	during one year baseline period	188,411	11.33
CKD excluding dialysis or end stage of renal disease	during one year baseline period	101,093	6.08
Sickle cell disease	during one year baseline period	2,485	0.15
Neurodevelopmental disorders	during one year baseline period	80,989	4.87
cancer excluding NMSC	during one year baseline period	88,905	5.35
Total patients who met the inclusion criteria		1,150,000	69.15
Exclusion Criteria			
Hospitalization	30 days prior to Index date	40,346	2.43
Active liver disease	any time prior to index date	124,043	7.46
Dialysis or end stage of renal disease	any time prior to index date	38,017	2.29
Pregnant or breastfeeding	9 months prior to index date	51,815	3.12
Total individuals who met the exclusion criteria (final count)		226,958	13.65

Trial Similar Cohort Standard Risk (as described in Section 9.3.2.2.2)

Table 6 presents the derivation of the Trial Similar Standard Risk cohort through the sequential application of inclusion and exclusion criteria.

Table 6. Attrition table for TSC Standard Risk

	Time Window	N	%
Inclusion Criteria			
Source cohort		1,663,017	100.00
Exclusion Criteria			
≥65 years	at the index date	300,270	18.06
BMI≥30 kg/m2	at index date or closest to index date	567,037	34.10
Current smoker	during one year baseline period	440,235	26.47
Immunosuppressive disease			
Bone marrow or organ transplantation	during one year baseline period	1,899	0.11
Primary immune deficiencies	during one year baseline period		
Treatment with biologics (eg, infliximab, ustekinumab)	90 days prior to index date	10,674	0.64
Immunomodulators with methotrexate, 6MP, azathioprine	90 days prior to index date	17,103	1.03
cancer chemotherapy	90 days prior to index date	9,519	0.57
HIV infection	during one year baseline period	4,089	0.25
Chronic lung disease with asthma, COPD, ILD	during one year baseline period	201,796	12.13
Hypertension	during one year baseline period	409,138	24.60
Cardiovascular disease			
Myocardial infarction	during one year baseline period	15,727	0.95
Stroke	during one year baseline period	16,901	1.02
Transient ischemic attack (TIA)	during one year baseline period	7,746	0.47
Heart failure (HF)	during one year baseline period	68,166	4.10
Angina with prescribed nitroglycerin	during one year baseline period	23,238	1.40
Coronary artery bypass graft surgery (CABG)	during one year baseline period	14,831	0.89
Percutaneous coronary intervention (PCI)	during one year baseline period	25,139	1.51
Carotid endarterectomy	during one year baseline period	287	0.02
Aortic bypass	during one year baseline period	36	0.00
Type 1 or Type 2 diabetes mellitus	during one year baseline period	188,411	11.33
CKD excluding dialysis or end stage of renal disease	during one year baseline period	102,308	6.15
Sickle cell disease	during one year baseline period	2,485	0.15

Table 6. Attrition table for TSC Standard Risk

	Time Window	N	%
Neurodevelopmental disorders	during one year baseline period	57,402	3.45
cancer excluding NMSC	during one year baseline period	88,905	5.35
Hospitalization	30 days prior to Index date	40,346	2.43
Active liver disease	any time prior to index date	124,043	7.46
Dialysis or end stage of renal disease	any time prior to index date	34,011	2.05
Pregnant or breastfeeding	9 months prior to index date	51,815	3.12
Total individuals who met the exclusion criteria		1,072,548	64.49
Total individuals who met the inclusion and exclusion criteria		590,469	35.51

Paxlovid Cohort (as described in Section 9.3.2.3)

Table 7 presents the attrition table for the Paxlovid cohort after each step of the inclusion and exclusion criteria. Among patients in the eligible Paxlovid cohort , the cohort drops from 36,687 to 16,583 individuals via the criteria applied, with the largest decreases occurring when applying the requirement for integrated delivery network (IDN) linkage (a loss of about 8,500 individuals) and when removing individuals with missing or unknown age (about 2,300 individuals removed). Additional attrition comes from baseline treatment exclusions and restricting the index date to on or before June 20, 2022.

Table 7. Attrition Table for Paxlovid Cohort

Step	N
1. Have a prescription of Paxlovid in this data release (covid19_optum_ehr_202209)	36,687
1.1 patients with prescription of Molnupiravir (removed)	315
2. + Have at least 12 months of >=1 healthcare activity prior to the first Paxlovid prescription (index date)	35,410
3. + Have IDN information to allow linkage of outpatient and inpatient records	26,914
4. + remove individuals with missing, unknown, or multiple values for gender	26,860
4.1 + remove individuals with unknown age	24,547
5. + remove individuals with COVID-related treatments including contraindicated meds during 28 days prior to index and with baseline hosp. within 30 days prior to the index date	22,980
6. + index date on or before 2022/06/20	16,583
7. + age >=12	16,583

10.1.2. Exploratory Objectives

Table 8 presents the derivation of the Source Cohort who exhibited post-COVID conditions through the sequential application of inclusion and exclusion criteria.

Table 8. Attrition table for post-COVID condition cohort

Step	N
Individuals with COVID-19	2,200,127
First COVID-19 infection on or after 2020/01/01	2,197,942
≥1 year enrollment before index date	1,926,090
Within integrated delivery network	1,669,952
Exclude unknown sex	1,663,017
Age ≥18 years	1,393,923
Follow-up ≥12 weeks	1,101,716
Without any primary PCC 365 days before index date and in 30-day acute period	686,070
Index COVID-19 in Omicron era (on or after January 1, 2022)	107,114
Without any cardiovascular PCC 365 days before index date and in 30-day acute period	980,980
Index COVID-19 in Omicron era (on or after January 1, 2022)	128,632
Without any pulmonary PCC 365 days before index date and in 30-day acute period	743,649
Index COVID-19 in Omicron era (on or after January 1, 2022)	116,666
Without any secondary PCC 365 days before index date and in 30-day acute period	1,080,845
Index COVID-19 in Omicron era (on or after January 1, 2022)	141,799

PCC, post–COVID-19 conditions

10.2. Descriptive data

10.2.1. Primary & Secondary Objectives

10.2.1.1. Objective 1: Describe the distribution of demographics, co-morbid conditions, medical history, selected biomarkers, and healthcare utilization at baseline for COVID-19 patients (including subpopulation with long COVID)

Table 9 illustrates the difference in patient demographics and baseline characteristics between the Paxlovid and non-Paxlovid groups prior to and after applying propensity score matching. After applying the matching, patient demographics and baseline characteristics are balanced between the two groups. Before PSM, several differences in characteristics between patients in the Paxlovid versus non-Paxlovid groups existed, such as with patients in the Paxlovid group being less racially diverse, older, using more Medicare and less Medicaid, having a greater number of comorbidities, a higher Deyo–Charlson Comorbidity Index Score, and having higher COVID-19 vaccination rates.

Table 9. Patient demographics and baseline clinical characteristics by Paxlovid use

	Before PSM			After PSM		
	Nirmatrelvir/ Ritonavir N=12,440	Non-nirmatrelvir/ Ritonavir N=234,123	Standardized Difference	Nirmatrelvir/ Ritonavir N=12,439	Non-nirmatrelvir/ Ritonavir N=36,490	Standardized Difference
Age, years, mean ± SD	59.8 ± 15.5	49.7 ± 19.3	0.575	59.8 ± 15.5	58.1 ± 17.4	0.011
Age bracket (inclusive), n (%)						
12–17 years	89 (0.7)	11,674 (5.0)	0.259	89 (0.7)	580 (1.6)	0.051
18–29 years	435 (3.5)	29,824 (12.7)	0.343	435 (3.5)	1965 (5.4)	0.043
30–39 years	877 (7.0)	34,756 (14.8)	0.252	877 (7.1)	3192 (8.7)	0.018
40–49 years	1580 (12.7)	37,494 (16.0)	0.095	1580 (12.7)	4980 (13.6)	0.003
50–59 years	2370 (19.1)	39,006 (16.7)	0.062	2370 (19.1)	6719 (18.4)	0.011
60–64 years	1916 (15.4)	24,908 (10.6)	0.142	1916 (15.4)	5029 (13.8)	0.031
65–74 years	3138 (25.2)	31,655 (13.5)	0.299	3137 (25.2)	7558 (20.7)	0.069
75–84 years	1560 (12.5)	16,963 (7.2)	0.178	1560 (12.5)	4392 (12.0)	0.015
≥85 years	475 (3.8)	7843 (3.3)	0.025	475 (3.8)	2075 (5.7)	0.103
Male sex, n (%)	5053 (40.6)	93,208 (39.8)	0.016	5053 (40.6)	14,657 (40.2)	0.007
Race, n (%)						
White	10,375 (83.4)	172,623 (73.7)	0.237	10,374 (83.4)	29,825 (81.7)	0.003
African American	943 (7.6)	31,257 (13.4)	0.189	943 (7.6)	2922 (8.0)	0.004
Asian	350 (2.8)	4812 (2.1)	0.049	350 (2.8)	1029 (2.8)	0.002
Other/unknown	772 (6.2)	25,431 (10.9)	0.167	772 (6.2)	2714 (7.4)	0.011
Ethnicity, n (%)						
Hispanic	516 (4.1)	18,841 (8.0)	0.164	516 (4.1)	1683 (4.6)	0.005
Non-Hispanic	10,590 (85.1)	179,473 (76.7)	0.217	10,589 (85.1)	29,825 (81.7)	0.024
Unknown	1334 (10.7)	35,809 (15.3)	0.136	1334 (10.7)	4982 (13.7)	0.025
Cohort entry month/year, n (%)						
Dec 2021	99 (0.8)	37,993 (16.2)	0.575	99 (0.8)	396 (1.1)	0.000
Jan 2022	609 (4.9)	117,606 (50.2)	1.177	609 (4.9)	2436 (6.7)	0.000
Feb 2022	292 (2.3)	22,604 (9.7)	0.311	292 (2.3)	1168 (3.2)	0.000
Mar 2022	294 (2.4)	8172 (3.5)	0.067	294 (2.4)	1176 (3.2)	0.000
Apr 2022	1736 (14.0)	11,617 (5.0)	0.311	1736 (14.0)	6,207 (17.0)	0.000
May 2022	6044 (48.6)	22,201 (9.5)	0.955	6044 (48.6)	15,903 (43.6)	0.000
Jun 2022	3366 (27.1)	13,930 (5.9)	0.593	3365 (27.1)	9204 (25.2)	0.000
Insurance type, n (%)						

Table 9. Patient demographics and baseline clinical characteristics by Paxlovid use

	Before PSM			After PSM		
	Nirmatrelvir/ Ritonavir N=12,440	**Non-nirmatrelvir/ Ritonavir N=234,123**	**Standardized Difference**	**Nirmatrelvir/ Ritonavir N=12,439**	**Non-nirmatrelvir/ Ritonavir N=36,490**	**Standardized Difference**
Commercial	7408 (59.5)	147,301 (62.9)	0.069	7408 (59.6)	22,253 (61.0)	0.009
Medicare	3044 (24.5)	34,257 (14.6)	0.250	3044 (24.5)	8462 (23.2)	0.002
Medicaid	443 (3.6)	20,334 (8.7)	0.215	443 (3.6)	1556 (4.3)	0.006
Other payer type	279 (2.2)	8895 (3.8)	0.091	279 (2.2)	931 (2.6)	0.002
Uninsured	71 (0.6)	2484 (1.1)	0.055	71 (0.6)	213 (0.6)	0.006
Unknown	1195 (9.6)	20,852 (8.9)	0.024	1194 (9.6)	3075 (8.4)	0.020
Geographic region, n (%)						
Northeast	3713 (29.8)	76,683 (32.8)	0.063	3713 (29.8)	13,093 (35.9)	0.055
Midwest	4924 (39.6)	93,962 (40.1)	0.011	4923 (39.6)	13,261 (36.3)	0.036
West	746 (6.0)	7472 (3.2)	0.134	746 (6.0)	2109 (5.8)	0.015
South	2645 (21.3)	46,395 (19.8)	0.036	2645 (21.3)	6698 (18.4)	0.031
Other/Unknown	412 (3.3)	9611 (4.1)	0.042	412 (3.3)	1329 (3.6)	0.006
Comorbidities,[a] n (%)						
Asthma	1556 (12.5)	26,814 (11.5)	0.032	1555 (12.5)	4180 (11.5)	0.012
COPD	775 (6.2)	13,580 (5.8)	0.018	775 (6.2)	2381 (6.5)	0.023
Coronary heart disease	1141 (9.2)	14,560 (6.2)	0.111	1141 (9.2)	3097 (8.5)	0.004
Hypertension	5464 (43.9)	72,442 (30.9)	0.271	5463 (43.9)	14,316 (39.2)	0.023
Chronic kidney disease	818 (6.6)	13,192 (5.6)	0.039	818 (6.6)	2553 (7.0)	0.034
Smoker	3672 (29.5)	95,124 (40.6)	0.234	3672 (29.5)	11,834 (32.4)	0.019
Body mass index ≥30 kg/m^2 or obesity	5841 (47.0)	110,596 (47.2)	0.006	5840 (46.9)	16,174 (44.3)	0.024
Hyperlipidemia	5687 (45.7)	64,236 (27.4)	0.387	5686 (45.7)	14,470 (39.7)	0.032
Diabetes mellitus		2183 (17.5)	29,359 (12.5)	0.140	2182 (17.5)	5551 (15.2)
Cancer	1405 (11.3)	14,702 (6.3)	0.178	1405 (11.3)	3621 (9.9)	0.006
Comorbidity index,[b] mean ± SD	1.19 ± 2.1	0.88 ± 1.8	0.163	1.19 ± 2.1	1.11 ± 2.0	0.004
Receipt of ≥1 COVID-19 vaccination, n (%)	8710 (70.0)	111,903 (47.8)	0.464	8709 (70.0)	24,082 (66.0)	0.014
Number of previous SARS-CoV-2 infections, n (%)						
0	11,186 (89.9)	208,403 (89.0)	0.029	11,185 (89.9)	32,464 (89.0)	0.017
1	1077 (8.7)	21,874 (9.3)	0.024	1077 (8.7)	3399 (9.3)	0.014
≥2	177 (1.4)	3846 (1.6)	0.018	177 (1.4)	627 (1.7)	0.009
Age, years, mean ± SD	59.8 ± 15.5	49.7 ± 19.3	0.575	59.8 ± 15.5	58.1 ± 17.4	0.011

COPD=chronic obstructive pulmonary disease; PSM=propensity score matching; SD=standard deviation.
Data cutoff for this analysis was July 20, 2022.
aReported in ≥5% of patients in either group.
bDeyo-Charlson Comorbidity Index Score.

Table 10 summarizes comorbid conditions reported in <5% of both groups which propensity score matching balances.

Table 10. Baseline clinical characteristics before and after PSM reported in <5% in both groups

Comorbidity, n (%)	Before PSM Nirmatrelvir / Ritonavir N=12,440	Before PSM Non-nirmatrelvir / Ritonavir N=234,123	Before PSM Standardized Difference	After PSM Nirmatrelvir / Ritonavir N=12,439	After PSM Non-nirmatrelvir / Ritonavir N=36,490	After PSM Standardized Difference
Multiple sclerosis	70 (0.6)	951 (0.4)	0.023	70 (0.6)	168 (0.5)	0.016
Sjögren's syndrome	59 (0.5)	720 (0.3)	0.027	59 (0.5)	142 (0.4)	0.016
Guillain-Barré	6 (0.0)	57 (0.0)	0.013	6 (0.0)	5 (0.0)	0.021
Idiopathic thrombocytopenia purpura	9 (0.1)	212 (0.1)	0.006	9 (0.1)	40 (0.1)	0.012
Autoimmune thyroiditis	159 (1.3)	2154 (0.9)	0.034	159 (1.3)	415 (1.1)	0.011
Giant cell arteritis	4 (0.0)	69 (0.0)	0.002	4 (0.0)	20 (0.1)	0.013
Psoriasis	237 (1.9)	2332 (1.0)	0.076	237 (1.9)	487 (1.3)	0.041
Systemic or cutaneous lupus erythematosus	85 (0.7)	1074 (0.5)	0.030	85 (0.7)	180 (0.5)	0.021
Autoimmune arthritis/rheumatoid arthritis	262 (2.1)	2968 (1.3)	0.065	262 (2.1)	605 (1.7)	0.031
Interstitial lung disease	103 (0.8)	1643 (0.7)	0.014	103 (0.8)	317 (0.9)	0.007
Cardiomyopathies	190 (1.5)	3124 (1.3)	0.016	190 (1.5)	588 (1.6)	0.009
Cerebrovascular disease or stroke (including transient ischemic attack)	498 (4.0)	7764 (3.3)	0.037	498 (4.0)	1561 (4.3)	0.023
HIV infection	52 (0.4)	860 (0.4)	0.008	52 (0.4)	121 (0.3)	0.021

PSM=propensity score matching.
Values shown are n (%).
Data cutoff for this analysis was July 20, 2022.

10.2.2. Exploratory Objectives

Objective 1: Identify predictors of COVID-19 severe outcomes/manifestations and Long COVID with machine learning (ML) methods

Objective 2: Predict risk of developing severe outcomes/manifestation and Long COVID with machine learning (ML) methods at the patient level

Table 11 summarizes the time between index COVID-19 infection and development of primary or secondary post-COVID-19 conditions (PCC). Across PCC outcome categories, newly developed primary, pulmonary, and cardiovascular PCCs occurred in approximately 1–3% of patients, with slightly lower rates in the Omicron-era subset. Secondary PCCs were less common (0.3–0.4%). Among patients who developed PCC, the time from index to first PCC event was consistent across domains, with median onset occurring around 64–67 days post-infection.

Table 11. Descriptive statistics of newly developed primary or secondary PCC outcomes

Outcome	n	%
Newly developed primary PCC in 31–120 days	22,723	3.3

Table 11. Descriptive statistics of newly developed primary or secondary PCC outcomes

Outcome	n		%	
Index COVID-19 infection in Omicron era	3329		3.1	
Newly developed cardiovascular PCC in 31–120 days	13,537		1.4	
Index COVID-19 infection in Omicron era	1909		1.5	
Newly developed pulmonary PCC in 31–120 days	20,031		2.7	
Index COVID-19 infection in Omicron era	2703		2.3	
Newly developed secondary PCC in 31–120 days	4072		0.3	
Index COVID-19 infection in Omicron era	566		0.4	
Time, days	**1st Quartile**	**3rd Quartile**	**Mean**	**Median**
From index date to first newly developed primary PCC date	45	90	69	65
From index date to first newly developed cardiovascular PCC date	46	92	70	67
From index date to first newly developed pulmonary PCC date	44	90	68	64
From index date to first newly developed secondary PCC date	47	91	70	67

PCC, post–COVID-19 condition

Table 12 describes the differences in patient characteristics between those who did not develop and did develop primary PCC within 31-120 days. Patients who developed primary PCC were older, with a higher proportion aged ≥65 (27% vs 16%), and entered the cohort slightly more often in 2020. They also had substantially higher comorbidity burden, including higher rates of asthma, COPD, coronary heart disease, cerebrovascular disease, hypertension, chronic kidney disease, obesity (BMI ≥30), diabetes, and cancer, along with a higher mean Charlson Comorbidity Index. Pre-index and peri-index healthcare utilization was consistently higher in the PCC group, including more hospitalizations, ER visits, physician visits, and greater use of COVID-19–related treatments such as remdesivir, steroids, and heparin.

Table 12. Patient characteristics by newly developed primary PCC group during the full study period: demographics, comorbidities and medical history, concomitant treatments, and healthcare utilization

Patient Characteristics	Analysis cohort (no primary PCC 365 days before index date or in 30-day acute period) n=686,070		Newly developed primary PCC in 31–120 days n=22,723		No newly developed primary PCC in 31–120 days n=663,347	
Demographics	**n**	**%**	**n**	**%**	**n**	**%**
Year of cohort entry						
2020	257,511	37.53	9415	41.43	248,096	37.40
2021	321,445	46.85	9979	43.92	311,466	46.95
2022	107,114	15.61	3329	14.65	103,785	15.65
Age group, years						
<65	573,017	83.52	16,596	73.04	556,421	83.88
≥65	113,053	16.48	6127	26.96	106,926	16.12
Age, years						
Mean (SD)	46.82 (17.29)		52.79 (17.65)		46.61 (17.24)	
Median (IQR)	46 (32–60)		54 (39–65)		46 (32–59)	
Sex						

Table 12. Patient characteristics by newly developed primary PCC group during the full study period: demographics, comorbidities and medical history, concomitant treatments, and healthcare utilization

Patient Characteristics	Analysis cohort (no primary PCC 365 days before index date or in 30-day acute period) n=686,070		Newly developed primary PCC in 31–120 days n=22,723		No newly developed primary PCC in 31–120 days n=663,347	
Male	273,958	39.93	8888	39.11	265,070	39.96
Female	412,112	60.07	13,835	60.89	398,277	60.04
Race						
White	504,989	73.61	16,864	74.22	488,125	73.59
Black	86,593	12.62	3225	14.19	83,368	12.57
Asian	14,310	2.09	369	1.62	13,941	2.10
Other/unknown	30,056	4.38	917	4.04	29,139	4.39
Ethnicity						
Hispanic	59,577	8.68	1986	8.74	57,591	8.68
Not Hispanic	535,656	78.08	17,885	78.71	517,771	78.05
Unknown	90,837	13.24	2852	12.55	87,985	13.26
Insurance						
Commercial	490,001	71.42	15,923	70.07	474,078	71.47
Medicare	58,093	8.47	3171	13.96	54,922	8.28
Medicaid	48,796	7.11	1778	7.82	47,018	7.09
Other payor type	14,144	2.06	422	1.86	13,722	2.07
Uninsured	14,494	2.11	268	1.18	14,226	2.14
Unknown	58,036	8.46	1054	4.64	56,982	8.59
Geographic region						
Northeast	177,632	25.89	6456	28.41	171,176	25.80
Midwest	315,208	45.94	10,417	45.84	304,791	45.95
West	31,890	4.65	1010	4.44	30,880	4.66
South	131,284	19.14	3923	17.26	127,361	19.20
Other/unknown	30,056	4.38	917	4.04	29,139	4.39
Comorbidities and medical history	**n**	**%**	**n**	**%**	**n**	**%**
Autoimmune diseases						
Multiple sclerosis	2292	0.33	112	0.49	2180	0.33
Sjogren syndrome	1367	0.20	85	0.37	1282	0.19
Guillain-Barre	116	0.02	11	0.05	105	0.02
Idiopathic thrombocytopenia purpura	499	0.07	33	0.15	466	0.07
Autoimmune thyroiditis	4616	0.67	191	0.84	4425	0.67
Giant cell arteritis	153	0.02	4	0.02	149	0.02
Psoriasis	5233	0.76	232	1.02	5001	0.75
Systemic or cutaneous lupus erythematosus	2114	0.31	124	0.55	1990	0.30
Autoimmune arthritis/rheumatoid arthritis	5969	0.87	383	1.69	5586	0.84
Respiratory conditions						
Asthma	41,019	5.98	2188	9.63	38,831	5.85
COPD	19,065	2.78	1530	6.73	17,535	2.64
ILD	1425	0.21	117	0.51	1308	0.20
Cardiovascular or cerebrovascular conditions						
Coronary heart disease	21,982	3.20	1705	7.50	20,277	3.06
Cardiomyopathies	2761	0.40	261	1.15	2500	0.38
Cerebrovascular disease or stroke (including transient ischemic attack)	12,755	1.86	871	3.83	11,884	1.79
Hypertension	150,406	21.92	7976	35.10	142,430	21.47
Liver or renal conditions						
Chronic kidney disease	29,264	4.27	1961	8.63	27,303	4.12

Table 12. Patient characteristics by newly developed primary PCC group during the full study period: demographics, comorbidities and medical history, concomitant treatments, and healthcare utilization

Patient Characteristics	Analysis cohort (no primary PCC 365 days before index date or in 30-day acute period) n=686,070		Newly developed primary PCC in 31–120 days n=22,723		No newly developed primary PCC in 31–120 days n=663,347	
Liver disease	19,059	2.78	1042	4.59	18,017	2.72
Infections						
HBV	551	0.08	22	0.10	529	0.08
HCV	1407	0.21	79	0.35	1328	0.20
HIV infection	1736	0.25	68	0.30	1668	0.25
Other						
Smoking	172,091	25.08	7469	32.87	164,622	24.82
BMI ≥30	232,237	33.85	9931	43.70	222,306	33.51
Hyperlipidemia	133,166	19.41	6679	29.39	126,487	19.07
Diabetes mellitus	67,961	9.91	3745	16.48	64,216	9.68
Cancer	31,319	4.56	1714	7.54	29,605	4.46
Sickle cell disease	848	0.12	40	0.18	808	0.12
Deyo-Charlson Comorbidity Index score						
Mean (SD)	0.51 (1.28)		1.00 (1.84)		0.50 (1.26)	
Median (IQR)	0 (0–0)		0 (0–1)		0 (0–0)	
DIC diagnosis (ICD code D65) during 365 days before index or in the 30-day acute period	69	0.01	7	0.03	62	0.01
Concomitant treatments	**n**	**%**	**n**	**%**	**n**	**%**
Treatments for COVID-19						
Nirmatrelvir/ritonavir	649	0.09	21	0.09	628	0.09
Anti-SARS-CoV-2 antibody products						
Bamlanivimab/etesevimab	11,709	1.71	485	2.13	11,224	1.69
Casirivimab/imdevimab	23,415	3.41	665	2.93	22,750	3.43
Sotrovimab	2149	0.31	116	0.51	2033	0.31
Tixagevimab/cilgavimab	29	0.00	3	0.01	26	0.00
Bebtelovimab	190	0.03	7	0.03	183	0.03
Convalescent plasma	0	0.00	0	0.00	0	0.00
Antiviral therapy						
Remdesivir	8797	1.28	831	3.66	7966	1.20
Molnupiravir	627	0.09	24	0.11	603	0.09
Chloroquine/hydroxychloroquine	258	0.04	20	0.09	238	0.04
Azithromycin	32,048	4.67	1625	7.15	30,423	4.59
Lopinavir/ritonavir	0	0.00	0	0.00	0	0.00
Ivermectin	1927	0.28	97	0.43	1830	0.28
Nitazoxanide	5	0.00	0	0.00	5	0.00
Ribavirin	1	0.00	0	0.00	1	0.00
Interferon-beta	32	0.00	2	0.01	30	0.00
Immunomodulators						
Dexamethasone	37,723	5.50	2286	10.06	35,437	5.34
Methylprednisolone	22,475	3.28	1147	5.05	21,328	3.22
Fluvoxamine	266	0.04	13	0.06	253	0.04
Interleukin inhibitors						
Tocilizumab	963	0.14	153	0.67	810	0.12
Sarilumab	64	0.01	13	0.06	51	0.01
Antithrombotic therapy						
Heparin	26,536	3.87	2052	9.03	24,484	3.69
COVID-19 vaccines	120,363	17.54	3977	17.50	116,386	17.55
Healthcare utilization	**30 days before index**	**Within 30 days of index**	**30 days before index**	**Within 30 days of index**	**30 days before index**	**Within 30 days of index**
Hospitalization						

Table 12. Patient characteristics by newly developed primary PCC group during the full study period: demographics, comorbidities and medical history, concomitant treatments, and healthcare utilization

Patient Characteristics	Analysis cohort (no primary PCC 365 days before index date or in 30-day acute period) n=686,070		Newly developed primary PCC in 31–120 days n=22,723		No newly developed primary PCC in 31–120 days n=663,347	
Mean (SD)	0.01 (0.12)	0.08 (0.29)	0.03 (0.18)	0.18 (0.42)	0.01 (0.12)	0.08 (0.28)
Median (IQR)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)
Length of stay						
Mean (SD)	7.22 (12.13)	6.99 (9.10)	10.54 (15.21)	11.11 (15.57)	6.97 (11.82)	6.67 (8.30)
Median (IQR)	4 (3–8)	5 (3–8)	6 (3–11)	7 (4–13)	4 (3–8)	5 (3–8)
Emergency room visits						
Mean (SD)	0.05 (0.28)	0.27 (0.58)	0.09 (0.39)	0.39 (0.75)	0.05 (0.28)	0.26 (0.57)
Median (IQR)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–1)	0 (0–0)	0 (0–0)
Physician office visits						
Mean (SD)	0.71 (1.26)	1.35 (1.72)	0.94 (1.52)	1.89 (2.27)	0.70 (1.24)	1.33 (1.69)
Median (IQR)	0 (0–1)	1 (0–2)	0 (0–1)	1 (0–3)	0 (0–1)	1 (0–2)

BMI, body mass index; COPD, chronic obstructive pulmonary disease; DIC, disseminated intravascular coagulation; HBV, hepatitis B virus, HCV, hepatitis C virus; HIV, human immunodeficiency virus; ICD, International Classification of Diseases, Tenth Revision, Clinical Modification; ILD, interstitial lung disease; IQR, interquartile range; PCC, post–COVID-19 conditions.

Table 13 describes the differences in patient characteristics between those who did not develop and did develop secondary PCC within 31-120 days. Patients who developed secondary PCC were much older (median 65 vs 48 years; 52% vs 19% aged ≥65) and had a substantially higher burden of comorbidities, including COPD, coronary heart disease, cardiomyopathy, cerebrovascular disease, hypertension, chronic kidney disease, diabetes, hyperlipidemia, obesity, and cancer. They also had markedly higher healthcare utilization, with more frequent hospitalizations, longer stays, more ER visits, more physician visits, and greater use of acute COVID-19 treatments such as remdesivir, dexamethasone, methylprednisolone, and heparin.

Table 13. Patient characteristics by newly developed secondary PCC group during the full study period: demographics, comorbidities and medical history, concomitant treatments, and healthcare utilization

Patient characteristics	Analysis cohort (no secondary PCC 365 days before index date or in 30-day acute period) n= 1,080,845		Newly developed secondary PCC in 31–120 days n=4072		No newly developed secondary PCC in 31–120 days n=1,076,773	
Demographics	**n**	**%**	**n**	**%**	**n**	**%**
Year of cohort entry						
2020	445,058	41.18	1777	43.64	443,281	41.17
2021	493,988	45.70	1729	42.46	492,259	45.72
2022	141,799	13.12	566	13.90	141,233	13.12
Age group, years						
<65	873,791	80.84	1955	48.01	871,836	80.97
≥65	207,054	19.16	2117	51.99	204,937	19.03
Age continuous, years						
Mean (SD)	48.45 (17.51)		63.35 (17.44)		48.39 (17.49)	
Median (IQR)	48 (34–61)		65 (52–77)		48 (34–61)	
Sex						
Male	438,049	40.53	1764	43.32	436,285	40.52
Female	642,796	59.47	2308	56.68	640,488	59.48

Table 13. Patient characteristics by newly developed secondary PCC group during the full study period: demographics, comorbidities and medical history, concomitant treatments, and healthcare utilization

Patient characteristics	Analysis cohort (no secondary PCC 365 days before index date or in 30-day acute period) n= 1,080,845		Newly developed secondary PCC in 31–120 days n=4072		No newly developed secondary PCC in 31–120 days n=1,076,773	
Race						
White	799,149	73.94	3166	77.75	795,983	73.92
Black	143,348	13.26	561	13.78	142,787	13.26
Asian	20,962	1.94	61	1.50	20,901	1.94
Other/unknown	46,077	4.26	166	4.08	45,911	4.26
Ethnicity						
Hispanic	96,472	8.93	259	6.36	96,213	8.94
Not Hispanic	856,106	79.21	3361	82.54	852,745	79.19
Unknown	128,267	11.87	452	11.10	127,815	11.87
Insurance						
Commercial	782,716	72.42	2525	62.01	780,191	72.46
Medicare	108,100	10.00	1052	25.83	107,048	9.94
Medicaid	79,094	7.32	254	6.24	78,840	7.32
Other payor type	21,339	1.97	51	1.25	21,288	1.98
Uninsured	21,459	1.99	23	0.56	21,436	1.99
Unknown	64,409	5.96	127	3.12	64,282	5.97
Geographic region						
Northeast	262,947	24.33	939	23.06	262,008	24.33
Midwest	514,818	47.63	2050	50.34	512,768	47.62
West	45,677	4.23	132	3.24	45,545	4.23
South	211,326	19.55	785	19.28	210,541	19.55
Other/unknown	46,077	4.26	166	4.08	45,911	4.26
Comorbidities and medical history	**n**	**%**	**n**	**%**	**n**	**%**
Autoimmune diseases						
Multiple sclerosis	3676	0.34	36	0.88	3640	0.34
Sjogren syndrome	2726	0.25	23	0.56	2703	0.25
Guillain-Barre	237	0.02	4	0.10	233	0.02
Idiopathic thrombocytopenia purpura	976	0.09	7	0.17	969	0.09
Autoimmune thyroiditis	7432	0.69	26	0.64	7406	0.69
Giant cell arteritis	352	0.03	4	0.10	348	0.03
Psoriasis	9007	0.83	57	1.40	8950	0.83
Systemic or cutaneous lupus erythematosus	4397	0.41	25	0.61	4372	0.41
Autoimmune arthritis/rheumatoid arthritis	11,924	1.10	105	2.58	11,819	1.10
Respiratory conditions						
Asthma	88,411	8.18	483	11.86	87,928	8.17
COPD	58,441	5.41	672	16.50	57,769	5.37
ILD	5511	0.51	86	2.11	5425	0.50
Cardiovascular or cerebrovascular conditions						
Coronary heart disease	62,024	5.74	771	18.93	61,253	5.69
Cardiomyopathies	15,243	1.41	207	5.08	15,036	1.40
Cerebrovascular disease or stroke (including transient ischemic attack)	29,242	2.71	464	11.39	28,778	2.67
Hypertension	295,896	27.38	2339	57.44	293,557	27.26
Liver or renal conditions						
Chronic kidney disease	66,331	6.14	974	23.92	65,357	6.07
Liver disease	39,211	3.63	343	8.42	38,868	3.61
Infections						

Table 13. Patient characteristics by newly developed secondary PCC group during the full study period: demographics, comorbidities and medical history, concomitant treatments, and healthcare utilization

Patient characteristics	Analysis cohort (no secondary PCC 365 days before index date or in 30-day acute period) n= 1,080,845		Newly developed secondary PCC in 31–120 days n=4072		No newly developed secondary PCC in 31–120 days n=1,076,773	
HBV	911	0.08	7	0.17	904	0.08
HCV	3033	0.28	38	0.93	2995	0.28
HIV infection	3053	0.28	14	0.34	3039	0.28
Other						
Smoking	315,901	29.23	1741	42.76	314,160	29.18
BMI ≥30 or obesity	418,698	38.74	1905	46.78	416,793	38.71
Hyperlipidemia	253,498	23.45	1904	46.76	251,594	23.37
Diabetes mellitus	135,781	12.56	1262	30.99	134,519	12.49
Cancer	60,616	5.61	571	14.02	60,045	5.58
Sickle cell disease	1601	0.15	10	0.25	1591	0.15
Deyo-Charlson Comorbidity Index Score						
Mean (SD)	0.74 (1.63)		2.35 (2.79)		0.73 (1.62)	
Median (IQR)	0 (0–1)		1 (0–4)		0 (0–1)	
DIC diagnosis (ICD code D65) during 365 days before index or in the 30-day acute period	244	0.02	9	0.22	235	0.02
Concomitant treatments	**n**	**%**	**n**	**%**	**n**	**%**
Treatments for COVID-19						
Nirmatrelvir/ritonavir	927	0.09	3	0.07	924	0.09
Anti-SARS-CoV-2 antibody products						
Bamlanivimab/etesevimab	19,485	1.80	77	1.89	19,408	1.80
Casirivimab/imdevimab	34,810	3.22	101	2.48	34,709	3.22
Sotrovimab	3,252	0.30	18	0.44	3234	0.30
Tixagevimab/cilgavimab	57	0.01	1	0.02	56	0.01
Bebtelovimab	307	0.03	2	0.05	305	0.03
Convalescent plasma	0	0	0	0	0	0
Antiviral therapy						
Remdesivir	31,041	2.87	344	8.45	30,697	2.85
Molnupiravir	970	0.09	4	0.10	966	0.09
Chloroquine/hydroxychloroquine	521	0.05	5	0.12	516	0.05
Azithromycin	72,567	6.71	411	10.09	72,156	6.70
Lopinavir/ritonavir	2	0.00	0	0	2	0.00
Ivermectin	3601	0.33	21	0.52	3580	0.33
Nitazoxanide	10	0.00	0	0	10	0.00
Ribavirin	3	0.00	0	0	3	0.00
Interferon-beta	39	0.00	0	0	39	0.00
Immunomodulators						
Dexamethasone	92,454	8.55	809	19.87	91,645	8.51
Methylprednisolone	47,552	4.40	302	7.42	47,250	4.39
Fluvoxamine	456	0.04	3	0.07	453	0.04
Interleukin inhibitors						
Tocilizumab	4039	0.37	84	2.06	3955	0.37
Sarilumab	213	0.02	0	0	213	0.02
Antithrombotic therapy						
Heparin	74,456	6.89	884	21.71	73,572	6.83
COVID-19 vaccines	168,653	15.60	787	19.33	167,866	15.59
Healthcare utilization	**30 days before index**	**Within 30 days of index**	**30 days before index**	**Within 30 days of index**	**30 days before index**	**Within 30 days of index**
Hospitalization						
Mean (SD)	0.02 (0.16)	0.14 (0.37)	0.09 (0.30)	0.46 (0.63)	0.02 (0.16)	0.13 (0.37)

Table 13. Patient characteristics by newly developed secondary PCC group during the full study period: demographics, comorbidities and medical history, concomitant treatments, and healthcare utilization

Patient characteristics	Analysis cohort (no secondary PCC 365 days before index date or in 30-day acute period) n= 1,080,845		Newly developed secondary PCC in 31–120 days n=4072		No newly developed secondary PCC in 31–120 days n=1,076,773	
Median (IQR)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–1)	0 (0–0)	0 (0–0)
Length of stay						
Mean (SD)	8.04 (11.38)	8.39 (10.58)	12.99 (15.15)	17.88 (20.29)	7.97 (11.13)	8.27 (10.35)
Median (IQR)	5 (6)	6 (6)	7 (11)	10 (18)	5 (6)	6 (6)
Emergency room visits						
Mean (SD)	0.08 (0.36)	0.38 (0.71)	0.19 (0.70)	0.71 (1.02)	0.08 (0.36)	0.37 (0.71)
Median (IQR)	0 (0–0)	0 (0–1)	0 (0–0)	0 (0–1)	0 (0–0)	0 (0–1)
Physician office visits						
Mean (SD)	0.79 (1.38)	1.55 (1.99)	1.37 (2.14)	2.66 (3.22)	0.79 (1.37)	1.55 (1.98)
Median (IQR)	0 (0–1)	1 (0–2)	1 (0–2)	2 (0–4)	0 (0–1)	1 (0–2)

BMI, body mass index; COPD, chronic obstructive pulmonary disease; DIC, disseminated intravascular coagulation; HBV, hepatitis B virus, HCV, hepatitis C virus; HIV, human immunodeficiency virus; ICD, International Classification of Diseases, Tenth Revision, Clinical Modification; ILD, interstitial lung disease; IQR, interquartile range; PCC, post–COVID-19 conditions.

Similar differences between patients with newly developed primary PCC and no newly developed primary PCC in the Omicron period (Table 14) were observed with the full study period (Table 12).

Table 14. Patient characteristics by newly developed primary PCC group during the Omicron period: demographics, comorbidities and medical history, concomitant treatments, and healthcare utilization

Patient characteristics	Analysis cohort (no primary PCC 365 days before index date or in 30-day acute period) n=107,114		Newly developed primary PCC in 31–120 days n=3329		No newly developed primary PCC in 31–120 days n=103,785	
Demographics	**n**	**%**	**n**	**%**	**n**	**%**
Age group, years						
<65	88,505	82.63	2348	70.53	86,157	83.01
≥65	18,609	17.37	981	29.47	17,628	16.99
Age, years						
Mean (SD)	47.52 (17.05)		53.38 (17.94)		47.33 (16.99)	
Median (IQR)	47 (34–60)		55 (39–67)		47 (33–60)	
Sex						
Male	36,231	33.82	1,220	36.65	35,011	33.73
Female	70,883	66.18	2,109	63.35	68,774	66.27
Race						
White	80,044	74.73	2470	74.20	77,574	74.74
Black	11,728	10.95	442	13.28	11,286	10.87
Asian	2803	2.62	55	1.65	2748	2.65
Other/unknown	4664	4.35	135	4.06	4529	4.36
Ethnicity						
Hispanic	9601	8.96	326	9.79	9275	8.94
Not Hispanic	81,971	76.53	2508	75.34	79,463	76.57
Unknown	15,542	14.51	495	14.87	15,047	14.50
Insurance						
Commercial	66,772	62.34	1841	55.30	64,931	62.56
Medicare	10,242	9.56	578	17.36	9664	9.31

Table 14. Patient characteristics by newly developed primary PCC group during the Omicron period: demographics, comorbidities and medical history, concomitant treatments, and healthcare utilization

Patient characteristics	Analysis cohort (no primary PCC 365 days before index date or in 30-day acute period) n=107,114		Newly developed primary PCC in 31–120 days n=3329		No newly developed primary PCC in 31–120 days n=103,785	
Medicaid	9878	9.22	394	11.84	9484	9.14
Other payor type	4727	4.41	156	4.69	4571	4.40
Uninsured	852	0.80	22	0.66	830	0.80
Unknown	12,222	11.41	237	7.12	11,985	11.55
Geographic region						
Northeast	35,806	33.43	1223	36.74	34,583	33.32
Midwest	40,769	38.06	1175	35.30	39,594	38.15
West	4005	3.74	148	4.45	3857	3.72
South	21,870	20.42	648	19.47	21,222	20.45
Other/unknown	4664	4.35	135	4.06	4529	4.36
Comorbidities and medical history	**n**	**%**	**n**	**%**	**n**	**%**
Autoimmune diseases						
Multiple sclerosis	479	0.45	20	0.60	459	0.44
Sjogren syndrome	340	0.32	19	0.57	321	0.31
Guillain-Barre	26	0.02	0	0	26	0.03
Idiopathic thrombocytopenia purpura	124	0.12	11	0.33	113	0.11
Autoimmune thyroiditis	1085	1.01	28	0.84	1057	1.02
Giant cell arteritis	27	0.03	2	0.06	25	0.02
Psoriasis	1203	1.12	41	1.23	1162	1.12
Systemic or cutaneous lupus erythematosus	517	0.48	21	0.63	496	0.48
Autoimmune arthritis/rheumatoid arthritis	1361	1.27	75	2.25	1286	1.24
Respiratory conditions						
Asthma	9029	8.43	433	13.01	8596	8.28
COPD	4006	3.74	287	8.62	3719	3.58
ILD	360	0.34	30	0.90	330	0.32
Cardiovascular or cerebrovascular conditions						
Coronary heart disease	4493	4.19	300	9.01	4193	4.04
Cardiomyopathies	560	0.52	39	1.17	521	0.50
Cerebrovascular disease or stroke (including transient ischemic attack)	2666	2.49	171	5.14	2495	2.40
Hypertension	29,655	27.69	1321	39.68	28,334	27.3
Liver or renal conditions						
Chronic kidney disease	5735	5.35	343	10.30	5392	5.20
Liver disease	4377	4.09	215	6.46	4162	4.01
Infections						
HBV	125	0.12	4	0.12	121	0.12
HCV	234	0.22	16	0.48	218	0.21
HIV infection	334	0.31	13	0.39	321	0.31
Other						
Smoking	37,914	35.40	1372	41.21	36,542	35.21
BMI ≥30	44,854	41.88	1556	46.74	43,298	41.72
Hyperlipidemia	27,330	25.51	1110	33.34	26,220	25.26
Diabetes mellitus	13,489	12.59	611	18.35	12,878	12.41
Cancer	6388	5.96	287	8.62	6101	5.88
Sickle cell disease	179	0.17	9	0.27	170	0.16
Deyo-Charlson Comorbidity Index score						
Mean (SD)	0.70 (1.49)		1.25 (2.06)		0.68 (1.46)	

Table 14. Patient characteristics by newly developed primary PCC group during the Omicron period: demographics, comorbidities and medical history, concomitant treatments, and healthcare utilization

Patient characteristics	Analysis cohort (no primary PCC 365 days before index date or in 30-day acute period) n=107,114		Newly developed primary PCC in 31–120 days n=3329		No newly developed primary PCC in 31–120 days n=103,785	
Median (IQR)	0 (0–0)		0 (0–2)		0 (0–0)	
DIC diagnosis (ICD code D65) during 365 days before index or in the 30-day acute period	6	0.01	1	0.03	5	0.00
Concomitant treatments	**n**	**%**	**n**	**%**	**n**	**%**
Treatments for COVID-19						
Nirmatrelvir/ritonavir	593	0.55	20	0.60	573	0.55
Anti-SARS-CoV-2 antibody products						
Bamlanivimab/etesevimab	141	0.13	6	0.18	135	0.13
Casirivimab/imdevimab	326	0.30	14	0.42	312	0.30
Sotrovimab	1594	1.49	87	2.61	1507	1.45
Tixagevimab/cilgavimab	29	0.03	3	0.09	26	0.03
Bebtelovimab	190	0.18	7	0.21	183	0.18
Convalescent plasma	0	0	0	0	0	0
Antiviral therapy						
Remdesivir	571	0.53	72	2.16	499	0.48
Molnupiravir	627	0.59	24	0.72	603	0.58
Chloroquine/hydroxychloroquine	60	0.06	7	0.21	53	0.05
Azithromycin	5329	4.98	236	7.09	5093	4.91
Lopinavir/ritonavir	0	0	0	0	0	0
Ivermectin	141	0.13	4	0.12	137	0.13
Nitazoxanide	1	0.00	0	0	1	0.00
Ribavirin	1	0.00	0	0	1	0.00
Interferon-beta	6	0.01	1	0.03	5	0.00
Immunomodulators						
Dexamethasone	4686	4.37	280	8.41	4406	4.25
Methylprednisolone	3381	3.16	169	5.08	3212	3.09
Fluvoxamine	77	0.07	6	0.18	71	0.07
Interleukin inhibitors						
Tocilizumab	22	0.02	7	0.21	15	0.01
Sarilumab	6	0.01	2	0.06	4	0.00
Antithrombotic therapy						
Heparin	1990	1.86	179	5.38	1811	1.74
COVID-19 vaccines	54,029	50.44	1727	51.88	52,302	50.39
Healthcare utilization	**30 days before index**	**Within 30 days of index**	**30 days before index**	**Within 30 days of index**	**30 days before index**	**Within 30 days of index**
Hospitalization						
Mean (SD)	0.01 (0.12)	0.06 (0.26)	0.03 (0.18)	0.16 (0.41)	0.01 (0.12)	0.06 (0.25)
Median (IQR)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–1)	0 (0–0)	0 (0–0)
Length of stay						
Mean (SD)	6.57 (9.78)	5.83 (7.99)	7.48 (9.31)	8.10 (11.09)	6.50 (9.81)	5.64 (7.64)
Median (IQR)	4 (2–8)	4 (1–7)	4 (2–9)	4 (2–9)	4 (2–7)	3 (1–7)
Emergency room visits						
Mean (SD)	0.06 (0.31)	0.19 (0.52)	0.11 (0.44)	0.38 (0.81)	0.06 (0.31)	0.19 (0.51)
Median (IQR)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–1)	0 (0–0)	0 (0–0)
Physician office visits						
Mean (SD)	0.96 (1.40)	1.43 (1.70)	1.08 (1.53)	1.89 (2.16)	0.96 (1.39)	1.42 (1.68)

Table 14. Patient characteristics by newly developed primary PCC group during the Omicron period: demographics, comorbidities and medical history, concomitant treatments, and healthcare utilization

Patient characteristics	Analysis cohort (no primary PCC 365 days before index date or in 30-day acute period) n=107,114		Newly developed primary PCC in 31–120 days n=3329		No newly developed primary PCC in 31–120 days n=103,785	
Median (IQR)	1 (0–1)	1 (0–2)	1 (0–2)	1 (0–3)	0 (0–1)	1 (0–2)

BMI, body mass index; COPD, chronic obstructive pulmonary disease; DIC, disseminated intravascular coagulation; HBV, hepatitis B virus, HCV, hepatitis C virus; HIV, human immunodeficiency virus; ICD, International Classification of Diseases, Tenth Revision, Clinical Modification; ILD, interstitial lung disease; IQR, interquartile range; PCC, post–COVID-19 conditions.

Similar differences between patients with newly developed secondary PCC and no newly developed secondary PCC in the Omicron period (Table 15) were observed with the full study period (Table 13).

Table 15. Patient characteristics by newly developed secondary PCC group during the Omicron period: demographics, comorbidities and medical history, concomitant treatments, and healthcare utilization

Patient characteristics	Analysis cohort (no secondary PCC 365 days before index date or in 30-day acute period) n= 141,799		Newly developed secondary PCC in 31–120 days n= 566		No newly developed secondary PCC in 31–120 days n= 141,233	
Demographics	**n**	**%**	**n**	**%**	**n**	**%**
Age group, years						
<65	112,495	79.33	248	43.82	112,247	79.48
≥65	29,304	20.67	318	56.18	28,986	20.52
Age continuous, years						
Mean (SD)	49.21 (17.50)		64.68 (17.85)		49.14 (17.47)	
Median (IQR)	49 (35–62)		67 (53–80)		49 (35–62)	
Sex						
Male	49,163	34.67	236	41.70	48,927	34.64
Female	92,636	65.33	330	58.30	92,306	65.36
Race						
White	106,483	75.09	438	77.39	106,045	75.09
Black	16,177	11.41	70	12.37	16,107	11.40
Asian	3384	2.39	11	1.94	3373	2.39
Other/unknown	6122	4.32	28	4.95	6094	4.31
Ethnicity						
Hispanic	12,315	8.68	52	9.19	12,263	8.68
Not Hispanic	109,387	77.14	431	76.15	108,956	77.15
Unknown	20,097	14.17	83	14.66	20,014	14.17
Insurance						
Commercial	86,698	61.14	239	42.23	86,459	61.22
Medicare	17,037	12.01	183	32.33	16,854	11.93
Medicaid	13,720	9.68	44	7.77	13,676	9.68
Other payor type	6257	4.41	26	4.59	6231	4.41
Uninsured	1081	0.76	2	0.35	1079	0.76
Unknown	13,405	9.45	32	5.65	13,373	9.47
Geographic region						
Northeast	47,161	33.26	163	28.8	46,998	33.28
Midwest	54,841	38.68	216	38.16	54,625	38.68
West	4943	3.49	27	4.77	4916	3.48
South	28,732	20.26	132	23.32	28,600	20.25
Other/unknown	6122	4.32	28	4.95	6094	4.31

Table 15. Patient characteristics by newly developed secondary PCC group during the Omicron period: demographics, comorbidities and medical history, concomitant treatments, and healthcare utilization

Patient characteristics	Analysis cohort (no secondary PCC 365 days before index date or in 30-day acute period) n= 141,799		Newly developed secondary PCC in 31–120 days n= 566		No newly developed secondary PCC in 31–120 days n= 141,233	
Comorbidities and medical history	**n**	**%**	**n**	**%**	**n**	**%**
Autoimmune diseases						
Multiple sclerosis	655	0.46	7	1.24	648	0.46
Sjogren syndrome	548	0.39	2	0.35	546	0.39
Guillain-Barre	47	0.03	0	0	47	0.03
Idiopathic thrombocytopenia purpura	215	0.15	2	0.35	213	0.15
Autoimmune thyroiditis	1489	1.05	5	0.88	1484	1.05
Giant cell arteritis	60	0.04	1	0.18	59	0.04
Psoriasis	1692	1.19	14	2.47	1678	1.19
Systemic or cutaneous lupus erythematosus	868	0.61	4	0.71	864	0.61
Autoimmune arthritis/rheumatoid arthritis	2210	1.56	22	3.89	2188	1.55
Respiratory conditions						
Asthma	15,376	10.84	64	11.31	15,312	10.84
COPD	9997	7.05	89	15.72	9908	7.02
ILD	1113	0.78	17	3	1,096	0.78
Cardiovascular or cerebrovascular conditions						
Coronary heart disease	10,719	7.56	134	23.67	10,585	7.49
Cardiomyopathies	2725	1.92	43	7.60	2682	1.90
Cerebrovascular disease or stroke (including transient ischemic attack)	5248	3.70	63	11.13	5185	3.67
Hypertension	47,320	33.37	351	62.01	46,969	33.26
Liver or Renal conditions						
Chronic kidney disease	10,894	7.68	161	28.45	10,733	7.60
Liver disease	7535	5.31	61	10.78	7474	5.29
Infections						
HBV	175	0.12	2	0.35	173	0.12
HCV	471	0.33	4	0.71	467	0.33
HIV infection	522	0.37	1	0.18	521	0.37
Other						
Smoking	57,083	40.26	278	49.12	56,805	40.22
BMI ≥30 or obesity	64,070	45.18	260	45.94	63,810	45.18
Hyperlipidemia	42,337	29.86	293	51.77	42,044	29.77
Diabetes mellitus	21,718	15.32	183	32.33	21,535	15.25
Cancer	10,512	7.41	81	14.31	10,431	7.39
Sickle cell disease	290	0.20	2	0.35	288	0.20
Deyo-Charlson Comorbidity Index Score						
Mean (SD)	0.99 (1.88)		2.74 (2.93)		0.99 (1.87)	
Median (IQR)	0 (0–1)		2 (0–4)		0 (0–1)	
DIC diagnosis (ICD code D65) during 365 days before index or in the 30-day acute period	18	0.01	0	0	18	0.01
Concomitant treatments	**n**	**%**	**n**	**%**	**n**	**%**
Treatments for COVID-19						
Nirmatrelvir/ritonavir	850	0.60	3	0.53	847	0.60
Anti-SARS-CoV-2 antibody products						
Bamlanivimab/etesevimab	237	0.17	0	0	237	0.17
Casirivimab/imdevimab	514	0.36	1	0.18	513	0.36

Table 15. Patient characteristics by newly developed secondary PCC group during the Omicron period: demographics, comorbidities and medical history, concomitant treatments, and healthcare utilization

Patient characteristics	Analysis cohort (no secondary PCC 365 days before index date or in 30-day acute period) n= 141,799		Newly developed secondary PCC in 31–120 days n= 566		No newly developed secondary PCC in 31–120 days n= 141,233	
Sotrovimab	2436	1.72	14	2.47	2422	1.71
Tixagevimab/cilgavimab	55	0.04	1	0.18	54	0.04
Bebtelovimab	307	0.22	2	0.35	305	0.22
Convalescent plasma	0	0	0	0	0	0
Antiviral therapy						
Remdesivir	1627	1.15	27	4.77	1600	1.13
Molnupiravir	970	0.68	4	0.71	966	0.68
Chloroquine/hydroxychloroquine	91	0.06	0	0	91	0.06
Azithromycin	8411	5.93	36	6.36	8375	5.93
Lopinavir/ritonavir	0	0	0	0	0	0
Ivermectin	182	0.13	3	0.53	179	0.13
Nitazoxanide	1	0.00	0	0	1	0.00
Ribavirin	1	0.00	0	0	1	0.00
Interferon-beta	6	0.00	0	0	6	0.00
Immunomodulators						
Dexamethasone	8516	6.01	89	15.72	8427	5.97
Methylprednisolone	5621	3.96	42	7.42	5579	3.95
Fluvoxamine	120	0.08	0	0	120	0.08
Interleukin inhibitors						
Tocilizumab	96	0.07	0	0	96	0.07
Sarilumab	19	0.01	0	0	19	0.01
Antithrombotic therapy						
Heparin	4544	3.20	71	12.54	4473	3.17
COVID-19 vaccines	72,478	51.11	301	53.18	72,177	51.10
Healthcare utilization	**30 days before index**	**Within 30 days of index**	**30 days before index**	**Within 30 days of index**	**30 days before index**	**Within 30 days of index**
Hospitalization						
Mean (SD)	0.02 (0.15)	0.10 (0.33)	0.08 (0.28)	0.42 (0.67)	0.02 (0.15)	0.10 (0.33)
Median (IQR)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–1)	0 (0–0)	0 (0–0)
Length of stay						
Mean (SD)	6.66 (9.52)	6.59 (8.67)	7.68 (8.90)	10.56 (12.85)	6.65 (9.53)	6.53 (8.57)
Median (IQR)	4 (2–8)	4 (2–8)	6 (1–9)	6 (3–12)	4 (2–8)	4 (2–8)
Emergency room visits						
Mean (SD)	0.08 (0.39)	0.26 (0.65)	0.21 (0.97)	0.68 (1.06)	0.08 (0.39)	0.26 (0.65)
Median (IQR)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–1)	0 (0–0)	0 (0–0)
Physician office visits						
Mean (SD)	1.06 (1.53)	1.60 (1.89)	1.36 (1.85)	2.58 (2.86)	1.06 (1.53)	1.60 (1.88)
Median (IQR)	1 (0–2)	1 (0–2)	1 (0–2)	2 (0–4)	1 (0–1)	1 (0–2)

BMI, body mass index; COPD, chronic obstructive pulmonary disease; DIC, disseminated intravascular coagulation; HBV, hepatitis B virus, HCV, hepatitis C virus; HIV, human immunodeficiency virus; ICD, International Classification of Diseases, Tenth Revision, Clinical Modification; ILD, interstitial lung disease; IQR, interquartile range; PCC, post–COVID-19 conditions

10.3. Main results

10.3.1. Primary Objectives

10.3.1.1. Objective 1: Describe the distribution of demographics, co-morbid conditions, medical history, selected biomarkers, and healthcare utilization at baseline for COVID-19 patients (including subpopulation with long COVID)

Table 16 describes the healthcare utilization within 12 months before the index date before and after PSM. Before matching, patients treated with Paxlovid had substantially lower healthcare utilization across all domains, including fewer hospitalizations, ER visits, physician visits, and urgent care visits (standardized differences often 0.15–0.30). After PSM, these imbalances were almost entirely eliminated, with all standardized differences dropping to ≤0.04, indicating strong covariate balance. Overall, matching successfully aligned the treatment and comparison groups on prior 12-month healthcare utilization

Table 16. Healthcare utilization within 12 months before the index date before and after PSM

	Before PSM			After PSM		
	Nirmatrelvir/ Ritonavir N=12,440	Non-nirmatrelvir/ Ritonavir N=234,123	Standardized Difference	Nirmatrelvir/ Ritonavir N=12,439	Non-nirmatrelvir/ Ritonavir N=36,490	Standardized Difference
Number of hospitalizations						
0	11,723 (94.2)	216,604 (92.5)	0.069	11,722 (94.2)	34,274 (93.9)	0.005
1	613 (4.9)	13,783 (5.9)	0.042	613 (4.9)	1859 (5.1)	0.002
≥2	104 (0.8)	3736 (1.6)	0.069	104 (0.8)	357 (1.0)	0.006
Mean ± SD	0.07 ± 0.31	0.10 ± 0.41	0.082	0.07 ± 0.31	0.07 ± 0.33	0.007
Length of stay, days						
Median, IQR	3.00, 4.00	4.00, 6.00	-	3.00, 4.00	3.00, 5.00	-
Emergency room visits						
0	10,361 (83.3)	166,788 (71.2)	0.290	10,360 (83.3)	29,863 (81.8)	0.007
1	1330 (10.7)	36,229 (15.5)	0.142	1330 (10.7)	4143 (11.4)	0.005
≥2	749 (6.0)	31,106 (13.3)	0.248	749 (6.0)	2484 (6.8)	0.004
Mean ± SD	0.29 ± 0.87	0.62 ± 1.89	0.226	0.29 ± 0.87	0.33 ± 1.01	0.020
Physician office visits						
0	978 (7.9)	33,916 (14.5)	0.211	978 (7.9)	3627 (9.9)	0.016
1	1506 (12.1)	28,686 (12.3)	0.004	1506 (12.1)	4685 (12.8)	0.003
≥2	9956 (80.0)	171,521 (73.3)	0.161	9955 (80.0)	28,178 (77.2)	0.013
Mean ± SD	6.22 ± 7.28	5.94 ± 8.03	0.037	6.22 ± 7.28	6.25 ± 7.98	0.031
Telemedicine visits						
0	6158 (49.5)	114,862 (49.1)	0.009	6157 (49.5)	16,822 (46.1)	0.041
1	1805 (14.5)	34,241 (14.6)	0.003	1805 (14.5)	5433 (14.9)	0.005
≥2	4477 (36.0)	85,020 (36.3)	0.007	4477 (36.0)	14,235 (39.0)	0.039
Urgent care visits						
0	11,743 (94.4)	206,198 (88.1)	0.225	11,742 (94.4)	34,039 (93.3)	0.011

Table 16. Healthcare utilization within 12 months before the index date before and after PSM

	Before PSM			After PSM		
	Nirmatrelvir/ Ritonavir N=12,440	**Non-nirmatrelvir/ Ritonavir N=234,123**	**Standardized Difference**	**Nirmatrelvir/ Ritonavir N=12,439**	**Non-nirmatrelvir/ Ritonavir N=36,490**	**Standardized Difference**
1	462 (3.7)	16,254 (6.9)	0.144	462 (3.7)	1601 (4.4)	0.008
≥2	235 (1.9)	11,671 (5.0)	0.171	235 (1.9)	850 (2.3)	0.008
Mean ± SD	0.09 ± 0.49	0.23 ± 0.86	0.193	0.09 ± 0.49	0.11 ± 0.53	0.006

IQR=interquartile range; PSM=propensity score matching; SD=standard deviation.
Values shown are n (%) unless otherwise specified.
Data cutoff for this analysis was July 20, 2022.

Table 17 describes healthcare utilization between the Paxlovid and non- Paxlovid treated groups in the 15 days and 30 days following index date and outlines sensitivity analyses to account for missing data. Across all analyses, patients treated with Paxlovid had substantially lower 15-day and 30-day hospitalization risks than matched untreated patients. In the primary analysis, relative risks were 0.17 (30-day) and 0.12 (15-day). Sensitivity analyses that made extreme assumptions about missing adjudication (treating all unknown cases as hospitalizations or as non-hospitalizations) slightly shifted absolute rates but did not materially change the conclusion, with relative risks remaining low (~0.15–0.26), consistently supporting a strong protective association of Paxlovid against hospitalization. The results of the sensitivity analyses do not show any major differences compared to the original results for hospitalization among patients with COVID-19 by Paxlovid treatment status.

Table 17. Actual data and sensitivity analysis accounting for missing data from the adjudicated medical chart review

	Hospitalization Within 30 Days		Hospitalization Within 15 Days	
	Nirmatrelvir/Ritonavir	**Non-nirmatrelvir/ Ritonavir**	**Nirmatrelvir/Ritonavir**	**Non-nirmatrelvir/ Ritonavir**
Hospitalization among patients with COVID-19 by nirmatrelvir/ritonavir treatment status after PSM				
Patients at risk, n	2,808	10,849	2,808	10,849
Events, n	34	752	22	708
Incidence proportion, % (95% CI)	1.21 (0.84, 1.69)	6.93 (6.46, 7.43)	0.78 (0.49, 1.18)	6.53 (6.07, 7.01)
Relative risk (95% CI)	0.17 (0.12, 0.24)	-	0.12 (0.08, 0.18)	-
Sensitivity analysis: Assume all unknown and unadjudicated cases were cases				
Patients at risk	2,808	10,849	2,808	10,849
Events	34	622	22	578
Incidence proportion, % (95% CI)	1.21 (0.84, 1.69)	5.73 (5.30, 6.19)	0.78 (0.49, 1.18)	5.33 (4.91, 5.77)
Relative risk (95% CI)	0.21 (0.15, 0.30)	-	0.15 (0.10, 0.22)	-
Assume all unknown and unadjudicated cases were non-cases				
Patients at risk	2,808	10,849	2,808	10,849
Events	33	492	21	448

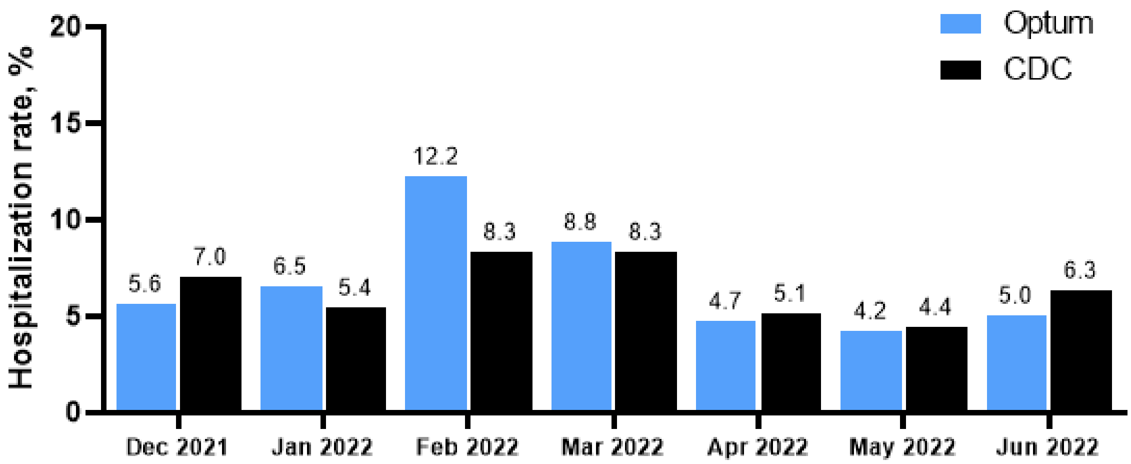
Table 17. Actual data and sensitivity analysis accounting for missing data from the adjudicated medical chart review

	Hospitalization Within 30 Days		Hospitalization Within 15 Days	
	Nirmatrelvir/Ritonavir	**Non-nirmatrelvir/ Ritonavir**	**Nirmatrelvir/Ritonavir**	**Non-nirmatrelvir/ Ritonavir**
Incidence proportion, % (95% CI)	1.18 (0.81, 1.65)	4.53 (4.15, 4.94)	0.75 (0.46, 1.14)	4.13 (3.76, 4.52)
Relative risk (95% CI)	0.26 (0.18, 0.37)	-	0.18 (0.12, 0.28)	-
Applied observed proportion to unknown and unadjudicated cases				
Patients at risk	2,808	10,849	2,808	10,849
Events	34	578	22	534
Incidence proportion, % (95% CI)	1.21 (0.84, 1.69)	5.33 (4.91, 5.77)	0.78 (0.49, 1.18)	4.92 (4.52, 5.35)
Relative risk (95% CI)	0.22 (0.16, 0.32)	-	0.16 (0.10, 0.24)	-

Data cutoff for this analysis was May 28, 2022.
Relative risk and 95% CIs were calculated using modified Poisson regression with a robust error variance

Figure 4. Hospitalization by month: all patients

Figure 4 shows hospitalization rates by month from 2021 to 2022 among the Source Cohort. During the study period, Optum and CDC show similar trends, with hospitalization rates peaking in February 2022 (Optum 12.2%, CDC 8.3%) and declining steadily through April–May 2022. By June 2022, rates increase slightly in both sources (Optum 5.0%, CDC 6.3%).



Light blue bars represent hospitalization rates for all Optum® patients with COVID-19 meeting study eligibility criteria. Data are through July 20, 2022.
[a]CDC COVID-19 hospitalization rates during the same time period including all 'yes' or 'no' values in the denominator. The data do not include missing/unknown hospitalization status in the denominator.
CDC=US Centers for Disease Control and Prevention.
The COVID-19 case surveillance database includes patient-level data reported by US states and autonomous reporting entities, including New York City and the District of Columbia, as well as US territories and affiliates.

10.3.1.2. Objective 2: Describe time to clinical events (e.g. hospitalization, ICU admission)

Table 18 shows hospitalizations among patients with COVID-19 by Paxlovid treatment status after PSM. In the PSM groups, the incidence proportion of hospitalization within 30 days in the non-Paxlovid treated group was more than six times greater than that of the Paxlovid treated group. The incidence proportion of hospitalization within 15 days in the non-Paxlovid treated group was more than eight times greater than that of the Paxlovid treated group.

Table 18. Hospitalization among patients with COVID-19 by nirmatrelvir/ritonavir treatment status after PSM

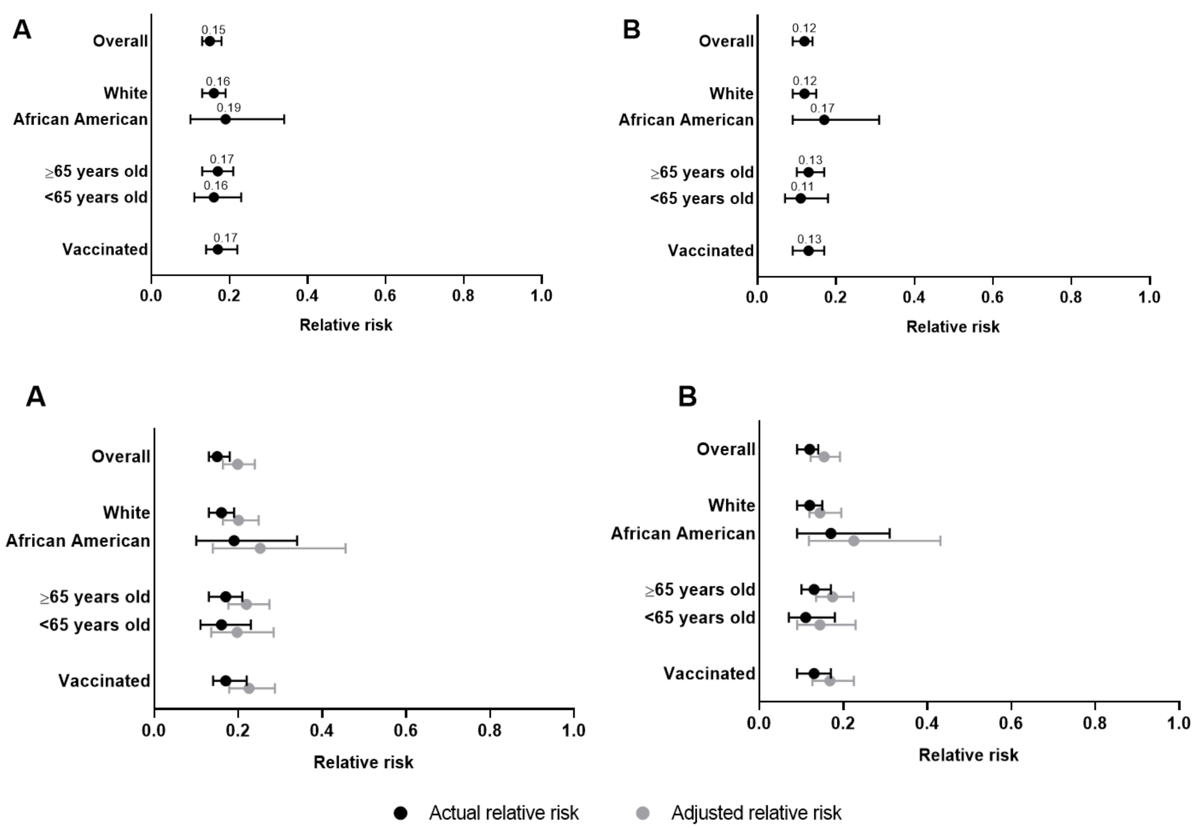
	Nirmatrelvir/ Ritonavir	Non-nirmatrelvir/ Ritonavir
Hospitalization within 30 days		
Patients at risk, n	12,439	36,490
Events, n	112	2157

Incidence proportion, % (95% CI)	0.90 (0.74, 1.08)	5.91 (5.67, 6.16)
Relative risk (95% CI)[a]	0.15 (0.13, 0.18)	-
Sensitivity analysis		
True events, n[b]	109.28	1622.86
Crude relative risk (95% CI)[b]	0.198 (0.163, 0.240)	-
Adjusted relative risk (95% CI)[c]	0.198 (0.163, 0.239)	-
Hospitalization within 15 days		
Patients at risk, n	12,439	36,490
Events, n	80	2026
Incidence proportion, % (95% CI)	0.64 (0.51, 0.80)	5.55 (5.32, 5.79)
Relative risk (95% CI)	0.12 (0.09, 0.14)	-
Sensitivity analysis		
True events, n[b]	77.28	1491.86
Crude relative risk (95% CI)[b]	0.152 (0.121, 0.191)	-
Adjusted relative risk (95% CI)[c]	0.153 (0.121, 0.191)	-

PSM=propensity score matching.
Data cutoff for this analysis was July 20, 2022.
Relative risk and 95% CIs were calculated using modified Poisson regression with a robust error variance.21
a All covariates were well balanced, so no adjustment was needed in final model.
bSensitivity analysis to account for hospitalizations on the day of COVID-19 diagnosis. The analysis uses as a positive predictive value of 0.66 to estimate true events (ie, excluding day of diagnosis hospitalizations estimated to be incidental) and associated crude relative risk.
cAdjusted relative accounts for the ratio of the relative risk to the crude relative risk.

Figure 5 illustrates the risk reduction ratios for hospitalization within (A) 30 and (B) 15 days among subgroups of patients with COVID-19 after PSM. Relative risks of hospitalization associated with treatment, stratified by subgroups (overall, White, African American, ≥65 years, <65 years, vaccinated) are relayed. Each panel on top and bottom (A and B) shows point estimates with horizontal confidence intervals. In the bottom set of images, two estimate types are shown: actual relative risk (black point) and adjusted relative risk (gray point). Across all subgroups in both A and B, relative risks remain well below 1.0, indicating consistently lower hospitalization risk for the treated group compared with the comparison group. In African American subgroups, confidence intervals are wider than in other groups, indicating greater variability. Overall, age >=65 and African American race had slightly higher risk reduction ratio as compared to Age <65 and White race.

Figure 5. Risk reduction ratios for hospitalization within (A) 30 and (B) 15 days among subgroups of patients with COVID-19 after PSM



Relative risk and 95% CIs were calculated using modified Poisson regression with a robust error variance, adjusting for unbalanced variables after PSM in subgroup analyses as follows:

White patients: The covariates of cohort month/year, region, medical history of hyperlipidemia were adjusted in the model

African American patients: The covariates of cohort month/year, region, medical history of hypertension, hyperlipidemia and diabetes, and baseline physician office visits were adjusted in the model.

≥65-year-old patients: The covariates of cohort month/year, age(continuous), ethnicity, region, baseline hyperlimidemia, number of physician office visit and COVID-19 vaccines status were adjusted in the model.

<65-year-old patients: The covariates of cohort month/year, age (continuous), Deyo-Charlson Comorbidity Index Score and medical history of hypertension, hyperlipidemia, and diabetes mellitus were adjusted in the model.

Vaccinated patients: The covariates of cohort month/year, ethnicity, region, medical history of hypertension and hyperlipidemia, and baseline telemedicine visits were adjusted in the mode.

The database may not completely collect vaccination data, which precluded assessing effectiveness in the unvaccinated patient subgroup. Error bars depict 95% CIs. PSM=propensity score matching. Data cutoff for this analysis was July 20, 2022.

Table 19 shows the events and median time to COVID-19 Complications/interventions since COVID Diagnosis cross study endpoints/outcomes. Across all cohorts, most acute complications (for example, pneumonia, kidney failure, thrombotic events, ARDS, heart failure, sepsis, mechanical ventilation, multi-organ dysfunction) occurred very early after COVID-19 diagnosis, with median times of 1 day and narrow IQRs, indicating that these events clustered tightly around the point of diagnosis or immediate clinical presentation. As expected, the hospitalized groups show slightly shorter times to complications and higher event counts compared with non-hospitalized groups. In contrast, longer-term conditions such as renal impairment, hepatic impairment, diarrhea, hypersensitivity reactions, and dysgeusia show much wider time distributions and substantially later median onset (spanning weeks to months), reflecting their more delayed or variable clinical course.

Table 19. Time to COVID-19 Complications/interventions since COVID Diagnosis

Study Endpoints	Events	Mean Time (Days)	SD	Median Time	IQR
		Overall			
Source Cohort					
Pneumonia	135,158	3.45	5.18	1.00	2.00
Kidney failure	93,359	3.38	5.62	1.00	1.00
Thrombotic event	95,576	4.98	7.18	1.00	5.00
ARDS	17,461	3.70	5.07	1.00	4.00
Heart failure	72,235	4.04	6.43	1.00	2.00
Sepsis/septic shock	49,452	3.44	5.44	1.00	2.00
Mechanical ventilation/ECMO	54,963	3.88	5.29	1.00	3.00
Hospitalization	212,016	3.03	4.98	1.00	1.00
All-cause mortality	33,694	13.94	7.54	13.00	11.00
In hospital death	9,821	11.14	7.34	10.00	11.00
Multi-organ dysfunction/failure	212,843	3.28	5.37	1.00	1.00
Vasopressor use	73,142	5.81	7.01	3.00	6.00
Renal impairment	168,309	65.76	127.41	2.00	65.00
Hepatic impairment	65,984	126.48	162.22	57.00	185.00
Dysgeusia	14,534	32.77	92.20	1.00	0.00
Diarrhea	80,334	109.06	158.84	19.00	165.00
Hypersensitivity reaction/allergic reaction	167,931	87.92	135.85	19.00	121.00
High Risk Trial Similar Cohort					
Pneumonia	81,949	3.58	5.29	1.00	3.00
Kidney failure	52,756	3.43	5.66	1.00	1.00
Thrombotic event	58,630	5.09	7.28	1.00	5.00
ARDS	10,441	3.67	5.00	1.00	4.00
Heart failure	41,609	4.15	6.56	1.00	2.00
Sepsis/septic shock	27,967	3.35	5.28	1.00	1.00
Mechanical ventilation/ECMO	31,365	3.93	5.22	1.00	4.00
Hospitalization	124,189	2.76	4.47	1.00	1.00
All-cause mortality	21,285	13.97	7.53	13.00	11.00
In hospital death	6,506	10.98	7.26	10.00	11.00

Table 19. Time to COVID-19 Complications/interventions since COVID Diagnosis

Study Endpoints	Events	Mean Time (Days)	SD	Median Time	IQR
Multi-organ dysfunction/failure	124,579	3.37	5.45	1.00	1.00
Vasopressor use	43,301	5.75	6.94	3.00	6.00
Renal impairment	101,944	73.26	133.67	4.00	83.00
Hepatic impairment	24,178	163.34	182.07	97.00	256.00
Dysgeusia	8,524	37.12	97.36	1.00	2.00
Diarrhea	48,320	111.51	160.24	20.00	170.00
Hypersensitivity reaction/allergic reaction	109,985	90.30	135.25	24.00	127.00
Standard Risk Trial Similar Cohort					
Pneumonia	27,177	2.79	4.36	1.00	1.00
Kidney failure	10,037	2.54	4.30	1.00	0.00
Thrombotic event	10,250	4.04	6.19	1.00	2.00
ARDS	3,785	3.32	4.82	1.00	2.00
Heart failure	6,152	3.34	5.56	1.00	1.00
Sepsis/septic shock	8,428	2.79	4.48	1.00	1.00
Mechanical ventilation/ECMO	10,361	3.04	4.26	1.00	2.00
Hospitalization	41,449	2.29	3.71	1.00	0.00
All-cause mortality	3,212	14.28	7.58	14.00	12.00
In hospital death	1,228	12.36	7.65	11.00	12.00
Multi-organ dysfunction/failure	34,310	2.51	3.97	1.00	1.00
Vasopressor use	13,049	4.81	6.24	2.00	4.00
Renal impairment	16,335	66.56	138.42	1.00	44.00
Hepatic impairment	7,545	130.56	178.57	37.00	210.00
Dysgeusia	5,331	20.95	73.34	1.00	0.00
Diarrhea	17,964	96.09	155.38	5.00	138.00
hypersensitivity reaction/allergic reaction	32,041	90.49	147.76	6.00	126.00
		Hospitalized			
Source Cohort					
Pneumonia	94,429	3.16	4.73	1.00	2.00
Kidney failure	70,491	2.87	4.84	1.00	0.00
Thrombotic event	61,625	3.98	6.11	1.00	3.00
ARDS	15,889	3.72	5.06	1.00	4.00
Heart failure	51,856	3.33	5.54	1.00	1.00
Sepsis/septic shock	43,901	3.45	5.44	1.00	2.00
Mechanical ventilation/ECMO	50,720	3.94	5.33	1.00	4.00
Hospitalization	212,016	3.03	4.98	1.00	1.00
All-cause mortality	25,522	14.31	7.56	14.00	12.00
In hospital death	9,821	11.14	7.34	10.00	11.00
Multi-organ dysfunction/failure	157,532	2.59	4.11	1.00	1.00
Vasopressor use	33,052	7.46	7.51	4.00	9.00
Renal impairment	90,044	22.83	79.57	1.00	3.00
Hepatic impairment	22,923	64.52	130.73	3.00	51.00

Table 19. Time to COVID-19 Complications/interventions since COVID Diagnosis

Study Endpoints	Events	Mean Time (Days)	SD	Median Time	IQR
Dysgeusia	652	67.94	133.00	1.00	57.50
Diarrhea	22,657	58.96	127.41	3.00	32.00
Hypersensitivity reaction/allergic reaction	30,493	43.35	107.49	1.00	15.00
High Risk Trial Similar Cohort					
Pneumonia	60,064	3.13	4.66	1.00	2.00
Kidney failure	42,827	2.85	4.74	1.00	0.00
Thrombotic event	38,626	3.89	5.97	1.00	2.00
ARDS	10,000	3.68	4.99	1.00	4.00
Heart failure	31,136	3.32	5.49	1.00	1.00
Sepsis/septic shock	26,669	3.31	5.21	1.00	1.00
Mechanical ventilation/ECMO	30,604	3.91	5.18	1.00	4.00
Hospitalization	124,189	2.76	4.47	1.00	1.00
All-cause mortality	16,954	14.25	7.54	14.00	12.00
In hospital death	6,506	10.98	7.26	10.00	11.00
Multi-organ dysfunction/failure	97,075	2.60	4.05	1.00	1.00
Vasopressor use	18,013	7.44	7.34	4.00	9.00
Renal impairment	54,956	23.29	81.16	1.00	4.00
Hepatic impairment	8,830	79.35	146.62	6.00	85.00
Dysgeusia	418	71.89	137.80	1.00	61.00
Diarrhea	13,282	52.95	123.03	2.00	19.00
Hypersensitivity reaction/allergic reaction	17,794	44.51	109.79	1.00	15.00
Standard Risk Trial Similar Cohort					
Pneumonia	17,973	2.58	3.90	1.00	1.00
Kidney failure	8,570	2.43	4.03	1.00	0.00
Thrombotic event	7,400	3.70	5.71	1.00	2.00
ARDS	3,619	3.38	4.86	1.00	3.00
Heart failure	5,365	3.17	5.25	1.00	1.00
Sepsis/septic shock	8,022	2.78	4.44	1.00	1.00
Mechanical ventilation/ECMO	10,106	3.03	4.23	1.00	2.00
Hospitalization	41,449	2.29	3.71	1.00	0.00
All-cause mortality	2,754	14.60	7.56	14.00	11.00
In hospital death	1,228	12.36	7.65	11.00	12.00
Multi-organ dysfunction/failure	29,185	2.28	3.36	1.00	1.00
Vasopressor use	5,462	6.38	6.70	3.00	8.00
Renal impairment	10,601	18.24	73.18	1.00	2.00
Hepatic impairment	3,316	43.97	112.95	1.00	14.00
Dysgeusia	83	35.52	90.43	1.00	7.00
Diarrhea	3,741	33.50	100.23	1.00	6.00
Hypersensitivity reaction/allergic reaction	5,091	27.43	88.98	1.00	3.00
		Non-Hospitalized			
Source Cohort					

Table 19. Time to COVID-19 Complications/interventions since COVID Diagnosis

Study Endpoints	Events	Mean Time (Days)	SD	Median Time	IQR
Pneumonia	40,729	4.14	6.04	1.00	4.00
Kidney failure	22,868	4.95	7.30	1.00	4.00
Thrombotic event	33,951	6.79	8.50	1.00	10.00
ARDS	1,572	3.53	5.13	1.00	2.00
Heart failure	20,379	5.84	8.01	1.00	7.00
Sepsis/septic shock	5,551	3.40	5.45	1.00	2.00
Mechanical ventilation/ECMO	4,243	3.22	4.72	1.00	2.00
Hospitalization	.	.	.	.	.
All-cause mortality	8,172	12.78	7.38	12.00	10.00
In hospital death	.	.	.	.	.
Multi-organ dysfunction/failure	55,311	5.23	7.60	1.00	5.00
Vasopressor use	40,090	4.45	6.26	2.00	3.00
Renal impairment	78,265	115.14	151.88	50.00	164.00
Hepatic impairment	43,061	159.47	167.61	102.00	211.00
Dysgeusia	13,882	31.12	89.49	1.00	0.00
Diarrhea	57,677	128.73	165.50	55.00	202.00
Hypersensitivity reaction/allergic reaction	137,438	97.80	139.46	33.00	140.00
High Risk Trial Similar Cohort					
Pneumonia	21,885	4.82	6.57	1.00	6.00
Kidney failure	9,929	5.94	8.09	1.00	7.00
Thrombotic event	20,004	7.41	8.85	1.00	12.00
ARDS	441	3.42	5.26	1.00	2.00
Heart failure	10,473	6.62	8.54	1.00	10.00
Sepsis/septic shock	1,298	4.15	6.56	1.00	2.00
Mechanical ventilation/ECMO	761	4.67	6.48	1.00	5.00
Hospitalization	.	.	.	.	.
All-cause mortality	4,331	12.89	7.41	12.00	10.00
In hospital death	.	.	.	.	.
Multi-organ dysfunction/failure	27,504	6.10	8.20	1.00	8.00
Vasopressor use	25,288	4.55	6.38	2.00	3.00
Renal impairment	46,988	131.70	157.24	71.00	181.00
Hepatic impairment	15,348	211.67	182.92	159.00	266.00
Dysgeusia	8,106	35.33	94.47	1.00	0.00
Diarrhea	35,038	133.71	166.98	63.00	212.00
Hypersensitivity reaction/allergic reaction	92,191	99.14	137.90	37.00	142.00
Standard Risk Trial Similar Cohort					
Pneumonia	9,204	3.18	5.11	1.00	1.00
Kidney failure	1,467	3.20	5.61	1.00	0.00
Thrombotic event	2,850	4.92	7.21	1.00	5.00
ARDS	166	2.17	3.69	1.00	0.00
Heart failure	787	4.57	7.19	1.00	2.00
Sepsis/septic shock	406	3.01	5.20	1.00	1.00

Table 19. Time to COVID-19 Complications/interventions since COVID Diagnosis

Study Endpoints	Events	Mean Time (Days)	SD	Median Time	IQR
Mechanical ventilation/ECMO	255	3.63	5.34	1.00	3.00
Hospitalization	.	.	.	.	.
All-cause mortality	458	12.38	7.46	12.00	10.00
In hospital death	.	.	.	.	.
Multi-organ dysfunction/failure	5,125	3.81	6.27	1.00	1.00
Vasopressor use	7,587	3.68	5.62	2.00	2.00
Renal impairment	5,734	155.90	179.96	86.00	256.00
Hepatic impairment	4,229	198.45	190.81	140.00	280.00
Dysgeusia	5,248	20.72	73.02	1.00	0.00
Diarrhea	14,223	112.56	162.94	15.00	174.00
Hypersensitivity reaction/allergic reaction	26,950	102.41	153.52	16.00	153.00

Table 20 shows the time to COVID-19 Complications/interventions since First Paxlovid (Paxlovid) Prescription. Acute complications—including pneumonia, kidney failure, thrombotic events, heart failure, sepsis, and hospitalization—occurred about 7–13 days after treatment initiation, with narrow IQRs indicating clustered early onset. In contrast, longer-latency outcomes such as renal impairment, hepatic impairment, diarrhea, hypersensitivity reactions, and dysgeusia occurred much later, with median times ranging from 23 to 34 days and wide variability. Hospitalized patients generally experienced complications slightly earlier and with less variation than non-hospitalized patients, while non-hospitalized individuals showed broader and later onset patterns for several conditions.

Table 20. Time to COVID-19 Complications/interventions since First nirmatrelvir/ritonavir (Paxlovid) Prescription

Study Endpoints	Events	Mean Time	SD	Median Time	IQR
			Overall		
Paxlovid Cohort					
Pneumonia	81	9.91	8.30	7.00	14.00
Kidney failure	116	11.62	8.98	9.50	16.00
Thrombotic event	304	12.24	9.07	11.00	15.50
Heart failure	179	12.67	8.74	13.00	16.00
Sepsis/septic shock	23	10.74	10.09	6.00	17.00
Mechanical ventilation/ECMO	20	11.10	8.30	9.50	11.00
Hospitalization	191	11.53	8.27	11.00	14.00
All-cause mortality	9	10.33	9.14	8.00	18.00
In hospital death	2	12.50	13.44	12.50	19.00
Multi-organ dysfunction/failure	384	12.07	8.89	11.00	16.50
Vasopressor use	151	11.07	9.83	9.00	17.00
Renal impairment	446	32.46	31.83	23.00	36.00
Hepatic impairment	244	36.26	33.27	29.00	37.00
Dysgeusia	5	50.20	61.23	34.00	40.00
Diarrhea	192	27.54	34.25	14.00	40.50

Table 20. Time to COVID-19 Complications/interventions since First nirmatrelvir/ritonavir (Paxlovid) Prescription

Study Endpoints	Events	Mean Time	SD	Median Time	IQR
Hypersensitivity reaction/allergic reaction	1,034	21.53	31.57	8.00	30.00
		Hospitalized			
Paxlovid Cohort					
Pneumonia	22	11.27	7.20	10.00	12.00
Kidney failure	32	8.44	7.61	6.50	8.50
Thrombotic event	51	9.80	6.97	9.00	11.00
Heart failure	28	10.43	7.34	9.50	10.00
Sepsis/septic shock	20	10.45	9.85	5.50	16.50
Mechanical ventilation/ECMO	20	11.10	8.30	9.50	11.00
Hospitalization	191	11.53	8.27	11.00	14.00
All-cause mortality	3	16.00	11.27	22.00	20.00
In hospital death	2	12.50	13.44	12.50	19.00
Multi-organ dysfunction/failure	91	10.27	7.94	8.00	14.00
Vasopressor use	33	14.52	6.50	15.00	7.00
Renal impairment	51	14.37	13.85	10.00	18.00
Hepatic impairment	17	24.88	29.41	11.00	24.00
Dysgeusia	.	.	.	.	.
Diarrhea	21	14.33	19.55	10.00	12.00
Hypersensitivity reaction/allergic reaction	25	20.40	38.46	6.00	14.00
		Non-Hospitalized			
Paxlovid Cohort					
Pneumonia	59	9.41	8.68	7.00	14.00
Kidney failure	84	12.83	9.21	11.00	15.00
Thrombotic event	253	12.74	9.37	12.00	18.00
Heart failure	151	13.09	8.93	13.00	18.00
Sepsis/septic shock	3	12.67	13.87	9.00	27.00
Mechanical ventilation/ECMO	.	.	.	.	.
Hospitalization	.	.	.	.	.
All-cause mortality	6	7.50	7.34	6.00	7.00
In hospital death	.	.	.	.	.
Multi-organ dysfunction/failure	293	12.62	9.11	13.00	17.00
Vasopressor use	118	10.11	10.39	4.00	17.00
Renal impairment	395	34.79	32.74	26.00	39.00
Hepatic impairment	227	37.11	33.44	32.00	36.00
Dysgeusia	5	50.20	61.23	34.00	40.00
Diarrhea	171	29.16	35.34	16.00	42.00
Hypersensitivity reaction/allergic reaction	1,009	21.56	31.41	8.00	30.00

10.3.1.3. Objective 3: Estimate background incidence of COVID-19 manifestations/complications and safety outcome of interests following COVID-19 infection or Paxlovid exposure

Table 21 shows the incidence of COVID-19 Complications/Interventions within 30 Days of COVID-19 Infection in the Source Cohort and Trial-similar Cohorts by Hospitalization Status. Across the source and trial-similar cohorts, acute COVID-19 complications within 30 days were common, with the highest incidence rates observed for pneumonia, hospitalization, multi-organ dysfunction, and vasopressor use. Rates were consistently highest in the High-Risk trial-similar cohort, intermediate in the Source cohort, and lowest in the Standard-Risk cohort—mirroring underlying differences in baseline comorbidity and severity. Hospitalization rates were particularly elevated in the High-Risk cohort (1,800 per 1,000 person-years), compared with 1,675 in the Source cohort and 998 in the Standard-Risk cohort. Despite these gradients, patterns across endpoints remained qualitatively similar, with respiratory, renal, thrombotic, and systemic complications clustering as the most frequent events early in the course of infection.

Table 21. Incidence of COVID-19 Complications/Interventions within 30 Days of COVID-19 Infection in the Source Cohort and Trial-similar Cohorts by Hospitalization Status, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Overall Person-time	Incidence Rate per 1000 person years	95% CI	
Source Cohort						
Pneumonia	1,644,030	128,987	116,289.33	1,109.19	1,103.15	1,115.26
Kidney failure	1,606,875	65,565	117,966.59	555.79	551.56	560.06
Thrombotic event	1,583,397	61,565	116,478.85	528.55	524.39	532.74
ARDS	1,662,756	17,419	125,263.77	139.06	137.01	141.14
Heart failure	1,613,247	43,796	119,962.17	365.08	361.68	368.52
Sepsis/septic shock	1,651,512	46,510	122,603.93	379.35	375.92	382.82
ICU/Mechanical ventilation/ECMO	1,649,617	51,912	122,305.72	424.44	420.81	428.11
Hospitalization	1,583,536	181,107	108,094.77	1,675.45	1,667.75	1,683.18
All-cause mortality	1,663,017	33,694	135,111.10	249.38	246.73	252.06
In hospital death	1,663,017	9,821	126,260.84	77.78	76.26	79.34
Multi-organ dysfunction/failure	1,551,501	152,200	107,739.46	1,412.67	1,405.59	1,419.78
Vasopressor use	1,621,780	67,719	119,108.61	568.55	564.28	572.85
High Risk Trial Similar Cohort						
Pneumonia	934,725	79,351	66,043.49	1,201.50	1,193.17	1,209.89
Kidney failure	916,851	41,930	67,315.24	622.89	616.96	628.88
Thrombotic event	896,513	40,239	65,903.25	610.58	604.64	616.57
ARDS	944,280	10,429	71,403.68	146.06	143.28	148.89
Heart failure	917,586	27,421	68,370.51	401.06	396.35	405.84
Sepsis/septic shock	940,198	27,165	70,053.65	387.77	383.19	392.41
ICU/Mechanical ventilation/ECMO	939,400	30,508	69,907.64	436.40	431.54	441.33
Hospitalization	911,157	111,974	61,961.43	1,807.16	1,796.60	1,817.77
All-cause mortality	944,347	21,285	76,630.40	277.76	274.06	281.52
In hospital death	944,347	6,506	71,986.85	90.38	88.21	92.60
Multi-organ dysfunction/failure	883,686	95,538	61,113.29	1,563.29	1,553.41	1,573.24

Table 21. Incidence of COVID-19 Complications/Interventions within 30 Days of COVID-19 Infection in the Source Cohort and Trial-similar Cohorts by Hospitalization Status, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Overall Person-time	Incidence Rate per 1000 person years	95% CI	
Vasopressor use	921,786	40,850	67,832.02	602.22	596.41	608.09
Standard Risk Trial Similar Cohort						
Pneumonia	589,785	27,112	42,432.16	638.95	631.39	646.60
Kidney failure	590,354	10,026	43,735.99	229.24	224.80	233.77
Thrombotic event	589,810	10,060	43,706.82	230.17	225.72	234.71
ARDS	590,467	3,784	44,169.28	85.67	82.98	88.44
Heart failure	590,469	6,152	44,017.74	139.76	136.31	143.30
Sepsis/septic shock	590,397	8,424	43,839.09	192.16	188.10	196.31
ICU/Mechanical ventilation/ECMO	590,368	10,350	43,740.73	236.62	232.11	241.22
Hospitalization	589,089	41,285	41,376.24	997.79	988.22	1,007.47
All-cause mortality	590,469	3,212	48,360.26	66.42	64.16	68.76
In hospital death	590,469	1,228	44,399.20	27.66	26.15	29.25
Multi-organ dysfunction/failure	589,207	34,128	41,923.96	814.05	805.45	822.73
Vasopressor use	588,401	12,957	43,436.45	298.30	293.21	303.48

Table 22 shows the incidence of COVID-19 Complications/Interventions within 30 Days of COVID-19 Infection in the Source Cohort and Trial-similar Cohorts by Hospitalization Status. Severe acute COVID-19 complications occurred at very high incidence rates, with the greatest burden consistently observed in the High-Risk trial-similar cohort, followed by the Source cohort, and lowest rates in the Standard-Risk cohort. Pneumonia, multi-organ dysfunction/failure, and hospitalization-related interventions (ICU/mechanical ventilation/ECMO, vasopressor use) showed the highest incidence rates across all cohorts, often exceeding 9,000 to 31,000 per 1,000 person-years depending on cohort and endpoint. Mortality and in-hospital death rates were also highest in the High-Risk cohort, reflecting its greater underlying clinical risk. Despite differences in magnitude, the pattern of which complications are most frequent is similar across cohorts, with respiratory, renal, and systemic complications dominating the early hospitalization period.

Table 22. Incidence of COVID-19 Complications/Interventions within 30 Days of COVID-19 Infection in the Source Cohort and Trial-similar Cohorts by Hospitalization Status, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Hospitalized Person-time	Incidence Rate per 1000 person years	95% CI	
Source Cohort						
Pneumonia	204,947	90,247	9,431.88	9,568.29	9,506.07	9,630.93
Kidney failure	188,684	52,300	10,938.12	4,781.44	4,740.64	4,822.60
Thrombotic event	185,126	42,722	11,296.06	3,782.03	3,746.33	3,818.06
ARDS	212,354	15,877	15,037.66	1,055.82	1,039.52	1,072.37
Heart failure	191,068	34,784	12,323.67	2,822.54	2,793.03	2,852.36

Table 22. Incidence of COVID-19 Complications/Interventions within 30 Days of COVID-19 Infection in the Source Cohort and Trial-similar Cohorts by Hospitalization Status, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Hospitalized Person-time	Incidence Rate per 1000 person years	95% CI	
Sepsis/septic shock	206,668	41,597	12,996.63	3,200.60	3,169.99	3,231.51
ICU/Mechanical ventilation/ECMO	205,930	48,159	12,706.04	3,790.25	3,756.55	3,824.25
Hospitalization	181,448	181,107	1,485.05	121,953.81	121,393.44	122,516.77
All-cause mortality	212,456	25,522	16,353.81	1,560.61	1,541.59	1,579.88
In hospital death	212,456	9,821	15,934.84	616.32	604.25	628.63
Multi-organ dysfunction/failure	171,289	120,424	4,811.09	25,030.51	24,889.54	25,172.28
Vasopressor use	201,992	30,425	13,632.82	2,231.75	2,206.81	2,256.97
High Risk Trial Similar Cohort						
Pneumonia	121,338	58,262	5,208.45	11,186.04	11,095.58	11,277.24
Kidney failure	114,480	35,631	6,320.86	5,637.05	5,578.82	5,695.89
Thrombotic event	110,493	29,027	6,447.12	4,502.32	4,450.82	4,554.42
ARDS	124,426	9,996	8,703.90	1,148.45	1,126.16	1,171.19
Heart failure	114,286	22,988	7,167.20	3,207.39	3,166.20	3,249.12
Sepsis/septic shock	122,550	25,957	7,563.65	3,431.81	3,390.31	3,473.81
ICU/Mechanical ventilation/ECMO	122,308	29,799	7,425.99	4,012.80	3,967.50	4,058.62
Hospitalization	112,204	111,974	848.38	131,985.58	131,214.77	132,760.91
All-cause mortality	124,451	16,954	9,490.68	1,786.38	1,759.70	1,813.48
In hospital death	124,451	6,506	9,258.08	702.74	685.87	720.02
Multi-organ dysfunction/failure	104,675	79,316	2,526.66	31,391.66	31,173.95	31,610.89
Vasopressor use	120,129	17,065	8,106.48	2,105.11	2,073.76	2,136.93
Standard Risk Trial Similar Cohort						
Pneumonia	41,438	17,955	1,919.53	9,353.87	9,218.05	9,491.70
Kidney failure	41,462	8,563	2,627.85	3,258.55	3,190.26	3,328.31
Thrombotic event	41,418	7,359	2,712.52	2,712.97	2,651.69	2,775.67
ARDS	41,474	3,619	2,968.93	1,218.96	1,179.89	1,259.33
Heart failure	41,475	5,365	2,855.43	1,878.88	1,829.27	1,929.83
Sepsis/septic shock	41,463	8,019	2,658.21	3,016.69	2,951.38	3,083.44
ICU/Mechanical ventilation/ECMO	41,456	10,097	2,548.70	3,961.63	3,885.11	4,039.67
Hospitalization	41,311	41,285	258.95	159,433.14	157,902.63	160,978.50
All-cause mortality	41,475	2,754	3,290.45	836.97	806.29	868.82
In hospital death	41,475	1,228	3,188.42	385.14	364.19	407.30
Multi-organ dysfunction/failure	41,380	29,117	1,128.68	25,797.48	25,502.86	26,095.50
Vasopressor use	41,399	5,444	2,889.09	1,884.33	1,834.94	1,935.06

Overall, during the full study period, incidence of complications such as pneumonia, hospitalization and all-cause mortality were higher in the High Risk Trial Similar Cohort as compared to the Source Cohort and Standard Risk Trial Similar Cohort (Table 21). The same differences are also observed across Hospitalized patients (Table 22). However, among Non-Hospitalized patients (Table 23), the same differences are not observed.

Table 23. Incidence of COVID-19 Complications/Interventions within 30 Days of COVID-19 Infection in the Source Cohort and Trial-similar Cohorts by Hospitalization Status, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Non-Hospitalized Person-time	Incidence Rate per 1000 person years	95% CI	
Source Cohort						
Pneumonia	1,439,083	38,740	106,857.45	362.54	358.95	366.17
Kidney failure	1,418,191	13,265	107,028.47	123.94	121.85	126.07
Thrombotic event	1,398,271	18,843	105,182.79	179.15	176.61	181.72
ARDS	1,450,402	1,542	110,226.12	13.99	13.31	14.71
Heart failure	1,422,179	9,012	107,638.51	83.72	82.01	85.47
Sepsis/septic shock	1,444,844	4,913	109,607.30	44.82	43.59	46.10
ICU/Mechanical ventilation/ECMO	1,443,687	3,753	109,599.69	34.24	33.17	35.36
Hospitalization	1,402,088	0	106,609.72	0.00	0.00	3,688.88
All-cause mortality	1,450,561	8,172	118,757.29	68.81	67.34	70.32
In hospital death	1,450,561	0	110,326.01	0.00	0.00	3,688.88
Multi-organ dysfunction/failure	1,380,212	31,776	102,928.38	308.72	305.34	312.13
Vasopressor use	1,419,788	37,294	105,475.79	353.58	350.01	357.19
High Risk Trial Similar Cohort						
Pneumonia	813,387	21,089	60,835.04	346.66	342.01	351.37
Kidney failure	802,371	6,299	60,994.38	103.27	100.75	105.85
Thrombotic event	786,020	11,212	59,456.13	188.58	185.12	192.10
ARDS	819,854	433	62,699.78	6.91	6.29	7.59
Heart failure	803,300	4,433	61,203.31	72.43	70.33	74.60
Sepsis/septic shock	817,648	1,208	62,490.00	19.33	18.27	20.45
ICU/Mechanical ventilation/ECMO	817,092	709	62,481.65	11.35	10.54	12.21
Hospitalization	798,953	0	61,113.05	0.00	0.00	3,688.88
All-cause mortality	819,896	4,331	67,139.72	64.51	62.61	66.46
In hospital death	819,896	0	62,728.78	0.00	0.00	3,688.88
Multi-organ dysfunction/failure	779,011	16,222	58,586.63	276.89	272.66	281.18
Vasopressor use	801,657	23,785	59,725.55	398.24	393.21	403.33
Standard Risk Trial Similar Cohort						
Pneumonia	548,347	9,157	40,512.63	226.03	221.45	230.71
Kidney failure	548,892	1,463	41,108.14	35.59	33.81	37.46
Thrombotic event	548,392	2,701	40,994.30	65.89	63.45	68.42
ARDS	548,993	165	41,200.35	4.00	3.44	4.67
Heart failure	548,994	787	41,162.31	19.12	17.83	20.50
Sepsis/septic shock	548,934	405	41,180.87	9.83	8.92	10.84
ICU/Mechanical ventilation/ECMO	548,912	253	41,192.03	6.14	5.43	6.95
Hospitalization	547,778	0	41,117.29	0.00	0.00	3,688.88
All-cause mortality	548,994	458	45,069.81	10.16	9.27	11.14
In hospital death	548,994	0	41,210.78	0.00	0.00	3,688.88

Table 23. Incidence of COVID-19 Complications/Interventions within 30 Days of COVID-19 Infection in the Source Cohort and Trial-similar Cohorts by Hospitalization Status, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Non-Hospitalized Person-time	Incidence Rate per 1000 person years	95% CI	
Multi-organ dysfunction/failure	547,827	5,011	40,795.28	122.83	119.48	126.28
Vasopressor use	547,002	7,513	40,547.36	185.29	181.15	189.53

Overall, the incidence of pneumonia, hospitalization, mortality and multi-organ dysfunction/failure are greater in the Pre-Vaccine period (Table 24) as compared to the Vaccine period (Table 27). Among Hospitalized patients in the Pre-Vaccine period (Table 25), these differences are substantially increased compared to the Vaccine period (Table 28). The incidence of these outcomes is dramatically lower in both the Non-Hospitalized groups in both periods (Table 26, Table 29).

Table 24. Incidence of COVID-19 Complications/Interventions within 30 Days of COVID-19 Infection in the Source Cohort and Trial-similar Cohorts by Hospitalization Status, 1/1/2020-10/31/2020 (Pre-vaccine Period)

Study Endpoints	Patients at Risk	Events	Overall Person-time	Incidence Rate per 1000 person years	95% CI	
Source Cohort						
Pneumonia	279,833	46,587	19,297.00	2,414.21	2,392.39	2,436.23
Kidney failure	270,652	16,507	20,751.72	795.45	783.41	807.68
Thrombotic event	268,997	13,638	20,803.91	655.55	644.64	666.65
ARDS	284,925	5,850	22,539.61	259.54	252.98	266.28
Heart failure	274,019	11,718	21,351.11	548.82	538.98	558.85
Sepsis/septic shock	282,158	14,206	21,794.57	651.81	641.18	662.62
ICU/Mechanical ventilation/ECMO	281,751	14,252	21,788.41	654.11	643.46	664.94
Hospitalization	268,687	41,697	18,758.66	2,222.81	2,201.58	2,244.25
All-cause mortality	285,016	9,491	22,995.34	412.74	404.52	421.12
In hospital death	285,016	2,367	22,888.36	103.42	99.33	107.67
Multi-organ dysfunction/failure	260,330	35,151	18,611.11	1,888.71	1,869.07	1,908.56
Vasopressor use	277,688	10,607	21,763.03	487.39	478.20	496.75
High Risk Trial Similar Cohort						
Pneumonia	160,920	28,265	11,002.72	2,568.91	2,539.14	2,599.03
Kidney failure	156,441	10,623	11,915.11	891.56	874.76	908.67
Thrombotic event	154,330	8,860	11,859.67	747.07	731.68	762.79
ARDS	163,445	3,508	12,920.22	271.51	262.68	280.65
Heart failure	157,823	7,315	12,253.05	596.99	583.47	610.83
Sepsis/septic shock	162,473	8,318	12,538.09	663.42	649.31	677.83
ICU/Mechanical ventilation/ECMO	162,404	8,425	12,542.50	671.72	657.53	686.21
Hospitalization	157,011	26,877	10,782.43	2,492.67	2,463.04	2,522.65

Table 24. Incidence of COVID-19 Complications/Interventions within 30 Days of COVID-19 Infection in the Source Cohort and Trial-similar Cohorts by Hospitalization Status, 1/1/2020-10/31/2020 (Pre-vaccine Period)

			Overall			
Study Endpoints	**Patients at Risk**	**Events**	**Person-time**	**Incidence Rate per 1000 person years**	**95% CI**	
All-cause mortality	163,469	5,941	13,168.74	451.14	439.82	462.76
In hospital death	163,469	1,575	13,126.30	119.99	114.21	126.06
Multi-organ dysfunction/failure	150,249	22,246	10,609.39	2,096.82	2,069.45	2,124.56
Vasopressor use	159,821	5,828	12,542.72	464.65	452.87	476.74
Standard Risk Trial Similar Cohort						
Pneumonia	96,795	9,207	7,186.74	1,281.11	1,255.21	1,307.55
Kidney failure	96,945	2,113	7,729.37	273.37	261.96	285.28
Thrombotic event	96,870	1,917	7,740.90	247.65	236.80	258.98
ARDS	96,964	1,037	7,808.34	132.81	124.97	141.14
Heart failure	96,964	1,457	7,779.33	187.29	177.92	197.16
Sepsis/septic shock	96,952	2,217	7,720.51	287.16	275.45	299.36
ICU/Mechanical ventilation/ECMO	96,946	2,376	7,715.37	307.96	295.82	320.59
Hospitalization	96,795	8,736	7,219.00	1,210.14	1,185.03	1,235.78
All-cause mortality	96,964	575	7,940.28	72.42	66.73	78.58
In hospital death	96,964	214	7,876.26	27.17	23.76	31.07
Multi-organ dysfunction/failure	96,739	6,831	7,363.91	927.63	905.89	949.89
Vasopressor use	96,696	1,649	7,759.65	212.51	202.50	223.02

Table 25. Incidence of COVID-19 Complications/Interventions within 30 Days of COVID-19 Infection in the Source Cohort and Trial-similar Cohorts by Hospitalization Status, 1/1/2020-10/31/2020 (Pre-vaccine Period)

			Hospitalized			
Study Endpoints	**Patients at Risk**	**Events**	**Person-time**	**Incidence Rate per 1000 person years**	**95% CI**	
Source Cohort						
Pneumonia	47,073	33,335	1,298.68	25,668.36	25,394.29	25,945.40
Kidney failure	42,708	13,214	2,423.96	5,451.41	5,359.25	5,545.16
Thrombotic event	42,737	9,693	2,656.66	3,648.57	3,576.65	3,721.93
ARDS	49,170	5,115	3,436.75	1,488.32	1,448.09	1,529.68
Heart failure	44,040	9,459	2,789.09	3,391.43	3,323.77	3,460.47
Sepsis/septic shock	47,666	12,429	2,853.86	4,355.16	4,279.26	4,432.40
ICU/Mechanical ventilation/ECMO	47,481	12,868	2,838.43	4,533.49	4,455.84	4,612.51
Hospitalization	41,761	41,697	310.21	134,415.64	133,131.64	135,712.01
All-cause mortality	49,205	6,863	3,750.54	1,829.87	1,787.09	1,873.68
In hospital death	49,205	2,367	3,739.07	633.05	608.05	659.07
Multi-organ dysfunction/failure	38,999	27,969	1,074.43	26,031.51	25,728.22	26,338.39
Vasopressor use	46,753	7,933	3,144.24	2,523.03	2,468.12	2,579.17

Table 25. Incidence of COVID-19 Complications/Interventions within 30 Days of COVID-19 Infection in the Source Cohort and Trial-similar Cohorts by Hospitalization Status, 1/1/2020-10/31/2020 (Pre-vaccine Period)

Hospitalized						
Study Endpoints	**Patients at Risk**	**Events**	**Person-time**	**Incidence Rate per 1000 person years**	**95% CI**	
High Risk Trial Similar Cohort						
Pneumonia	28,949	21,860	693.07	31,540.68	31,125.32	31,961.58
Kidney failure	27,069	9,380	1,450.05	6,468.75	6,339.16	6,600.99
Thrombotic event	26,558	6,743	1,581.51	4,263.64	4,163.08	4,366.63
ARDS	29,826	3,357	2,050.57	1,637.11	1,582.65	1,693.43
Heart failure	27,414	6,444	1,679.14	3,837.68	3,745.12	3,932.54
Sepsis/septic shock	29,324	8,058	1,711.35	4,708.58	4,606.88	4,812.51
ICU/Mechanical ventilation/ECMO	29,292	8,247	1,713.03	4,814.27	4,711.48	4,919.30
Hospitalization	26,925	26,877	186.73	143,935.37	142,224.84	145,666.48
All-cause mortality	29,834	4,680	2,252.06	2,078.10	2,019.41	2,138.50
In hospital death	29,834	1,575	2,245.97	701.26	667.47	736.76
Multi-organ dysfunction/failure	24,874	19,204	580.80	33,064.77	32,600.41	33,535.74
Vasopressor use	28,874	4,565	1,945.80	2,346.08	2,279.00	2,415.14
Standard Risk Trial Similar Cohort						
Pneumonia	8,754	6,403	222.94	28,720.32	28,025.40	29,432.48
Kidney failure	8,760	1,887	565.44	3,337.21	3,189.98	3,491.23
Thrombotic event	8,749	1,457	597.07	2,440.27	2,318.13	2,568.84
ARDS	8,761	977	631.38	1,547.41	1,453.36	1,647.55
Heart failure	8,761	1,326	606.89	2,184.93	2,070.43	2,305.75
Sepsis/septic shock	8,759	2,132	546.09	3,904.13	3,741.87	4,073.41
ICU/Mechanical ventilation/ECMO	8,758	2,314	538.96	4,293.46	4,122.04	4,472.00
Hospitalization	8,738	8,736	49.77	175,532.18	171,889.65	179,251.90
All-cause mortality	8,761	500	699.37	714.93	654.93	780.42
In hospital death	8,761	214	695.08	307.88	269.27	352.02
Multi-organ dysfunction/failure	8,746	6,056	253.34	23,904.49	23,309.95	24,514.19
Vasopressor use	8,745	1,279	619.19	2,065.61	1,955.45	2,181.98

Table 26. Incidence of COVID-19 Complications/Interventions within 30 Days of COVID-19 Infection in the Source Cohort and Trial-similar Cohorts by Hospitalization Status, 1/1/2020-10/31/2020 (Pre-vaccine Period)

Non-Hospitalized						
Study Endpoints	**Patients at Risk**	**Events**	**Person-time**	**Incidence Rate per 1000 person years**	**95% CI**	
Source Cohort						
Pneumonia	232,760	13,252	17,998.32	736.29	723.86	748.93
Kidney failure	227,944	3,293	18,327.76	179.67	173.64	185.92
Thrombotic event	226,260	3,945	18,147.25	217.39	210.71	224.28
ARDS	235,755	735	19,102.86	38.48	35.79	41.36
Heart failure	229,979	2,259	18,562.02	121.70	116.78	126.82

Table 26. Incidence of COVID-19 Complications/Interventions within 30 Days of COVID-19 Infection in the Source Cohort and Trial-similar Cohorts by Hospitalization Status, 1/1/2020-10/31/2020 (Pre-vaccine Period)

Non-Hospitalized						
Study Endpoints	**Patients at Risk**	**Events**	**Person-time**	**Incidence Rate per 1000 person years**	**95% CI**	
Sepsis/septic shock	234,492	1,777	18,940.71	93.82	89.56	98.28
ICU/Mechanical ventilation/ECMO	234,270	1,384	18,949.98	73.03	69.29	76.99
Hospitalization	226,926	0	18,448.45	0.00	0.00	3,688.88
All-cause mortality	235,811	2,628	19,244.80	136.56	131.43	141.88
In hospital death	235,811	0	19,149.29	0.00	0.00	3,688.88
Multi-organ dysfunction/failure	221,331	7,182	17,536.68	409.54	400.18	419.12
Vasopressor use	230,935	2,674	18,618.80	143.62	138.28	149.17
High Risk Trial Similar Cohort						
Pneumonia	131,971	6,405	10,309.65	621.26	606.23	636.67
Kidney failure	129,372	1,243	10,465.06	118.78	112.35	125.57
Thrombotic event	127,772	2,117	10,278.16	205.97	197.38	214.93
ARDS	133,619	151	10,869.65	13.89	11.84	16.29
Heart failure	130,409	871	10,573.91	82.37	77.08	88.03
Sepsis/septic shock	133,149	260	10,826.75	24.01	21.27	27.12
ICU/Mechanical ventilation/ECMO	133,112	178	10,829.46	16.44	14.19	19.04
Hospitalization	130,086	0	10,595.70	0.00	0.00	3,688.88
All-cause mortality	133,635	1,261	10,916.69	115.51	109.31	122.07
In hospital death	133,635	0	10,880.33	0.00	0.00	3,688.88
Multi-organ dysfunction/failure	125,375	3,042	10,028.59	303.33	292.74	314.31
Vasopressor use	130,947	1,263	10,596.93	119.19	112.79	125.94
Standard Risk Trial Similar Cohort						
Pneumonia	88,041	2,804	6,963.80	402.65	388.02	417.84
Kidney failure	88,185	226	7,163.93	31.55	27.69	35.94
Thrombotic event	88,121	460	7,143.84	64.39	58.77	70.55
ARDS	88,203	60	7,176.96	8.36	6.49	10.77
Heart failure	88,203	131	7,172.44	18.26	15.39	21.68
Sepsis/septic shock	88,193	85	7,174.42	11.85	9.58	14.65
ICU/Mechanical ventilation/ECMO	88,188	62	7,176.41	8.64	6.74	11.08
Hospitalization	88,057	0	7,169.23	0.00	0.00	3,688.88
All-cause mortality	88,203	75	7,240.91	10.36	8.26	12.99
In hospital death	88,203	0	7,181.18	0.00	0.00	3,688.88
Multi-organ dysfunction/failure	87,993	775	7,110.57	108.99	101.58	116.94
Vasopressor use	87,951	370	7,140.46	51.82	46.80	57.38

Table 27. Incidence of COVID-19 Complications/Interventions within 30 Days of COVID-19 Infection in the Source Cohort and Trial-similar Cohorts by Hospitalization Status, 12/13/2020-07/20/2022 (Vaccine Period)

	Overall					
Study Endpoints	**Patients at Risk**	**Events**	**Person-time**	**Incidence Rate per 1000 person years**	**95% CI**	
Source Cohort						
Pneumonia	1,178,153	56,370	83,723.20	673.29	667.76	678.87
Kidney failure	1,156,545	41,513	83,131.97	499.36	494.58	504.19
Thrombotic event	1,136,190	40,724	81,690.28	498.52	493.70	503.38
ARDS	1,189,953	9,627	87,653.17	109.83	107.66	112.05
Heart failure	1,157,422	26,661	84,210.76	316.60	312.82	320.42
Sepsis/septic shock	1,182,748	26,679	86,062.05	310.00	306.30	313.74
ICU/Mechanical ventilation/ECMO	1,181,574	31,664	85,793.66	369.07	365.03	373.16
Hospitalization	1,136,007	117,494	76,347.20	1,538.94	1,530.17	1,547.77
All-cause mortality	1,190,097	19,375	96,906.01	199.94	197.14	202.77
In hospital death	1,190,097	6,015	88,192.67	68.20	66.50	69.95
Multi-organ dysfunction/failure	1,117,710	98,828	76,283.51	1,295.54	1,287.48	1,303.64
Vasopressor use	1,161,162	52,423	82,792.74	633.18	627.79	638.63
High Risk Trial Similar Cohort						
Pneumonia	663,264	34,169	47,260.38	722.99	715.37	730.70
Kidney failure	653,489	26,138	47,075.46	555.24	548.55	562.01
Thrombotic event	636,664	26,463	45,816.02	577.59	570.68	584.59
ARDS	669,391	5,680	49,557.29	114.61	111.67	117.64
Heart failure	651,668	16,559	47,588.25	347.96	342.70	353.30
Sepsis/septic shock	666,765	15,329	48,768.91	314.32	309.38	319.33
ICU/Mechanical ventilation/ECMO	666,159	18,339	48,625.17	377.15	371.73	382.65
Hospitalization	646,574	70,449	43,480.32	1,620.25	1,608.33	1,632.26
All-cause mortality	669,424	12,144	54,454.88	223.01	219.08	227.01
In hospital death	669,424	3,974	49,866.59	79.69	77.25	82.21
Multi-organ dysfunction/failure	630,289	61,022	42,970.56	1,420.09	1,408.87	1,431.40
Vasopressor use	653,306	32,129	46,660.71	688.57	681.08	696.14
Standard Risk Trial Similar Cohort						
Pneumonia	428,663	12,933	30,356.84	426.03	418.75	433.44
Kidney failure	429,063	6,939	30,817.99	225.16	219.93	230.52
Thrombotic event	428,650	7,163	30,782.86	232.69	227.37	238.15
ARDS	429,148	2,436	31,126.60	78.26	75.21	81.43
Heart failure	429,150	4,061	31,024.33	130.90	126.93	134.99
Sepsis/septic shock	429,093	5,378	30,920.22	173.93	169.35	178.64
ICU/Mechanical ventilation/ECMO	429,082	7,000	30,834.61	227.02	221.76	232.40
Hospitalization	428,094	28,327	29,223.49	969.32	958.10	980.68
All-cause mortality	429,150	2,332	35,148.88	66.35	63.71	69.10
In hospital death	429,150	900	31,269.06	28.78	26.96	30.73
Multi-organ dysfunction/failure	428,226	23,827	29,563.00	805.97	795.81	816.27

Table 27. Incidence of COVID-19 Complications/Interventions within 30 Days of COVID-19 Infection in the Source Cohort and Trial-similar Cohorts by Hospitalization Status, 12/13/2020-07/20/2022 (Vaccine Period)

Overall						
Study Endpoints	**Patients at Risk**	**Events**	**Person-time**	**Incidence Rate per 1000 person years**	**95% CI**	
Vasopressor use	427,588	10,640	30,477.42	349.11	342.54	355.81

Table 28. Incidence of COVID-19 Complications/Interventions within 30 Days of COVID-19 Infection in the Source Cohort and Trial-similar Cohorts by Hospitalization Status, 12/13/2020-07/20/2022 (Vaccine Period)

Hospitalized						
Study Endpoints	**Patients at Risk**	**Events**	**Person-time**	**Incidence Rate per 1000 person years**	**95% CI**	
Source Cohort						
Pneumonia	133,100	38,591	7,493.73	5,149.77	5,098.65	5,201.41
Kidney failure	123,743	32,821	7,208.71	4,552.96	4,503.97	4,602.49
Thrombotic event	120,395	27,780	7,289.92	3,810.74	3,766.19	3,855.82
ARDS	137,591	8,956	9,762.23	917.41	898.61	936.61
Heart failure	124,145	20,833	8,056.93	2,585.72	2,550.85	2,621.08
Sepsis/septic shock	134,070	24,030	8,558.58	2,807.71	2,772.43	2,843.44
ICU/Mechanical ventilation/ECMO	133,589	29,650	8,298.16	3,573.08	3,532.64	3,613.98
Hospitalization	117,699	117,494	994.21	118,177.67	117,503.86	118,855.34
All-cause mortality	137,647	15,132	10,660.17	1,419.49	1,397.05	1,442.29
In hospital death	137,647	6,015	10,257.73	586.39	571.75	601.40
Multi-organ dysfunction/failure	112,172	77,550	3,207.50	24,177.74	24,008.17	24,348.50
Vasopressor use	130,925	19,278	8,795.57	2,191.79	2,161.06	2,222.94
High Risk Trial Similar Cohort						
Pneumonia	76,598	24,117	4,153.21	5,806.84	5,734.01	5,880.59
Kidney failure	72,879	21,743	4,051.82	5,366.22	5,295.37	5,438.03
Thrombotic event	69,722	18,563	4,022.80	4,614.44	4,548.54	4,681.30
ARDS	78,472	5,447	5,504.38	989.58	963.64	1,016.21
Heart failure	72,078	13,471	4,551.44	2,959.72	2,910.16	3,010.13
Sepsis/septic shock	77,332	14,527	4,856.99	2,990.95	2,942.70	3,039.98
ICU/Mechanical ventilation/ECMO	77,129	17,889	4,719.99	3,790.05	3,734.91	3,846.00
Hospitalization	70,581	70,449	547.10	128,768.23	127,820.86	129,722.61
All-cause mortality	78,486	9,873	6,022.60	1,639.33	1,607.31	1,671.98
In hospital death	78,486	3,974	5,799.23	685.26	664.29	706.90
Multi-organ dysfunction/failure	66,463	49,660	1,637.83	30,320.53	30,055.02	30,588.38
Vasopressor use	75,699	10,543	5,078.72	2,075.92	2,036.67	2,115.92
Standard Risk Trial Similar Cohort						
Pneumonia	28,437	8,318	1,597.55	5,206.72	5,096.02	5,319.82
Kidney failure	28,457	5,820	1,783.97	3,262.39	3,179.64	3,347.29
Thrombotic event	28,429	5,182	1,828.60	2,833.86	2,757.74	2,912.08
ARDS	28,466	2,345	2,021.43	1,160.07	1,114.05	1,207.98

Table 28. Incidence of COVID-19 Complications/Interventions within 30 Days of COVID-19 Infection in the Source Cohort and Trial-similar Cohorts by Hospitalization Status, 12/13/2020-07/20/2022 (Vaccine Period)

			Hospitalized			
Study Endpoints	**Patients at Risk**	**Events**	**Person-time**	**Incidence Rate per 1000 person years**	**95% CI**	
Heart failure	28,467	3,483	1,948.56	1,787.47	1,729.08	1,847.83
Sepsis/septic shock	28,458	5,100	1,829.85	2,787.12	2,711.66	2,864.67
ICU/Mechanical ventilation/ECMO	28,452	6,833	1,735.57	3,937.03	3,844.78	4,031.49
Hospitalization	28,344	28,327	183.44	154,424.43	152,636.55	156,233.25
All-cause mortality	28,467	1,999	2,254.52	886.66	848.63	926.40
In hospital death	28,467	900	2,158.67	416.92	390.56	445.07
Multi-organ dysfunction/failure	28,396	20,040	757.77	26,445.88	26,082.25	26,814.57
Vasopressor use	28,414	3,692	1,960.24	1,883.45	1,823.66	1,945.19

Table 29. Incidence of COVID-19 Complications/Interventions within 30 Days of COVID-19 Infection in the Source Cohort and Trial-similar Cohorts by Hospitalization Status, 12/13/2020-07/20/2022 (Vaccine Period)

			Non-Hospitalized			
Study Endpoints	**Patients at Risk**	**Events**	**Person-time**	**Incidence Rate per 1000 person years**	**95% CI**	
Source Cohort						
Pneumonia	1,045,053	17,779	76,229.47	233.23	229.83	236.68
Kidney failure	1,032,802	8,692	75,923.26	114.48	112.10	116.92
Thrombotic event	1,015,795	12,944	74,400.36	173.98	171.01	177.00
ARDS	1,052,362	671	77,890.94	8.61	7.99	9.29
Heart failure	1,033,277	5,828	76,153.83	76.53	74.59	78.52
Sepsis/septic shock	1,048,678	2,649	77,503.47	34.18	32.90	35.51
ICU/Mechanical ventilation/ECMO	1,047,985	2,014	77,495.50	25.99	24.88	27.15
Hospitalization	1,018,308	0	75,352.98	0.00	0.00	3,688.88
All-cause mortality	1,052,450	4,243	86,245.84	49.20	47.74	50.70
In hospital death	1,052,450	0	77,934.94	0.00	0.00	3,688.88
Multi-organ dysfunction/failure	1,005,538	21,278	73,076.01	291.18	287.29	295.12
Vasopressor use	1,030,237	33,145	73,997.17	447.92	443.13	452.77
High Risk Trial Similar Cohort						
Pneumonia	586,666	10,052	43,107.17	233.19	228.67	237.79
Kidney failure	580,610	4,395	43,023.64	102.15	99.18	105.22
Thrombotic event	566,942	7,900	41,793.22	189.03	184.90	193.24
ARDS	590,919	233	44,052.91	5.29	4.65	6.01
Heart failure	579,590	3,088	43,036.81	71.75	69.27	74.33
Sepsis/septic shock	589,433	802	43,911.92	18.26	17.04	19.57
ICU/Mechanical ventilation/ECMO	589,030	450	43,905.17	10.25	9.35	11.24
Hospitalization	575,993	0	42,933.22	0.00	0.00	3,688.88

Table 29. Incidence of COVID-19 Complications/Interventions within 30 Days of COVID-19 Infection in the Source Cohort and Trial-similar Cohorts by Hospitalization Status, 12/13/2020-07/20/2022 (Vaccine Period)

			Non-Hospitalized			
Study Endpoints	**Patients at Risk**	**Events**	**Person-time**	**Incidence Rate per 1000 person years**	**95% CI**	
All-cause mortality	590,938	2,271	48,432.28	46.89	45.00	48.86
In hospital death	590,938	0	44,067.36	0.00	0.00	3,688.88
Multi-organ dysfunction/failure	563,826	11,362	41,332.73	274.89	269.88	279.99
Vasopressor use	577,607	21,586	41,582.00	519.12	512.24	526.09
Standard Risk Trial Similar Cohort						
Pneumonia	400,226	4,615	28,759.29	160.47	155.91	165.17
Kidney failure	400,606	1,119	29,034.03	38.54	36.35	40.87
Thrombotic event	400,221	1,981	28,954.26	68.42	65.47	71.50
ARDS	400,682	91	29,105.16	3.13	2.55	3.84
Heart failure	400,683	578	29,075.77	19.88	18.32	21.57
Sepsis/septic shock	400,635	278	29,090.37	9.56	8.50	10.75
ICU/Mechanical ventilation/ECMO	400,630	167	29,099.04	5.74	4.93	6.68
Hospitalization	399,750	0	29,040.05	0.00	0.00	3,688.88
All-cause mortality	400,683	333	32,894.36	10.12	9.09	11.27
In hospital death	400,683	0	29,110.38	0.00	0.00	3,688.88
Multi-organ dysfunction/failure	399,830	3,787	28,805.23	131.47	127.35	135.72
Vasopressor use	399,174	6,948	28,517.18	243.64	237.98	249.44

Similar incidence of outcomes are also observed during the Omicron period (Table 30), with a greater burden among the Hospitalized patients (Table 31) as compared to the Non-Hospitalized patients (Table 32).

Table 30. Incidence of COVID-19 Complications/Interventions within 30 Days of COVID-19 Infection in the Source Cohort and Trial-similar Cohorts by Hospitalization Status, 12/15/2021-07/20/2022 (Omicron Period)

			Overall			
Study Endpoints	**Patients at Risk**	**Events**	**Person-time**	**Incidence Rate per 1000 person years**	**95% CI**	
Source Cohort						
Pneumonia	512,793	10,769	32,850.68	327.82	321.68	334.07
Kidney failure	504,800	12,452	32,173.37	387.03	380.29	393.89
Thrombotic event	494,969	12,819	31,480.36	407.21	400.22	414.32
ARDS	518,480	1,438	33,767.87	42.58	40.44	44.84
Heart failure	504,355	8,210	32,403.97	253.36	247.94	258.90
Sepsis/septic shock	515,204	7,128	33,222.90	214.55	209.63	219.59
ICU/Mechanical ventilation/ECMO	515,000	7,926	33,188.61	238.82	233.62	244.13
Hospitalization	494,355	32,911	30,188.53	1,090.18	1,078.47	1,102.02

Table 30. Incidence of COVID-19 Complications/Interventions within 30 Days of COVID-19 Infection in the Source Cohort and Trial-similar Cohorts by Hospitalization Status, 12/15/2021-07/20/2022 (Omicron Period)

			Overall			
Study Endpoints	**Patients at Risk**	**Events**	**Person-time**	**Incidence Rate per 1000 person years**	**95% CI**	
All-cause mortality	518,547	4,680	42,384.24	110.42	107.30	113.63
In hospital death	518,547	1,229	33,846.93	36.31	34.34	38.40
Multi-organ dysfunction/failure	487,328	25,225	30,188.55	835.58	825.33	845.96
Vasopressor use	505,661	12,399	32,288.19	384.01	377.31	390.83
High Risk Trial Similar Cohort						
Pneumonia	291,267	6,538	18,968.87	344.67	336.42	353.13
Kidney failure	288,066	7,727	18,670.28	413.87	404.74	423.20
Thrombotic event	280,125	8,338	18,095.50	460.78	450.99	470.78
ARDS	294,320	833	19,495.94	42.73	39.92	45.73
Heart failure	286,708	5,046	18,740.05	269.26	261.94	276.80
Sepsis/septic shock	293,149	3,997	19,240.37	207.74	201.40	214.28
ICU/Mechanical ventilation/ECMO	292,998	4,539	19,217.94	236.19	229.41	243.16
Hospitalization	284,146	19,120	17,677.51	1,081.60	1,066.38	1,097.04
All-cause mortality	294,336	2,858	24,048.00	118.85	114.57	123.28
In hospital death	294,336	814	19,539.62	41.66	38.89	44.62
Multi-organ dysfunction/failure	277,811	15,882	17,473.08	908.94	894.91	923.19
Vasopressor use	287,209	6,989	18,675.97	374.22	365.55	383.10
Standard Risk Trial Similar Cohort						
Pneumonia	179,069	1,785	10,813.76	165.07	157.59	172.91
Kidney failure	179,316	1,637	10,838.30	151.04	143.90	158.54
Thrombotic event	179,126	1,806	10,817.61	166.95	159.43	174.83
ARDS	179,352	277	10,916.09	25.38	22.56	28.55
Heart failure	179,353	1,010	10,876.24	92.86	87.31	98.77
Sepsis/septic shock	179,325	1,015	10,873.22	93.35	87.78	99.27
ICU/Mechanical ventilation/ECMO	179,319	1,339	10,854.17	123.36	116.93	130.15
Hospitalization	178,847	6,069	10,540.64	575.77	561.47	590.44
All-cause mortality	179,353	440	14,712.39	29.91	27.24	32.84
In hospital death	179,353	147	10,930.50	13.45	11.44	15.81
Multi-organ dysfunction/failure	178,920	4,453	10,646.70	418.25	406.15	430.72
Vasopressor use	178,650	1,951	10,785.55	180.89	173.04	189.10

Table 31. Incidence of COVID-19 Complications/Interventions within 30 Days of COVID-19 Infection in the Source Cohort and Trial-similar Cohorts by Hospitalization Status, 12/15/2021-07/20/2022 (Omicron Period)

Hospitalized						
Study Endpoints	**Patients at Risk**	**Events**	**Person-time**	**Incidence Rate per 1000 person years**	**95% CI**	
Source Cohort						
Pneumonia	39,217	6,856	2,327.44	2,945.72	2,876.81	3,016.28
Kidney failure	36,025	9,001	1,960.29	4,591.67	4,497.79	4,687.52
Thrombotic event	34,861	7,940	1,942.46	4,087.60	3,998.67	4,178.50
ARDS	41,123	1,242	2,782.73	446.32	422.18	471.85
Heart failure	35,976	5,821	2,159.20	2,695.91	2,627.54	2,766.06
Sepsis/septic shock	39,614	6,104	2,399.90	2,543.43	2,480.42	2,608.05
ICU/Mechanical ventilation/ECMO	39,529	7,185	2,359.17	3,045.56	2,975.95	3,116.80
Hospitalization	32,948	32,911	313.66	104,925.09	103,797.60	106,064.83
All-cause mortality	41,152	3,458	3,231.58	1,070.07	1,034.99	1,106.33
In hospital death	41,152	1,229	2,850.07	431.22	407.77	456.01
Multi-organ dysfunction/failure	31,565	17,565	1,107.40	15,861.47	15,628.63	16,097.78
Vasopressor use	38,614	4,988	2,427.35	2,054.92	1,998.68	2,112.75
High Risk Trial Similar Cohort						
Pneumonia	21,484	4,213	1,231.55	3,420.90	3,319.15	3,525.78
Kidney failure	20,394	5,855	1,051.46	5,568.47	5,427.65	5,712.95
Thrombotic event	19,278	5,254	1,010.38	5,200.01	5,061.29	5,342.54
ARDS	22,276	742	1,483.96	500.01	465.30	537.32
Heart failure	19,956	3,675	1,158.55	3,172.06	3,071.14	3,276.29
Sepsis/septic shock	21,815	3,585	1,292.12	2,774.51	2,685.16	2,866.83
ICU/Mechanical ventilation/ECMO	21,773	4,287	1,267.93	3,381.10	3,281.39	3,483.84
Hospitalization	19,143	19,120	153.54	124,531.11	122,778.41	126,308.83
All-cause mortality	22,283	2,180	1,735.08	1,256.43	1,204.78	1,310.29
In hospital death	22,283	814	1,523.19	534.41	498.93	572.41
Multi-organ dysfunction/failure	18,037	11,535	532.12	21,677.53	21,285.53	22,076.76
Vasopressor use	21,359	2,362	1,345.37	1,755.65	1,686.26	1,827.90
Standard Risk Trial Similar Cohort						
Pneumonia	6,114	1,018	341.36	2,982.23	2,804.55	3,171.17
Kidney failure	6,124	1,236	329.69	3,748.98	3,545.70	3,963.92
Thrombotic event	6,117	1,142	334.71	3,411.90	3,219.65	3,615.64
ARDS	6,126	240	387.36	619.58	545.95	703.14
Heart failure	6,127	787	357.12	2,203.73	2,055.02	2,363.20
Sepsis/septic shock	6,124	903	349.39	2,584.50	2,421.31	2,758.69
ICU/Mechanical ventilation/ECMO	6,118	1,276	328.41	3,885.44	3,678.00	4,104.59
Hospitalization	6,071	6,069	41.24	147,171.84	143,515.37	150,921.47
All-cause mortality	6,127	353	488.42	722.74	651.15	802.21
In hospital death	6,127	147	400.39	367.15	312.34	431.56
Multi-organ dysfunction/failure	6,098	3,287	200.71	16,376.49	15,826.10	16,946.02

Table 31. Incidence of COVID-19 Complications/Interventions within 30 Days of COVID-19 Infection in the Source Cohort and Trial-similar Cohorts by Hospitalization Status, 12/15/2021-07/20/2022 (Omicron Period)

			Hospitalized			
Study Endpoints	**Patients at Risk**	**Events**	**Person-time**	**Incidence Rate per 1000 person years**	**95% CI**	
Vasopressor use	6,110	751	361.90	2,075.17	1,931.94	2,229.03

Table 32. Incidence of COVID-19 Complications/Interventions within 30 Days of COVID-19 Infection in the Source Cohort and Trial-similar Cohorts by Hospitalization Status, 12/15/2021-07/20/2022 (Omicron Period)

			Non-Hospitalized			
Study Endpoints	**Patients at Risk**	**Events**	**Person-time**	**Incidence Rate per 1000 person years**	**95% CI**	
Source Cohort						
Pneumonia	473,576	3,913	30,523.24	128.20	124.24	132.28
Kidney failure	468,775	3,451	30,213.08	114.22	110.47	118.10
Thrombotic event	460,108	4,879	29,537.89	165.18	160.61	169.88
ARDS	477,357	196	30,985.14	6.33	5.50	7.28
Heart failure	468,379	2,389	30,244.77	78.99	75.88	82.22
Sepsis/septic shock	475,590	1,024	30,823.00	33.22	31.25	35.32
ICU/Mechanical ventilation/ECMO	475,471	741	30,829.44	24.04	22.37	25.83
Hospitalization	461,407	0	29,874.87	0.00	0.00	3,688.88
All-cause mortality	477,395	1,222	39,152.67	31.21	29.51	33.01
In hospital death	477,395	0	30,996.86	0.00	0.00	3,688.88
Multi-organ dysfunction/failure	455,763	7,660	29,081.15	263.40	257.57	269.37
Vasopressor use	467,047	7,411	29,860.84	248.18	242.60	253.90
High Risk Trial Similar Cohort						
Pneumonia	269,783	2,325	17,737.33	131.08	125.86	136.52
Kidney failure	267,672	1,872	17,618.82	106.25	101.54	111.17
Thrombotic event	260,847	3,084	17,085.12	180.51	174.25	186.99
ARDS	272,044	91	18,011.98	5.05	4.11	6.21
Heart failure	266,752	1,371	17,581.50	77.98	73.96	82.22
Sepsis/septic shock	271,334	412	17,948.25	22.95	20.84	25.28
ICU/Mechanical ventilation/ECMO	271,225	252	17,950.01	14.04	12.41	15.88
Hospitalization	265,003	0	17,523.97	0.00	0.00	3,688.88
All-cause mortality	272,053	678	22,312.92	30.39	28.18	32.76
In hospital death	272,053	0	18,016.43	0.00	0.00	3,688.88
Multi-organ dysfunction/failure	259,774	4,347	16,940.97	256.60	249.08	264.34
Vasopressor use	265,850	4,627	17,330.60	266.98	259.40	274.79
Standard Risk Trial Similar Cohort						
Pneumonia	172,955	767	10,472.41	73.24	68.24	78.61
Kidney failure	173,192	401	10,508.61	38.16	34.60	42.08
Thrombotic event	173,009	664	10,482.90	63.34	58.70	68.35
ARDS	173,226	37	10,528.73	3.51	2.55	4.85

Table 32. Incidence of COVID-19 Complications/Interventions within 30 Days of COVID-19 Infection in the Source Cohort and Trial-similar Cohorts by Hospitalization Status, 12/15/2021-07/20/2022 (Omicron Period)

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate per 1000 person years	95% CI	
			Non-Hospitalized			
Heart failure	173,226	223	10,519.12	21.20	18.59	24.17
Sepsis/septic shock	173,201	112	10,523.82	10.64	8.84	12.81
ICU/Mechanical ventilation/ECMO	173,201	63	10,525.77	5.99	4.68	7.66
Hospitalization	172,776	0	10,499.41	0.00	0.00	3,688.88
All-cause mortality	173,226	87	14,223.98	6.12	4.96	7.55
In hospital death	173,226	0	10,530.11	0.00	0.00	3,688.88
Multi-organ dysfunction/failure	172,822	1,166	10,445.98	111.62	105.40	118.22
Vasopressor use	172,540	1,200	10,423.65	115.12	108.79	121.82

In the Paxlovid cohort (Table 33), the incidence of all outcomes were substantially lower than in the Pre-Vaccine and even Vaccine periods.

Table 33. Incidence of COVID-19 Complications/Interventions within 30 Days of index date among Paxlovid Cohort by Hospitalization Status

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate per 1000 person years	95% CI	
			Overall			
Paxlovid Cohort						
Pneumonia	16,434	71	927.97	76.51	60.63	96.55
Kidney failure	16,273	75	917.72	81.72	65.17	102.48
Thrombotic event	15,670	130	872.40	149.01	125.48	176.96
ARDS	16,578	0	941.25	0.00	0.00	3,688.88
Heart failure	16,153	51	909.62	56.07	42.61	73.77
Sepsis/septic shock	16,536	23	937.01	24.55	16.31	36.94
ICU/Mechanical ventilation/ECMO	16,527	19	936.91	20.28	12.94	31.79
Hospitalization	16,089	168	899.59	186.75	160.54	217.24
All-cause mortality	16,583	9	1,361.57	6.61	3.44	12.70
In hospital death	16,583	2	941.65	2.12	0.53	8.49
Multi-organ dysfunction/failure	15,584	168	866.44	193.90	166.69	225.55
Vasopressor use	16,127	127	903.86	140.51	118.08	167.20
			Hospitalized			
Paxlovid Cohort						
Pneumonia	184	19	13.08	1,453.05	926.83	2,278.03
Kidney failure	179	26	12.29	2,115.98	1,440.71	3,107.74
Thrombotic event	163	33	10.73	3,075.59	2,186.52	4,326.18
ARDS	191	0	14.55	0.00	0.00	3,688.88
Heart failure	178	18	12.91	1,394.08	878.33	2,212.68

Table 33. Incidence of COVID-19 Complications/Interventions within 30 Days of index date among Paxlovid Cohort by Hospitalization Status

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate per 1000 person years	95% CI	
Sepsis/septic shock	189	20	13.45	1,487.17	959.46	2,305.14
ICU/Mechanical ventilation/ECMO	189	19	13.52	1,405.38	896.42	2,203.29
Hospitalization	168	168	5.28	31,810.26	27,346.12	37,003.17
All-cause mortality	191	3	15.57	192.64	62.13	597.30
In hospital death	191	2	14.55	137.47	34.38	549.65
Multi-organ dysfunction/failure	151	58	8.56	6,776.87	5,239.15	8,765.92
Vasopressor use	180	28	12.70	2,204.57	1,522.17	3,192.90
			Non-Hospitalized			
Paxlovid Cohort						
Pneumonia	16,250	52	914.90	56.84	43.31	74.59
Kidney failure	16,094	49	905.43	54.12	40.90	71.60
Thrombotic event	15,507	97	861.67	112.57	92.26	137.36
ARDS	16,387	0	926.70	0.00	0.00	3,688.88
Heart failure	15,975	33	896.70	36.80	26.16	51.77
Sepsis/septic shock	16,347	3	923.56	3.25	1.05	10.07
ICU/Mechanical ventilation/ECMO	16,338	0	923.39	0.00	0.00	3,688.88
Hospitalization	15,921	0	894.31	0.00	0.00	3,688.88
All-cause mortality	16,392	6	1,346.00	4.46	2.00	9.92
In hospital death	16,392	0	927.10	0.00	0.00	3,688.88
Multi-organ dysfunction/failure	15,433	110	857.88	128.22	106.37	154.57
Vasopressor use	15,947	99	891.16	111.09	91.23	135.28

Overall, the Source Cohort and High Risk Trial Similar Cohort had similar incidence rates of health outcomes (potential safety related endpoints) as compared to the Standard Risk Trial Similar Cohort, which had lower incidence rates across all health outcomes (Table 34). The incidence of all health outcomes was higher in Hospitalized patients compared to Non-Hospitalized patients (Table 34).

Table 34. Incidence of Potential Safety Endpoints in the Source Cohort and Trial-similar Cohorts by Hospitalization Status, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate per 1000 person years	95% CI	
			Overall			
Source Cohort						
Renal impairment	1,581,154	112,305	1,220,502.07	92.02	91.48	92.56
Hepatic impairment	1,628,679	49,427	1,303,281.71	37.93	37.59	38.26
Dysgeusia	1,661,550	14,392	1,350,550.61	10.66	10.48	10.83
Diarrhea	1,632,786	74,339	1,282,892.39	57.95	57.53	58.36

Table 34. Incidence of Potential Safety Endpoints in the Source Cohort and Trial-similar Cohorts by Hospitalization Status, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate per 1000 person years	95% CI	
Hypersensitivity reaction/allergic reaction	1,570,300	110,732	1,202,650.69	92.07	91.53	92.62
High Risk Trial Similar Cohort						
Renal impairment	900,354	73,922	712,335.41	103.77	103.03	104.53
Hepatic impairment	944,347	24,178	785,675.95	30.77	30.39	31.16
Dysgeusia	943,360	8,421	791,883.75	10.63	10.41	10.86
Diarrhea	926,104	44,923	749,679.85	59.92	59.37	60.48
Hypersensitivity reaction/allergic reaction	874,179	66,606	688,430.77	96.75	96.02	97.49
Standard Risk Trial Similar Cohort						
Renal impairment	590,354	16,314	446,629.02	36.53	35.97	37.09
Hepatic impairment	590,469	7,545	452,662.94	16.67	16.30	17.05
Dysgeusia	590,198	5,311	451,709.50	11.76	11.45	12.08
Diarrhea	586,818	17,562	441,837.46	39.75	39.16	40.34
Hypersensitivity reaction/allergic reaction	588,902	31,750	435,072.19	72.98	72.18	73.78
			Hospitalized			
Source Cohort						
Renal impairment	182,181	64,092	106,497.62	601.82	597.18	606.49
Hepatic impairment	204,498	18,059	154,911.95	116.58	114.89	118.29
Dysgeusia	212,334	642	173,274.05	3.71	3.43	4.00
Diarrhea	207,279	21,205	151,520.56	139.95	138.08	141.84
Hypersensitivity reaction/allergic reaction	200,227	21,316	144,191.27	147.83	145.86	149.83
High Risk Trial Similar Cohort						
Renal impairment	110,844	43,514	62,239.72	699.14	692.60	705.74
Hepatic impairment	124,451	8,830	97,096.76	90.94	89.06	92.86
Dysgeusia	124,395	413	102,652.00	4.02	3.65	4.43
Diarrhea	122,308	12,727	90,010.77	141.39	138.96	143.87
Hypersensitivity reaction/allergic reaction	117,421	12,313	85,501.11	144.01	141.49	146.58
Standard Risk Trial Similar Cohort						
Renal impairment	41,462	10,594	26,575.21	398.64	391.12	406.31
Hepatic impairment	41,475	3,316	31,559.27	105.07	101.56	108.71
Dysgeusia	41,474	83	33,826.36	2.45	1.98	3.04
Diarrhea	41,405	3,720	30,722.99	121.08	117.25	125.04
Hypersensitivity reaction/allergic reaction	41,449	5,080	29,625.10	171.48	166.83	176.26

Table 34. Incidence of Potential Safety Endpoints in the Source Cohort and Trial-similar Cohorts by Hospitalization Status, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate per 1000 person years	95% CI	
			Non-Hospitalized			
Source Cohort						
Renal impairment	1,398,973	48,213	1,114,004.45	43.28	42.89	43.67
Hepatic impairment	1,424,181	31,368	1,148,369.76	27.32	27.02	27.62
Dysgeusia	1,449,216	13,750	1,177,276.56	11.68	11.49	11.88
Diarrhea	1,425,507	53,134	1,131,371.82	46.96	46.57	47.37
Hypersensitivity reaction/allergic reaction	1,370,073	89,416	1,058,459.41	84.48	83.93	85.03
High Risk Trial Similar Cohort						
Renal impairment	789,510	30,408	650,095.69	46.77	46.25	47.30
Hepatic impairment	819,896	15,348	688,579.19	22.29	21.94	22.65
Dysgeusia	818,965	8,008	689,231.76	11.62	11.37	11.88
Diarrhea	803,796	32,196	659,669.08	48.81	48.28	49.34
Hypersensitivity reaction/allergic reaction	756,758	54,293	602,929.66	90.05	89.29	90.81
Standard Risk Trial Similar Cohort						
Renal impairment	548,892	5,720	420,053.82	13.62	13.27	13.98
Hepatic impairment	548,994	4,229	421,103.67	10.04	9.74	10.35
Dysgeusia	548,724	5,228	417,883.13	12.51	12.18	12.85
Diarrhea	545,413	13,842	411,114.48	33.67	33.11	34.24
Hypersensitivity reaction/allergic reaction	547,453	26,670	405,447.09	65.78	65.00	66.57

Across all cohorts, overall, the incidence rates of health outcomes were higher during the Vaccine Period (Table 36) as compared to the Pre-Vaccine Period (Table 35).

Table 35. Incidence of Potential Safety Endpoints in the Source Cohort and Trial-similar Cohorts by Hospitalization Status, 1/1/2020-10/31/2020 (Pre-vaccine Period)

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate per 1000 person years	95% CI	
			Overall			
Source Cohort						
Renal impairment	267,043	29,566	378,969.21	78.02	77.13	78.91
Hepatic impairment	279,146	13,531	410,833.92	32.94	32.39	33.50
Dysgeusia	284,788	3,502	428,357.32	8.18	7.91	8.45
Diarrhea	279,454	20,127	401,822.41	50.09	49.40	50.79

Table 35. Incidence of Potential Safety Endpoints in the Source Cohort and Trial-similar Cohorts by Hospitalization Status, 1/1/2020-10/31/2020 (Pre-vaccine Period)

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate per 1000 person years	95% CI	
Hypersensitivity reaction/allergic reaction	269,114	24,240	378,674.72	64.01	63.21	64.82
High Risk Trial Similar Cohort						
Renal impairment	154,192	19,663	218,054.38	90.17	88.92	91.44
Hepatic impairment	163,469	6,810	244,596.48	27.84	27.19	28.51
Dysgeusia	163,312	2,016	248,188.48	8.12	7.78	8.49
Diarrhea	160,178	12,249	231,750.11	52.85	51.93	53.80
Hypersensitivity reaction/allergic reaction	151,630	15,074	213,611.70	70.57	69.45	71.70
Standard Risk Trial Similar Cohort						
Renal impairment	96,945	3,840	143,755.91	26.71	25.88	27.57
Hepatic impairment	96,964	1,996	145,952.24	13.68	13.09	14.29
Dysgeusia	96,930	1,329	146,091.01	9.10	8.62	9.60
Diarrhea	96,453	4,410	142,035.17	31.05	30.15	31.98
Hypersensitivity reaction/allergic reaction	96,772	6,193	140,403.03	44.11	43.02	45.22
			Hospitalized			
Source Cohort						
Renal impairment	41,706	16,631	38,046.53	437.12	430.53	443.82
Hepatic impairment	47,444	4,716	56,808.92	83.02	80.68	85.42
Dysgeusia	49,167	223	63,655.78	3.50	3.07	4.00
Diarrhea	47,905	6,415	54,349.51	118.03	115.18	120.96
Hypersensitivity reaction/allergic reaction	46,283	5,551	52,545.79	105.64	102.90	108.46
High Risk Trial Similar Cohort						
Renal impairment	26,537	11,724	22,411.20	523.13	513.75	532.69
Hepatic impairment	29,834	2,356	36,007.75	65.43	62.84	68.13
Dysgeusia	29,817	153	38,178.07	4.01	3.42	4.70
Diarrhea	29,284	3,925	32,687.25	120.08	116.38	123.89
Hypersensitivity reaction/allergic reaction	28,100	3,331	31,532.33	105.64	102.11	109.29
Standard Risk Trial Similar Cohort						
Renal impairment	8,760	2,401	9,587.71	250.42	240.61	260.65
Hepatic impairment	8,761	763	11,521.25	66.23	61.69	71.10
Dysgeusia	8,761	29	12,342.81	2.35	1.63	3.38
Diarrhea	8,743	1,070	10,906.88	98.10	92.40	104.16
Hypersensitivity reaction/allergic reaction	8,755	1,184	10,740.11	110.24	104.14	116.70

Table 35. Incidence of Potential Safety Endpoints in the Source Cohort and Trial-similar Cohorts by Hospitalization Status, 1/1/2020-10/31/2020 (Pre-vaccine Period)

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate per 1000 person years	95% CI	
			Non-Hospitalized			
Source Cohort						
Renal impairment	225,337	12,935	340,922.68	37.94	37.29	38.60
Hepatic impairment	231,702	8,815	354,025.00	24.90	24.39	25.43
Dysgeusia	235,621	3,279	364,701.54	8.99	8.69	9.30
Diarrhea	231,549	13,712	347,472.90	39.46	38.81	40.13
Hypersensitivity reaction/allergic reaction	222,831	18,689	326,128.93	57.31	56.49	58.13
High Risk Trial Similar Cohort						
Renal impairment	127,655	7,939	195,643.18	40.58	39.70	41.48
Hepatic impairment	133,635	4,454	208,588.73	21.35	20.74	21.99
Dysgeusia	133,495	1,863	210,010.41	8.87	8.48	9.28
Diarrhea	130,894	8,324	199,062.86	41.82	40.93	42.72
Hypersensitivity reaction/allergic reaction	123,530	11,743	182,079.37	64.49	63.34	65.67
Standard Risk Trial Similar Cohort						
Renal impairment	88,185	1,439	134,168.20	10.73	10.19	11.29
Hepatic impairment	88,203	1,233	134,430.99	9.17	8.67	9.70
Dysgeusia	88,169	1,300	133,748.19	9.72	9.21	10.26
Diarrhea	87,710	3,340	131,128.29	25.47	24.62	26.35
Hypersensitivity reaction/allergic reaction	88,017	5,009	129,662.92	38.63	37.58	39.72

Table 36. Incidence of Potential Safety Endpoints in the Source Cohort and Trial-similar Cohorts by Hospitalization Status, 12/13/2020-07/20/2022 (Vaccine Period)

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate per 1000 person years	95% CI	
			Overall			
Source Cohort						
Renal impairment	1,137,054	67,993	621,715.61	109.36	108.55	110.19
Hepatic impairment	1,165,455	29,362	657,970.70	44.63	44.12	45.14
Dysgeusia	1,189,061	7,249	682,050.16	10.63	10.39	10.88
Diarrhea	1,168,994	43,523	651,246.95	66.83	66.21	67.46
Hypersensitivity reaction/allergic reaction	1,123,289	72,123	607,190.69	118.78	117.92	119.65
High Risk Trial Similar Cohort						

Table 36. Incidence of Potential Safety Endpoints in the Source Cohort and Trial-similar Cohorts by Hospitalization Status, 12/13/2020-07/20/2022 (Vaccine Period)

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate per 1000 person years	95% CI	
Renal impairment	640,929	44,089	363,291.06	121.36	120.23	122.50
Hepatic impairment	669,424	14,028	396,543.22	35.38	34.80	35.97
Dysgeusia	668,711	4,302	399,312.73	10.77	10.46	11.10
Diarrhea	656,713	25,922	380,451.76	68.13	67.31	68.97
Hypersensitivity reaction/allergic reaction	618,763	42,256	347,700.95	121.53	120.38	122.69
Standard Risk Trial Similar Cohort						
Renal impairment	429,063	10,630	221,515.44	47.99	47.08	48.91
Hepatic impairment	429,150	4,682	224,425.19	20.86	20.27	21.47
Dysgeusia	428,969	2,587	224,467.55	11.53	11.09	11.98
Diarrhea	426,412	10,800	219,670.63	49.16	48.25	50.10
Hypersensitivity reaction/allergic reaction	427,908	21,982	215,307.74	102.10	100.76	103.45
			Hospitalized			
Source Cohort						
Renal impairment	118,970	39,376	51,855.31	759.34	751.88	766.88
Hepatic impairment	132,389	11,252	73,543.84	153.00	150.20	155.85
Dysgeusia	137,579	295	82,396.24	3.58	3.19	4.01
Diarrhea	134,431	12,073	73,303.02	164.70	161.79	167.66
Hypersensitivity reaction/allergic reaction	129,766	12,965	69,008.70	187.87	184.67	191.14
High Risk Trial Similar Cohort						
Renal impairment	70,193	26,057	29,571.92	881.14	870.51	891.90
Hepatic impairment	78,486	5,426	44,892.05	120.87	117.69	124.13
Dysgeusia	78,455	182	47,477.66	3.83	3.32	4.43
Diarrhea	77,201	7,068	42,389.71	166.74	162.90	170.67
Hypersensitivity reaction/allergic reaction	74,028	7,223	39,817.22	181.40	177.27	185.64
Standard Risk Trial Similar Cohort						
Renal impairment	28,457	7,089	13,158.47	538.74	526.34	551.43
Hepatic impairment	28,467	2,219	15,504.32	143.12	137.29	149.20
Dysgeusia	28,466	41	16,663.43	2.46	1.81	3.34
Diarrhea	28,423	2,283	15,392.30	148.32	142.36	154.53
Hypersensitivity reaction/allergic reaction	28,449	3,323	14,677.07	226.41	218.84	234.24
			Non-Hospitalized			
Source Cohort						
Renal impairment	1,018,084	28,617	569,860.30	50.22	49.64	50.80

Table 36. Incidence of Potential Safety Endpoints in the Source Cohort and Trial-similar Cohorts by Hospitalization Status, 12/13/2020-07/20/2022 (Vaccine Period)

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate per 1000 person years	95% CI	
Hepatic impairment	1,033,066	18,110	584,426.85	30.99	30.54	31.44
Dysgeusia	1,051,482	6,954	599,653.92	11.60	11.33	11.87
Diarrhea	1,034,563	31,450	577,943.93	54.42	53.82	55.02
Hypersensitivity reaction/allergic reaction	993,523	59,158	538,181.99	109.92	109.04	110.81
High Risk Trial Similar Cohort						
Renal impairment	570,736	18,032	333,719.14	54.03	53.25	54.83
Hepatic impairment	590,938	8,602	351,651.17	24.46	23.95	24.98
Dysgeusia	590,256	4,120	351,835.07	11.71	11.36	12.07
Diarrhea	579,512	18,854	338,062.05	55.77	54.98	56.57
Hypersensitivity reaction/allergic reaction	544,735	35,033	307,883.73	113.79	112.60	114.98
Standard Risk Trial Similar Cohort						
Renal impairment	400,606	3,541	208,356.97	16.99	16.44	17.56
Hepatic impairment	400,683	2,463	208,920.87	11.79	11.33	12.26
Dysgeusia	400,503	2,546	207,804.12	12.25	11.79	12.74
Diarrhea	397,989	8,517	204,278.33	41.69	40.82	42.59
Hypersensitivity reaction/allergic reaction	399,459	18,659	200,630.67	93.00	91.68	94.35

The Omicron period (Table 37) had overall higher incidence rates of renal impairment and hypersensitivity/allergic reaction, compared to the full study time period (Table 34). Incidence rates for hepatic impairment, dysgeusia and diarrhea were somewhat similar between the two periods.

Table 37. Incidence of Potential Safety Endpoints in the Source Cohort and Trial-similar Cohorts by Hospitalization Status, 12/15/2021-07/20/2022 (Omicron Period)

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate per 1000 person years	95% CI	
			Overall			
Source Cohort						
Renal impairment	495,629	19,382	122,856.23	157.76	155.56	160.00
Hepatic impairment	507,130	8,205	128,968.87	63.62	62.26	65.01
Dysgeusia	518,173	768	134,307.87	5.72	5.33	6.14
Diarrhea	508,634	11,638	128,580.47	90.51	88.88	92.17
Hypersensitivity reaction/allergic reaction	486,599	23,166	118,662.62	195.23	192.73	197.76
High Risk Trial Similar Cohort						

Table 37. Incidence of Potential Safety Endpoints in the Source Cohort and Trial-similar Cohorts by Hospitalization Status, 12/15/2021-07/20/2022 (Omicron Period)

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate per 1000 person years	95% CI	
Renal impairment	282,186	12,347	74,593.88	165.52	162.63	168.47
Hepatic impairment	294,336	3,691	80,239.81	46.00	44.54	47.51
Dysgeusia	294,091	480	80,832.11	5.94	5.43	6.49
Diarrhea	288,444	6,780	77,443.78	87.55	85.49	89.66
Hypersensitivity reaction/allergic reaction	270,248	13,564	70,041.89	193.66	190.42	196.94
Standard Risk Trial Similar Cohort						
Renal impairment	179,316	2,448	36,449.04	67.16	64.55	69.88
Hepatic impairment	179,353	1,052	36,756.27	28.62	26.94	30.40
Dysgeusia	179,288	201	36,906.67	5.45	4.74	6.25
Diarrhea	178,009	2,684	36,119.99	74.31	71.55	77.17
Hypersensitivity reaction/allergic reaction	178,646	6,769	35,470.84	190.83	186.34	195.43
			Hospitalized			
Source Cohort						
Renal impairment	34,230	10,507	7,181.93	1,462.98	1,435.27	1,491.22
Hepatic impairment	39,139	2,921	10,596.23	275.66	265.85	285.84
Dysgeusia	41,129	37	12,042.90	3.07	2.23	4.24
Diarrhea	39,947	2,661	10,840.48	245.47	236.32	254.98
Hypersensitivity reaction/allergic reaction	38,368	2,987	10,127.47	294.94	284.55	305.71
High Risk Trial Similar Cohort						
Renal impairment	19,438	6,826	3,794.70	1,798.82	1,756.65	1,842.01
Hepatic impairment	22,283	1,339	5,986.61	223.67	212.00	235.97
Dysgeusia	22,274	19	6,314.97	3.01	1.92	4.72
Diarrhea	21,842	1,446	5,741.20	251.86	239.21	265.19
Hypersensitivity reaction/allergic reaction	20,890	1,638	5,342.29	306.61	292.12	321.82
Standard Risk Trial Similar Cohort						
Renal impairment	6,124	1,479	1,154.04	1,281.58	1,217.90	1,348.59
Hepatic impairment	6,127	424	1,402.92	302.23	274.79	332.41
Dysgeusia	6,127	4	1,511.41	2.65	0.99	7.05
Diarrhea	6,111	379	1,408.24	269.13	243.35	297.64
Hypersensitivity reaction/allergic reaction	6,121	598	1,349.56	443.11	408.98	480.09
			Non-Hospitalized			
Source Cohort						
Renal impairment	461,399	8,875	115,674.30	76.72	75.14	78.34

Table 37. Incidence of Potential Safety Endpoints in the Source Cohort and Trial-similar Cohorts by Hospitalization Status, 12/15/2021-07/20/2022 (Omicron Period)

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate per 1000 person years	95% CI	
Hepatic impairment	467,991	5,284	118,372.64	44.64	43.45	45.86
Dysgeusia	477,044	731	122,264.97	5.98	5.56	6.43
Diarrhea	468,687	8,977	117,739.99	76.24	74.68	77.84
Hypersensitivity reaction/allergic reaction	448,231	20,179	108,535.15	185.92	183.37	188.50
High Risk Trial Similar Cohort						
Renal impairment	262,748	5,521	70,799.18	77.98	75.95	80.07
Hepatic impairment	272,053	2,352	74,253.19	31.68	30.42	32.98
Dysgeusia	271,817	461	74,517.14	6.19	5.65	6.78
Diarrhea	266,602	5,334	71,702.59	74.39	72.42	76.41
Hypersensitivity reaction/allergic reaction	249,358	11,926	64,699.59	184.33	181.05	187.67
Standard Risk Trial Similar Cohort						
Renal impairment	173,192	969	35,295.00	27.45	25.78	29.24
Hepatic impairment	173,226	628	35,353.34	17.76	16.43	19.21
Dysgeusia	173,161	197	35,395.26	5.57	4.84	6.40
Diarrhea	171,898	2,305	34,711.75	66.40	63.75	69.17
Hypersensitivity reaction/allergic reaction	172,525	6,171	34,121.29	180.85	176.40	185.42

With the exception of dysgeusia, the Paxlovid cohort (Table 38) had higher incidence rates of all other health outcomes as compared to the full study period overall (Table 34).

Table 38. Incidence of Potential Safety Endpoints among Paxlovid Cohort by Hospitalization Status

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate per 1000 person years	95% CI	
			Overall			
Paxlovid Cohort						
Renal impairment	15,801	210	1,812.71	115.85	101.19	132.63
Hepatic impairment	16,090	130	1,867.58	69.61	58.62	82.67
Dysgeusia	16,573	5	1,963.65	2.55	1.06	6.12
Diarrhea	16,298	166	1,901.12	87.32	75.00	101.66
Hypersensitivity reaction/allergic reaction	15,199	546	1,704.40	320.35	294.57	348.38
			Hospitalized			
Paxlovid Cohort						

Table 38. Incidence of Potential Safety Endpoints among Paxlovid Cohort by Hospitalization Status

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate per 1000 person years	95% CI	
Renal impairment	170	41	26.17	1,566.45	1,153.40	2,127.41
Hepatic impairment	175	12	30.23	397.01	225.47	699.07
Dysgeusia	191	0	37.13	0.00	0.00	3,688.88
Diarrhea	184	21	32.56	644.99	420.54	989.24
Hypersensitivity reaction/allergic reaction	170	12	31.22	384.37	218.29	676.82
			Non-Hospitalized			
Paxlovid Cohort						
Renal impairment	15,631	169	1,786.53	94.60	81.36	109.99
Hepatic impairment	15,915	118	1,837.35	64.22	53.62	76.92
Dysgeusia	16,382	5	1,926.53	2.60	1.08	6.24
Diarrhea	16,114	145	1,868.56	77.60	65.94	91.32
Hypersensitivity reaction/allergic reaction	15,029	534	1,673.18	319.15	293.20	347.40

10.3.1.4. Objective 4: Estimate incidence of long COVID-19 or post-acute sequalae SARS CoV-2 (PASC) and assess health effects of Long COVID

In the Source Cohort, the incidence rates of any symptom and of post-COVID syndrome were highest at 4 weeks and decreased at 12 weeks and then further at 6 months (Table 39). A similar decrease in incidence rates were also observed in the Hospitalized (Table 40) and Non-Hospitalized (Table 41). At any time period, the Hospitalized patients had higher incidences of any symptom and post-COVID syndrome.

Table 39. Incidence of Long COVID in the Source Cohort by Follow-up Intervals, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
			Overall			
Any below medical condition						
Any below medical condition	967,343	539,650	342,665.65	1,574.86	1,570.66	1,579.07
Post-COVID syndrome						
Post-COVID syndrome	1,662,649	17,743	1,360,921.44	13.04	12.85	13.23
General symptoms						
Fatigue	1,584,560	177,703	1,163,142.74	152.78	152.07	153.49
Intermittent fever	1,628,224	151,263	1,212,003.15	124.80	124.18	125.44

Table 39. Incidence of Long COVID in the Source Cohort by Follow-up Intervals, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Post-exertional malaise	1,652,435	33,771	1,333,153.71	25.33	25.06	25.60
Multisystem inflammatory syndrome (MIS)	1,662,977	599	1,367,331.59	0.44	0.40	0.48
Respiratory symptoms						
Dyspnea or Shortness of breath	1,585,845	259,735	1,082,807.44	239.87	238.95	240.80
Cough	1,603,114	170,408	1,107,598.78	153.85	153.13	154.59
Nasal congestion	1,641,280	65,568	1,303,237.81	50.31	49.93	50.70
Lung function abnormalities	1,656,383	15,145	1,351,809.01	11.20	11.03	11.38
Hypoxemia	1,654,993	77,094	1,298,264.90	59.38	58.97	59.80
Cardiovascular and cerebrovascular symptoms						
Chest pain	1,585,903	163,124	1,176,658.74	138.63	137.96	139.31
Palpitations or Fast-beating or pounding heart	1,639,525	41,703	1,316,045.78	31.69	31.39	31.99
Myocarditis	1,662,834	1,588	1,366,385.60	1.16	1.11	1.22
Pericarditis	1,662,636	958	1,366,659.42	0.70	0.66	0.75
Myocardial infarction	1,653,999	24,950	1,345,257.96	18.55	18.32	18.78
Angina	1,648,805	17,302	1,342,325.68	12.89	12.70	13.08
Atrial fibrillation	1,623,384	43,890	1,307,481.31	33.57	33.26	33.88
Atrial flutter	1,657,908	8,486	1,358,056.94	6.25	6.12	6.38
Sinus tachycardia	1,640,709	72,412	1,293,176.22	56.00	55.59	56.41
Sinus bradycardia	1,650,311	30,373	1,334,989.23	22.75	22.50	23.01
Heart Failure	1,613,247	66,992	1,284,770.34	52.14	51.75	52.54
Stroke	1,652,380	16,009	1,348,542.53	11.87	11.69	12.06
TIA	1,658,572	6,852	1,359,299.22	5.04	4.92	5.16
Neurological symptoms						
Headache	1,647,811	10,864	1,329,666.06	8.17	8.02	8.33
Insomnia	1,630,643	40,603	1,308,573.71	31.03	30.73	31.33
Cognitive impairment	1,638,572	52,944	1,314,250.36	40.28	39.94	40.63
Confusion	1,661,313	6,963	1,362,260.70	5.11	4.99	5.23
Anosmia or Loss of smell	1,661,800	15,439	1,349,503.83	11.44	11.26	11.62
Ageusia or Loss of taste	1,661,550	14,393	1,350,550.61	10.66	10.48	10.83
Depression	1,559,238	85,833	1,198,107.10	71.64	71.16	72.12
Anxiety Disorders	1,511,320	145,793	1,127,358.01	129.32	128.66	129.99
Post-traumatic Stress Disorder	1,652,988	10,532	1,351,453.01	7.79	7.65	7.94
Substance Use Disorders	1,632,819	38,412	1,315,972.73	29.19	28.90	29.48
Suicidal behavior and suicide ideation	1,657,312	9,831	1,356,094.02	7.25	7.11	7.39
Dizziness on standing (lightheadedness)	1,628,019	63,007	1,291,128.42	48.80	48.42	49.18

Table 39. Incidence of Long COVID in the Source Cohort by Follow-up Intervals, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Pins-and-needles feelings	1,649,513	22,881	1,339,519.43	17.08	16.86	17.30
Dysautonomia	1,661,092	2,534	1,364,237.87	1.86	1.79	1.93
Digestive symptoms						
Abdominal pain	1,558,902	146,345	1,176,676.70	124.37	123.74	125.01
Diarrhea	1,632,786	74,541	1,282,892.39	58.10	57.69	58.52
Nausea	1,636,149	57,521	1,300,253.74	44.24	43.88	44.60
Constipation	1,627,014	58,946	1,296,024.83	45.48	45.12	45.85
Musculoskeletal and Skin						
Arthralgia or joint pain	1,544,221	139,500	1,168,847.75	119.35	118.72	119.98
Myalgia or muscle pain	1,645,094	46,724	1,312,254.04	35.61	35.29	35.93
Body aches	1,643,454	58,741	1,304,704.27	45.02	44.66	45.39
Rash	1,631,607	48,358	1,308,077.40	36.97	36.64	37.30
Alopecia	1,662,531	675	1,366,904.80	0.49	0.46	0.53
Hair loss	1,658,004	13,389	1,353,310.37	9.89	9.73	10.06
Endocrine symptoms						
Diabetes mellitus (Type I & II)	1,510,436	97,073	1,154,056.64	84.11	83.59	84.65
Diabetic ketoacidosis	1,661,098	5,722	1,362,143.20	4.20	4.09	4.31
Thyroiditis	1,655,654	6,181	1,356,778.28	4.56	4.44	4.67
Hypothyroidism	1,580,260	57,990	1,249,537.57	46.41	46.03	46.79
Hyperthyroidism	1,657,046	6,053	1,357,903.34	4.46	4.35	4.57
Menstrual/period issues	1,622,679	49,315	1,298,601.26	37.98	37.64	38.31
Hematologic symptoms						
DVT	1,656,167	15,432	1,350,921.28	11.42	11.24	11.61
Pulmonary embolism	1,657,529	17,925	1,350,013.83	13.28	13.09	13.47
Renal symptoms						
Acute kidney injury	1,637,891	83,097	1,294,158.71	64.21	63.77	64.65
Chronic kidney disease	1,591,015	74,111	1,254,121.11	59.09	58.67	59.52
Dialysis	1,652,664	21,123	1,346,209.85	15.69	15.48	15.90
			>=4 Weeks			
Any below medical condition						
Any below medical condition	496,893	154,901	337,173.39	459.41	457.13	461.70
Post-COVID syndrome						
Post-COVID syndrome	1,458,541	11,178	1,354,754.66	8.25	8.10	8.41
General symptoms						
Fatigue	1,312,393	84,909	1,156,555.97	73.42	72.92	73.91
Intermittent fever	1,328,485	32,949	1,205,697.12	27.33	27.03	27.62
Post-exertional malaise	1,439,685	15,340	1,326,962.12	11.56	11.38	11.75
Multisystem inflammatory syndrome (MIS)	1,464,058	158	1,361,339.06	0.12	0.10	0.14
Respiratory symptoms						

Table 39. Incidence of Long COVID in the Source Cohort by Follow-up Intervals, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Dyspnea or Shortness of breath	1,229,990	72,018	1,075,873.07	66.94	66.45	67.43
Cough	1,268,451	28,629	1,100,660.97	26.01	25.71	26.31
Nasal congestion	1,409,343	26,323	1,297,135.93	20.29	20.05	20.54
Lung function abnormalities	1,453,888	9,221	1,345,789.82	6.85	6.71	6.99
Hypoxemia	1,402,004	11,190	1,292,071.83	8.66	8.50	8.82
Cardiovascular and cerebrovascular symptoms						
Chest pain	1,324,885	85,790	1,170,099.26	73.32	72.83	73.81
Palpitations or Fast-beating or pounding heart	1,433,291	31,300	1,309,895.15	23.90	23.63	24.16
Myocarditis	1,463,431	490	1,360,392.85	0.36	0.33	0.39
Pericarditis	1,463,761	520	1,360,667.11	0.38	0.35	0.42
Myocardial infarction	1,445,821	9,052	1,339,333.85	6.76	6.62	6.90
Angina	1,447,622	12,498	1,336,319.11	9.35	9.19	9.52
Atrial fibrillation	1,409,982	14,971	1,301,692.19	11.50	11.32	11.69
Atrial flutter	1,456,722	3,857	1,352,081.07	2.85	2.76	2.94
Sinus tachycardia	1,406,243	27,540	1,286,922.87	21.40	21.15	21.65
Sinus bradycardia	1,440,826	14,996	1,328,942.77	11.28	11.11	11.47
Heart Failure	1,391,721	22,988	1,279,103.74	17.97	17.74	18.21
Stroke	1,449,903	8,782	1,342,572.72	6.54	6.41	6.68
TIA	1,458,850	4,694	1,353,308.64	3.47	3.37	3.57
Neurological symptoms						
Headache	1,441,560	2,492	1,323,626.12	1.88	1.81	1.96
Insomnia	1,423,626	27,774	1,302,468.05	21.32	21.08	21.58
Cognitive impairment	1,425,100	28,198	1,308,231.16	21.55	21.30	21.81
Confusion	1,459,749	2,114	1,356,283.35	1.56	1.49	1.63
Anosmia or Loss of smell	1,450,379	2,230	1,343,456.89	1.66	1.59	1.73
Ageusia or Loss of taste	1,451,132	2,201	1,344,512.44	1.64	1.57	1.71
Depression	1,336,922	50,903	1,191,943.53	42.71	42.34	43.08
Anxiety Disorders	1,274,927	87,976	1,121,085.85	78.47	77.96	78.99
Post-traumatic Stress Disorder	1,452,006	7,013	1,345,436.23	5.21	5.09	5.34
Substance Use Disorders	1,421,601	20,280	1,309,956.46	15.48	15.27	15.70
Suicidal behavior and suicide ideation	1,455,507	5,429	1,350,089.36	4.02	3.92	4.13
Dizziness on standing (lightheadedness)	1,414,394	42,909	1,284,964.74	33.39	33.08	33.71
Pins-and-needles feelings	1,448,780	19,361	1,333,482.42	14.52	14.32	14.73
Dysautonomia	1,462,083	1,747	1,358,245.45	1.29	1.23	1.35
Digestive symptoms						
Abdominal pain	1,334,620	108,011	1,170,387.90	92.29	91.74	92.84
Diarrhea	1,400,986	34,652	1,276,700.07	27.14	26.86	27.43
Nausea	1,415,796	31,459	1,294,068.32	24.31	24.04	24.58

Table 39. Incidence of Long COVID in the Source Cohort by Follow-up Intervals, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Constipation	1,415,178	38,756	1,289,917.04	30.05	29.75	30.35
Musculoskeletal and Skin						
Arthralgia or joint pain	1,338,751	120,638	1,162,704.18	103.76	103.17	104.34
Myalgia or muscle pain	1,424,290	21,124	1,306,147.55	16.17	15.96	16.39
Body aches	1,416,128	24,281	1,298,613.97	18.70	18.46	18.93
Rash	1,427,141	38,779	1,301,972.13	29.78	29.49	30.08
Alopecia	1,463,966	588	1,360,914.84	0.43	0.40	0.47
Hair loss	1,458,809	12,213	1,347,305.37	9.06	8.91	9.23
Endocrine symptoms						
Diabetes mellitus (Type I & II)	1,271,997	30,754	1,148,407.67	26.78	26.48	27.08
Diabetic ketoacidosis	1,459,563	1,601	1,356,163.97	1.18	1.12	1.24
Thyroiditis	1,456,211	4,567	1,350,778.09	3.38	3.28	3.48
Hypothyroidism	1,365,174	28,572	1,243,603.71	22.98	22.71	23.24
Hyperthyroidism	1,457,227	3,992	1,351,904.32	2.95	2.86	3.05
Menstrual/period issues	1,421,342	43,179	1,292,523.04	33.41	33.09	33.72
Hematologic symptoms						
DVT	1,451,888	7,217	1,344,886.67	5.37	5.24	5.49
Pulmonary embolism	1,449,467	5,705	1,343,944.86	4.24	4.14	4.36
Renal symptoms						
Acute kidney injury	1,399,039	21,197	1,288,456.97	16.45	16.23	16.67
Chronic kidney disease	1,370,655	33,153	1,248,380.58	26.56	26.27	26.84
Dialysis	1,446,281	7,429	1,340,183.91	5.54	5.42	5.67
			>=12 Weeks			
Any below medical condition						
Any below medical condition	387,332	106,820	321,392.40	332.37	330.38	334.37
Post-COVID syndrome						
Post-COVID syndrome	1,300,256	6,925	1,331,839.59	5.20	5.08	5.32
General symptoms						
Fatigue	1,151,282	63,400	1,133,192.92	55.95	55.51	56.39
Intermittent fever	1,178,565	25,665	1,183,934.78	21.68	21.41	21.95
Post-exertional malaise	1,282,012	9,967	1,304,116.71	7.64	7.49	7.79
Multisystem inflammatory syndrome (MIS)	1,308,087	64	1,338,713.18	0.05	0.04	0.06
Respiratory symptoms						
Dyspnea or Shortness of breath	1,074,332	49,822	1,053,362.73	47.30	46.89	47.72
Cough	1,108,638	20,070	1,077,517.69	18.63	18.37	18.89
Nasal congestion	1,254,717	21,871	1,274,697.19	17.16	16.93	17.39
Lung function abnormalities	1,296,863	6,324	1,323,009.10	4.78	4.66	4.90
Hypoxemia	1,249,114	7,244	1,269,884.19	5.70	5.58	5.84
Cardiovascular and cerebrovascular symptoms						

Table 39. Incidence of Long COVID in the Source Cohort by Follow-up Intervals, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Chest pain	1,162,068	64,445	1,146,486.48	56.21	55.78	56.65
Palpitations or Fast-beating or pounding heart	1,272,486	23,072	1,286,579.56	17.93	17.70	18.17
Myocarditis	1,307,444	287	1,337,763.02	0.21	0.19	0.24
Pericarditis	1,307,791	380	1,338,039.68	0.28	0.26	0.31
Myocardial infarction	1,290,886	6,849	1,316,839.29	5.20	5.08	5.33
Angina	1,290,517	9,466	1,313,519.72	7.21	7.06	7.35
Atrial fibrillation	1,257,884	10,490	1,279,605.64	8.20	8.04	8.36
Atrial flutter	1,300,959	2,756	1,329,476.68	2.07	2.00	2.15
Sinus tachycardia	1,249,064	19,198	1,264,143.73	15.19	14.97	15.40
Sinus bradycardia	1,284,633	11,667	1,306,262.05	8.93	8.77	9.10
Heart Failure	1,240,568	16,290	1,257,117.26	12.96	12.76	13.16
Stroke	1,294,094	6,649	1,319,958.90	5.04	4.92	5.16
TIA	1,302,568	3,671	1,330,632.22	2.76	2.67	2.85
Neurological symptoms						
Headache	1,284,809	1,183	1,300,881.74	0.91	0.86	0.96
Insomnia	1,264,498	20,452	1,279,378.43	15.99	15.77	16.21
Cognitive impairment	1,268,411	20,887	1,285,481.60	16.25	16.03	16.47
Confusion	1,304,231	1,464	1,333,714.99	1.10	1.04	1.16
Anosmia or Loss of smell	1,294,358	1,651	1,320,824.47	1.25	1.19	1.31
Ageusia or Loss of taste	1,295,176	1,715	1,321,886.69	1.30	1.24	1.36
Depression	1,176,233	36,375	1,168,603.67	31.13	30.81	31.45
Anxiety Disorders	1,113,057	63,347	1,097,611.44	57.71	57.27	58.17
Post-traumatic Stress Disorder	1,295,457	5,237	1,322,720.70	3.96	3.85	4.07
Substance Use Disorders	1,265,351	15,243	1,287,273.67	11.84	11.66	12.03
Suicidal behavior and suicide ideation	1,299,215	4,078	1,327,412.74	3.07	2.98	3.17
Dizziness on standing (lightheadedness)	1,254,553	33,859	1,261,756.18	26.83	26.55	27.12
Pins-and-needles feelings	1,290,516	15,477	1,310,500.30	11.81	11.63	12.00
Dysautonomia	1,305,995	1,315	1,335,599.56	0.98	0.93	1.04
Digestive symptoms						
Abdominal pain	1,168,439	83,863	1,146,204.68	73.17	72.67	73.66
Diarrhea	1,243,790	27,261	1,253,872.25	21.74	21.49	22.00
Nausea	1,257,321	24,692	1,271,057.07	19.43	19.19	19.67
Constipation	1,256,001	29,158	1,266,807.00	23.02	22.75	23.28
Musculoskeletal and Skin						
Arthralgia or joint pain	1,169,994	94,820	1,138,108.92	83.31	82.79	83.85
Myalgia or muscle pain	1,267,403	16,870	1,283,370.15	13.15	12.95	13.35
Body aches	1,259,647	19,416	1,275,889.57	15.22	15.01	15.43
Rash	1,267,196	30,566	1,278,753.59	23.90	23.64	24.17
Alopecia	1,307,977	467	1,338,283.28	0.35	0.32	0.38

Table 39. Incidence of Long COVID in the Source Cohort by Follow-up Intervals, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Hair loss	1,300,839	9,594	1,324,334.29	7.24	7.10	7.39
Endocrine symptoms						
Diabetes mellitus (Type I & II)	1,125,675	21,678	1,127,164.52	19.23	18.98	19.49
Diabetic ketoacidosis	1,303,844	1,254	1,333,569.77	0.94	0.89	0.99
Thyroiditis	1,299,952	3,360	1,328,109.37	2.53	2.45	2.62
Hypothyroidism	1,210,757	19,930	1,221,204.68	16.32	16.10	16.55
Hyperthyroidism	1,301,045	3,004	1,329,244.57	2.26	2.18	2.34
Menstrual/period issues	1,260,319	33,899	1,269,118.83	26.71	26.43	27.00
Hematologic symptoms						
DVT	1,295,478	4,906	1,322,198.17	3.71	3.61	3.82
Pulmonary embolism	1,293,512	3,579	1,321,334.06	2.71	2.62	2.80
Renal symptoms						
Acute kidney injury	1,248,737	16,090	1,266,560.66	12.70	12.51	12.90
Chronic kidney disease	1,218,076	24,639	1,226,196.16	20.09	19.85	20.35
Dialysis	1,291,432	5,025	1,317,703.17	3.81	3.71	3.92
			>=6 months			
Any below medical condition						
Any below medical condition	245,692	55,213	268,635.39	205.53	203.82	207.25
Post-COVID syndrome						
Post-COVID syndrome	996,564	4,601	1,213,247.33	3.79	3.68	3.90
General symptoms						
Fatigue	856,896	38,673	1,019,101.37	37.95	37.57	38.33
Intermittent fever	892,088	16,091	1,072,361.04	15.01	14.78	15.24
Post-exertional malaise	978,077	6,026	1,185,447.94	5.08	4.96	5.21
Multisystem inflammatory syndrome (MIS)	1,002,093	47	1,219,108.54	0.04	0.03	0.05
Respiratory symptoms						
Dyspnea or Shortness of breath	796,018	29,955	945,471.36	31.68	31.33	32.04
Cough	815,030	11,217	963,429.19	11.64	11.43	11.86
Nasal congestion	956,471	14,698	1,158,426.99	12.69	12.48	12.90
Lung function abnormalities	991,303	3,714	1,203,692.89	3.09	2.99	3.19
Hypoxemia	951,160	4,402	1,153,539.07	3.82	3.71	3.93
Cardiovascular and cerebrovascular symptoms						
Chest pain	867,646	40,217	1,032,389.84	38.96	38.58	39.34
Palpitations or Fast-beating or pounding heart	966,849	14,334	1,167,493.04	12.28	12.08	12.48
Myocarditis	1,001,487	171	1,218,173.61	0.14	0.12	0.16
Pericarditis	1,001,707	226	1,218,406.26	0.19	0.16	0.21
Myocardial infarction	986,978	4,428	1,198,110.78	3.70	3.59	3.81
Angina	984,955	5,843	1,194,239.45	4.89	4.77	5.02

Table 39. Incidence of Long COVID in the Source Cohort by Follow-up Intervals, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Atrial fibrillation	959,521	6,381	1,163,108.04	5.49	5.35	5.62
Atrial flutter	995,619	1,668	1,210,163.44	1.38	1.31	1.45
Sinus tachycardia	948,895	11,573	1,147,119.05	10.09	9.91	10.27
Sinus bradycardia	979,791	7,370	1,187,258.04	6.21	6.07	6.35
Heart Failure	943,855	9,830	1,141,328.58	8.61	8.44	8.79
Stroke	989,321	4,287	1,200,911.23	3.57	3.47	3.68
TIA	996,694	2,385	1,211,125.87	1.97	1.89	2.05
Neurological symptoms						
Headache	978,584	175	1,181,235.64	0.15	0.13	0.17
Insomnia	961,060	12,314	1,161,162.29	10.60	10.42	10.79
Cognitive impairment	965,359	13,047	1,167,271.15	11.18	10.99	11.37
Confusion	998,697	908	1,214,291.34	0.75	0.70	0.80
Anosmia or Loss of smell	988,987	946	1,201,490.22	0.79	0.74	0.84
Ageusia or Loss of taste	989,667	946	1,202,501.28	0.79	0.74	0.84
Depression	879,496	19,277	1,053,494.02	18.30	18.04	18.56
Anxiety Disorders	827,803	36,126	987,484.60	36.58	36.21	36.96
Post-traumatic Stress Disorder	990,646	3,113	1,203,686.18	2.59	2.50	2.68
Substance Use Disorders	964,370	9,021	1,169,883.11	7.71	7.55	7.87
Suicidal behavior and suicide ideation	994,011	2,426	1,208,170.36	2.01	1.93	2.09
Dizziness on standing (lightheadedness)	950,006	21,630	1,143,215.25	18.92	18.67	19.17
Pins-and-needles feelings	983,406	9,881	1,190,696.21	8.30	8.14	8.46
Dysautonomia	1,000,042	804	1,216,036.14	0.66	0.62	0.71
Digestive symptoms						
Abdominal pain	868,607	51,241	1,030,351.14	49.73	49.30	50.16
Diarrhea	943,002	17,191	1,136,729.37	15.12	14.90	15.35
Nausea	954,668	15,291	1,153,163.55	13.26	13.05	13.47
Constipation	952,720	17,882	1,148,730.36	15.57	15.34	15.80
Musculoskeletal and Skin						
Arthralgia or joint pain	865,331	58,999	1,020,518.20	57.81	57.35	58.28
Myalgia or muscle pain	963,640	10,874	1,164,891.31	9.33	9.16	9.51
Body aches	957,629	12,562	1,158,134.64	10.85	10.66	11.04
Rash	961,743	19,224	1,159,781.20	16.58	16.34	16.81
Alopecia	1,001,888	290	1,218,649.75	0.24	0.21	0.27
Hair loss	991,042	3,416	1,203,637.99	2.84	2.74	2.94
Endocrine symptoms						
Diabetes mellitus (Type I & II)	848,521	12,793	1,019,373.62	12.55	12.33	12.77
Diabetic ketoacidosis	998,440	799	1,214,216.15	0.66	0.61	0.71
Thyroiditis	994,719	1,974	1,208,876.76	1.63	1.56	1.71

Table 39. Incidence of Long COVID in the Source Cohort by Follow-up Intervals, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Hypothyroidism	917,011	10,614	1,106,829.86	9.59	9.41	9.77
Hyperthyroidism	995,521	1,769	1,209,881.69	1.46	1.40	1.53
Menstrual/period issues	954,667	20,991	1,150,204.45	18.25	18.01	18.50
Hematologic symptoms						
DVT	990,539	3,015	1,203,072.71	2.51	2.42	2.60
Pulmonary embolism	989,388	2,192	1,202,518.49	1.82	1.75	1.90
Renal symptoms						
Acute kidney injury	950,835	10,258	1,150,264.54	8.92	8.75	9.09
Chronic kidney disease	922,742	15,170	1,111,097.20	13.65	13.44	13.87
Dialysis	987,425	3,083	1,198,918.37	2.57	2.48	2.66

Table 40. Incidence of Long COVID in the Source Cohort by Follow-up Intervals among Patients Hospitalized, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
			Overall			
Any below medical condition						
Any below medical condition	110,840	101,912	7,583.13	13,439.30	13,357.04	13,522.06
Post-COVID syndrome						
Post-COVID syndrome	212,443	5,576	171,738.69	32.47	31.63	33.33
General symptoms						
Fatigue	197,780	46,876	126,592.23	370.29	366.95	373.66
Intermittent fever	207,893	29,160	143,081.17	203.80	201.48	206.15
Post-exertional malaise	209,124	15,232	160,425.35	94.95	93.45	96.47
Multisystem inflammatory syndrome (MIS)	212,454	346	173,834.54	1.99	1.79	2.21
Respiratory symptoms						
Dyspnea or Shortness of breath	192,192	102,689	71,864.64	1,428.92	1,420.21	1,437.69
Cough	205,157	24,602	138,823.95	177.22	175.02	179.45
Nasal congestion	211,190	3,301	170,450.08	19.37	18.72	20.04
Lung function abnormalities	210,386	7,514	167,156.75	44.95	43.95	45.98
Hypoxemia	208,533	60,806	120,162.90	506.03	502.02	510.07
Cardiovascular and cerebrovascular symptoms						
Chest pain	197,561	36,024	131,828.08	273.26	270.46	276.10
Palpitations or Fast-beating or pounding heart	209,631	5,911	166,668.25	35.47	34.57	36.38
Myocarditis	212,430	927	173,341.66	5.35	5.01	5.70
Pericarditis	212,357	438	173,613.83	2.52	2.30	2.77

Table 40. Incidence of Long COVID in the Source Cohort by Follow-up Intervals among Patients Hospitalized, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Myocardial infarction	208,508	16,786	161,027.79	104.24	102.68	105.83
Angina	208,148	5,648	166,147.16	33.99	33.12	34.89
Atrial fibrillation	198,123	25,502	148,239.04	172.03	169.93	174.16
Atrial flutter	210,429	5,115	169,347.73	30.20	29.39	31.04
Sinus tachycardia	205,915	32,528	142,875.31	227.67	225.21	230.16
Sinus bradycardia	208,785	14,869	160,296.72	92.76	91.28	94.26
Heart Failure	191,068	42,531	131,787.87	322.72	319.67	325.81
Stroke	208,461	8,339	165,595.37	50.36	49.29	51.45
TIA	211,061	2,665	171,046.55	15.58	15.00	16.18
Neurological symptoms						
Headache	210,147	1,955	168,158.78	11.63	11.12	12.15
Insomnia	207,537	11,317	160,686.08	70.43	69.14	71.74
Cognitive impairment	204,697	25,754	151,852.16	169.60	167.54	171.68
Confusion	211,556	5,453	170,045.71	32.07	31.23	32.93
Anosmia or Loss of smell	212,400	681	173,276.07	3.93	3.65	4.24
Ageusia or Loss of taste	212,334	643	173,274.05	3.71	3.44	4.01
Depression	195,555	24,813	136,489.98	181.79	179.55	184.07
Anxiety Disorders	193,523	37,325	129,225.26	288.84	285.92	291.78
Post-traumatic Stress Disorder	210,936	2,754	170,496.07	16.15	15.56	16.77
Substance Use Disorders	204,479	13,534	157,451.30	85.96	84.52	87.42
Suicidal behavior and suicide ideation	210,825	3,676	169,814.86	21.65	20.96	22.36
Dizziness on standing (lightheadedness)	206,341	12,474	158,683.14	78.61	77.24	80.00
Pins-and-needles feelings	210,745	3,382	169,891.86	19.91	19.25	20.59
Dysautonomia	212,043	769	173,107.19	4.44	4.14	4.77
Digestive symptoms						
Abdominal pain	196,749	25,425	140,878.53	180.47	178.27	182.71
Diarrhea	207,279	21,358	151,520.56	140.96	139.08	142.86
Nausea	208,388	10,148	161,998.20	62.64	61.44	63.87
Constipation	204,653	20,959	152,011.19	137.88	136.02	139.76
Musculoskeletal and Skin						
Arthralgia or joint pain	195,867	19,913	144,642.30	137.67	135.77	139.60
Myalgia or muscle pain	210,313	5,871	166,749.45	35.21	34.32	36.12
Body aches	208,970	13,338	161,154.87	82.77	81.37	84.18
Rash	208,946	6,769	165,772.54	40.83	39.87	41.82
Alopecia	212,436	63	174,015.33	0.36	0.28	0.46
Hair loss	212,161	2,136	171,933.60	12.42	11.91	12.96
Endocrine symptoms						
Diabetes mellitus (Type I & II)	173,045	43,034	106,615.80	403.64	399.84	407.47
Diabetic ketoacidosis	211,515	4,064	170,396.08	23.85	23.13	24.60

Table 40. Incidence of Long COVID in the Source Cohort by Follow-up Intervals among Patients Hospitalized, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Thyroiditis	211,830	885	172,762.35	5.12	4.80	5.47
Hypothyroidism	197,484	18,986	147,454.04	128.76	126.94	130.60
Hyperthyroidism	211,467	1,648	171,947.83	9.58	9.13	10.06
Menstrual/period issues	209,633	4,036	168,347.20	23.97	23.25	24.73
Hematologic symptoms						
DVT	210,262	8,703	166,195.04	52.37	51.28	53.48
Pulmonary embolism	210,633	11,453	164,288.82	69.71	68.45	71.00
Renal symptoms						
Acute kidney injury	200,330	59,171	126,539.43	467.61	463.86	471.39
Chronic kidney disease	186,372	36,064	128,595.20	280.45	277.57	283.36
Dialysis	206,953	15,097	160,633.38	93.98	92.50	95.50
			>=4 Weeks			
Any below medical condition						
Any below medical condition	10,039	2,719	7,013.11	387.70	373.40	402.55
Post-COVID syndrome						
Post-COVID syndrome	176,531	3,760	170,373.59	22.07	21.38	22.79
General symptoms						
Fatigue	138,914	13,914	125,128.41	111.20	109.37	113.06
Intermittent fever	153,199	4,674	141,696.92	32.99	32.05	33.95
Post-exertional malaise	167,502	5,367	159,000.20	33.75	32.86	34.67
Multisystem inflammatory syndrome (MIS)	177,886	53	172,527.55	0.31	0.24	0.40
Respiratory symptoms						
Dyspnea or Shortness of breath	83,714	10,302	70,439.33	146.25	143.46	149.11
Cough	153,134	4,219	137,429.87	30.70	29.79	31.64
Nasal congestion	175,700	1,872	169,138.95	11.07	10.58	11.58
Lung function abnormalities	173,608	3,767	165,841.74	22.71	22.00	23.45
Hypoxemia	127,851	4,859	118,701.27	40.93	39.80	42.10
Cardiovascular and cerebrovascular symptoms						
Chest pain	145,221	13,293	130,402.82	101.94	100.22	103.69
Palpitations or Fast-beating or pounding heart	173,964	4,108	165,336.64	24.85	24.10	25.62
Myocarditis	177,504	124	172,035.69	0.72	0.60	0.86
Pericarditis	177,824	153	172,307.59	0.89	0.76	1.04
Myocardial infarction	165,827	3,409	159,776.53	21.34	20.63	22.06
Angina	172,457	3,184	164,842.34	19.32	18.66	20.00
Atrial fibrillation	152,214	4,018	147,104.08	27.31	26.48	28.17
Atrial flutter	173,888	1,408	168,055.09	8.38	7.95	8.83
Sinus tachycardia	151,450	6,884	141,431.28	48.67	47.54	49.84
Sinus bradycardia	166,414	3,807	158,958.09	23.95	23.20	24.72
Heart Failure	137,470	7,462	130,753.77	57.07	55.79	58.38

Table 40. Incidence of Long COVID in the Source Cohort by Follow-up Intervals among Patients Hospitalized, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Stroke	170,977	2,989	164,302.75	18.19	17.55	18.86
TIA	175,943	1,338	169,741.77	7.88	7.47	8.32
Neurological symptoms						
Headache	174,658	457	166,851.22	2.74	2.50	3.00
Insomnia	168,134	4,551	159,346.29	28.56	27.74	29.40
Cognitive impairment	158,878	7,583	150,540.67	50.37	49.25	51.52
Confusion	174,400	1,102	168,748.62	6.53	6.16	6.93
Anosmia or Loss of smell	177,597	145	171,968.37	0.84	0.72	0.99
Ageusia or Loss of taste	177,607	179	171,967.20	1.04	0.90	1.21
Depression	147,132	5,715	135,156.43	42.28	41.20	43.40
Anxiety Disorders	138,169	8,595	127,880.20	67.21	65.81	68.65
Post-traumatic Stress Disorder	175,140	912	169,181.11	5.39	5.05	5.75
Substance Use Disorders	162,330	3,078	156,138.92	19.71	19.03	20.42
Suicidal behavior and suicide ideation	174,335	997	168,497.60	5.92	5.56	6.30
Dizziness on standing (lightheadedness)	167,656	6,669	157,346.24	42.38	41.38	43.41
Pins-and-needles feelings	175,867	2,569	168,578.55	15.24	14.66	15.84
Dysautonomia	177,449	354	171,801.46	2.06	1.86	2.29
Digestive symptoms						
Abdominal pain	153,407	13,093	139,505.67	93.85	92.26	95.47
Diarrhea	159,665	5,308	150,154.77	35.35	34.41	36.31
Nausea	169,361	4,475	160,647.38	27.86	27.05	28.68
Constipation	160,496	7,460	150,654.70	49.52	48.41	50.65
Musculoskeletal and Skin						
Arthralgia or joint pain	159,573	15,077	143,347.46	105.18	103.51	106.87
Myalgia or muscle pain	173,182	2,579	165,428.26	15.59	15.00	16.20
Body aches	167,193	3,771	159,820.80	23.60	22.85	24.36
Rash	173,020	4,375	164,445.36	26.60	25.83	27.41
Alopecia	178,130	51	172,711.53	0.30	0.22	0.39
Hair loss	177,820	2,065	170,629.13	12.10	11.59	12.64
Endocrine symptoms						
Diabetes mellitus (Type I & II)	113,982	4,151	105,584.30	39.31	38.14	40.53
Diabetic ketoacidosis	174,599	531	169,100.69	3.14	2.88	3.42
Thyroiditis	177,121	361	171,456.31	2.11	1.90	2.33
Hypothyroidism	152,924	2,757	146,243.72	18.85	18.16	19.57
Hyperthyroidism	176,457	606	170,644.70	3.55	3.28	3.85
Menstrual/period issues	174,697	3,129	167,036.54	18.73	18.09	19.40
Hematologic symptoms						
DVT	171,653	2,618	164,866.93	15.88	15.28	16.50
Pulmonary embolism	169,084	2,180	162,928.84	13.38	12.83	13.95

Table 40. Incidence of Long COVID in the Source Cohort by Follow-up Intervals among Patients Hospitalized, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Renal symptoms						
Acute kidney injury	131,233	6,671	125,487.04	53.16	51.90	54.45
Chronic kidney disease	135,619	6,939	127,515.42	54.42	53.15	55.71
Dialysis	165,737	3,401	159,286.43	21.35	20.65	22.08
			>=12 Weeks			
Any below medical condition						
Any below medical condition	7,625	1,593	6,673.28	238.71	227.27	250.73
Post-COVID syndrome						
Post-COVID syndrome	155,039	2,110	167,380.32	12.61	12.08	13.16
General symptoms						
Fatigue	119,368	8,908	122,412.60	72.77	71.28	74.30
Intermittent fever	134,013	3,097	139,016.37	22.28	21.51	23.08
Post-exertional malaise	146,691	2,847	156,112.88	18.24	17.58	18.92
Multisystem inflammatory syndrome (MIS)	157,527	25	169,686.55	0.15	0.10	0.22
Respiratory symptoms						
Dyspnea or Shortness of breath	69,484	5,995	68,451.09	87.58	85.39	89.83
Cough	132,508	2,552	134,544.21	18.97	18.25	19.72
Nasal congestion	155,246	1,557	166,281.98	9.36	8.91	9.84
Lung function abnormalities	152,857	2,404	162,937.16	14.75	14.18	15.36
Hypoxemia	110,839	2,663	116,326.47	22.89	22.04	23.78
Cardiovascular and cerebrovascular symptoms						
Chest pain	124,685	9,435	127,535.87	73.98	72.50	75.49
Palpitations or Fast-beating or pounding heart	152,749	2,849	162,373.92	17.55	16.91	18.20
Myocarditis	157,171	57	169,198.42	0.34	0.26	0.44
Pericarditis	157,458	102	169,464.93	0.60	0.50	0.73
Myocardial infarction	146,837	2,418	157,121.75	15.39	14.79	16.02
Angina	152,019	2,406	161,985.79	14.85	14.27	15.46
Atrial fibrillation	135,198	2,520	144,715.15	17.41	16.75	18.11
Atrial flutter	153,885	920	165,259.71	5.57	5.22	5.94
Sinus tachycardia	131,874	3,962	138,713.00	28.56	27.69	29.47
Sinus bradycardia	146,773	2,756	156,207.57	17.64	17.00	18.31
Heart Failure	122,110	4,889	128,574.52	38.02	36.97	39.11
Stroke	151,083	2,162	161,520.87	13.39	12.83	13.96
TIA	155,543	1,007	166,892.31	6.03	5.67	6.42
Neurological symptoms						
Headache	154,200	208	163,995.49	1.27	1.11	1.45
Insomnia	147,536	3,080	156,472.48	19.68	19.00	20.39
Cognitive impairment	139,794	5,012	147,876.84	33.89	32.97	34.85
Confusion	154,482	696	165,967.26	4.19	3.89	4.52

Table 40. Incidence of Long COVID in the Source Cohort by Follow-up Intervals among Patients Hospitalized, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Anosmia or Loss of smell	157,215	108	169,122.77	0.64	0.53	0.77
Ageusia or Loss of taste	157,236	142	169,123.18	0.84	0.71	0.99
Depression	127,711	3,669	132,437.49	27.70	26.82	28.62
Anxiety Disorders	119,795	5,572	125,318.92	44.46	43.31	45.65
Post-traumatic Stress Disorder	154,789	623	166,340.42	3.75	3.46	4.05
Substance Use Disorders	143,002	2,192	153,448.82	14.28	13.70	14.90
Suicidal behavior and suicide ideation	154,099	690	165,675.62	4.16	3.87	4.49
Dizziness on standing (lightheadedness)	146,913	5,084	154,447.62	32.92	32.03	33.84
Pins-and-needles feelings	155,174	2,029	165,686.23	12.25	11.73	12.79
Dysautonomia	157,061	239	168,955.90	1.41	1.25	1.61
Digestive symptoms						
Abdominal pain	132,700	9,883	136,607.93	72.35	70.93	73.79
Diarrhea	139,935	3,851	147,399.62	26.13	25.31	26.97
Nausea	148,802	3,374	157,773.99	21.39	20.68	22.12
Constipation	140,514	5,071	147,863.30	34.30	33.36	35.25
Musculoskeletal and Skin						
Arthralgia or joint pain	138,123	11,930	140,323.89	85.02	83.51	86.56
Myalgia or muscle pain	152,693	2,044	162,561.36	12.57	12.04	13.13
Body aches	147,104	2,754	157,015.26	17.54	16.90	18.21
Rash	152,189	3,248	161,537.88	20.11	19.43	20.81
Alopecia	157,755	37	169,866.90	0.22	0.16	0.30
Hair loss	157,126	1,714	167,726.45	10.22	9.75	10.71
Endocrine symptoms						
Diabetes mellitus (Type I & II)	99,732	2,709	103,575.16	26.15	25.19	27.16
Diabetic ketoacidosis	154,520	390	166,297.48	2.35	2.12	2.59
Thyroiditis	156,759	270	168,613.37	1.60	1.42	1.80
Hypothyroidism	134,858	1,925	143,717.13	13.39	12.81	14.01
Hyperthyroidism	156,135	431	167,808.03	2.57	2.34	2.82
Menstrual/period issues	154,012	2,507	164,142.75	15.27	14.69	15.88
Hematologic symptoms						
DVT	151,325	1,506	162,030.19	9.29	8.84	9.78
Pulmonary embolism	149,049	1,105	160,139.41	6.90	6.51	7.32
Renal symptoms						
Acute kidney injury	116,949	4,585	123,447.22	37.14	36.08	38.23
Chronic kidney disease	119,520	4,825	125,243.64	38.52	37.45	39.63
Dialysis	146,618	1,961	156,613.39	12.52	11.98	13.09
			>=6 months			
Any below medical condition						

Table 40. Incidence of Long COVID in the Source Cohort by Follow-up Intervals among Patients Hospitalized, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Any below medical condition	5,209	863	5,776.13	149.41	139.77	159.72
Post-COVID syndrome						
Post-COVID syndrome	125,261	1,329	155,854.07	8.53	8.08	9.00
General symptoms						
Fatigue	93,460	5,263	112,472.86	46.79	45.55	48.08
Intermittent fever	106,198	1,948	128,253.56	15.19	14.53	15.88
Post-exertional malaise	117,657	1,587	144,864.91	10.96	10.43	11.51
Multisystem inflammatory syndrome (MIS)	127,294	19	157,943.23	0.12	0.08	0.19
Respiratory symptoms						
Dyspnea or Shortness of breath	52,201	3,409	61,882.48	55.09	53.27	56.97
Cough	103,152	1,303	123,212.86	10.58	10.02	11.17
Nasal congestion	125,063	1,129	154,575.91	7.30	6.89	7.74
Lung function abnormalities	122,528	1,279	151,208.96	8.46	8.01	8.94
Hypoxemia	87,332	1,521	107,269.90	14.18	13.48	14.91
Cardiovascular and cerebrovascular symptoms						
Chest pain	97,442	5,953	117,098.38	50.84	49.56	52.15
Palpitations or Fast-beating or pounding heart	122,359	1,760	150,620.30	11.69	11.15	12.24
Myocarditis	126,979	29	157,469.74	0.18	0.13	0.27
Pericarditis	127,186	56	157,709.57	0.36	0.27	0.46
Myocardial infarction	118,354	1,502	146,076.09	10.28	9.78	10.82
Angina	121,965	1,493	150,346.71	9.93	9.44	10.45
Atrial fibrillation	109,015	1,518	134,549.41	11.28	10.73	11.86
Atrial flutter	124,097	528	153,702.26	3.44	3.15	3.74
Sinus tachycardia	104,840	2,239	128,286.55	17.45	16.75	18.19
Sinus bradycardia	117,713	1,717	144,953.91	11.85	11.30	12.42
Heart Failure	97,524	2,880	119,061.65	24.19	23.32	25.09
Stroke	121,664	1,396	150,113.14	9.30	8.82	9.80
TIA	125,423	676	155,205.91	4.36	4.04	4.70
Neurological symptoms						
Headache	123,902	29	152,234.65	0.19	0.13	0.27
Insomnia	117,997	1,824	145,061.12	12.57	12.01	13.17
Cognitive impairment	111,932	3,022	137,095.16	22.04	21.27	22.84
Confusion	124,702	408	154,397.94	2.64	2.40	2.91
Anosmia or Loss of smell	126,951	61	157,368.54	0.39	0.30	0.50
Ageusia or Loss of taste	126,960	94	157,364.61	0.60	0.49	0.73
Depression	100,120	1,886	121,816.19	15.48	14.80	16.20
Anxiety Disorders	94,588	3,272	115,641.41	28.29	27.34	29.28

Table 40. Incidence of Long COVID in the Source Cohort by Follow-up Intervals among Patients Hospitalized, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Post-traumatic Stress Disorder	124,894	371	154,740.12	2.40	2.17	2.65
Substance Use Disorders	115,372	1,356	142,752.49	9.50	9.01	10.02
Suicidal behavior and suicide ideation	124,382	406	154,139.07	2.63	2.39	2.90
Dizziness on standing (lightheadedness)	116,970	3,271	142,893.24	22.89	22.12	23.69
Pins-and-needles feelings	124,688	1,308	153,876.61	8.50	8.05	8.97
Dysautonomia	126,832	143	157,219.12	0.91	0.77	1.07
Digestive symptoms						
Abdominal pain	104,298	6,272	125,708.14	49.89	48.67	51.14
Diarrhea	111,642	2,447	136,470.94	17.93	17.23	18.66
Nausea	119,088	2,140	146,277.68	14.63	14.02	15.26
Constipation	112,010	3,122	136,854.67	22.81	22.03	23.63
Musculoskeletal and Skin						
Arthralgia or joint pain	107,451	7,568	128,561.31	58.87	57.56	60.21
Myalgia or muscle pain	122,515	1,357	150,865.02	8.99	8.53	9.49
Body aches	118,143	1,713	145,817.12	11.75	11.20	12.32
Rash	121,887	2,088	149,810.35	13.94	13.35	14.55
Alopecia	127,462	24	158,101.28	0.15	0.10	0.23
Hair loss	125,604	275	155,574.54	1.77	1.57	1.99
Endocrine symptoms						
Diabetes mellitus (Type I & II)	78,728	1,640	95,475.82	17.18	16.37	18.03
Diabetic ketoacidosis	124,841	248	154,779.80	1.60	1.42	1.82
Thyroiditis	126,568	173	156,891.82	1.10	0.95	1.28
Hypothyroidism	108,227	1,123	133,391.59	8.42	7.94	8.93
Hyperthyroidism	126,007	254	156,115.65	1.63	1.44	1.84
Menstrual/period issues	123,566	1,616	152,343.68	10.61	10.10	11.14
Hematologic symptoms						
DVT	121,823	852	150,598.97	5.66	5.29	6.05
Pulmonary embolism	120,115	640	148,922.02	4.30	3.98	4.64
Renal symptoms						
Acute kidney injury	93,691	2,859	114,446.73	24.98	24.08	25.91
Chronic kidney disease	95,398	3,077	115,908.08	26.55	25.63	27.50
Dialysis	117,969	1,139	145,500.33	7.83	7.39	8.30

Table 41. Incidence of Long COVID in the Source Cohort by Follow-up Intervals among Patients Non-Hospitalized, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
			Overall			
Any below medical condition						
Any below medical condition	856,503	437,738	335,082.52	1,306.36	1,302.50	1,310.23
Post-COVID syndrome						
Post-COVID syndrome	1,450,206	12,167	1,189,182.75	10.23	10.05	10.42
General symptoms						
Fatigue	1,386,780	130,827	1,036,550.51	126.21	125.53	126.90
Intermittent fever	1,420,331	122,103	1,068,921.98	114.23	113.59	114.87
Post-exertional malaise	1,443,311	18,539	1,172,728.37	15.81	15.58	16.04
Multisystem inflammatory syndrome (MIS)	1,450,523	253	1,193,497.05	0.21	0.19	0.24
Respiratory symptoms						
Dyspnea or Shortness of breath	1,393,653	157,046	1,010,942.80	155.35	154.58	156.12
Cough	1,397,957	145,806	968,774.84	150.51	149.74	151.28
Nasal congestion	1,430,090	62,267	1,132,787.73	54.97	54.54	55.40
Lung function abnormalities	1,445,997	7,631	1,184,652.26	6.44	6.30	6.59
Hypoxemia	1,446,460	16,288	1,178,102.00	13.83	13.62	14.04
Cardiovascular and cerebrovascular symptoms						
Chest pain	1,388,342	127,100	1,044,830.66	121.65	120.98	122.32
Palpitations or Fast-beating or pounding heart	1,429,894	35,792	1,149,377.53	31.14	30.82	31.47
Myocarditis	1,450,404	661	1,193,043.95	0.55	0.51	0.60
Pericarditis	1,450,279	520	1,193,045.59	0.44	0.40	0.48
Myocardial infarction	1,445,491	8,164	1,184,230.17	6.89	6.75	7.05
Angina	1,440,657	11,654	1,176,178.52	9.91	9.73	10.09
Atrial fibrillation	1,425,261	18,388	1,159,242.28	15.86	15.63	16.09
Atrial flutter	1,447,479	3,371	1,188,709.20	2.84	2.74	2.93
Sinus tachycardia	1,434,794	39,884	1,150,300.91	34.67	34.33	35.02
Sinus bradycardia	1,441,526	15,504	1,174,692.51	13.20	12.99	13.41
Heart Failure	1,422,179	24,461	1,152,982.47	21.22	20.95	21.48
Stroke	1,443,919	7,670	1,182,947.16	6.48	6.34	6.63
TIA	1,447,511	4,187	1,188,252.67	3.52	3.42	3.63
Neurological symptoms						
Headache	1,437,664	8,909	1,161,507.29	7.67	7.51	7.83
Insomnia	1,423,106	29,286	1,147,887.63	25.51	25.22	25.81
Cognitive impairment	1,433,875	27,190	1,162,398.20	23.39	23.12	23.67
Confusion	1,449,757	1,510	1,192,214.99	1.27	1.20	1.33
Anosmia or Loss of smell	1,449,400	14,758	1,176,227.76	12.55	12.35	12.75
Ageusia or Loss of taste	1,449,216	13,750	1,177,276.56	11.68	11.49	11.88
Depression	1,363,683	61,020	1,061,617.12	57.48	57.02	57.94
Anxiety Disorders	1,317,797	108,468	998,132.74	108.67	108.03	109.32

Table 41. Incidence of Long COVID in the Source Cohort by Follow-up Intervals among Patients Non-Hospitalized, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Post-traumatic Stress Disorder	1,442,052	7,778	1,180,956.94	6.59	6.44	6.73
Substance Use Disorders	1,428,340	24,878	1,158,521.43	21.47	21.21	21.74
Suicidal behavior and suicide ideation	1,446,487	6,155	1,186,279.16	5.19	5.06	5.32
Dizziness on standing (lightheadedness)	1,421,678	50,533	1,132,445.28	44.62	44.24	45.01
Pins-and-needles feelings	1,438,768	19,499	1,169,627.57	16.67	16.44	16.91
Dysautonomia	1,449,049	1,765	1,191,130.68	1.48	1.41	1.55
Digestive symptoms						
Abdominal pain	1,362,153	120,920	1,035,798.18	116.74	116.09	117.40
Diarrhea	1,425,507	53,183	1,131,371.82	47.01	46.61	47.41
Nausea	1,427,761	47,373	1,138,255.54	41.62	41.25	42.00
Constipation	1,422,361	37,987	1,144,013.64	33.21	32.87	33.54
Musculoskeletal and Skin						
Arthralgia or joint pain	1,348,354	119,587	1,024,205.45	116.76	116.10	117.42
Myalgia or muscle pain	1,434,781	40,853	1,145,504.59	35.66	35.32	36.01
Body aches	1,434,484	45,403	1,143,549.40	39.70	39.34	40.07
Rash	1,422,661	41,589	1,142,304.85	36.41	36.06	36.76
Alopecia	1,450,095	612	1,192,889.46	0.51	0.47	0.56
Hair loss	1,445,843	11,253	1,181,376.77	9.53	9.35	9.70
Endocrine symptoms						
Diabetes mellitus (Type I & II)	1,337,391	54,039	1,047,440.83	51.59	51.16	52.03
Diabetic ketoacidosis	1,449,583	1,658	1,191,747.11	1.39	1.33	1.46
Thyroiditis	1,443,824	5,296	1,184,015.92	4.47	4.35	4.60
Hypothyroidism	1,382,776	39,004	1,102,083.53	35.39	35.04	35.74
Hyperthyroidism	1,445,579	4,405	1,185,955.51	3.71	3.61	3.83
Menstrual/period issues	1,413,046	45,279	1,130,254.06	40.06	39.69	40.43
Hematologic symptoms						
DVT	1,445,905	6,729	1,184,726.23	5.68	5.55	5.82
Pulmonary embolism	1,446,896	6,472	1,185,725.02	5.46	5.33	5.59
Renal symptoms						
Acute kidney injury	1,437,561	23,926	1,167,619.28	20.49	20.23	20.75
Chronic kidney disease	1,404,643	38,047	1,125,525.91	33.80	33.47	34.15
Dialysis	1,445,711	6,026	1,185,576.47	5.08	4.96	5.21
			>=4 Weeks			
Any below medical condition						
Any below medical condition	486,854	152,182	330,160.28	460.93	458.62	463.26
Post-COVID syndrome						
Post-COVID syndrome	1,282,010	7,418	1,184,381.08	6.26	6.12	6.41
General symptoms						

Table 41. Incidence of Long COVID in the Source Cohort by Follow-up Intervals among Patients Non-Hospitalized, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Fatigue	1,173,479	70,995	1,031,427.56	68.83	68.33	69.34
Intermittent fever	1,175,286	28,275	1,064,000.20	26.57	26.27	26.89
Post-exertional malaise	1,272,183	9,973	1,167,961.92	8.54	8.37	8.71
Multisystem inflammatory syndrome (MIS)	1,286,172	105	1,188,811.51	0.09	0.07	0.11
Respiratory symptoms						
Dyspnea or Shortness of breath	1,146,276	61,716	1,005,433.74	61.38	60.90	61.87
Cough	1,115,317	24,410	963,231.10	25.34	25.03	25.66
Nasal congestion	1,233,643	24,451	1,127,996.99	21.68	21.41	21.95
Lung function abnormalities	1,280,280	5,454	1,179,948.07	4.62	4.50	4.75
Hypoxemia	1,274,153	6,331	1,173,370.56	5.40	5.26	5.53
Cardiovascular and cerebrovascular symptoms						
Chest pain	1,179,664	72,497	1,039,696.45	69.73	69.22	70.24
Palpitations or Fast-beating or pounding heart	1,259,327	27,192	1,144,558.52	23.76	23.48	24.04
Myocarditis	1,285,927	366	1,188,357.16	0.31	0.28	0.34
Pericarditis	1,285,937	367	1,188,359.52	0.31	0.28	0.34
Myocardial infarction	1,279,994	5,643	1,179,557.32	4.78	4.66	4.91
Angina	1,275,165	9,314	1,171,476.76	7.95	7.79	8.11
Atrial fibrillation	1,257,768	10,953	1,154,588.11	9.49	9.31	9.67
Atrial flutter	1,282,834	2,449	1,184,025.98	2.07	1.99	2.15
Sinus tachycardia	1,254,793	20,656	1,145,491.59	18.03	17.79	18.28
Sinus bradycardia	1,274,412	11,189	1,169,984.68	9.56	9.39	9.74
Heart Failure	1,254,251	15,526	1,148,349.97	13.52	13.31	13.74
Stroke	1,278,926	5,793	1,178,269.97	4.92	4.79	5.05
TIA	1,282,907	3,356	1,183,566.87	2.84	2.74	2.93
Neurological symptoms						
Headache	1,266,902	2,035	1,156,774.90	1.76	1.68	1.84
Insomnia	1,255,492	23,223	1,143,121.77	20.32	20.06	20.58
Cognitive impairment	1,266,222	20,615	1,157,690.49	17.81	17.57	18.05
Confusion	1,285,349	1,012	1,187,534.73	0.85	0.80	0.91
Anosmia or Loss of smell	1,272,782	2,085	1,171,488.52	1.78	1.71	1.86
Ageusia or Loss of taste	1,273,525	2,022	1,172,545.25	1.72	1.65	1.80
Depression	1,189,790	45,188	1,056,787.10	42.76	42.37	43.16
Anxiety Disorders	1,136,758	79,381	993,205.65	79.92	79.37	80.48
Post-traumatic Stress Disorder	1,276,866	6,101	1,176,255.12	5.19	5.06	5.32
Substance Use Disorders	1,259,271	17,202	1,153,817.54	14.91	14.69	15.13
Suicidal behavior and suicide ideation	1,281,172	4,432	1,181,591.75	3.75	3.64	3.86

Table 41. Incidence of Long COVID in the Source Cohort by Follow-up Intervals among Patients Non-Hospitalized, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Dizziness on standing (lightheadedness)	1,246,738	36,240	1,127,618.49	32.14	31.81	32.47
Pins-and-needles feelings	1,272,913	16,792	1,164,903.87	14.41	14.20	14.64
Dysautonomia	1,284,634	1,393	1,186,443.99	1.17	1.11	1.24
Digestive symptoms						
Abdominal pain	1,181,213	94,918	1,030,882.23	92.07	91.49	92.66
Diarrhea	1,241,321	29,344	1,126,545.31	26.05	25.75	26.35
Nausea	1,246,435	26,984	1,133,420.94	23.81	23.53	24.09
Constipation	1,254,682	31,296	1,139,262.34	27.47	27.17	27.78
Musculoskeletal and Skin						
Arthralgia or joint pain	1,179,178	105,561	1,019,356.73	103.56	102.93	104.18
Myalgia or muscle pain	1,251,108	18,545	1,140,719.29	16.26	16.03	16.49
Body aches	1,248,935	20,510	1,138,793.17	18.01	17.77	18.26
Rash	1,254,121	34,404	1,137,526.77	30.24	29.93	30.57
Alopecia	1,285,836	537	1,188,203.31	0.45	0.42	0.49
Hair loss	1,280,989	10,148	1,176,676.24	8.62	8.46	8.79
Endocrine symptoms						
Diabetes mellitus (Type I & II)	1,158,015	26,603	1,042,823.37	25.51	25.21	25.82
Diabetic ketoacidosis	1,284,964	1,070	1,187,063.27	0.90	0.85	0.96
Thyroiditis	1,279,090	4,206	1,179,321.78	3.57	3.46	3.68
Hypothyroidism	1,212,250	25,815	1,097,359.99	23.52	23.24	23.81
Hyperthyroidism	1,280,770	3,386	1,181,259.62	2.87	2.77	2.97
Menstrual/period issues	1,246,645	40,050	1,125,486.50	35.58	35.24	35.94
Hematologic symptoms						
DVT	1,280,235	4,599	1,180,019.74	3.90	3.79	4.01
Pulmonary embolism	1,280,383	3,525	1,181,016.02	2.98	2.89	3.09
Renal symptoms						
Acute kidney injury	1,267,806	14,526	1,162,969.93	12.49	12.29	12.70
Chronic kidney disease	1,235,036	26,214	1,120,865.16	23.39	23.11	23.67
Dialysis	1,280,544	4,028	1,180,897.48	3.41	3.31	3.52
			>=12 Weeks			
Any below medical condition						
Any below medical condition	379,707	105,227	314,719.12	334.35	332.34	336.38
Post-COVID syndrome						
Post-COVID syndrome	1,145,217	4,815	1,164,459.27	4.13	4.02	4.25
General symptoms						
Fatigue	1,031,914	54,492	1,010,780.32	53.91	53.46	54.37
Intermittent fever	1,044,552	22,568	1,044,918.41	21.60	21.32	21.88
Post-exertional malaise	1,135,321	7,120	1,148,003.83	6.20	6.06	6.35
Multisystem inflammatory syndrome (MIS)	1,150,560	39	1,169,026.63	0.03	0.02	0.05

Table 41. Incidence of Long COVID in the Source Cohort by Follow-up Intervals among Patients Non-Hospitalized, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Respiratory symptoms						
Dyspnea or Shortness of breath	1,004,848	43,827	984,911.64	44.50	44.08	44.92
Cough	976,130	17,518	942,973.49	18.58	18.30	18.86
Nasal congestion	1,099,471	20,314	1,108,415.21	18.33	18.08	18.58
Lung function abnormalities	1,144,006	3,920	1,160,071.94	3.38	3.28	3.49
Hypoxemia	1,138,275	4,581	1,153,557.72	3.97	3.86	4.09
Cardiovascular and cerebrovascular symptoms						
Chest pain	1,037,383	55,010	1,018,950.61	53.99	53.54	54.44
Palpitations or Fast-beating or pounding heart	1,119,737	20,223	1,124,205.64	17.99	17.74	18.24
Myocarditis	1,150,273	230	1,168,564.59	0.20	0.17	0.22
Pericarditis	1,150,333	278	1,168,574.75	0.24	0.21	0.27
Myocardial infarction	1,144,049	4,431	1,159,717.54	3.82	3.71	3.94
Angina	1,138,498	7,060	1,151,533.94	6.13	5.99	6.28
Atrial fibrillation	1,122,686	7,970	1,134,890.49	7.02	6.87	7.18
Atrial flutter	1,147,074	1,836	1,164,216.96	1.58	1.51	1.65
Sinus tachycardia	1,117,190	15,236	1,125,430.73	13.54	13.33	13.76
Sinus bradycardia	1,137,860	8,911	1,150,054.48	7.75	7.59	7.91
Heart Failure	1,118,458	11,401	1,128,542.74	10.10	9.92	10.29
Stroke	1,143,011	4,487	1,158,438.03	3.87	3.76	3.99
TIA	1,147,025	2,664	1,163,739.91	2.29	2.20	2.38
Neurological symptoms						
Headache	1,130,609	975	1,136,886.25	0.86	0.81	0.91
Insomnia	1,116,962	17,372	1,122,905.95	15.47	15.24	15.70
Cognitive impairment	1,128,617	15,875	1,137,604.75	13.95	13.74	14.17
Confusion	1,149,749	768	1,167,747.73	0.66	0.61	0.71
Anosmia or Loss of smell	1,137,143	1,543	1,151,701.69	1.34	1.28	1.41
Ageusia or Loss of taste	1,137,940	1,573	1,152,763.51	1.36	1.30	1.43
Depression	1,048,522	32,706	1,036,166.18	31.56	31.22	31.91
Anxiety Disorders	993,262	57,775	972,292.52	59.42	58.94	59.91
Post-traumatic Stress Disorder	1,140,668	4,614	1,156,380.29	3.99	3.88	4.11
Substance Use Disorders	1,122,349	13,051	1,133,824.85	11.51	11.32	11.71
Suicidal behavior and suicide ideation	1,145,116	3,388	1,161,737.12	2.92	2.82	3.02
Dizziness on standing (lightheadedness)	1,107,640	28,775	1,107,308.55	25.99	25.69	26.29
Pins-and-needles feelings	1,135,342	13,448	1,144,814.06	11.75	11.55	11.95
Dysautonomia	1,148,934	1,076	1,166,643.67	0.92	0.87	0.98
Digestive symptoms						
Abdominal pain	1,035,739	73,980	1,009,596.76	73.28	72.75	73.81
Diarrhea	1,103,855	23,410	1,106,472.62	21.16	20.89	21.43

Table 41. Incidence of Long COVID in the Source Cohort by Follow-up Intervals among Patients Non-Hospitalized, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Nausea	1,108,519	21,318	1,113,283.08	19.15	18.89	19.41
Constipation	1,115,487	24,087	1,118,943.70	21.53	21.26	21.80
Musculoskeletal and Skin						
Arthralgia or joint pain	1,031,871	82,890	997,785.04	83.07	82.51	83.64
Myalgia or muscle pain	1,114,710	14,826	1,120,808.79	13.23	13.02	13.44
Body aches	1,112,543	16,662	1,118,874.31	14.89	14.67	15.12
Rash	1,115,007	27,318	1,117,215.72	24.45	24.16	24.74
Alopecia	1,150,222	430	1,168,416.38	0.37	0.34	0.41
Hair loss	1,143,713	7,880	1,156,607.84	6.81	6.66	6.97
Endocrine symptoms						
Diabetes mellitus (Type I & II)	1,025,943	18,969	1,023,589.36	18.53	18.27	18.80
Diabetic ketoacidosis	1,149,324	864	1,167,272.29	0.74	0.69	0.79
Thyroiditis	1,143,193	3,090	1,159,496.00	2.66	2.57	2.76
Hypothyroidism	1,075,899	18,005	1,077,487.55	16.71	16.47	16.96
Hyperthyroidism	1,144,910	2,573	1,161,436.54	2.22	2.13	2.30
Menstrual/period issues	1,106,307	31,392	1,104,976.08	28.41	28.10	28.73
Hematologic symptoms						
DVT	1,144,153	3,400	1,160,167.98	2.93	2.83	3.03
Pulmonary embolism	1,144,463	2,474	1,161,194.65	2.13	2.05	2.22
Renal symptoms						
Acute kidney injury	1,131,788	11,505	1,143,113.44	10.06	9.88	10.25
Chronic kidney disease	1,098,556	19,814	1,100,952.52	18.00	17.75	18.25
Dialysis	1,144,814	3,064	1,161,089.78	2.64	2.55	2.73
			>=6 months			
Any below medical condition						
Any below medical condition	240,483	54,350	262,859.26	206.76	205.03	208.51
Post-COVID syndrome						
Post-COVID syndrome	871,303	3,272	1,057,393.26	3.09	2.99	3.20
General symptoms						
Fatigue	763,436	33,410	906,628.52	36.85	36.46	37.25
Intermittent fever	785,890	14,143	944,107.47	14.98	14.74	15.23
Post-exertional malaise	860,420	4,439	1,040,583.03	4.27	4.14	4.39
Multisystem inflammatory syndrome (MIS)	874,799	28	1,061,165.31	0.03	0.02	0.04
Respiratory symptoms						
Dyspnea or Shortness of breath	743,817	26,546	883,588.88	30.04	29.68	30.41
Cough	711,878	9,914	840,216.33	11.80	11.57	12.03
Nasal congestion	831,408	13,569	1,003,851.08	13.52	13.29	13.75
Lung function abnormalities	868,775	2,435	1,052,483.93	2.31	2.22	2.41
Hypoxemia	863,828	2,881	1,046,269.17	2.75	2.66	2.86

Table 41. Incidence of Long COVID in the Source Cohort by Follow-up Intervals among Patients Non-Hospitalized, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Cardiovascular and cerebrovascular symptoms						
Chest pain	770,204	34,264	915,291.46	37.44	37.04	37.83
Palpitations or Fast-beating or pounding heart	844,490	12,574	1,016,872.74	12.37	12.15	12.58
Myocarditis	874,508	142	1,060,703.87	0.13	0.11	0.16
Pericarditis	874,521	170	1,060,696.69	0.16	0.14	0.19
Myocardial infarction	868,624	2,926	1,052,034.68	2.78	2.68	2.88
Angina	862,990	4,350	1,043,892.74	4.17	4.05	4.29
Atrial fibrillation	850,506	4,863	1,028,558.62	4.73	4.60	4.86
Atrial flutter	871,522	1,140	1,056,461.19	1.08	1.02	1.14
Sinus tachycardia	844,055	9,334	1,018,832.50	9.16	8.98	9.35
Sinus bradycardia	862,078	5,653	1,042,304.13	5.42	5.28	5.57
Heart Failure	846,331	6,950	1,022,266.93	6.80	6.64	6.96
Stroke	867,657	2,891	1,050,798.09	2.75	2.65	2.85
TIA	871,271	1,709	1,055,919.97	1.62	1.54	1.70
Neurological symptoms						
Headache	854,682	146	1,029,000.99	0.14	0.12	0.17
Insomnia	843,063	10,490	1,016,101.17	10.32	10.13	10.52
Cognitive impairment	853,427	10,025	1,030,175.99	9.73	9.54	9.92
Confusion	873,995	500	1,059,893.40	0.47	0.43	0.52
Anosmia or Loss of smell	862,036	885	1,044,121.68	0.85	0.79	0.91
Ageusia or Loss of taste	862,707	852	1,045,136.67	0.82	0.76	0.87
Depression	779,376	17,391	931,677.83	18.67	18.39	18.95
Anxiety Disorders	733,215	32,854	871,843.20	37.68	37.28	38.09
Post-traumatic Stress Disorder	865,752	2,742	1,048,946.05	2.61	2.52	2.71
Substance Use Disorders	848,998	7,665	1,027,130.62	7.46	7.30	7.63
Suicidal behavior and suicide ideation	869,629	2,020	1,054,031.29	1.92	1.84	2.00
Dizziness on standing (lightheadedness)	833,036	18,359	1,000,322.01	18.35	18.09	18.62
Pins-and-needles feelings	858,718	8,573	1,036,819.59	8.27	8.10	8.45
Dysautonomia	873,210	661	1,058,817.02	0.62	0.58	0.67
Digestive symptoms						
Abdominal pain	764,309	44,969	904,643.00	49.71	49.25	50.17
Diarrhea	831,360	14,744	1,000,258.43	14.74	14.50	14.98
Nausea	835,580	13,151	1,006,885.87	13.06	12.84	13.29
Constipation	840,710	14,760	1,011,875.69	14.59	14.35	14.82
Musculoskeletal and Skin						
Arthralgia or joint pain	757,880	51,431	891,956.89	57.66	57.17	58.16
Myalgia or muscle pain	841,125	9,517	1,014,026.30	9.39	9.20	9.58

Table 41. Incidence of Long COVID in the Source Cohort by Follow-up Intervals among Patients Non-Hospitalized, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Body aches	839,486	10,849	1,012,317.52	10.72	10.52	10.92
Rash	839,856	17,136	1,009,970.85	16.97	16.72	17.22
Alopecia	874,426	266	1,060,548.47	0.25	0.22	0.28
Hair loss	865,438	3,141	1,048,063.46	3.00	2.89	3.10
Endocrine symptoms						
Diabetes mellitus (Type I & II)	769,793	11,153	923,897.80	12.07	11.85	12.30
Diabetic ketoacidosis	873,599	551	1,059,436.34	0.52	0.48	0.57
Thyroiditis	868,151	1,801	1,051,984.94	1.71	1.64	1.79
Hypothyroidism	808,784	9,491	973,438.27	9.75	9.56	9.95
Hyperthyroidism	869,514	1,515	1,053,766.04	1.44	1.37	1.51
Menstrual/period issues	831,101	19,375	997,860.77	19.42	19.15	19.69
Hematologic symptoms						
DVT	868,716	2,163	1,052,473.74	2.06	1.97	2.14
Pulmonary embolism	869,273	1,552	1,053,596.47	1.47	1.40	1.55
Renal symptoms						
Acute kidney injury	857,144	7,399	1,035,817.81	7.14	6.98	7.31
Chronic kidney disease	827,344	12,093	995,189.12	12.15	11.94	12.37
Dialysis	869,456	1,944	1,053,418.04	1.85	1.77	1.93

The High Risk Trial Similar Cohort (Table 42) had higher incidence rates of any symptom and of post-COVID syndrome at all time periods compared to the Standard Risk Trial Similar Cohort (Table 43). Consistent with the Source Cohort, the incidence rates peaked at 4 weeks and decreased through 6 months.

Table 42. Incidence of Long COVID in the High-Risk Trial Similar Cohort by Follow-up Intervals, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
			Overall			
Any below medical condition						
Any below medical condition	463,725	279,944	153,456.71	1,824.25	1,817.51	1,831.02
Post-COVID syndrome						
Post-COVID syndrome	944,109	11,531	797,630.22	14.46	14.20	14.72
General symptoms						
Fatigue	892,823	113,476	667,866.31	169.91	168.92	170.90
Intermittent fever	924,555	82,149	712,734.67	115.26	114.47	116.05
Post-exertional malaise	938,418	21,000	780,760.30	26.90	26.54	27.26
Multisystem inflammatory syndrome (MIS)	944,338	207	801,994.81	0.26	0.23	0.30
Respiratory symptoms						

Table 42. Incidence of Long COVID in the High-Risk Trial Similar Cohort by Follow-up Intervals, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Dyspnea or Shortness of breath	895,513	161,710	621,217.04	260.31	259.05	261.58
Cough	903,707	102,044	637,103.75	160.17	159.19	161.15
Nasal congestion	929,818	38,750	762,042.45	50.85	50.35	51.36
Lung function abnormalities	940,423	9,635	792,147.19	12.16	11.92	12.41
Hypoxemia	940,672	48,042	759,355.42	63.27	62.70	63.84
Cardiovascular and cerebrovascular symptoms						
Chest pain	893,428	98,015	681,529.57	143.82	142.92	144.72
Palpitations or Fast-beating or pounding heart	927,942	26,104	767,734.13	34.00	33.59	34.42
Myocarditis	944,236	835	801,414.64	1.04	0.97	1.12
Pericarditis	944,144	506	801,565.21	0.63	0.58	0.69
Myocardial infarction	939,930	15,630	788,905.51	19.81	19.50	20.13
Angina	935,304	11,688	785,211.47	14.89	14.62	15.16
Atrial fibrillation	919,437	30,483	761,490.01	40.03	39.58	40.48
Atrial flutter	941,490	5,532	796,037.97	6.95	6.77	7.14
Sinus tachycardia	932,476	40,416	760,407.68	53.15	52.64	53.67
Sinus bradycardia	936,344	19,380	781,077.08	24.81	24.47	25.16
Heart Failure	917,586	42,644	752,601.05	56.66	56.13	57.20
Stroke	937,681	10,483	789,706.40	13.27	13.02	13.53
TIA	941,352	4,668	796,366.18	5.86	5.70	6.03
Neurological symptoms						
Headache	934,334	5,930	778,624.28	7.62	7.43	7.81
Insomnia	921,495	26,674	761,395.59	35.03	34.62	35.46
Cognitive impairment	929,499	33,786	768,092.64	43.99	43.52	44.46
Confusion	943,711	4,412	798,987.90	5.52	5.36	5.69
Anosmia or Loss of smell	943,522	8,830	791,470.23	11.16	10.93	11.39
Ageusia or Loss of taste	943,360	8,422	791,883.75	10.64	10.41	10.87
Depression	873,291	54,430	688,629.17	79.04	78.38	79.71
Anxiety Disorders	839,694	88,707	642,475.03	138.07	137.17	138.98
Post-traumatic Stress Disorder	937,884	6,251	791,960.47	7.89	7.70	8.09
Substance Use Disorders	928,059	20,166	774,324.61	26.04	25.69	26.41
Suicidal behavior and suicide ideation	940,938	5,074	795,676.39	6.38	6.20	6.56
Dizziness on standing (lightheadedness)	920,856	40,302	751,590.80	53.62	53.10	54.15
Pins-and-needles feelings	934,734	14,849	783,006.93	18.96	18.66	19.27
Dysautonomia	943,143	1,534	799,951.59	1.92	1.82	2.02
Digestive symptoms						
Abdominal pain	883,781	85,564	688,600.97	124.26	123.43	125.09
Diarrhea	926,104	45,036	749,679.85	60.07	59.52	60.63
Nausea	928,340	34,749	760,541.01	45.69	45.21	46.17

Table 42. Incidence of Long COVID in the High-Risk Trial Similar Cohort by Follow-up Intervals, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Constipation	923,055	36,257	757,960.85	47.83	47.35	48.33
Musculoskeletal and Skin						
Arthralgia or joint pain	858,864	92,450	662,640.60	139.52	138.62	140.42
Myalgia or muscle pain	932,068	27,824	767,153.76	36.27	35.85	36.70
Body aches	931,952	35,034	763,299.27	45.90	45.42	46.38
Rash	923,201	30,344	762,797.93	39.78	39.34	40.23
Alopecia	944,039	411	801,601.51	0.51	0.47	0.57
Hair loss	940,992	8,679	792,502.37	10.95	10.72	11.18
Endocrine symptoms						
Diabetes mellitus (Type I & II)	840,559	61,351	658,249.43	93.20	92.47	93.94
Diabetic ketoacidosis	943,489	3,111	799,246.85	3.89	3.76	4.03
Thyroiditis	939,273	3,843	794,752.54	4.84	4.69	4.99
Hypothyroidism	885,727	38,746	718,883.47	53.90	53.36	54.44
Hyperthyroidism	940,283	3,786	795,550.13	4.76	4.61	4.91
Menstrual/period issues	919,078	30,078	758,510.46	39.65	39.21	40.11
Hematologic symptoms						
DVT	940,532	9,468	791,908.98	11.96	11.72	12.20
Pulmonary embolism	941,341	11,174	791,222.19	14.12	13.86	14.39
Renal symptoms						
Acute kidney injury	933,757	52,358	759,760.15	68.91	68.33	69.51
Chronic kidney disease	904,371	49,013	732,261.51	66.93	66.34	67.53
Dialysis	944,347	10,325	796,028.57	12.97	12.72	13.22
			>=4 Weeks			
Any below medical condition						
Any below medical condition	231,603	85,072	150,837.20	564.00	560.22	567.80
Post-COVID syndrome						
Post-COVID syndrome	835,305	7,335	794,438.27	9.23	9.02	9.45
General symptoms						
Fatigue	740,734	54,834	664,394.67	82.53	81.84	83.23
Intermittent fever	763,885	18,399	709,463.90	25.93	25.56	26.31
Post-exertional malaise	824,049	9,429	777,551.23	12.13	11.88	12.37
Multisystem inflammatory syndrome (MIS)	838,980	62	798,920.33	0.08	0.06	0.10
Respiratory symptoms						
Dyspnea or Shortness of breath	694,500	47,503	617,512.08	76.93	76.24	77.62
Cough	717,913	18,285	633,422.48	28.87	28.45	29.29
Nasal congestion	805,739	16,578	758,897.20	21.84	21.52	22.18
Lung function abnormalities	832,705	5,986	789,053.36	7.59	7.40	7.78
Hypoxemia	801,286	6,718	756,148.33	8.88	8.68	9.10
Cardiovascular and cerebrovascular symptoms						

Table 42. Incidence of Long COVID in the High-Risk Trial Similar Cohort by Follow-up Intervals, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Chest pain	752,913	54,299	678,085.99	80.08	79.41	80.75
Palpitations or Fast-beating or pounding heart	818,434	20,135	764,564.50	26.34	25.97	26.70
Myocarditis	838,580	281	798,340.78	0.35	0.31	0.40
Pericarditis	838,739	286	798,490.15	0.36	0.32	0.40
Myocardial infarction	828,389	5,608	785,865.40	7.14	6.95	7.33
Angina	828,110	8,506	782,116.76	10.88	10.65	11.11
Atrial fibrillation	803,015	10,450	758,524.82	13.78	13.52	14.04
Atrial flutter	834,385	2,521	792,968.29	3.18	3.06	3.31
Sinus tachycardia	807,911	16,206	757,174.54	21.40	21.08	21.74
Sinus bradycardia	824,259	9,845	777,965.54	12.65	12.41	12.91
Heart Failure	797,159	15,142	749,698.68	20.20	19.88	20.52
Stroke	829,800	5,826	786,640.51	7.41	7.22	7.60
TIA	835,297	3,238	793,291.02	4.08	3.94	4.23
Neurological symptoms						
Headache	825,004	1,510	775,519.90	1.95	1.85	2.05
Insomnia	811,115	18,722	758,243.16	24.69	24.34	25.05
Cognitive impairment	814,448	18,020	764,994.14	23.56	23.21	23.90
Confusion	836,441	1,283	795,922.02	1.61	1.53	1.70
Anosmia or Loss of smell	831,068	1,448	788,362.77	1.84	1.75	1.93
Ageusia or Loss of taste	831,320	1,449	788,779.99	1.84	1.75	1.93
Depression	753,941	33,288	685,440.01	48.56	48.05	49.09
Anxiety Disorders	713,244	54,997	639,233.51	86.04	85.32	86.76
Post-traumatic Stress Disorder	831,365	4,345	788,870.60	5.51	5.35	5.67
Substance Use Disorders	817,099	11,863	771,230.75	15.38	15.11	15.66
Suicidal behavior and suicide ideation	834,197	3,011	792,594.20	3.80	3.67	3.94
Dizziness on standing (lightheadedness)	806,330	27,942	748,403.58	37.34	36.90	37.78
Pins-and-needles feelings	828,323	12,821	779,904.18	16.44	16.16	16.73
Dysautonomia	837,628	1,081	796,876.69	1.36	1.28	1.44
Digestive symptoms						
Abdominal pain	764,853	65,245	685,331.69	95.20	94.47	95.94
Diarrhea	800,694	21,146	746,473.42	28.33	27.95	28.71
Nausea	809,671	18,966	757,338.32	25.04	24.69	25.40
Constipation	809,679	24,183	754,807.02	32.04	31.64	32.45
Musculoskeletal and Skin						
Arthralgia or joint pain	749,665	80,447	659,466.62	121.99	121.15	122.83
Myalgia or muscle pain	814,544	13,683	764,005.91	17.91	17.61	18.21
Body aches	810,024	15,020	760,167.32	19.76	19.45	20.08
Rash	814,703	24,868	759,656.11	32.74	32.33	33.15
Alopecia	838,791	363	798,528.19	0.45	0.41	0.50

Table 42. Incidence of Long COVID in the High-Risk Trial Similar Cohort by Follow-up Intervals, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Hair loss	835,392	7,986	789,419.67	10.12	9.90	10.34
Endocrine symptoms						
Diabetes mellitus (Type I & II)	711,174	20,589	655,368.64	31.42	30.99	31.85
Diabetic ketoacidosis	836,634	873	796,179.43	1.10	1.03	1.17
Thyroiditis	833,576	2,931	791,673.62	3.70	3.57	3.84
Hypothyroidism	769,665	19,310	715,844.04	26.98	26.60	27.36
Hyperthyroidism	834,288	2,520	792,471.30	3.18	3.06	3.31
Menstrual/period issues	812,317	26,514	755,382.76	35.10	34.68	35.53
Hematologic symptoms						
DVT	831,733	4,481	788,802.33	5.68	5.52	5.85
Pulmonary embolism	830,116	3,613	788,092.07	4.58	4.44	4.74
Renal symptoms						
Acute kidney injury	802,119	12,918	756,851.64	17.07	16.78	17.37
Chronic kidney disease	783,869	22,713	729,292.82	31.14	30.74	31.55
Dialysis	834,790	3,705	792,904.11	4.67	4.53	4.83
			>=12 Weeks			
Any below medical condition						
Any below medical condition	179,005	57,503	143,193.40	401.58	398.31	404.87
Post-COVID syndrome						
Post-COVID syndrome	752,902	4,525	782,408.34	5.78	5.62	5.95
General symptoms						
Fatigue	656,191	41,198	652,029.27	63.18	62.58	63.80
Intermittent fever	685,603	14,477	698,000.26	20.74	20.41	21.08
Post-exertional malaise	742,197	6,201	765,588.09	8.10	7.90	8.30
Multisystem inflammatory syndrome (MIS)	758,205	22	787,092.72	0.03	0.02	0.04
Respiratory symptoms						
Dyspnea or Shortness of breath	612,559	33,067	605,558.39	54.61	54.02	55.20
Cough	634,285	12,640	621,214.13	20.35	20.00	20.71
Nasal congestion	725,376	13,763	747,127.24	18.42	18.12	18.73
Lung function abnormalities	751,135	4,091	777,109.46	5.26	5.11	5.43
Hypoxemia	722,354	4,365	744,578.95	5.86	5.69	6.04
Cardiovascular and cerebrovascular symptoms						
Chest pain	667,230	41,027	665,553.96	61.64	61.05	62.24
Palpitations or Fast-beating or pounding heart	734,491	14,864	752,286.40	19.76	19.44	20.08
Myocarditis	757,799	171	786,511.40	0.22	0.19	0.25
Pericarditis	757,962	209	786,662.19	0.27	0.23	0.30
Myocardial infarction	748,149	4,309	774,102.65	5.57	5.40	5.74
Angina	746,490	6,472	770,164.65	8.40	8.20	8.61

Table 42. Incidence of Long COVID in the High-Risk Trial Similar Cohort by Follow-up Intervals, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Atrial fibrillation	724,438	7,374	747,005.16	9.87	9.65	10.10
Atrial flutter	753,673	1,823	781,144.84	2.33	2.23	2.44
Sinus tachycardia	726,039	11,406	745,200.12	15.31	15.03	15.59
Sinus bradycardia	743,223	7,698	766,087.97	10.05	9.83	10.28
Heart Failure	718,606	10,786	738,163.40	14.61	14.34	14.89
Stroke	749,042	4,439	774,808.56	5.73	5.56	5.90
TIA	754,289	2,541	781,428.20	3.25	3.13	3.38
Neurological symptoms						
Headache	743,718	728	763,617.38	0.95	0.89	1.03
Insomnia	728,150	13,870	746,094.03	18.59	18.28	18.90
Cognitive impairment	733,067	13,448	753,067.25	17.86	17.56	18.16
Confusion	755,924	930	784,127.12	1.19	1.11	1.27
Anosmia or Loss of smell	750,198	1,089	776,523.17	1.40	1.32	1.49
Ageusia or Loss of taste	750,502	1,150	776,946.14	1.48	1.40	1.57
Depression	669,991	23,879	673,132.35	35.47	35.03	35.93
Anxiety Disorders	628,889	39,793	626,891.68	63.48	62.86	64.10
Post-traumatic Stress Disorder	750,202	3,240	776,984.06	4.17	4.03	4.32
Substance Use Disorders	735,820	9,002	759,318.20	11.86	11.61	12.10
Suicidal behavior and suicide ideation	753,222	2,283	780,735.56	2.92	2.81	3.05
Dizziness on standing (lightheadedness)	723,040	22,221	736,199.79	30.18	29.79	30.58
Pins-and-needles feelings	746,069	10,245	767,847.15	13.34	13.09	13.60
Dysautonomia	756,783	814	785,038.62	1.04	0.97	1.11
Digestive symptoms						
Abdominal pain	677,207	51,119	672,465.05	76.02	75.36	76.68
Diarrhea	718,902	16,790	734,484.26	22.86	22.52	23.21
Nausea	727,257	14,956	745,260.39	20.07	19.75	20.39
Constipation	726,668	18,304	742,638.62	24.65	24.29	25.01
Musculoskeletal and Skin						
Arthralgia or joint pain	660,468	63,271	646,337.36	97.89	97.13	98.66
Myalgia or muscle pain	732,856	10,871	752,035.41	14.46	14.19	14.73
Body aches	728,740	12,097	748,253.22	16.17	15.88	16.46
Rash	731,267	19,654	747,435.68	26.30	25.93	26.67
Alopecia	757,998	289	786,697.12	0.37	0.33	0.41
Hair loss	753,280	6,275	777,359.70	8.07	7.88	8.27
Endocrine symptoms						
Diabetes mellitus (Type I & II)	636,210	14,459	644,378.55	22.44	22.08	22.81
Diabetic ketoacidosis	755,988	688	784,368.78	0.88	0.81	0.95
Thyroiditis	752,621	2,171	779,821.06	2.78	2.67	2.90
Hypothyroidism	689,772	13,440	704,145.26	19.09	18.77	19.41
Hyperthyroidism	753,369	1,898	780,620.94	2.43	2.32	2.54

Table 42. Incidence of Long COVID in the High-Risk Trial Similar Cohort by Follow-up Intervals, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Menstrual/period issues	728,217	20,714	743,049.21	27.88	27.50	28.26
Hematologic symptoms						
DVT	750,566	3,021	776,919.55	3.89	3.75	4.03
Pulmonary embolism	749,201	2,256	776,254.83	2.91	2.79	3.03
Renal symptoms						
Acute kidney injury	724,580	9,992	745,435.07	13.40	13.14	13.67
Chronic kidney disease	704,160	16,981	717,586.71	23.66	23.31	24.02
Dialysis	754,135	2,538	781,083.49	3.25	3.13	3.38
>=6 months						
Any below medical condition						
Any below medical condition	109,826	28,558	117,477.09	243.09	240.29	245.93
Post-COVID syndrome						
Post-COVID syndrome	583,657	3,000	716,004.93	4.19	4.04	4.34
General symptoms						
Fatigue	492,273	25,125	588,275.81	42.71	42.19	43.24
Intermittent fever	524,725	9,220	635,017.13	14.52	14.23	14.82
Post-exertional malaise	572,585	3,813	699,040.96	5.45	5.28	5.63
Multisystem inflammatory syndrome (MIS)	587,495	19	720,038.52	0.03	0.02	0.04
Respiratory symptoms						
Dyspnea or Shortness of breath	457,119	19,863	545,040.84	36.44	35.94	36.95
Cough	469,554	7,031	556,853.21	12.63	12.34	12.93
Nasal congestion	559,251	9,311	682,075.09	13.65	13.38	13.93
Lung function abnormalities	580,676	2,414	710,229.15	3.40	3.27	3.54
Hypoxemia	556,079	2,689	679,314.04	3.96	3.81	4.11
Cardiovascular and cerebrovascular symptoms						
Chest pain	502,990	25,683	601,671.48	42.69	42.17	43.21
Palpitations or Fast-beating or pounding heart	563,986	9,210	685,561.56	13.43	13.16	13.71
Myocarditis	587,116	108	719,467.14	0.15	0.12	0.18
Pericarditis	587,223	116	719,599.58	0.16	0.13	0.19
Myocardial infarction	578,590	2,840	707,534.47	4.01	3.87	4.16
Angina	576,042	4,051	703,311.11	5.76	5.59	5.94
Atrial fibrillation	558,635	4,505	681,954.33	6.61	6.42	6.80
Atrial flutter	583,334	1,112	714,256.04	1.56	1.47	1.65
Sinus tachycardia	557,878	7,005	679,321.04	10.31	10.07	10.56
Sinus bradycardia	573,061	4,889	699,341.28	6.99	6.80	7.19
Heart Failure	552,719	6,540	673,109.69	9.72	9.48	9.95
Stroke	579,073	2,863	708,096.27	4.04	3.90	4.19
TIA	583,697	1,668	714,454.05	2.33	2.23	2.45

Table 42. Incidence of Long COVID in the High-Risk Trial Similar Cohort by Follow-up Intervals, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Neurological symptoms						
Headache	572,903	126	696,550.29	0.18	0.15	0.22
Insomnia	559,123	8,344	679,968.18	12.27	12.01	12.54
Cognitive impairment	564,059	8,480	686,843.98	12.35	12.09	12.61
Confusion	585,480	584	717,178.21	0.81	0.75	0.88
Anosmia or Loss of smell	579,794	627	709,603.55	0.88	0.82	0.96
Ageusia or Loss of taste	580,044	634	710,008.11	0.89	0.83	0.97
Depression	505,520	12,610	609,109.90	20.70	20.34	21.07
Anxiety Disorders	471,711	22,524	566,052.34	39.79	39.28	40.31
Post-traumatic Stress Disorder	580,270	1,927	710,297.53	2.71	2.59	2.84
Substance Use Disorders	567,233	5,352	693,239.94	7.72	7.52	7.93
Suicidal behavior and suicide ideation	582,959	1,350	713,889.41	1.89	1.79	2.00
Dizziness on standing (lightheadedness)	553,221	14,321	669,812.26	21.38	21.03	21.73
Pins-and-needles feelings	574,709	6,550	700,696.18	9.35	9.12	9.58
Dysautonomia	586,126	502	718,019.37	0.70	0.64	0.76
Digestive symptoms						
Abdominal pain	508,779	31,481	607,122.45	51.85	51.28	52.43
Diarrhea	550,975	10,639	668,780.43	15.91	15.61	16.21
Nausea	558,320	9,307	679,141.91	13.70	13.43	13.99
Constipation	557,124	11,274	676,342.06	16.67	16.36	16.98
Musculoskeletal and Skin						
Arthralgia or joint pain	491,424	39,259	580,961.52	67.58	66.91	68.25
Myalgia or muscle pain	563,324	7,058	685,606.24	10.29	10.06	10.54
Body aches	560,230	7,942	682,237.58	11.64	11.39	11.90
Rash	560,759	12,360	680,737.43	18.16	17.84	18.48
Alopecia	587,261	183	719,636.42	0.25	0.22	0.29
Hair loss	579,970	2,117	709,563.47	2.98	2.86	3.11
Endocrine symptoms						
Diabetes mellitus (Type I & II)	484,096	8,467	584,945.93	14.47	14.17	14.79
Diabetic ketoacidosis	585,546	438	717,426.21	0.61	0.56	0.67
Thyroiditis	582,426	1,273	713,018.25	1.79	1.69	1.89
Hypothyroidism	527,413	7,022	640,672.27	10.96	10.71	11.22
Hyperthyroidism	583,016	1,120	713,741.11	1.57	1.48	1.66
Menstrual/period issues	557,401	12,673	676,318.04	18.74	18.42	19.07
Hematologic symptoms						
DVT	580,397	1,899	710,120.12	2.67	2.56	2.80
Pulmonary embolism	579,538	1,386	709,643.69	1.95	1.85	2.06

Table 42. Incidence of Long COVID in the High-Risk Trial Similar Cohort by Follow-up Intervals, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Renal symptoms						
Acute kidney injury	558,039	6,507	680,089.63	9.57	9.34	9.80
Chronic kidney disease	538,774	10,515	652,831.40	16.11	15.80	16.42
Dialysis	583,479	1,616	714,071.15	2.26	2.16	2.38

Table 43. Incidence of Long COVID in the Standard-Risk Trial Similar Cohort by Follow-up Intervals, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
			Overall			
Any below medical condition						
Any below medical condition	499,499	248,248	195,088.93	1,272.49	1,267.49	1,277.50
Post-COVID syndrome						
Post-COVID syndrome	590,404	3,721	456,408.21	8.15	7.90	8.42
General symptoms						
Fatigue	582,027	40,644	419,901.14	96.79	95.86	97.74
Intermittent fever	582,040	55,470	409,378.72	135.50	134.38	136.63
Post-exertional malaise	589,863	5,429	452,769.44	11.99	11.68	12.31
Multisystem inflammatory syndrome (MIS)	590,461	262	457,525.47	0.57	0.51	0.65
Respiratory symptoms						
Dyspnea or Shortness of breath	586,525	64,139	401,592.55	159.71	158.48	160.95
Cough	580,589	56,231	387,790.93	145.00	143.81	146.21
Nasal congestion	585,411	22,955	438,079.22	52.40	51.73	53.08
Lung function abnormalities	590,193	2,303	456,054.16	5.05	4.85	5.26
Hypoxemia	590,418	14,938	445,531.33	33.53	33.00	34.07
Cardiovascular and cerebrovascular symptoms						
Chest pain	583,466	44,738	419,755.92	106.58	105.60	107.57
Palpitations or Fast-beating or pounding heart	587,916	10,810	447,837.80	24.14	23.69	24.60
Myocarditis	590,456	494	457,285.38	1.08	0.99	1.18
Pericarditis	590,443	251	457,473.41	0.55	0.49	0.62
Myocardial infarction	590,469	2,553	456,076.50	5.60	5.39	5.82
Angina	590,469	1,580	456,579.24	3.46	3.29	3.64
Atrial fibrillation	590,090	4,259	454,684.21	9.37	9.09	9.65
Atrial flutter	590,429	784	457,199.86	1.71	1.60	1.84
Sinus tachycardia	589,080	18,265	442,910.23	41.24	40.65	41.84
Sinus bradycardia	589,897	5,072	453,585.96	11.18	10.88	11.49
Heart Failure	590,469	8,076	452,519.17	17.85	17.46	18.24
Stroke	590,469	1,652	456,633.45	3.62	3.45	3.80

Table 43. Incidence of Long COVID in the Standard-Risk Trial Similar Cohort by Follow-up Intervals, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
TIA	590,469	712	457,196.93	1.56	1.45	1.68
Neurological symptoms						
Headache	588,431	3,956	449,081.36	8.81	8.54	9.09
Insomnia	587,828	7,345	450,131.83	16.32	15.95	16.70
Cognitive impairment	589,257	7,184	452,087.27	15.89	15.53	16.26
Confusion	590,468	558	457,247.40	1.22	1.12	1.33
Anosmia or Loss of smell	590,229	5,996	451,028.86	13.29	12.96	13.64
Ageusia or Loss of taste	590,198	5,311	451,709.50	11.76	11.45	12.08
Depression	582,424	17,814	436,216.66	40.84	40.24	41.44
Anxiety Disorders	573,737	37,641	417,539.25	90.15	89.24	91.07
Post-traumatic Stress Disorder	589,761	2,233	455,656.28	4.90	4.70	5.11
Substance Use Disorders	589,071	9,951	450,267.52	22.10	21.67	22.54
Suicidal behavior and suicide ideation	590,115	2,789	455,672.85	6.12	5.90	6.35
Dizziness on standing (lightheadedness)	587,339	13,247	446,079.53	29.70	29.20	30.21
Pins-and-needles feelings	589,156	4,703	453,360.55	10.37	10.08	10.67
Dysautonomia	590,333	541	457,224.45	1.18	1.09	1.29
Digestive symptoms						
Abdominal pain	577,937	38,759	423,237.22	91.58	90.67	92.49
Diarrhea	586,818	17,576	441,837.46	39.78	39.20	40.37
Nausea	587,605	14,159	445,364.00	31.79	31.27	32.32
Constipation	586,581	11,288	447,417.18	25.23	24.77	25.70
Musculoskeletal and Skin						
Arthralgia or joint pain	577,103	30,726	428,069.41	71.78	70.98	72.59
Myalgia or muscle pain	588,214	13,802	444,515.64	31.05	30.54	31.57
Body aches	588,331	16,673	442,817.72	37.65	37.09	38.23
Rash	585,228	12,105	446,171.45	27.13	26.65	27.62
Alopecia	590,336	210	457,449.56	0.46	0.40	0.53
Hair loss	589,418	3,237	454,633.16	7.12	6.88	7.37
Endocrine symptoms						
Diabetes mellitus (Type I & II)	590,469	22,403	440,463.34	50.86	50.20	51.53
Diabetic ketoacidosis	590,469	1,194	456,892.26	2.61	2.47	2.77
Thyroiditis	589,343	1,631	455,624.75	3.58	3.41	3.76
Hypothyroidism	584,862	11,692	443,895.26	26.34	25.87	26.82
Hyperthyroidism	589,904	1,290	456,284.42	2.83	2.68	2.99
Menstrual/period issues	584,027	14,161	442,996.28	31.97	31.44	32.50
Hematologic symptoms						
DVT	590,298	2,412	455,885.12	5.29	5.08	5.51
Pulmonary embolism	590,364	3,334	455,253.59	7.32	7.08	7.58
Renal symptoms						

Table 43. Incidence of Long COVID in the Standard-Risk Trial Similar Cohort by Follow-up Intervals, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Acute kidney injury	590,354	11,100	450,385.06	24.65	24.19	25.11
Chronic kidney disease	590,469	8,753	451,697.53	19.38	18.98	19.79
Dialysis	590,469	2,661	456,074.81	5.83	5.62	6.06
			>=4 Weeks			
Any below medical condition						
Any below medical condition	269,081	67,899	192,264.95	353.15	350.51	355.82
Post-COVID syndrome						
Post-COVID syndrome	509,912	2,290	453,956.43	5.04	4.84	5.26
General symptoms						
Fatigue	482,885	17,791	417,319.95	42.63	42.01	43.26
Intermittent fever	464,184	10,039	406,860.78	24.67	24.20	25.16
Post-exertional malaise	507,697	2,242	450,309.48	4.98	4.78	5.19
Multisystem inflammatory syndrome (MIS)	510,961	74	455,100.80	0.16	0.13	0.20
Respiratory symptoms						
Dyspnea or Shortness of breath	461,266	13,080	398,895.94	32.79	32.23	33.36
Cough	453,355	6,953	385,081.69	18.06	17.64	18.49
Nasal congestion	492,928	7,424	435,626.65	17.04	16.66	17.43
Lung function abnormalities	509,965	1,230	453,620.69	2.71	2.56	2.87
Hypoxemia	498,599	1,025	443,060.81	2.31	2.18	2.46
Cardiovascular and cerebrovascular symptoms						
Chest pain	482,261	19,140	417,172.30	45.88	45.24	46.54
Palpitations or Fast-beating or pounding heart	505,574	7,249	445,362.66	16.28	15.91	16.66
Myocarditis	510,816	136	454,859.71	0.30	0.25	0.35
Pericarditis	510,994	111	455,049.31	0.24	0.20	0.29
Myocardial infarction	509,764	705	453,655.21	1.55	1.44	1.67
Angina	510,679	1,062	454,150.00	2.34	2.20	2.48
Atrial fibrillation	508,551	1,267	452,263.07	2.80	2.65	2.96
Atrial flutter	510,726	271	454,776.98	0.60	0.53	0.67
Sinus tachycardia	498,542	5,254	440,415.54	11.93	11.61	12.26
Sinus bradycardia	508,056	2,043	451,143.85	4.53	4.34	4.73
Heart Failure	506,622	1,869	450,106.36	4.15	3.97	4.35
Stroke	510,426	722	454,208.26	1.59	1.48	1.71
TIA	510,899	423	454,771.61	0.93	0.85	1.02
Neurological symptoms						
Headache	505,848	536	446,641.17	1.20	1.10	1.31
Insomnia	506,221	4,582	447,675.75	10.24	9.94	10.54
Cognitive impairment	507,468	4,030	449,641.32	8.96	8.69	9.24
Confusion	510,778	110	454,821.58	0.24	0.20	0.29
Anosmia or Loss of smell	505,647	597	448,585.20	1.33	1.23	1.44

Table 43. Incidence of Long COVID in the Standard-Risk Trial Similar Cohort by Follow-up Intervals, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Ageusia or Loss of taste	506,222	532	449,271.12	1.18	1.09	1.29
Depression	496,733	10,306	433,727.11	23.76	23.31	24.23
Anxiety Disorders	482,309	22,267	414,997.73	53.66	52.96	54.37
Post-traumatic Stress Disorder	509,735	1,362	453,225.94	3.01	2.85	3.17
Substance Use Disorders	505,035	4,221	447,825.80	9.43	9.15	9.71
Suicidal behavior and suicide ideation	509,616	1,316	453,245.95	2.90	2.75	3.07
Dizziness on standing (lightheadedness)	503,649	7,939	443,613.95	17.90	17.51	18.29
Pins-and-needles feelings	509,029	3,666	450,923.66	8.13	7.87	8.40
Dysautonomia	510,848	342	454,799.29	0.75	0.68	0.84
Digestive symptoms						
Abdominal pain	489,554	27,056	420,723.41	64.31	63.55	65.08
Diarrhea	498,357	7,035	439,371.39	16.01	15.64	16.39
Nausea	501,734	6,559	442,897.19	14.81	14.46	15.17
Constipation	504,226	7,411	444,959.85	16.66	16.28	17.04
Musculoskeletal and Skin						
Arthralgia or joint pain	495,186	26,427	425,587.01	62.10	61.35	62.85
Myalgia or muscle pain	500,468	4,227	442,064.24	9.56	9.28	9.86
Body aches	498,534	4,706	440,363.38	10.69	10.39	11.00
Rash	503,787	9,167	443,713.50	20.66	20.24	21.09
Alopecia	510,996	181	455,025.91	0.40	0.34	0.46
Hair loss	509,817	2,805	452,205.00	6.20	5.98	6.44
Endocrine symptoms						
Diabetes mellitus (Type I & II)	496,089	5,093	438,010.47	11.63	11.31	11.95
Diabetic ketoacidosis	510,356	194	454,471.66	0.43	0.37	0.49
Thyroiditis	509,662	1,127	453,197.05	2.49	2.35	2.64
Hypothyroidism	500,685	5,691	441,441.76	12.89	12.56	13.23
Hyperthyroidism	510,221	836	453,857.80	1.84	1.72	1.97
Menstrual/period issues	503,420	12,126	440,538.26	27.53	27.04	28.02
Hematologic symptoms						
DVT	509,717	854	453,451.63	1.88	1.76	2.01
Pulmonary embolism	508,697	616	452,810.32	1.36	1.26	1.47
Renal symptoms						
Acute kidney injury	504,215	2,066	447,985.87	4.61	4.42	4.82
Chronic kidney disease	506,998	3,644	449,264.04	8.11	7.85	8.38
Dialysis	509,699	681	453,633.72	1.50	1.39	1.62
			>=12 Weeks			
Any below medical condition						

Table 43. Incidence of Long COVID in the Standard-Risk Trial Similar Cohort by Follow-up Intervals, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Any below medical condition	212,955	48,843	184,262.66	265.07	262.73	267.43
Post-COVID syndrome						
Post-COVID syndrome	445,873	1,453	444,807.85	3.27	3.10	3.44
General symptoms						
Fatigue	418,000	13,523	408,045.05	33.14	32.59	33.70
Intermittent fever	403,859	7,867	398,226.81	19.76	19.32	20.20
Post-exertional malaise	443,600	1,418	441,148.39	3.21	3.05	3.39
Multisystem inflammatory syndrome (MIS)	447,274	24	445,994.43	0.05	0.04	0.08
Respiratory symptoms						
Dyspnea or Shortness of breath	398,120	8,954	389,894.15	22.97	22.49	23.45
Cough	389,089	5,061	375,895.90	13.46	13.10	13.84
Nasal congestion	430,253	6,159	426,661.61	14.44	14.08	14.80
Lung function abnormalities	446,147	826	444,496.99	1.86	1.74	1.99
Hypoxemia	435,737	603	434,078.13	1.39	1.28	1.51
Cardiovascular and cerebrovascular symptoms						
Chest pain	417,297	14,294	407,886.49	35.04	34.47	35.62
Palpitations or Fast-beating or pounding heart	440,724	5,273	436,089.16	12.09	11.77	12.42
Myocarditis	447,142	83	445,754.09	0.19	0.15	0.23
Pericarditis	447,329	83	445,945.07	0.19	0.15	0.23
Myocardial infarction	446,162	546	444,558.77	1.23	1.13	1.34
Angina	446,838	814	445,018.48	1.83	1.71	1.96
Atrial fibrillation	444,967	899	443,167.86	2.03	1.90	2.17
Atrial flutter	447,089	201	445,675.85	0.45	0.39	0.52
Sinus tachycardia	434,841	3,650	431,313.65	8.46	8.19	8.74
Sinus bradycardia	444,353	1,591	442,029.40	3.60	3.43	3.78
Heart Failure	443,233	1,287	441,034.24	2.92	2.76	3.08
Stroke	446,713	551	445,095.03	1.24	1.14	1.35
TIA	447,194	347	445,661.44	0.78	0.70	0.87
Neurological symptoms						
Headache	442,050	249	437,515.26	0.57	0.50	0.64
Insomnia	441,910	3,377	438,482.46	7.70	7.45	7.97
Cognitive impairment	443,320	3,022	440,466.38	6.86	6.62	7.11
Confusion	447,115	60	445,717.46	0.13	0.11	0.17
Anosmia or Loss of smell	442,060	423	439,492.56	0.96	0.88	1.06
Ageusia or Loss of taste	442,642	407	440,179.07	0.92	0.84	1.02
Depression	431,561	7,546	424,397.81	17.78	17.38	18.19
Anxiety Disorders	416,107	16,295	405,526.22	40.18	39.57	40.80
Post-traumatic Stress Disorder	445,922	1,023	444,098.97	2.30	2.17	2.45

Table 43. Incidence of Long COVID in the Standard-Risk Trial Similar Cohort by Follow-up Intervals, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Substance Use Disorders	441,236	3,265	438,697.57	7.44	7.19	7.70
Suicidal behavior and suicide ideation	445,843	983	444,125.25	2.21	2.08	2.36
Dizziness on standing (lightheadedness)	439,285	6,282	434,406.09	14.46	14.11	14.82
Pins-and-needles feelings	444,891	2,919	441,747.75	6.61	6.37	6.85
Dysautonomia	447,145	255	445,689.39	0.57	0.51	0.65
Digestive symptoms						
Abdominal pain	423,311	21,352	411,216.45	51.92	51.23	52.63
Diarrhea	434,662	5,558	430,259.84	12.92	12.58	13.26
Nausea	437,715	5,220	433,737.99	12.03	11.71	12.37
Constipation	439,831	5,687	435,746.54	13.05	12.72	13.40
Musculoskeletal and Skin						
Arthralgia or joint pain	428,485	21,100	416,026.60	50.72	50.04	51.41
Myalgia or muscle pain	437,067	3,411	432,992.06	7.88	7.62	8.15
Body aches	435,204	3,859	431,300.01	8.95	8.67	9.23
Rash	439,321	7,239	434,489.97	16.66	16.28	17.05
Alopecia	447,321	145	445,920.04	0.33	0.28	0.38
Hair loss	445,743	2,188	443,032.76	4.94	4.74	5.15
Endocrine symptoms						
Diabetes mellitus (Type I & II)	432,776	3,791	428,953.84	8.84	8.56	9.12
Diabetic ketoacidosis	446,737	151	445,373.11	0.34	0.29	0.40
Thyroiditis	445,911	836	444,079.53	1.88	1.76	2.02
Hypothyroidism	436,604	4,070	432,278.02	9.42	9.13	9.71
Hyperthyroidism	446,452	621	444,736.91	1.40	1.29	1.51
Menstrual/period issues	438,150	9,531	431,189.92	22.10	21.67	22.55
Hematologic symptoms						
DVT	445,971	553	444,338.57	1.24	1.15	1.35
Pulmonary embolism	445,103	372	443,718.94	0.84	0.76	0.93
Renal symptoms						
Acute kidney injury	441,169	1,588	438,959.39	3.62	3.44	3.80
Chronic kidney disease	443,054	2,780	440,113.68	6.32	6.09	6.56
Dialysis	446,161	445	444,546.63	1.00	0.91	1.10
			>=6 months			
Any below medical condition						
Any below medical condition	140,598	27,041	157,231.62	171.98	169.94	174.04
Post-COVID syndrome						
Post-COVID syndrome	335,034	970	402,059.02	2.41	2.27	2.57
General symptoms						
Fatigue	308,856	8,486	366,116.25	23.18	22.69	23.68
Intermittent fever	300,897	4,884	358,647.16	13.62	13.24	14.01

Table 43. Incidence of Long COVID in the Standard-Risk Trial Similar Cohort by Follow-up Intervals, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Post-exertional malaise	332,533	852	398,324.68	2.14	2.00	2.29
Multisystem inflammatory syndrome (MIS)	335,936	19	403,041.43	0.05	0.03	0.07
Respiratory symptoms						
Dyspnea or Shortness of breath	294,305	5,576	350,022.61	15.93	15.52	16.35
Cough	283,875	2,899	335,613.82	8.64	8.33	8.96
Nasal congestion	321,740	4,071	384,862.33	10.58	10.26	10.91
Lung function abnormalities	334,839	456	401,573.06	1.14	1.04	1.25
Hypoxemia	326,711	383	392,057.48	0.98	0.88	1.08
Cardiovascular and cerebrovascular symptoms						
Chest pain	308,901	9,159	366,231.95	25.01	24.50	25.53
Palpitations or Fast-beating or pounding heart	329,325	3,372	393,172.61	8.58	8.29	8.87
Myocarditis	335,797	51	402,800.16	0.13	0.10	0.17
Pericarditis	335,934	51	402,972.11	0.13	0.10	0.17
Myocardial infarction	334,954	361	401,661.82	0.90	0.81	1.00
Angina	335,344	520	402,013.66	1.29	1.19	1.41
Atrial fibrillation	333,882	572	400,326.65	1.43	1.32	1.55
Atrial flutter	335,721	118	402,715.14	0.29	0.25	0.35
Sinus tachycardia	325,169	2,238	389,054.03	5.75	5.52	6.00
Sinus bradycardia	333,152	1,039	399,151.54	2.60	2.45	2.77
Heart Failure	332,354	826	398,269.47	2.07	1.94	2.22
Stroke	335,356	375	402,141.79	0.93	0.84	1.03
TIA	335,756	226	402,674.48	0.56	0.49	0.64
Neurological symptoms						
Headache	330,634	39	394,542.66	0.10	0.07	0.14
Insomnia	330,794	2,124	395,666.08	5.37	5.15	5.60
Cognitive impairment	332,136	1,938	397,605.16	4.87	4.66	5.10
Confusion	335,768	39	402,762.84	0.10	0.07	0.13
Anosmia or Loss of smell	331,047	237	396,674.19	0.60	0.53	0.68
Ageusia or Loss of taste	331,526	221	397,320.93	0.56	0.49	0.64
Depression	320,562	4,311	381,699.80	11.29	10.96	11.64
Anxiety Disorders	307,214	9,796	363,765.21	26.93	26.40	27.47
Post-traumatic Stress Disorder	334,618	632	401,172.61	1.58	1.46	1.70
Substance Use Disorders	330,617	2,052	396,062.53	5.18	4.96	5.41
Suicidal behavior and suicide ideation	334,586	600	401,210.52	1.50	1.38	1.62
Dizziness on standing (lightheadedness)	328,075	4,153	391,563.74	10.61	10.29	10.93

Table 43. Incidence of Long COVID in the Standard-Risk Trial Similar Cohort by Follow-up Intervals, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Pins-and-needles feelings	333,222	1,931	398,698.46	4.84	4.63	5.06
Dysautonomia	335,756	148	402,721.73	0.37	0.31	0.43
Digestive symptoms						
Abdominal pain	312,222	13,599	368,606.97	36.89	36.28	37.52
Diarrhea	324,724	3,565	387,921.61	9.19	8.89	9.50
Nausea	327,181	3,294	391,171.78	8.42	8.14	8.71
Constipation	328,847	3,524	392,999.66	8.97	8.68	9.27
Musculoskeletal and Skin						
Arthralgia or joint pain	316,079	13,663	372,863.20	36.64	36.03	37.26
Myalgia or muscle pain	326,609	2,234	390,410.48	5.72	5.49	5.96
Body aches	325,250	2,621	388,943.55	6.74	6.49	7.00
Rash	328,181	4,583	391,682.53	11.70	11.37	12.05
Alopecia	335,920	83	402,945.45	0.21	0.17	0.26
Hair loss	333,694	906	399,878.09	2.27	2.12	2.42
Endocrine symptoms						
Diabetes mellitus (Type I & II)	323,462	2,475	386,842.17	6.40	6.15	6.66
Diabetic ketoacidosis	335,499	100	402,463.69	0.25	0.20	0.30
Thyroiditis	334,658	497	401,171.97	1.24	1.14	1.35
Hypothyroidism	326,165	2,352	389,727.86	6.03	5.80	6.28
Hyperthyroidism	335,088	382	401,784.92	0.95	0.86	1.05
Menstrual/period issues	326,215	6,103	388,117.07	15.72	15.34	16.12
Hematologic symptoms						
DVT	334,734	366	401,431.18	0.91	0.82	1.01
Pulmonary embolism	334,162	232	400,927.12	0.58	0.51	0.66
Renal symptoms						
Acute kidney injury	330,792	1,039	396,404.69	2.62	2.47	2.79
Chronic kidney disease	331,921	1,869	397,272.36	4.70	4.50	4.92
Dialysis	334,914	311	401,632.36	0.77	0.69	0.87

The incidence rates of any symptom and post-COVID syndrome were higher in the Vaccine period (Table 45) as compared to the Pre-Vaccine period (Table 44). The Omicron period (Table 46) had the highest incidence rates of any symptom and post-COVID syndrome compared to the other periods during the 4 and 12 week marks, however after 6 months there was a dramatic decrease in these outcomes bringing rates to lower than both of the other periods.

Table 44. Incidence of Long COVID in the Source Cohort by Follow-up Intervals, 1/1/2020-10/31/2020 (Pre-vaccine Period)

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
			Overall			
Any below medical condition						

Table 44. Incidence of Long COVID in the Source Cohort by Follow-up Intervals, 1/1/2020-10/31/2020 (Pre-vaccine Period)

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Any below medical condition	163,347	112,845	99,302.60	1,136.38	1,129.76	1,143.03
Post-COVID syndrome						
Post-COVID syndrome	285,016	1,340	433,060.27	3.09	2.93	3.26
General symptoms						
Fatigue	270,689	44,607	362,410.05	123.08	121.95	124.23
Intermittent fever	276,652	37,307	371,110.05	100.53	99.51	101.55
Post-exertional malaise	282,595	9,502	420,100.18	22.62	22.17	23.08
Multisystem inflammatory syndrome (MIS)	285,016	40	433,623.68	0.09	0.07	0.13
Respiratory symptoms						
Dyspnea or Shortness of breath	268,776	64,400	328,005.40	196.34	194.83	197.86
Cough	268,537	52,960	331,660.49	159.68	158.33	161.05
Nasal congestion	282,631	11,727	417,136.23	28.11	27.61	28.63
Lung function abnormalities	283,817	3,891	427,779.75	9.10	8.81	9.39
Hypoxemia	282,993	19,394	407,726.57	47.57	46.90	48.24
Cardiovascular and cerebrovascular symptoms						
Chest pain	270,816	40,859	364,040.29	112.24	111.16	113.33
Palpitations or Fast-beating or pounding heart	281,305	11,282	415,144.86	27.18	26.68	27.68
Myocarditis	284,979	542	432,996.53	1.25	1.15	1.36
Pericarditis	284,940	327	433,162.32	0.75	0.68	0.84
Myocardial infarction	283,088	6,568	425,188.51	15.45	15.08	15.83
Angina	282,302	4,869	424,454.13	11.47	11.15	11.80
Atrial fibrillation	276,829	10,897	412,904.87	26.39	25.90	26.89
Atrial flutter	283,954	2,246	430,180.46	5.22	5.01	5.44
Sinus tachycardia	280,479	18,793	405,712.90	46.32	45.66	46.99
Sinus bradycardia	282,552	8,684	421,244.19	20.62	20.19	21.05
Heart Failure	274,019	18,718	402,328.04	46.52	45.86	47.20
Stroke	282,739	4,465	426,307.93	10.47	10.17	10.79
TIA	284,165	1,987	430,535.67	4.62	4.42	4.82
Neurological symptoms						
Headache	277,352	10,351	405,818.51	25.51	25.02	26.00
Insomnia	279,613	10,723	413,388.79	25.94	25.45	26.44
Cognitive impairment	279,748	14,856	413,213.69	35.95	35.38	36.54
Confusion	284,559	2,188	431,197.73	5.07	4.87	5.29
Anosmia or Loss of smell	284,780	3,863	427,823.13	9.03	8.75	9.32
Ageusia or Loss of taste	284,788	3,502	428,357.32	8.18	7.91	8.45
Depression	265,856	24,970	375,313.82	66.53	65.71	67.36
Anxiety Disorders	260,741	35,158	356,347.04	98.66	97.64	99.70
Post-traumatic Stress Disorder	283,504	2,652	428,352.07	6.19	5.96	6.43

Table 44. Incidence of Long COVID in the Source Cohort by Follow-up Intervals, 1/1/2020-10/31/2020 (Pre-vaccine Period)

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Substance Use Disorders	279,817	8,986	416,070.95	21.60	21.16	22.05
Suicidal behavior and suicide ideation	284,053	2,295	429,686.08	5.34	5.13	5.56
Dizziness on standing (lightheadedness)	278,757	16,939	405,792.76	41.74	41.12	42.38
Pins-and-needles feelings	282,849	6,691	423,335.00	15.81	15.43	16.19
Dysautonomia	284,634	736	432,329.72	1.70	1.58	1.83
Digestive symptoms						
Abdominal pain	267,180	38,461	365,570.36	105.21	104.16	106.27
Diarrhea	279,454	20,184	401,822.41	50.23	49.54	50.93
Nausea	280,487	14,213	410,369.06	34.63	34.07	35.21
Constipation	278,162	16,135	406,942.42	39.65	39.04	40.27
Musculoskeletal and Skin						
Arthralgia or joint pain	265,163	38,076	364,700.80	104.40	103.36	105.46
Myalgia or muscle pain	281,520	13,194	412,779.17	31.96	31.42	32.51
Body aches	281,298	13,818	412,451.36	33.50	32.95	34.07
Rash	279,782	13,284	412,063.85	32.24	31.69	32.79
Alopecia	284,928	202	433,306.48	0.47	0.41	0.54
Hair loss	284,267	3,559	428,245.26	8.31	8.04	8.59
Endocrine symptoms						
Diabetes mellitus (Type I & II)	254,352	24,312	359,067.29	67.71	66.86	68.57
Diabetic ketoacidosis	284,661	1,378	431,653.71	3.19	3.03	3.37
Thyroiditis	283,903	1,591	430,013.83	3.70	3.52	3.89
Hypothyroidism	269,988	14,327	394,236.87	36.34	35.75	36.94
Hyperthyroidism	283,926	1,614	430,071.90	3.75	3.57	3.94
Menstrual/period issues	278,889	13,460	410,058.08	32.82	32.28	33.38
Hematologic symptoms						
DVT	283,607	4,270	427,115.11	10.00	9.70	10.30
Pulmonary embolism	283,947	4,019	427,696.69	9.40	9.11	9.69
Renal symptoms						
Acute kidney injury	279,196	22,426	404,869.65	55.39	54.67	56.12
Chronic kidney disease	269,142	19,878	391,814.56	50.73	50.03	51.44
Dialysis	282,278	6,454	424,630.48	15.20	14.83	15.57
			>=4 Weeks			
Any below medical condition						
Any below medical condition	85,211	36,306	98,676.03	367.93	364.17	371.74
Post-COVID syndrome						
Post-COVID syndrome	272,742	1,334	432,573.24	3.08	2.92	3.25
General symptoms						
Fatigue	241,792	25,068	361,771.29	69.29	68.44	70.16
Intermittent fever	237,849	8,442	370,517.88	22.78	22.30	23.28

Table 44. Incidence of Long COVID in the Source Cohort by Follow-up Intervals, 1/1/2020-10/31/2020 (Pre-vaccine Period)

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Post-exertional malaise	266,880	5,095	419,563.62	12.14	11.82	12.48
Multisystem inflammatory syndrome (MIS)	272,748	40	433,136.81	0.09	0.07	0.13
Respiratory symptoms						
Dyspnea or Shortness of breath	218,490	20,757	327,295.46	63.42	62.56	64.29
Cough	217,767	12,353	330,918.74	37.33	36.68	37.99
Nasal congestion	265,837	7,007	416,621.04	16.82	16.43	17.22
Lung function abnormalities	270,645	2,645	427,287.28	6.19	5.96	6.43
Hypoxemia	257,659	3,525	407,195.31	8.66	8.38	8.95
Cardiovascular and cerebrovascular symptoms						
Chest pain	244,014	24,883	363,389.69	68.47	67.63	69.33
Palpitations or Fast-beating or pounding heart	267,219	9,330	414,617.39	22.50	22.05	22.96
Myocarditis	272,426	172	432,509.77	0.40	0.34	0.46
Pericarditis	272,554	195	432,673.82	0.45	0.39	0.52
Myocardial infarction	268,689	3,045	424,718.85	7.17	6.92	7.43
Angina	269,308	3,790	423,961.30	8.94	8.66	9.23
Atrial fibrillation	261,011	4,331	412,464.99	10.50	10.19	10.82
Atrial flutter	271,062	1,184	429,697.38	2.76	2.60	2.92
Sinus tachycardia	259,553	8,211	405,161.41	20.27	19.83	20.71
Sinus bradycardia	267,434	4,899	420,739.57	11.64	11.32	11.97
Heart Failure	255,094	6,940	401,928.50	17.27	16.87	17.68
Stroke	269,565	2,899	425,824.64	6.81	6.57	7.06
TIA	271,580	1,510	430,047.50	3.51	3.34	3.69
Neurological symptoms						
Headache	257,430	2,221	405,275.96	5.48	5.26	5.71
Insomnia	265,166	8,019	412,872.01	19.42	19.00	19.85
Cognitive impairment	263,680	8,777	412,718.34	21.27	20.83	21.72
Confusion	271,338	777	430,712.54	1.80	1.68	1.94
Anosmia or Loss of smell	269,566	841	427,320.61	1.97	1.84	2.11
Ageusia or Loss of taste	269,834	764	427,856.87	1.79	1.66	1.92
Depression	246,311	15,763	374,768.18	42.06	41.41	42.72
Anxiety Disorders	238,404	22,978	355,754.87	64.59	63.76	65.43
Post-traumatic Stress Disorder	270,622	1,957	427,856.67	4.57	4.38	4.78
Substance Use Disorders	264,613	5,505	415,566.24	13.25	12.90	13.60
Suicidal behavior and suicide ideation	271,135	1,563	429,193.68	3.64	3.47	3.83
Dizziness on standing (lightheadedness)	263,000	12,996	405,258.99	32.07	31.52	32.62

Table 44. Incidence of Long COVID in the Source Cohort by Follow-up Intervals, 1/1/2020-10/31/2020 (Pre-vaccine Period)

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Pins-and-needles feelings	269,919	5,964	422,832.68	14.10	13.75	14.47
Dysautonomia	272,250	571	431,841.75	1.32	1.22	1.44
Digestive symptoms						
Abdominal pain	248,044	30,583	364,984.56	83.79	82.86	84.74
Diarrhea	257,949	9,949	401,270.98	24.79	24.31	25.29
Nausea	263,339	9,021	409,825.94	22.01	21.56	22.47
Constipation	262,353	11,358	406,421.79	27.95	27.44	28.47
Musculoskeletal and Skin						
Arthralgia or joint pain	250,148	34,363	364,152.74	94.36	93.37	95.37
Myalgia or muscle pain	263,248	6,814	412,255.54	16.53	16.14	16.93
Body aches	263,206	7,398	411,929.69	17.96	17.56	18.37
Rash	265,866	11,321	411,545.17	27.51	27.01	28.02
Alopecia	272,642	184	432,819.05	0.43	0.37	0.49
Hair loss	271,763	3,311	427,753.50	7.74	7.48	8.01
Endocrine symptoms						
Diabetes mellitus (Type I & II)	231,367	9,196	358,629.75	25.64	25.12	26.17
Diabetic ketoacidosis	271,722	523	431,168.61	1.21	1.11	1.32
Thyroiditis	271,340	1,265	429,522.32	2.95	2.79	3.11
Hypothyroidism	253,005	7,791	393,746.35	19.79	19.35	20.23
Hyperthyroidism	271,294	1,161	429,581.36	2.70	2.55	2.86
Menstrual/period issues	265,594	12,357	409,542.60	30.17	29.65	30.71
Hematologic symptoms						
DVT	269,853	2,309	426,616.96	5.41	5.20	5.64
Pulmonary embolism	269,876	1,757	427,194.62	4.11	3.93	4.31
Renal symptoms						
Acute kidney injury	256,511	6,691	404,465.17	16.54	16.15	16.94
Chronic kidney disease	251,164	9,965	391,390.03	25.46	24.97	25.97
Dialysis	267,601	2,419	424,133.91	5.70	5.48	5.94
			>=12 Weeks			
Any below medical condition						
Any below medical condition	76,163	28,308	97,360.79	290.75	287.39	294.16
Post-COVID syndrome						
Post-COVID syndrome	266,610	1,331	431,743.20	3.08	2.92	3.25
General symptoms						
Fatigue	232,616	20,442	360,486.20	56.71	55.94	57.49
Intermittent fever	231,547	7,007	369,647.91	18.96	18.52	19.41
Post-exertional malaise	259,880	3,704	418,612.08	8.85	8.57	9.14
Multisystem inflammatory syndrome (MIS)	266,618	39	432,307.06	0.09	0.07	0.12
Respiratory symptoms						

Table 44. Incidence of Long COVID in the Source Cohort by Follow-up Intervals, 1/1/2020-10/31/2020 (Pre-vaccine Period)

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Dyspnea or Shortness of breath	210,272	16,254	326,144.61	49.84	49.08	50.61
Cough	209,976	9,397	329,848.94	28.49	27.92	29.07
Nasal congestion	259,332	6,442	415,729.28	15.50	15.12	15.88
Lung function abnormalities	264,142	2,077	426,398.21	4.87	4.67	5.09
Hypoxemia	251,720	2,598	406,382.50	6.39	6.15	6.64
Cardiovascular and cerebrovascular symptoms						
Chest pain	234,584	20,650	362,068.91	57.03	56.26	57.82
Palpitations or Fast-beating or pounding heart	259,583	7,740	413,561.73	18.72	18.30	19.14
Myocarditis	266,265	114	431,675.03	0.26	0.22	0.32
Pericarditis	266,404	163	431,841.55	0.38	0.32	0.44
Myocardial infarction	262,532	2,553	423,880.38	6.02	5.79	6.26
Angina	262,715	3,196	423,060.19	7.55	7.30	7.82
Atrial fibrillation	255,134	3,464	411,662.53	8.41	8.14	8.70
Atrial flutter	264,867	934	428,856.18	2.18	2.04	2.32
Sinus tachycardia	252,658	6,498	404,220.58	16.08	15.69	16.47
Sinus bradycardia	260,973	4,173	419,856.22	9.94	9.64	10.25
Heart Failure	249,434	5,563	401,145.48	13.87	13.51	14.24
Stroke	263,229	2,398	424,962.05	5.64	5.42	5.87
TIA	265,294	1,291	429,193.79	3.01	2.85	3.18
Neurological symptoms						
Headache	250,444	971	404,319.78	2.40	2.26	2.56
Insomnia	257,842	6,593	411,865.25	16.01	15.63	16.40
Cognitive impairment	256,927	7,163	411,792.63	17.39	17.00	17.80
Confusion	265,278	594	429,892.23	1.38	1.28	1.50
Anosmia or Loss of smell	263,289	630	426,467.77	1.48	1.37	1.60
Ageusia or Loss of taste	263,604	612	427,010.37	1.43	1.32	1.55
Depression	237,923	12,540	373,593.31	33.57	32.98	34.16
Anxiety Disorders	228,929	18,562	354,422.85	52.37	51.62	53.13
Post-traumatic Stress Disorder	264,221	1,623	426,985.66	3.80	3.62	3.99
Substance Use Disorders	257,913	4,623	414,647.03	11.15	10.83	11.48
Suicidal behavior and suicide ideation	264,812	1,297	428,335.26	3.03	2.87	3.20
Dizziness on standing (lightheadedness)	255,445	11,261	404,212.29	27.86	27.35	28.38
Pins-and-needles feelings	263,071	5,195	421,895.98	12.31	11.98	12.65
Dysautonomia	266,044	467	431,001.07	1.08	0.99	1.19
Digestive symptoms						
Abdominal pain	238,229	26,184	363,588.96	72.02	71.15	72.89
Diarrhea	251,114	8,577	400,328.30	21.42	20.98	21.88
Nausea	256,197	7,735	408,840.91	18.92	18.50	19.35

Table 44. Incidence of Long COVID in the Source Cohort by Follow-up Intervals, 1/1/2020-10/31/2020 (Pre-vaccine Period)

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Constipation	255,067	9,565	405,417.36	23.59	23.13	24.07
Musculoskeletal and Skin						
Arthralgia or joint pain	239,827	29,648	362,674.82	81.75	80.82	82.68
Myalgia or muscle pain	256,571	5,890	411,339.01	14.32	13.96	14.69
Body aches	256,409	6,395	410,999.35	15.56	15.18	15.95
Rash	258,360	9,735	410,507.30	23.71	23.25	24.19
Alopecia	266,496	167	431,986.96	0.39	0.33	0.45
Hair loss	265,090	2,761	426,830.72	6.47	6.23	6.71
Endocrine symptoms						
Diabetes mellitus (Type I & II)	225,200	7,399	357,775.14	20.68	20.22	21.16
Diabetic ketoacidosis	265,589	448	430,337.89	1.04	0.95	1.14
Thyroiditis	265,016	1,050	428,663.13	2.45	2.31	2.60
Hypothyroidism	245,886	6,075	392,765.40	15.47	15.08	15.86
Hyperthyroidism	264,993	949	428,725.91	2.21	2.08	2.36
Menstrual/period issues	257,811	10,613	408,458.94	25.98	25.49	26.48
Hematologic symptoms						
DVT	263,417	1,772	425,741.56	4.16	3.97	4.36
Pulmonary embolism	263,533	1,309	426,332.80	3.07	2.91	3.24
Renal symptoms						
Acute kidney injury	251,033	5,550	403,702.90	13.75	13.39	14.11
Chronic kidney disease	244,757	8,227	390,501.19	21.07	20.62	21.53
Dialysis	261,663	1,874	423,326.22	4.43	4.23	4.63
			>=6 months			
Any below medical condition						
Any below medical condition	65,694	19,052	93,614.69	203.52	200.65	206.43
Post-COVID syndrome						
Post-COVID syndrome	259,160	1,318	429,009.31	3.07	2.91	3.24
General symptoms						
Fatigue	221,534	14,933	356,455.87	41.89	41.23	42.57
Intermittent fever	223,798	5,356	366,820.80	14.60	14.22	15.00
Post-exertional malaise	251,894	2,601	415,695.37	6.26	6.02	6.50
Multisystem inflammatory syndrome (MIS)	259,175	33	429,575.57	0.08	0.06	0.11
Respiratory symptoms						
Dyspnea or Shortness of breath	200,760	11,789	322,701.03	36.53	35.88	37.20
Cough	201,060	6,104	326,602.76	18.69	18.23	19.16
Nasal congestion	250,835	5,112	412,618.65	12.39	12.05	12.73
Lung function abnormalities	256,292	1,509	423,524.79	3.56	3.39	3.75
Hypoxemia	244,381	1,879	403,699.15	4.65	4.45	4.87
Cardiovascular and cerebrovascular symptoms						

Table 44. Incidence of Long COVID in the Source Cohort by Follow-up Intervals, 1/1/2020-10/31/2020 (Pre-vaccine Period)

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Chest pain	223,281	15,445	357,950.52	43.15	42.47	43.83
Palpitations or Fast-beating or pounding heart	250,447	5,824	410,228.77	14.20	13.84	14.57
Myocarditis	258,816	79	428,941.73	0.18	0.15	0.23
Pericarditis	258,934	118	429,100.13	0.27	0.23	0.33
Myocardial infarction	254,844	1,944	421,062.89	4.62	4.42	4.83
Angina	254,650	2,391	420,108.22	5.69	5.47	5.92
Atrial fibrillation	247,655	2,562	408,926.10	6.27	6.03	6.51
Atrial flutter	257,339	689	426,096.08	1.62	1.50	1.74
Sinus tachycardia	244,385	4,769	401,198.95	11.89	11.55	12.23
Sinus bradycardia	252,943	3,172	416,922.50	7.61	7.35	7.88
Heart Failure	241,913	4,057	398,392.46	10.18	9.88	10.50
Stroke	255,501	1,853	422,128.16	4.39	4.19	4.59
TIA	257,671	1,005	426,399.44	2.36	2.22	2.51
Neurological symptoms						
Headache	242,771	61	401,541.58	0.15	0.12	0.20
Insomnia	248,899	4,771	408,598.90	11.68	11.35	12.01
Cognitive impairment	248,610	5,347	408,748.13	13.08	12.74	13.44
Confusion	257,868	450	427,172.61	1.05	0.96	1.16
Anosmia or Loss of smell	255,725	386	423,693.30	0.91	0.83	1.01
Ageusia or Loss of taste	256,005	381	424,221.79	0.90	0.81	0.99
Depression	227,345	8,204	369,746.86	22.19	21.71	22.67
Anxiety Disorders	217,449	13,083	350,254.17	37.35	36.72	38.00
Post-traumatic Stress Disorder	256,426	1,182	424,128.26	2.79	2.63	2.95
Substance Use Disorders	249,735	3,446	411,652.31	8.37	8.10	8.66
Suicidal behavior and suicide ideation	257,104	945	425,507.92	2.22	2.08	2.37
Dizziness on standing (lightheadedness)	245,876	8,660	400,713.34	21.61	21.16	22.07
Pins-and-needles feelings	254,523	3,960	418,765.23	9.46	9.17	9.76
Dysautonomia	258,519	345	428,240.03	0.81	0.73	0.90
Digestive symptoms						
Abdominal pain	225,514	19,642	358,947.35	54.72	53.96	55.49
Diarrhea	242,462	6,530	397,161.63	16.44	16.05	16.85
Nausea	247,280	5,786	405,577.72	14.27	13.90	14.64
Constipation	245,917	7,150	402,071.33	17.78	17.38	18.20
Musculoskeletal and Skin						
Arthralgia or joint pain	226,142	22,311	357,685.57	62.38	61.56	63.20
Myalgia or muscle pain	248,281	4,453	408,304.15	10.91	10.59	11.23
Body aches	247,870	4,881	407,870.72	11.97	11.64	12.31

Table 44. Incidence of Long COVID in the Source Cohort by Follow-up Intervals, 1/1/2020-10/31/2020 (Pre-vaccine Period)

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Rash	249,069	7,513	407,103.01	18.45	18.04	18.88
Alopecia	259,022	129	429,244.67	0.30	0.25	0.36
Hair loss	256,300	1,345	423,656.33	3.17	3.01	3.35
Endocrine symptoms						
Diabetes mellitus (Type I & II)	217,400	5,348	354,929.14	15.07	14.67	15.48
Diabetic ketoacidosis	258,112	338	427,594.97	0.79	0.71	0.88
Thyroiditis	257,357	783	425,857.51	1.84	1.71	1.97
Hypothyroidism	237,249	4,036	389,619.81	10.36	10.04	10.68
Hyperthyroidism	257,343	683	425,922.09	1.60	1.49	1.73
Menstrual/period issues	248,092	8,038	404,903.00	19.85	19.42	20.29
Hematologic symptoms						
DVT	255,738	1,290	422,926.73	3.05	2.89	3.22
Pulmonary embolism	255,934	943	423,548.71	2.23	2.09	2.37
Renal symptoms						
Acute kidney injury	243,481	4,198	400,939.01	10.47	10.16	10.79
Chronic kidney disease	236,656	6,150	387,543.16	15.87	15.48	16.27
Dialysis	254,269	1,361	420,614.89	3.24	3.07	3.41

Table 45. Incidence of Long COVID in the Source Cohort by Follow-up Intervals, 12/31/2020-07/20/2022 (Vaccine Period)

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
			Overall			
Any below medical condition						
Any below medical condition	697,753	356,540	184,664.62	1,930.74	1,924.42	1,937.09
Post-COVID syndrome						
Post-COVID syndrome	1,189,729	15,524	683,142.43	22.72	22.37	23.09
General symptoms						
Fatigue	1,135,732	106,422	594,457.42	179.02	177.95	180.10
Intermittent fever	1,167,027	93,932	623,270.10	150.71	149.75	151.68
Post-exertional malaise	1,183,368	19,488	674,034.89	28.91	28.51	29.32
Multisystem inflammatory syndrome (MIS)	1,190,057	534	688,602.00	0.78	0.71	0.84
Respiratory symptoms						
Dyspnea or Shortness of breath	1,137,788	159,796	558,491.10	286.12	284.72	287.53
Cough	1,154,016	82,104	585,842.45	140.15	139.19	141.11
Nasal congestion	1,172,309	43,786	653,916.41	66.96	66.34	67.59
Lung function abnormalities	1,185,281	9,394	681,270.07	13.79	13.51	14.07

Table 45. Incidence of Long COVID in the Source Cohort by Follow-up Intervals, 12/31/2020-07/20/2022 (Vaccine Period)

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Hypoxemia	1,185,023	46,972	657,268.28	71.47	70.82	72.12
Cardiovascular and cerebrovascular symptoms						
Chest pain	1,135,611	99,841	600,358.66	166.30	165.27	167.34
Palpitations or Fast-beating or pounding heart	1,172,702	24,434	664,640.34	36.76	36.31	37.23
Myocarditis	1,189,962	875	688,426.82	1.27	1.19	1.36
Pericarditis	1,189,834	524	688,532.12	0.76	0.70	0.83
Myocardial infarction	1,183,928	15,111	678,355.81	22.28	21.92	22.63
Angina	1,180,286	9,962	677,063.31	14.71	14.43	15.01
Atrial fibrillation	1,163,732	26,699	660,339.28	40.43	39.95	40.92
Atrial flutter	1,186,712	5,036	684,467.55	7.36	7.16	7.56
Sinus tachycardia	1,174,794	44,403	654,294.77	67.86	67.24	68.50
Sinus bradycardia	1,181,465	17,525	674,177.80	25.99	25.61	26.38
Heart Failure	1,157,422	39,216	651,007.94	60.24	59.65	60.84
Stroke	1,182,971	9,394	680,207.82	13.81	13.53	14.09
TIA	1,187,042	3,879	685,064.54	5.66	5.49	5.84
Neurological symptoms						
Headache	1,186,633	407	684,491.64	0.59	0.54	0.66
Insomnia	1,167,089	23,786	661,096.56	35.98	35.53	36.44
Cognitive impairment	1,173,958	30,574	665,138.04	45.97	45.45	46.49
Confusion	1,189,061	3,890	686,738.39	5.66	5.49	5.85
Anosmia or Loss of smell	1,189,257	7,775	681,696.43	11.41	11.16	11.66
Ageusia or Loss of taste	1,189,061	7,249	682,050.16	10.63	10.39	10.88
Depression	1,119,684	46,378	611,085.97	75.89	75.21	76.59
Anxiety Disorders	1,081,554	89,520	571,456.58	156.65	155.63	157.68
Post-traumatic Stress Disorder	1,182,730	6,456	680,851.27	9.48	9.25	9.72
Substance Use Disorders	1,168,289	24,876	662,984.41	37.52	37.06	37.99
Suicidal behavior and suicide ideation	1,186,020	6,329	683,264.82	9.26	9.04	9.49
Dizziness on standing (lightheadedness)	1,165,424	36,889	653,863.86	56.42	55.84	57.00
Pins-and-needles feelings	1,180,392	12,625	676,289.07	18.67	18.35	19.00
Dysautonomia	1,188,773	1,478	687,365.93	2.15	2.04	2.26
Digestive symptoms						
Abdominal pain	1,115,292	87,203	599,269.89	145.52	144.55	146.48
Diarrhea	1,168,994	43,644	651,246.95	67.02	66.39	67.65
Nausea	1,170,878	35,115	656,915.58	53.45	52.90	54.02
Constipation	1,164,923	34,601	656,041.98	52.74	52.19	53.30
Musculoskeletal and Skin						
Arthralgia or joint pain	1,105,589	79,710	596,291.21	133.68	132.75	134.61
Myalgia or muscle pain	1,177,808	26,174	665,018.69	39.36	38.88	39.84
Body aches	1,176,654	35,682	660,060.11	54.06	53.50	54.62

Table 45. Incidence of Long COVID in the Source Cohort by Follow-up Intervals, 12/31/2020-07/20/2022 (Vaccine Period)

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Rash	1,167,553	27,883	661,752.32	42.14	41.64	42.63
Alopecia	1,189,743	384	688,592.72	0.56	0.51	0.62
Hair loss	1,186,379	7,998	682,423.96	11.72	11.47	11.98
Endocrine symptoms						
Diabetes mellitus (Type I & II)	1,087,686	60,464	587,200.64	102.97	102.15	103.79
Diabetic ketoacidosis	1,188,724	3,677	686,222.10	5.36	5.19	5.53
Thyroiditis	1,184,697	3,777	683,599.10	5.53	5.35	5.70
Hypothyroidism	1,133,401	35,576	632,572.11	56.24	55.66	56.83
Hyperthyroidism	1,185,874	3,615	684,352.68	5.28	5.11	5.46
Menstrual/period issues	1,160,486	28,159	656,299.96	42.91	42.41	43.41
Hematologic symptoms						
DVT	1,185,445	9,240	681,266.49	13.56	13.29	13.84
Pulmonary embolism	1,186,356	11,571	680,213.87	17.01	16.70	17.32
Renal symptoms						
Acute kidney injury	1,173,790	49,709	655,973.31	75.78	75.12	76.45
Chronic kidney disease	1,143,660	44,250	637,111.88	69.45	68.81	70.10
Dialysis	1,183,670	11,756	679,722.76	17.30	16.99	17.61
			>=4 Weeks			
Any below medical condition						
Any below medical condition	354,175	96,477	180,151.16	535.53	532.17	538.92
Post-COVID syndrome						
Post-COVID syndrome	1,003,584	8,966	677,676.52	13.23	12.96	13.51
General symptoms						
Fatigue	909,475	45,919	588,825.26	77.98	77.27	78.70
Intermittent fever	926,467	19,803	617,843.54	32.05	31.61	32.50
Post-exertional malaise	993,922	7,786	668,621.85	11.64	11.39	11.91
Multisystem inflammatory syndrome (MIS)	1,009,099	98	683,310.32	0.14	0.12	0.18
Respiratory symptoms						
Dyspnea or Shortness of breath	859,630	40,113	552,646.69	72.58	71.88	73.30
Cough	904,310	10,089	580,052.81	17.39	17.06	17.74
Nasal congestion	968,505	14,968	648,574.23	23.08	22.71	23.45
Lung function abnormalities	1,002,056	5,296	675,961.33	7.83	7.63	8.05
Hypoxemia	970,674	5,942	651,860.33	9.12	8.89	9.35
Cardiovascular and cerebrovascular symptoms						
Chest pain	915,297	47,340	594,761.83	79.59	78.88	80.32
Palpitations or Fast-beating or pounding heart	987,216	17,011	659,255.50	25.80	25.42	26.19
Myocarditis	1,008,880	245	683,135.47	0.36	0.32	0.41
Pericarditis	1,009,071	261	683,242.91	0.38	0.34	0.43

Table 45. Incidence of Long COVID in the Source Cohort by Follow-up Intervals, 12/31/2020-07/20/2022 (Vaccine Period)

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Myocardial infarction	997,015	4,619	673,111.66	6.86	6.67	7.06
Angina	998,104	6,728	671,767.21	10.02	9.78	10.26
Atrial fibrillation	974,032	8,154	655,188.01	12.45	12.18	12.72
Atrial flutter	1,004,462	2,047	679,187.82	3.01	2.89	3.15
Sinus tachycardia	971,123	15,047	648,849.10	23.19	22.82	23.56
Sinus bradycardia	994,126	7,720	668,858.52	11.54	11.29	11.80
Heart Failure	963,552	12,438	645,925.93	19.26	18.92	19.60
Stroke	999,825	4,514	674,935.47	6.69	6.50	6.89
TIA	1,005,718	2,412	679,776.90	3.55	3.41	3.69
Neurological symptoms						
Headache	1,005,989	230	679,205.98	0.34	0.30	0.39
Insomnia	981,523	15,216	655,744.07	23.20	22.84	23.58
Cognitive impairment	984,154	14,888	659,837.43	22.56	22.20	22.93
Confusion	1,006,765	1,018	681,459.81	1.49	1.41	1.59
Anosmia or Loss of smell	1,002,094	963	676,381.75	1.42	1.34	1.52
Ageusia or Loss of taste	1,002,459	989	676,740.44	1.46	1.37	1.56
Depression	926,661	25,729	605,720.22	42.48	41.96	43.00
Anxiety Disorders	878,781	50,578	566,059.04	89.35	88.58	90.13
Post-traumatic Stress Disorder	1,000,628	3,978	675,548.32	5.89	5.71	6.07
Substance Use Disorders	979,265	11,765	657,697.09	17.89	17.57	18.21
Suicidal behavior and suicide ideation	1,003,211	3,076	677,971.08	4.54	4.38	4.70
Dizziness on standing (lightheadedness)	975,243	22,937	648,476.10	35.37	34.92	35.83
Pins-and-needles feelings	998,583	10,162	670,975.43	15.15	14.85	15.44
Dysautonomia	1,007,893	927	682,076.13	1.36	1.27	1.45
Digestive symptoms						
Abdominal pain	919,219	60,593	593,833.48	102.04	101.23	102.85
Diarrhea	969,145	19,112	645,858.21	29.59	29.18	30.01
Nausea	976,362	17,422	651,520.54	26.74	26.35	27.14
Constipation	976,247	21,379	650,687.49	32.86	32.42	33.30
Musculoskeletal and Skin						
Arthralgia or joint pain	922,117	66,381	590,942.76	112.33	111.48	113.19
Myalgia or muscle pain	984,662	10,756	659,673.48	16.31	16.00	16.62
Body aches	978,157	12,949	654,730.89	19.78	19.44	20.12
Rash	983,526	21,233	656,398.23	32.35	31.92	32.79
Alopecia	1,009,158	321	683,304.13	0.47	0.42	0.52
Hair loss	1,005,474	7,171	677,127.53	10.59	10.35	10.84
Endocrine symptoms						
Diabetes mellitus (Type I & II)	883,450	16,931	582,192.85	29.08	28.65	29.52
Diabetic ketoacidosis	1,006,177	856	680,942.62	1.26	1.18	1.34

Table 45. Incidence of Long COVID in the Source Cohort by Follow-up Intervals, 12/31/2020-07/20/2022 (Vaccine Period)

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Thyroiditis	1,003,628	2,625	678,306.99	3.87	3.73	4.02
Hypothyroidism	943,521	16,224	627,348.69	25.86	25.47	26.26
Hyperthyroidism	1,004,543	2,231	679,059.53	3.29	3.15	3.43
Menstrual/period issues	978,655	23,696	650,967.36	36.40	35.94	36.87
Hematologic symptoms						
DVT	1,001,216	3,838	675,950.35	5.68	5.50	5.86
Pulmonary embolism	999,263	3,101	674,873.14	4.59	4.44	4.76
Renal symptoms						
Acute kidney injury	968,455	11,166	650,868.20	17.16	16.84	17.48
Chronic kidney disease	949,693	18,001	631,986.63	28.48	28.07	28.90
Dialysis	998,671	3,855	674,413.65	5.72	5.54	5.90
			>=12 Weeks			
Any below medical condition						
Any below medical condition	258,964	61,481	166,480.30	369.30	366.39	372.23
Post-COVID syndrome						
Post-COVID syndrome	853,957	4,735	655,916.99	7.22	7.02	7.43
General symptoms						
Fatigue	761,900	31,729	567,353.23	55.92	55.31	56.54
Intermittent fever	785,688	14,663	597,325.10	24.55	24.15	24.95
Post-exertional malaise	846,202	4,546	647,114.89	7.03	6.82	7.23
Multisystem inflammatory syndrome (MIS)	861,777	20	661,838.20	0.03	0.02	0.05
Respiratory symptoms						
Dyspnea or Shortness of breath	716,271	25,254	531,850.57	47.48	46.90	48.07
Cough	756,144	6,226	558,494.04	11.15	10.87	11.43
Nasal congestion	823,355	11,578	627,422.57	18.45	18.12	18.79
Lung function abnormalities	854,241	3,291	654,422.08	5.03	4.86	5.20
Hypoxemia	826,074	3,445	630,792.90	5.46	5.28	5.65
Cardiovascular and cerebrovascular symptoms						
Chest pain	766,703	32,899	573,134.36	57.40	56.79	58.03
Palpitations or Fast-beating or pounding heart	837,591	11,432	637,472.27	17.93	17.61	18.27
Myocarditis	861,576	127	661,664.94	0.19	0.16	0.23
Pericarditis	861,770	168	661,772.07	0.25	0.22	0.30
Myocardial infarction	850,739	3,183	651,782.84	4.88	4.72	5.06
Angina	850,382	4,667	650,236.31	7.18	6.97	7.39
Atrial fibrillation	830,224	5,153	634,222.61	8.12	7.91	8.35
Atrial flutter	857,426	1,345	657,753.76	2.04	1.94	2.16
Sinus tachycardia	824,021	9,529	627,436.87	15.19	14.89	15.50
Sinus bradycardia	847,082	5,526	647,413.25	8.54	8.31	8.76
Heart Failure	820,356	7,948	625,028.81	12.72	12.44	13.00

Table 45. Incidence of Long COVID in the Source Cohort by Follow-up Intervals, 12/31/2020-07/20/2022 (Vaccine Period)

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Stroke	852,942	3,129	653,520.91	4.79	4.62	4.96
TIA	858,316	1,729	658,290.70	2.63	2.51	2.75
Neurological symptoms						
Headache	858,701	177	657,735.89	0.27	0.23	0.31
Insomnia	832,969	10,228	634,101.69	16.13	15.82	16.45
Cognitive impairment	837,084	10,087	638,395.72	15.80	15.50	16.11
Confusion	859,780	631	660,031.04	0.96	0.88	1.03
Anosmia or Loss of smell	854,945	694	654,936.74	1.06	0.98	1.14
Ageusia or Loss of taste	855,317	743	655,295.11	1.13	1.06	1.22
Depression	778,616	16,734	584,150.29	28.65	28.22	29.08
Anxiety Disorders	731,398	33,479	544,631.81	61.47	60.82	62.13
Post-traumatic Stress Disorder	853,155	2,725	654,053.70	4.17	4.01	4.33
Substance Use Disorders	832,648	8,159	636,323.16	12.82	12.55	13.10
Suicidal behavior and suicide ideation	855,841	2,116	656,490.14	3.22	3.09	3.36
Dizziness on standing (lightheadedness)	826,422	16,703	626,785.24	26.65	26.25	27.06
Pins-and-needles feelings	850,137	7,530	649,326.52	11.60	11.34	11.86
Dysautonomia	860,548	636	660,598.25	0.96	0.89	1.04
Digestive symptoms						
Abdominal pain	767,803	43,585	571,748.65	76.23	75.52	76.95
Diarrhea	821,876	13,925	624,387.61	22.30	21.93	22.68
Nausea	828,222	12,741	629,925.86	20.23	19.88	20.58
Constipation	827,680	14,729	629,034.52	23.42	23.04	23.80
Musculoskeletal and Skin						
Arthralgia or joint pain	768,961	48,336	568,584.30	85.01	84.26	85.77
Myalgia or muscle pain	837,447	7,975	638,210.34	12.50	12.23	12.77
Body aches	831,424	9,679	633,331.68	15.28	14.98	15.59
Rash	834,476	15,587	634,676.03	24.56	24.18	24.95
Alopecia	861,832	226	661,828.73	0.34	0.30	0.39
Hair loss	856,981	5,401	655,452.40	8.24	8.02	8.46
Endocrine symptoms						
Diabetes mellitus (Type I & II)	745,930	10,762	562,164.10	19.14	18.79	19.51
Diabetic ketoacidosis	859,092	620	659,501.51	0.94	0.87	1.02
Thyroiditis	856,329	1,770	656,839.83	2.69	2.57	2.82
Hypothyroidism	799,371	10,392	606,356.96	17.14	16.81	17.47
Hyperthyroidism	857,270	1,581	657,593.74	2.40	2.29	2.53
Menstrual/period issues	828,973	17,240	629,130.41	27.40	27.00	27.82
Hematologic symptoms						
DVT	853,896	2,339	654,482.61	3.57	3.43	3.72
Pulmonary embolism	852,259	1,694	653,460.49	2.59	2.47	2.72

Table 45. Incidence of Long COVID in the Source Cohort by Follow-up Intervals, 12/31/2020-07/20/2022 (Vaccine Period)

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Renal symptoms						
Acute kidney injury	825,738	7,818	630,016.32	12.41	12.14	12.69
Chronic kidney disease	806,174	12,264	611,052.97	20.07	19.72	20.43
Dialysis	852,178	2,321	653,052.97	3.55	3.41	3.70
			>=6 months			
Any below medical condition						
Any below medical condition	134,188	25,366	119,755.73	211.81	209.22	214.44
Post-COVID syndrome						
Post-COVID syndrome	559,102	2,450	540,558.08	4.53	4.36	4.72
General symptoms						
Fatigue	482,929	15,949	458,851.95	34.76	34.22	35.30
Intermittent fever	509,021	7,621	489,326.95	15.57	15.23	15.93
Post-exertional malaise	551,992	2,265	531,985.70	4.26	4.09	4.44
Multisystem inflammatory syndrome (MIS)	564,589	11	545,455.89	0.02	0.01	0.04
Respiratory symptoms						
Dyspnea or Shortness of breath	450,852	12,426	428,620.57	28.99	28.49	29.51
Cough	474,431	2,490	448,739.19	5.55	5.34	5.77
Nasal congestion	535,666	6,454	515,008.56	12.53	12.23	12.84
Lung function abnormalities	558,161	1,557	538,565.31	2.89	2.75	3.04
Hypoxemia	536,920	1,679	517,657.59	3.24	3.09	3.40
Cardiovascular and cerebrovascular symptoms						
Chest pain	487,848	17,033	464,684.02	36.66	36.11	37.21
Palpitations or Fast-beating or pounding heart	543,657	5,846	522,637.94	11.19	10.90	11.48
Myocarditis	564,436	55	545,301.40	0.10	0.08	0.13
Pericarditis	564,538	83	545,377.79	0.15	0.12	0.19
Myocardial infarction	556,056	1,664	536,427.42	3.10	2.96	3.26
Angina	554,689	2,339	534,558.25	4.38	4.20	4.56
Atrial fibrillation	540,968	2,540	521,050.75	4.87	4.69	5.07
Atrial flutter	561,080	662	541,728.80	1.22	1.13	1.32
Sinus tachycardia	534,320	4,672	514,224.95	9.09	8.83	9.35
Sinus bradycardia	552,109	2,815	532,009.64	5.29	5.10	5.49
Heart Failure	532,971	3,896	512,648.36	7.60	7.37	7.84
Stroke	557,491	1,638	537,882.87	3.05	2.90	3.20
TIA	561,580	914	542,123.96	1.69	1.58	1.80
Neurological symptoms						
Headache	561,496	93	541,352.59	0.17	0.14	0.21
Insomnia	540,922	5,081	520,030.05	9.77	9.51	10.04
Cognitive impairment	544,474	5,131	523,998.09	9.79	9.53	10.06
Confusion	563,047	302	543,829.02	0.56	0.50	0.62

Table 45. Incidence of Long COVID in the Source Cohort by Follow-up Intervals, 12/31/2020-07/20/2022 (Vaccine Period)

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Anosmia or Loss of smell	558,616	359	538,908.46	0.67	0.60	0.74
Ageusia or Loss of taste	558,899	345	539,234.57	0.64	0.58	0.71
Depression	496,630	7,068	474,387.30	14.90	14.56	15.25
Anxiety Disorders	462,569	15,614	440,438.77	35.45	34.90	36.01
Post-traumatic Stress Disorder	557,779	1,339	538,466.74	2.49	2.36	2.62
Substance Use Disorders	541,861	3,881	522,653.82	7.43	7.20	7.66
Suicidal behavior and suicide ideation	559,911	1,036	540,638.70	1.92	1.80	2.04
Dizziness on standing (lightheadedness)	534,394	8,762	512,812.71	17.09	16.73	17.45
Pins-and-needles feelings	553,715	3,970	533,422.19	7.44	7.22	7.68
Dysautonomia	563,541	311	544,307.67	0.57	0.51	0.64
Digestive symptoms						
Abdominal pain	486,076	21,764	462,485.96	47.06	46.44	47.69
Diarrhea	532,219	7,182	511,305.10	14.05	13.73	14.38
Nausea	536,920	6,439	516,181.11	12.47	12.17	12.78
Constipation	536,212	7,359	515,265.65	14.28	13.96	14.61
Musculoskeletal and Skin						
Arthralgia or joint pain	484,135	24,848	458,200.22	54.23	53.56	54.91
Myalgia or muscle pain	544,125	4,248	523,541.21	8.11	7.87	8.36
Body aches	540,089	5,220	519,476.33	10.05	9.78	10.33
Rash	541,082	7,947	520,105.84	15.28	14.95	15.62
Alopecia	564,593	104	545,432.75	0.19	0.16	0.23
Hair loss	558,097	1,405	538,674.37	2.61	2.48	2.75
Endocrine symptoms						
Diabetes mellitus (Type I & II)	478,708	5,155	457,989.35	11.26	10.95	11.57
Diabetic ketoacidosis	562,560	324	543,394.66	0.60	0.54	0.67
Thyroiditis	560,289	829	540,964.67	1.53	1.43	1.64
Hypothyroidism	516,823	4,528	496,052.24	9.13	8.87	9.40
Hyperthyroidism	560,907	776	541,580.49	1.43	1.34	1.54
Menstrual/period issues	536,167	8,697	514,901.80	16.89	16.54	17.25
Hematologic symptoms						
DVT	558,183	1,183	538,730.28	2.20	2.07	2.33
Pulmonary embolism	557,215	849	537,960.25	1.58	1.48	1.69
Renal symptoms						
Acute kidney injury	537,094	4,088	517,106.03	7.91	7.67	8.15
Chronic kidney disease	521,116	6,129	499,700.49	12.27	11.96	12.58
Dialysis	557,088	1,199	537,529.45	2.23	2.11	2.36

Table 46. Incidence of Long COVID in the Source Cohort by Follow-up Intervals, 12/15/2021-07/20/2022 (Omicron Period)

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
			Overall			
Any below medical condition						
Any below medical condition	294,139	111,510	42,669.56	2,613.34	2,598.05	2,628.72
Post-COVID syndrome						
Post-COVID syndrome	518,222	7,074	132,797.40	53.27	52.04	54.53
General symptoms						
Fatigue	494,300	30,320	119,855.30	252.97	250.14	255.84
Intermittent fever	506,720	32,195	123,522.69	260.64	257.81	263.50
Post-exertional malaise	515,535	5,339	132,436.77	40.31	39.25	41.41
Multisystem inflammatory syndrome (MIS)	518,532	94	134,670.44	0.70	0.57	0.85
Respiratory symptoms						
Dyspnea or Shortness of breath	494,997	39,148	117,030.44	334.51	331.21	337.84
Cough	508,221	452	130,470.67	3.46	3.16	3.80
Nasal congestion	508,552	14,459	127,899.75	113.05	111.22	114.91
Lung function abnormalities	516,055	2,604	133,264.73	19.54	18.80	20.31
Hypoxemia	516,248	9,415	131,326.76	71.69	70.26	73.15
Cardiovascular and cerebrovascular symptoms						
Chest pain	493,548	29,244	119,722.14	244.27	241.48	247.08
Palpitations or Fast-beating or pounding heart	510,239	7,076	130,379.34	54.27	53.02	55.55
Myocarditis	518,480	211	134,626.43	1.57	1.37	1.79
Pericarditis	518,407	149	134,610.34	1.11	0.94	1.30
Myocardial infarction	515,738	4,594	132,730.02	34.61	33.63	35.63
Angina	514,407	2,709	132,685.97	20.42	19.66	21.20
Atrial fibrillation	506,785	7,737	129,439.32	59.77	58.46	61.12
Atrial flutter	517,038	1,358	133,896.53	10.14	9.62	10.70
Sinus tachycardia	511,456	12,025	129,261.44	93.03	91.38	94.71
Sinus bradycardia	514,726	4,375	132,442.44	33.03	32.07	34.03
Heart Failure	504,355	11,164	127,712.18	87.42	85.81	89.05
Stroke	515,328	2,896	133,022.43	21.77	20.99	22.58
TIA	517,163	1,128	133,980.94	8.42	7.94	8.93
Neurological symptoms						
Headache	518,415	98	134,637.35	0.73	0.60	0.89
Insomnia	507,868	6,496	129,720.72	50.08	48.87	51.31
Cognitive impairment	510,994	9,032	130,396.82	69.27	67.85	70.71
Confusion	518,066	1,184	134,302.01	8.82	8.33	9.33
Anosmia or Loss of smell	518,240	705	134,350.94	5.25	4.87	5.65
Ageusia or Loss of taste	518,173	768	134,307.87	5.72	5.33	6.14
Depression	490,382	10,099	122,403.26	82.51	80.91	84.13

Table 46. Incidence of Long COVID in the Source Cohort by Follow-up Intervals, 12/15/2021-07/20/2022 (Omicron Period)

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Anxiety Disorders	468,411	25,773	112,208.21	229.69	226.90	232.51
Post-traumatic Stress Disorder	515,022	1,962	132,968.38	14.76	14.12	15.42
Substance Use Disorders	509,098	7,883	129,812.86	60.73	59.40	62.08
Suicidal behavior and suicide ideation	516,697	2,139	133,595.67	16.01	15.35	16.70
Dizziness on standing (lightheadedness)	507,198	10,750	128,462.10	83.68	82.12	85.28
Pins-and-needles feelings	514,192	3,318	132,519.68	25.04	24.20	25.90
Dysautonomia	517,901	456	134,369.33	3.39	3.10	3.72
Digestive symptoms						
Abdominal pain	484,311	26,041	117,745.21	221.16	218.49	223.87
Diarrhea	508,634	11,652	128,580.47	90.62	88.99	92.28
Nausea	509,926	9,788	129,443.71	75.62	74.13	77.13
Constipation	506,847	10,143	128,527.15	78.92	77.40	80.47
Musculoskeletal and Skin						
Arthralgia or joint pain	480,306	22,004	117,626.89	187.07	184.61	189.55
Myalgia or muscle pain	512,884	7,481	130,880.65	57.16	55.88	58.47
Body aches	512,639	10,303	130,210.60	79.13	77.61	80.67
Rash	507,776	8,241	129,589.43	63.59	62.24	64.98
Alopecia	518,365	104	134,621.74	0.77	0.64	0.94
Hair loss	516,725	1,823	133,725.36	13.63	13.02	14.27
Endocrine symptoms						
Diabetes mellitus (Type I & II)	475,016	16,402	116,718.87	140.53	138.39	142.69
Diabetic ketoacidosis	517,938	1,004	134,209.97	7.48	7.03	7.96
Thyroiditis	515,832	1,180	133,564.21	8.83	8.35	9.35
Hypothyroidism	493,238	10,565	124,436.18	84.90	83.30	86.54
Hyperthyroidism	516,560	1,054	133,793.07	7.88	7.42	8.37
Menstrual/period issues	504,223	8,024	128,208.69	62.59	61.23	63.97
Hematologic symptoms						
DVT	516,459	2,375	133,410.90	17.80	17.10	18.53
Pulmonary embolism	516,865	2,924	133,351.43	21.93	21.15	22.74
Renal symptoms						
Acute kidney injury	511,455	13,768	129,253.52	106.52	104.76	108.31
Chronic kidney disease	498,506	13,001	125,235.85	103.81	102.04	105.61
Dialysis	515,818	3,044	133,021.88	22.88	22.09	23.71
			>=4 Weeks			
Any below medical condition						
Any below medical condition	133,406	31,606	39,610.01	797.93	789.18	806.78
Post-COVID syndrome						

Table 46. Incidence of Long COVID in the Source Cohort by Follow-up Intervals, 12/15/2021-07/20/2022 (Omicron Period)

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Post-COVID syndrome	353,343	2,865	128,159.47	22.35	21.55	23.19
General symptoms						
Fatigue	324,332	11,057	115,366.38	95.84	94.07	97.65
Intermittent fever	330,548	5,251	119,115.23	44.08	42.91	45.29
Post-exertional malaise	352,002	1,738	127,883.98	13.59	12.97	14.25
Multisystem inflammatory syndrome (MIS)	356,883	17	130,129.68	0.13	0.08	0.21
Respiratory symptoms						
Dyspnea or Shortness of breath	317,536	9,946	112,560.48	88.36	86.64	90.12
Cough	347,387	103	125,973.11	0.82	0.67	0.99
Nasal congestion	341,180	3,327	123,412.48	26.96	26.06	27.89
Lung function abnormalities	353,963	1,230	128,728.81	9.55	9.04	10.10
Hypoxemia	349,468	1,388	126,807.67	10.95	10.39	11.54
Cardiovascular and cerebrovascular symptoms						
Chest pain	324,371	11,217	115,248.19	97.33	95.54	99.15
Palpitations or Fast-beating or pounding heart	348,040	4,171	125,838.57	33.15	32.16	34.17
Myocarditis	356,776	49	130,085.88	0.38	0.29	0.50
Pericarditis	356,760	56	130,069.46	0.43	0.33	0.56
Myocardial infarction	352,489	1,037	128,220.11	8.09	7.61	8.60
Angina	352,719	1,533	128,155.52	11.96	11.38	12.58
Atrial fibrillation	344,382	1,954	124,999.98	15.63	14.95	16.34
Atrial flutter	355,174	471	129,365.48	3.64	3.33	3.99
Sinus tachycardia	345,275	3,610	124,739.30	28.94	28.01	29.90
Sinus bradycardia	352,105	1,692	127,917.79	13.23	12.61	13.87
Heart Failure	341,002	2,969	123,304.59	24.08	23.23	24.96
Stroke	353,245	1,035	128,502.79	8.05	7.58	8.56
TIA	355,447	513	129,446.22	3.96	3.64	4.32
Neurological symptoms						
Headache	356,812	52	130,097.17	0.40	0.31	0.53
Insomnia	346,393	3,796	125,201.03	30.32	29.37	31.30
Cognitive impairment	347,601	3,546	125,895.38	28.17	27.25	29.11
Confusion	356,040	262	129,769.14	2.02	1.79	2.28
Anosmia or Loss of smell	356,185	90	129,812.04	0.69	0.56	0.85
Ageusia or Loss of taste	356,109	134	129,768.67	1.03	0.87	1.22
Depression	330,295	5,982	117,933.02	50.72	49.45	52.03
Anxiety Disorders	307,588	13,563	107,819.80	125.79	123.69	127.93
Post-traumatic Stress Disorder	353,290	1,033	128,432.91	8.04	7.57	8.55
Substance Use Disorders	346,404	3,161	125,331.08	25.22	24.36	26.12

Table 46. Incidence of Long COVID in the Source Cohort by Follow-up Intervals, 12/15/2021-07/20/2022 (Omicron Period)

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Suicidal behavior and suicide ideation	354,644	778	129,069.19	6.03	5.62	6.47
Dizziness on standing (lightheadedness)	344,211	5,682	123,940.38	45.84	44.67	47.05
Pins-and-needles feelings	352,717	2,344	127,986.76	18.31	17.59	19.07
Dysautonomia	356,286	252	129,830.11	1.94	1.72	2.20
Digestive symptoms						
Abdominal pain	322,137	15,881	113,290.12	140.18	138.02	142.38
Diarrhea	344,170	4,858	124,068.82	39.16	38.07	40.27
Nausea	346,096	4,360	124,917.99	34.90	33.88	35.95
Constipation	344,222	5,628	124,007.66	45.38	44.21	46.59
Musculoskeletal and Skin						
Arthralgia or joint pain	321,923	16,284	113,176.38	143.88	141.69	146.11
Myalgia or muscle pain	348,788	2,448	126,359.94	19.37	18.62	20.16
Body aches	347,425	2,994	125,707.46	23.82	22.98	24.69
Rash	346,443	5,722	125,060.93	45.75	44.58	46.96
Alopecia	356,771	72	130,080.38	0.55	0.44	0.70
Hair loss	355,215	1,449	129,186.26	11.22	10.65	11.81
Endocrine symptoms						
Diabetes mellitus (Type I & II)	314,435	4,270	112,464.09	37.97	36.85	39.12
Diabetic ketoacidosis	355,920	186	129,676.99	1.43	1.24	1.66
Thyroiditis	354,382	736	129,028.64	5.70	5.31	6.13
Hypothyroidism	332,830	4,391	120,015.08	36.59	35.52	37.69
Hyperthyroidism	354,961	582	129,256.63	4.50	4.15	4.88
Menstrual/period issues	343,765	6,117	123,689.80	49.45	48.23	50.71
Hematologic symptoms						
DVT	354,239	899	128,873.31	6.98	6.53	7.45
Pulmonary embolism	354,060	770	128,814.21	5.98	5.57	6.42
Renal symptoms						
Acute kidney injury	344,570	2,626	124,825.14	21.04	20.25	21.86
Chronic kidney disease	335,494	4,381	120,831.53	36.26	35.20	37.35
Dialysis	353,392	927	128,489.74	7.21	6.77	7.69
			>=12 Weeks			
Any below medical condition						
Any below medical condition	71,749	15,210	31,326.87	485.53	477.87	493.30
Post-COVID syndrome						
Post-COVID syndrome	240,287	832	112,519.47	7.39	6.91	7.91
General symptoms						
Fatigue	216,565	5,666	100,464.96	56.40	54.95	57.89
Intermittent fever	224,164	2,914	104,361.51	27.92	26.93	28.96
Post-exertional malaise	240,164	719	112,392.39	6.40	5.95	6.88

Table 46. Incidence of Long COVID in the Source Cohort by Follow-up Intervals, 12/15/2021-07/20/2022 (Omicron Period)

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Multisystem inflammatory syndrome (MIS)	244,302	3	114,523.96	0.03	0.01	0.08
Respiratory symptoms						
Dyspnea or Shortness of breath	211,511	4,464	97,926.51	45.59	44.27	46.94
Cough	236,151	36	110,560.33	0.33	0.24	0.45
Nasal congestion	231,594	1,750	108,232.23	16.17	15.43	16.95
Lung function abnormalities	241,655	550	113,169.73	4.86	4.47	5.28
Hypoxemia	238,458	549	111,428.84	4.93	4.53	5.36
Cardiovascular and cerebrovascular symptoms						
Chest pain	216,254	5,620	100,288.24	56.04	54.59	57.52
Palpitations or Fast-beating or pounding heart	236,079	1,957	110,338.08	17.74	16.97	18.54
Myocarditis	244,199	13	114,479.71	0.11	0.07	0.20
Pericarditis	244,195	27	114,465.44	0.24	0.16	0.34
Myocardial infarction	240,818	510	112,747.00	4.52	4.15	4.93
Angina	240,625	762	112,624.40	6.77	6.30	7.26
Atrial fibrillation	234,841	812	109,840.19	7.39	6.90	7.92
Atrial flutter	242,908	210	113,806.46	1.85	1.61	2.11
Sinus tachycardia	234,459	1,686	109,398.24	15.41	14.69	16.17
Sinus bradycardia	240,301	880	112,423.84	7.83	7.33	8.36
Heart Failure	231,919	1,349	108,213.47	12.47	11.82	13.15
Stroke	241,327	493	112,994.32	4.36	3.99	4.77
TIA	243,027	239	113,864.66	2.10	1.85	2.38
Neurological symptoms						
Headache	244,227	28	114,489.75	0.24	0.17	0.35
Insomnia	234,771	1,806	109,747.95	16.46	15.71	17.23
Cognitive impairment	236,492	1,719	110,507.02	15.56	14.84	16.31
Confusion	243,674	114	114,193.06	1.00	0.83	1.20
Anosmia or Loss of smell	243,753	50	114,226.13	0.44	0.33	0.58
Ageusia or Loss of taste	243,654	65	114,178.70	0.57	0.45	0.73
Depression	220,868	2,927	102,801.79	28.47	27.46	29.52
Anxiety Disorders	201,458	6,545	93,197.77	70.23	68.55	71.95
Post-traumatic Stress Disorder	241,086	526	112,883.60	4.66	4.28	5.08
Substance Use Disorders	235,568	1,699	109,972.65	15.45	14.73	16.20
Suicidal behavior and suicide ideation	242,361	394	113,504.91	3.47	3.15	3.83
Dizziness on standing (lightheadedness)	232,714	3,003	108,496.74	27.68	26.71	28.69
Pins-and-needles feelings	240,332	1,297	112,406.84	11.54	10.93	12.18
Dysautonomia	243,751	111	114,230.99	0.97	0.81	1.17

Table 46. Incidence of Long COVID in the Source Cohort by Follow-up Intervals, 12/15/2021-07/20/2022 (Omicron Period)

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Digestive symptoms						
Abdominal pain	212,582	8,405	98,119.45	85.66	83.85	87.51
Diarrhea	232,969	2,535	108,655.33	23.33	22.44	24.26
Nausea	234,459	2,333	109,448.41	21.32	20.47	22.20
Constipation	232,744	2,769	108,571.94	25.50	24.57	26.47
Musculoskeletal and Skin						
Arthralgia or joint pain	212,028	8,636	97,972.41	88.15	86.31	90.03
Myalgia or muscle pain	237,344	1,337	110,911.28	12.05	11.43	12.72
Body aches	236,246	1,590	110,293.88	14.42	13.73	15.14
Rash	234,590	3,205	109,568.72	29.25	28.26	30.28
Alopecia	244,196	37	114,474.72	0.32	0.23	0.45
Hair loss	242,587	912	113,572.13	8.03	7.53	8.57
Endocrine symptoms						
Diabetes mellitus (Type I & II)	210,960	1,923	98,185.84	19.59	18.73	20.48
Diabetic ketoacidosis	243,497	98	114,093.32	0.86	0.71	1.05
Thyroiditis	242,146	336	113,476.13	2.96	2.66	3.30
Hypothyroidism	224,970	2,056	105,114.49	19.56	18.73	20.42
Hyperthyroidism	242,644	309	113,691.17	2.72	2.43	3.04
Menstrual/period issues	231,996	3,331	108,198.12	30.79	29.76	31.85
Hematologic symptoms						
DVT	241,990	386	113,318.87	3.41	3.08	3.76
Pulmonary embolism	241,929	292	113,280.71	2.58	2.30	2.89
Renal symptoms						
Acute kidney injury	234,958	1,328	109,639.00	12.11	11.48	12.78
Chronic kidney disease	227,247	2,123	105,865.36	20.05	19.22	20.93
Dialysis	241,392	387	112,971.03	3.43	3.10	3.79
			>=6 months			
Any below medical condition						
Any below medical condition	14,413	841	10,109.12	83.19	77.76	89.01
Post-COVID syndrome						
Post-COVID syndrome	66,734	39	44,906.00	0.87	0.64	1.19
General symptoms						
Fatigue	57,858	347	38,983.06	8.90	8.01	9.89
Intermittent fever	61,287	150	40,997.37	3.66	3.12	4.29
Post-exertional malaise	66,558	37	44,737.21	0.83	0.60	1.14
Multisystem inflammatory syndrome (MIS)	68,114	0	45,820.75	0.00	0.00	3,688.88
Respiratory symptoms						
Dyspnea or Shortness of breath	56,368	218	37,800.99	5.77	5.05	6.59
Cough	65,510	1	44,092.30	0.02	0.00	0.16
Nasal congestion	63,839	98	42,949.73	2.28	1.87	2.78

Table 46. Incidence of Long COVID in the Source Cohort by Follow-up Intervals, 12/15/2021-07/20/2022 (Omicron Period)

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Lung function abnormalities	67,086	27	45,141.72	0.60	0.41	0.87
Hypoxemia	65,850	26	44,156.02	0.59	0.40	0.87
Cardiovascular and cerebrovascular symptoms						
Chest pain	57,829	340	38,905.54	8.74	7.86	9.72
Palpitations or Fast-beating or pounding heart	64,900	92	43,733.00	2.10	1.72	2.58
Myocarditis	68,081	0	45,801.61	0.00	0.00	3,688.88
Pericarditis	68,055	1	45,782.86	0.02	0.00	0.16
Myocardial infarction	66,812	24	44,916.49	0.53	0.36	0.80
Angina	66,689	48	44,874.89	1.07	0.81	1.42
Atrial fibrillation	64,972	21	43,673.69	0.48	0.31	0.74
Atrial flutter	67,600	6	45,463.97	0.13	0.06	0.29
Sinus tachycardia	64,213	81	43,139.16	1.88	1.51	2.33
Sinus bradycardia	66,432	37	44,684.50	0.83	0.60	1.14
Heart Failure	63,689	54	42,732.64	1.26	0.97	1.65
Stroke	66,959	18	45,036.79	0.40	0.25	0.63
TIA	67,585	17	45,470.21	0.37	0.23	0.60
Neurological symptoms						
Headache	68,094	2	45,810.09	0.04	0.01	0.18
Insomnia	64,774	101	43,641.53	2.31	1.90	2.81
Cognitive impairment	65,108	96	43,787.98	2.19	1.80	2.68
Confusion	67,852	4	45,632.44	0.09	0.03	0.23
Anosmia or Loss of smell	67,868	1	45,646.07	0.02	0.00	0.16
Ageusia or Loss of taste	67,834	1	45,627.21	0.02	0.00	0.16
Depression	59,775	171	40,375.30	4.24	3.65	4.92
Anxiety Disorders	53,078	415	35,993.99	11.53	10.47	12.69
Post-traumatic Stress Disorder	66,836	31	44,993.95	0.69	0.49	0.98
Substance Use Disorders	64,701	103	43,456.14	2.37	1.95	2.88
Suicidal behavior and suicide ideation	67,388	17	45,299.15	0.38	0.23	0.60
Dizziness on standing (lightheadedness)	63,311	172	42,669.20	4.03	3.47	4.68
Pins-and-needles feelings	66,258	80	44,624.56	1.79	1.44	2.23
Dysautonomia	67,872	4	45,660.80	0.09	0.03	0.23
Digestive symptoms						
Abdominal pain	55,478	522	37,475.13	13.93	12.78	15.18
Diarrhea	63,756	141	42,878.62	3.29	2.79	3.88
Nausea	64,358	145	43,310.74	3.35	2.85	3.94
Constipation	63,602	145	42,840.40	3.38	2.88	3.98
Musculoskeletal and Skin						

Table 46. Incidence of Long COVID in the Source Cohort by Follow-up Intervals, 12/15/2021-07/20/2022 (Omicron Period)

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Arthralgia or joint pain	55,154	553	37,485.56	14.75	13.57	16.04
Myalgia or muscle pain	65,204	87	43,902.83	1.98	1.61	2.45
Body aches	64,890	123	43,585.78	2.82	2.37	3.37
Rash	64,180	218	43,318.06	5.03	4.41	5.75
Alopecia	68,077	2	45,799.97	0.04	0.01	0.18
Hair loss	67,230	26	45,262.43	0.57	0.39	0.84
Endocrine symptoms						
Diabetes mellitus (Type I & II)	57,197	94	38,571.42	2.44	1.99	2.98
Diabetic ketoacidosis	67,782	6	45,584.94	0.13	0.06	0.29
Thyroiditis	67,352	24	45,349.63	0.53	0.36	0.79
Hypothyroidism	61,828	131	41,723.71	3.14	2.65	3.73
Hyperthyroidism	67,468	24	45,408.97	0.53	0.35	0.79
Menstrual/period issues	63,084	237	42,594.51	5.56	4.90	6.32
Hematologic symptoms						
DVT	67,165	21	45,168.33	0.46	0.30	0.71
Pulmonary embolism	67,193	24	45,166.92	0.53	0.36	0.79
Renal symptoms						
Acute kidney injury	64,593	74	43,291.73	1.71	1.36	2.15
Chronic kidney disease	61,875	122	41,582.45	2.93	2.46	3.50
Dialysis	66,917	24	44,969.21	0.53	0.36	0.80

Over longer periods of follow-up, particularly at the 12 week and 6 month marks, Paxlovid Users (Table 47, Table 48, Table 49) had substantially lower incidence rates of any symptom and post-COVID syndrome compared to other patients even though their overall incidence rates of these conditions began at similar levels. At 6 months, incidences rates of 0 are observed for any symptom and post-COVID syndrome in both Hospitalized and Non-Hospitalized Paxlovid users (Table 48, Table 49).

Table 47. Incidence of Long COVID among Paxlovid Users by Follow-up Intervals

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
			Overall			
Any below medical condition						
Any below medical condition	7,273	1,780	555.08	3,206.74	3,061.18	3,359.23
Post-COVID syndrome						
Post-COVID syndrome	16,546	210	1,939.21	108.29	94.59	123.98
General symptoms						
Fatigue	15,658	526	1,770.76	297.05	272.72	323.55

Table 47. Incidence of Long COVID among Paxlovid Users by Follow-up Intervals

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Intermittent fever	16,418	436	1,891.92	230.45	209.81	253.13
Post-exertional malaise	16,482	74	1,939.12	38.16	30.39	47.93
Multisystem inflammatory syndrome (MIS)	16,583	1	1,965.84	0.51	0.07	3.61
Respiratory symptoms						
Dyspnea or Shortness of breath	15,708	578	1,747.59	330.74	304.85	358.84
Cough	16,529	9	1,947.47	4.62	2.41	8.88
Nasal congestion	16,332	265	1,903.35	139.23	123.44	157.04
Lung function abnormalities	16,499	34	1,944.93	17.48	12.49	24.47
Hypoxemia	16,520	45	1,945.67	23.13	17.27	30.98
Cardiovascular and cerebrovascular symptoms						
Chest pain	15,716	470	1,783.57	263.52	240.74	288.45
Palpitations or Fast-beating or pounding heart	16,160	151	1,889.75	79.90	68.12	93.72
Myocarditis	16,579	2	1,965.40	1.02	0.26	4.07
Pericarditis	16,580	1	1,965.58	0.51	0.07	3.61
Myocardial infarction	16,531	29	1,952.21	14.85	10.32	21.38
Angina	16,388	56	1,924.12	29.10	22.40	37.82
Atrial fibrillation	16,108	105	1,881.00	55.82	46.10	67.59
Atrial flutter	16,542	14	1,957.69	7.15	4.24	12.08
Sinus tachycardia	16,423	108	1,926.62	56.06	46.42	67.69
Sinus bradycardia	16,425	66	1,935.79	34.09	26.79	43.40
Heart Failure	16,153	111	1,885.07	58.88	48.89	70.92
Stroke	16,473	35	1,943.55	18.01	12.93	25.08
TIA	16,522	24	1,952.72	12.29	8.24	18.34
Neurological symptoms						
Headache	16,582	2	1,965.48	1.02	0.25	4.07
Insomnia	15,973	115	1,870.88	61.47	51.20	73.80
Cognitive impairment	16,288	102	1,907.46	53.47	44.04	64.93
Confusion	16,576	5	1,963.10	2.55	1.06	6.12
Anosmia or Loss of smell	16,575	5	1,964.54	2.55	1.06	6.12
Ageusia or Loss of taste	16,573	5	1,963.65	2.55	1.06	6.12
Depression	15,403	203	1,775.85	114.31	99.62	131.17
Anxiety Disorders	14,439	452	1,624.21	278.29	253.78	305.16
Post-traumatic Stress Disorder	16,473	22	1,945.32	11.31	7.45	17.18
Substance Use Disorders	16,356	60	1,929.79	31.09	24.14	40.04
Suicidal behavior and suicide ideation	16,572	6	1,964.13	3.05	1.37	6.80
Dizziness on standing (lightheadedness)	16,122	175	1,875.36	93.32	80.47	108.22

Table 47. Incidence of Long COVID among Paxlovid Users by Follow-up Intervals

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Pins-and-needles feelings	16,399	69	1,935.07	35.66	28.16	45.15
Dysautonomia	16,549	4	1,960.80	2.04	0.77	5.44
Digestive symptoms						
Abdominal pain	15,561	330	1,778.29	185.57	166.59	206.71
Diarrhea	16,298	166	1,901.12	87.32	75.00	101.66
Nausea	16,335	161	1,910.01	84.29	72.23	98.37
Constipation	16,255	104	1,905.17	54.59	45.04	66.16
Musculoskeletal and Skin						
Arthralgia or joint pain	14,796	504	1,667.27	302.29	277.02	329.87
Myalgia or muscle pain	16,333	125	1,910.96	65.41	54.89	77.95
Body aches	16,450	140	1,928.98	72.58	61.50	85.65
Rash	16,203	134	1,902.36	70.44	59.47	83.43
Alopecia	16,573	0	1,964.82	0.00	0.00	3,688.88
Hair loss	16,475	24	1,948.53	12.32	8.26	18.38
Endocrine symptoms						
Diabetes mellitus (Type I & II)	14,160	265	1,581.63	167.55	148.54	188.99
Diabetic ketoacidosis	16,574	1	1,963.62	0.51	0.07	3.62
Thyroiditis	16,403	27	1,934.46	13.96	9.57	20.35
Hypothyroidism	15,044	273	1,721.52	158.58	140.84	178.55
Hyperthyroidism	16,488	18	1,952.13	9.22	5.81	14.64
Menstrual/period issues	16,006	134	1,878.27	71.34	60.23	84.50
Hematologic symptoms						
DVT	16,506	13	1,951.38	6.66	3.87	11.47
Pulmonary embolism	16,527	23	1,953.48	11.77	7.82	17.72
Renal symptoms						
Acute kidney injury	16,486	72	1,939.28	37.13	29.47	46.77
Chronic kidney disease	15,851	178	1,825.16	97.53	84.20	112.96
Dialysis	16,575	10	1,961.88	5.10	2.74	9.47
			>=4 Weeks			
Any below medical condition						
Any below medical condition	2,789	616	470.34	1,309.68	1,210.24	1,417.30
Post-COVID syndrome						
Post-COVID syndrome	9,329	66	1,770.27	37.28	29.29	47.46
General symptoms						
Fatigue	8,582	182	1,609.66	113.07	97.78	130.75
Intermittent fever	9,154	34	1,730.02	19.65	14.04	27.51
Post-exertional malaise	9,353	35	1,774.05	19.73	14.17	27.48
Multisystem inflammatory syndrome (MIS)	9,462	1	1,800.75	0.56	0.08	3.94
Respiratory symptoms						
Dyspnea or Shortness of breath	8,540	179	1,584.80	112.95	97.56	130.77

Table 47. Incidence of Long COVID among Paxlovid Users by Follow-up Intervals

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Cough	9,408	0	1,782.51	0.00	0.00	3,688.88
Nasal congestion	9,174	35	1,740.48	20.11	14.44	28.01
Lung function abnormalities	9,384	18	1,779.88	10.11	6.37	16.05
Hypoxemia	9,391	13	1,780.78	7.30	4.24	12.57
Cardiovascular and cerebrovascular symptoms						
Chest pain	8,668	171	1,622.23	105.41	90.74	122.46
Palpitations or Fast-beating or pounding heart	9,135	82	1,727.09	47.48	38.24	58.95
Myocarditis	9,459	2	1,800.35	1.11	0.28	4.44
Pericarditis	9,460	1	1,800.51	0.56	0.08	3.94
Myocardial infarction	9,409	11	1,787.32	6.15	3.41	11.11
Angina	9,284	27	1,759.53	15.35	10.52	22.38
Atrial fibrillation	9,084	53	1,718.71	30.84	23.56	40.36
Atrial flutter	9,426	6	1,792.87	3.35	1.50	7.45
Sinus tachycardia	9,287	28	1,762.14	15.89	10.97	23.01
Sinus bradycardia	9,324	32	1,771.61	18.06	12.77	25.54
Heart Failure	9,104	60	1,722.63	34.83	27.04	44.86
Stroke	9,372	20	1,779.27	11.24	7.25	17.42
TIA	9,405	10	1,787.87	5.59	3.01	10.40
Neurological symptoms						
Headache	9,460	0	1,800.39	0.00	0.00	3,688.88
Insomnia	9,022	59	1,710.85	34.49	26.72	44.51
Cognitive impairment	9,197	52	1,742.96	29.83	22.73	39.15
Confusion	9,454	4	1,797.95	2.22	0.84	5.93
Anosmia or Loss of smell	9,456	1	1,799.56	0.56	0.08	3.95
Ageusia or Loss of taste	9,452	3	1,798.61	1.67	0.54	5.17
Depression	8,582	86	1,621.35	53.04	42.94	65.53
Anxiety Disorders	7,846	233	1,473.74	158.10	139.05	179.76
Post-traumatic Stress Disorder	9,372	10	1,781.10	5.61	3.02	10.44
Substance Use Disorders	9,285	23	1,766.24	13.02	8.65	19.60
Suicidal behavior and suicide ideation	9,452	2	1,798.94	1.11	0.28	4.45
Dizziness on standing (lightheadedness)	9,079	92	1,713.32	53.70	43.77	65.87
Pins-and-needles feelings	9,316	44	1,770.64	24.85	18.49	33.39
Dysautonomia	9,435	2	1,795.93	1.11	0.28	4.45
Digestive symptoms						
Abdominal pain	8,642	179	1,618.35	110.61	95.53	128.06
Diarrhea	9,182	53	1,737.22	30.51	23.31	39.93
Nausea	9,208	46	1,745.94	26.35	19.74	35.18
Constipation	9,199	57	1,742.23	32.72	25.24	42.41
Musculoskeletal and Skin						
Arthralgia or joint pain	8,092	315	1,513.48	208.13	186.37	232.43

Table 47. Incidence of Long COVID among Paxlovid Users by Follow-up Intervals

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Myalgia or muscle pain	9,214	40	1,747.37	22.89	16.79	31.21
Body aches	9,293	24	1,764.60	13.60	9.12	20.29
Rash	9,147	71	1,738.46	40.84	32.37	51.54
Alopecia	9,456	0	1,799.88	0.00	0.00	3,688.88
Hair loss	9,381	13	1,784.16	7.29	4.23	12.55
Endocrine symptoms						
Diabetes mellitus (Type I & II)	7,685	110	1,438.16	76.49	63.45	92.20
Diabetic ketoacidosis	9,453	1	1,798.53	0.56	0.08	3.95
Thyroiditis	9,322	17	1,770.70	9.60	5.97	15.44
Hypothyroidism	8,330	127	1,568.82	80.95	68.03	96.33
Hyperthyroidism	9,393	9	1,787.71	5.03	2.62	9.68
Menstrual/period issues	9,051	83	1,718.11	48.31	38.96	59.90
Hematologic symptoms						
DVT	9,398	7	1,786.68	3.92	1.87	8.22
Pulmonary embolism	9,406	11	1,788.44	6.15	3.41	11.11
Renal symptoms						
Acute kidney injury	9,354	26	1,774.22	14.65	9.98	21.52
Chronic kidney disease	8,858	89	1,663.61	53.50	43.46	65.85
Dialysis	9,452	7	1,796.70	3.90	1.86	8.17
			>=12 Weeks			
Any below medical condition						
Any below medical condition	400	96	148.48	646.53	529.32	789.71
Post-COVID syndrome						
Post-COVID syndrome	1,743	6	696.39	8.62	3.87	19.18
General symptoms						
Fatigue	1,560	33	618.52	53.35	37.93	75.05
Intermittent fever	1,686	9	671.82	13.40	6.97	25.75
Post-exertional malaise	1,745	5	696.29	7.18	2.99	17.25
Multisystem inflammatory syndrome (MIS)	1,779	0	711.40	0.00	0.00	3,688.88
Respiratory symptoms						
Dyspnea or Shortness of breath	1,506	31	592.79	52.29	36.78	74.36
Cough	1,745	0	696.06	0.00	0.00	3,688.88
Nasal congestion	1,715	11	684.43	16.07	8.90	29.02
Lung function abnormalities	1,752	5	698.18	7.16	2.98	17.21
Hypoxemia	1,749	0	697.91	0.00	0.00	3,688.88
Cardiovascular and cerebrovascular symptoms						
Chest pain	1,562	23	618.30	37.20	24.72	55.98
Palpitations or Fast-beating or pounding heart	1,694	16	674.25	23.73	14.54	38.74
Myocarditis	1,779	0	711.40	0.00	0.00	3,688.88

Table 47. Incidence of Long COVID among Paxlovid Users by Follow-up Intervals

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Pericarditis	1,779	0	711.40	0.00	0.00	3,688.88
Myocardial infarction	1,761	1	703.53	1.42	0.20	10.09
Angina	1,727	6	687.98	8.72	3.92	19.41
Atrial fibrillation	1,682	7	670.87	10.43	4.97	21.89
Atrial flutter	1,765	1	706.33	1.42	0.20	10.05
Sinus tachycardia	1,740	6	693.39	8.65	3.89	19.26
Sinus bradycardia	1,744	9	697.30	12.91	6.72	24.81
Heart Failure	1,679	11	669.91	16.42	9.09	29.65
Stroke	1,752	5	699.40	7.15	2.98	17.18
TIA	1,763	2	704.77	2.84	0.71	11.35
Neurological symptoms						
Headache	1,778	0	711.15	0.00	0.00	3,688.88
Insomnia	1,682	11	669.75	16.42	9.10	29.66
Cognitive impairment	1,713	9	682.63	13.18	6.86	25.34
Confusion	1,775	2	709.17	2.82	0.71	11.28
Anosmia or Loss of smell	1,778	0	710.93	0.00	0.00	3,688.88
Ageusia or Loss of taste	1,776	1	710.24	1.41	0.20	10.00
Depression	1,593	10	633.48	15.79	8.49	29.34
Anxiety Disorders	1,437	32	571.03	56.04	39.63	79.24
Post-traumatic Stress Disorder	1,757	3	701.90	4.27	1.38	13.25
Substance Use Disorders	1,750	2	697.53	2.87	0.72	11.47
Suicidal behavior and suicide ideation	1,777	1	710.63	1.41	0.20	9.99
Dizziness on standing (lightheadedness)	1,676	17	666.13	25.52	15.87	41.05
Pins-and-needles feelings	1,745	6	697.29	8.60	3.87	19.15
Dysautonomia	1,774	0	709.69	0.00	0.00	3,688.88
Digestive symptoms						
Abdominal pain	1,568	32	619.90	51.62	36.51	73.00
Diarrhea	1,698	12	677.04	17.72	10.07	31.21
Nausea	1,712	10	684.27	14.61	7.86	27.16
Constipation	1,718	13	682.10	19.06	11.07	32.82
Musculoskeletal and Skin						
Arthralgia or joint pain	1,466	57	581.66	98.00	75.59	127.04
Myalgia or muscle pain	1,720	9	686.54	13.11	6.82	25.20
Body aches	1,738	5	694.49	7.20	3.00	17.30
Rash	1,719	15	686.30	21.86	13.18	36.25
Alopecia	1,779	0	711.40	0.00	0.00	3,688.88
Hair loss	1,762	2	703.87	2.84	0.71	11.36
Endocrine symptoms						
Diabetes mellitus (Type I & II)	1,379	28	544.88	51.39	35.48	74.42
Diabetic ketoacidosis	1,777	0	710.13	0.00	0.00	3,688.88

Table 47. Incidence of Long COVID among Paxlovid Users by Follow-up Intervals

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Thyroiditis	1,747	5	696.97	7.17	2.99	17.24
Hypothyroidism	1,542	23	613.56	37.49	24.91	56.41
Hyperthyroidism	1,769	1	707.51	1.41	0.20	10.03
Menstrual/period issues	1,705	15	678.34	22.11	13.33	36.68
Hematologic symptoms						
DVT	1,760	1	703.93	1.42	0.20	10.09
Pulmonary embolism	1,765	2	705.90	2.83	0.71	11.33
Renal symptoms						
Acute kidney injury	1,747	9	695.67	12.94	6.73	24.86
Chronic kidney disease	1,609	18	638.28	28.20	17.77	44.76
Dialysis	1,772	2	707.69	2.83	0.71	11.30
			>=6 months			
Any below medical condition						
Any below medical condition	46	0	28.21	0.00	0.00	3,688.88
Post-COVID syndrome						
Post-COVID syndrome	379	0	226.58	0.00	0.00	3,688.88
General symptoms						
Fatigue	323	0	193.48	0.00	0.00	3,688.88
Intermittent fever	363	1	217.00	4.61	0.65	32.72
Post-exertional malaise	377	0	225.33	0.00	0.00	3,688.88
Multisystem inflammatory syndrome (MIS)	387	0	231.31	0.00	0.00	3,688.88
Respiratory symptoms						
Dyspnea or Shortness of breath	303	1	181.56	5.51	0.78	39.10
Cough	378	0	225.71	0.00	0.00	3,688.88
Nasal congestion	370	0	221.69	0.00	0.00	3,688.88
Lung function abnormalities	375	0	224.11	0.00	0.00	3,688.88
Hypoxemia	375	0	224.28	0.00	0.00	3,688.88
Cardiovascular and cerebrovascular symptoms						
Chest pain	336	1	200.37	4.99	0.70	35.43
Palpitations or Fast-beating or pounding heart	362	0	216.54	0.00	0.00	3,688.88
Myocarditis	387	0	231.31	0.00	0.00	3,688.88
Pericarditis	387	0	231.31	0.00	0.00	3,688.88
Myocardial infarction	382	0	228.35	0.00	0.00	3,688.88
Angina	371	0	221.23	0.00	0.00	3,688.88
Atrial fibrillation	353	0	211.28	0.00	0.00	3,688.88
Atrial flutter	384	0	229.55	0.00	0.00	3,688.88
Sinus tachycardia	375	0	223.74	0.00	0.00	3,688.88
Sinus bradycardia	380	0	227.38	0.00	0.00	3,688.88
Heart Failure	361	0	216.22	0.00	0.00	3,688.88

Table 47. Incidence of Long COVID among Paxlovid Users by Follow-up Intervals

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Stroke	378	0	226.00	0.00	0.00	3,688.88
TIA	382	0	228.26	0.00	0.00	3,688.88
Neurological symptoms						
Headache	387	0	231.31	0.00	0.00	3,688.88
Insomnia	360	0	215.25	0.00	0.00	3,688.88
Cognitive impairment	366	0	219.05	0.00	0.00	3,688.88
Confusion	385	0	230.08	0.00	0.00	3,688.88
Anosmia or Loss of smell	387	0	231.31	0.00	0.00	3,688.88
Ageusia or Loss of taste	387	0	231.31	0.00	0.00	3,688.88
Depression	341	0	203.08	0.00	0.00	3,688.88
Anxiety Disorders	301	0	178.75	0.00	0.00	3,688.88
Post-traumatic Stress Disorder	379	0	226.84	0.00	0.00	3,688.88
Substance Use Disorders	375	0	223.86	0.00	0.00	3,688.88
Suicidal behavior and suicide ideation	387	0	231.31	0.00	0.00	3,688.88
Dizziness on standing (lightheadedness)	351	0	210.56	0.00	0.00	3,688.88
Pins-and-needles feelings	375	1	224.17	4.46	0.63	31.67
Dysautonomia	387	0	231.31	0.00	0.00	3,688.88
Digestive symptoms						
Abdominal pain	315	0	189.12	0.00	0.00	3,688.88
Diarrhea	369	0	220.39	0.00	0.00	3,688.88
Nausea	375	0	224.21	0.00	0.00	3,688.88
Constipation	364	0	216.37	0.00	0.00	3,688.88
Musculoskeletal and Skin						
Arthralgia or joint pain	312	0	186.70	0.00	0.00	3,688.88
Myalgia or muscle pain	372	0	222.77	0.00	0.00	3,688.88
Body aches	377	1	225.13	4.44	0.63	31.53
Rash	367	0	220.13	0.00	0.00	3,688.88
Alopecia	387	0	231.31	0.00	0.00	3,688.88
Hair loss	381	0	227.83	0.00	0.00	3,688.88
Endocrine symptoms						
Diabetes mellitus (Type I & II)	280	0	167.43	0.00	0.00	3,688.88
Diabetic ketoacidosis	386	0	230.39	0.00	0.00	3,688.88
Thyroiditis	373	0	223.38	0.00	0.00	3,688.88
Hypothyroidism	320	0	191.68	0.00	0.00	3,688.88
Hyperthyroidism	384	0	229.75	0.00	0.00	3,688.88
Menstrual/period issues	363	0	216.53	0.00	0.00	3,688.88
Hematologic symptoms						
DVT	381	0	227.95	0.00	0.00	3,688.88

Table 47. Incidence of Long COVID among Paxlovid Users by Follow-up Intervals

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Pulmonary embolism	385	0	230.23	0.00	0.00	3,688.88
Renal symptoms						
Acute kidney injury	372	0	222.14	0.00	0.00	3,688.88
Chronic kidney disease	334	0	199.37	0.00	0.00	3,688.88
Dialysis	383	0	228.85	0.00	0.00	3,688.88

Table 48. Incidence of Long COVID among Paxlovid Users Hospitalized with COVID-19 by Follow-up Intervals

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
			Overall			
Any below medical condition						
Any below medical condition	64	50	4.32	11,565.86	8,765.97	15,260.06
Post-COVID syndrome						
Post-COVID syndrome	191	11	36.34	302.72	167.65	546.63
General symptoms						
Fatigue	176	25	29.17	857.07	579.13	1,268.41
Intermittent fever	187	13	34.55	376.25	218.47	647.97
Post-exertional malaise	186	12	34.10	351.94	199.87	619.70
Multisystem inflammatory syndrome (MIS)	191	1	37.03	27.01	3.80	191.73
Respiratory symptoms						
Dyspnea or Shortness of breath	159	42	22.60	1,858.33	1,373.34	2,514.58
Cough	190	0	36.99	0.00	0.00	3,688.88
Nasal congestion	188	4	35.57	112.46	42.21	299.65
Lung function abnormalities	187	3	34.86	86.06	27.76	266.84
Hypoxemia	187	21	32.08	654.57	426.78	1,003.93
Cardiovascular and cerebrovascular symptoms						
Chest pain	171	26	29.34	886.20	603.39	1,301.56
Palpitations or Fast-beating or pounding heart	184	6	34.65	173.16	77.79	385.43
Myocarditis	191	0	37.13	0.00	0.00	3,688.88
Pericarditis	191	0	37.13	0.00	0.00	3,688.88
Myocardial infarction	191	13	34.14	380.83	221.13	655.87
Angina	185	5	35.44	141.10	58.73	339.00
Atrial fibrillation	179	12	32.34	371.09	210.75	653.44
Atrial flutter	191	1	37.06	26.99	3.80	191.57
Sinus tachycardia	184	11	33.50	328.38	181.86	592.96
Sinus bradycardia	186	14	33.89	413.11	244.67	697.53
Heart Failure	178	21	32.32	649.69	423.60	996.45

Table 48. Incidence of Long COVID among Paxlovid Users Hospitalized with COVID-19 by Follow-up Intervals

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Stroke	190	4	36.63	109.21	40.99	290.98
TIA	189	2	36.78	54.38	13.60	217.44
Neurological symptoms						
Headache	191	0	37.13	0.00	0.00	3,688.88
Insomnia	186	10	34.42	290.53	156.32	539.96
Cognitive impairment	181	11	33.36	329.70	182.59	595.35
Confusion	190	2	36.52	54.77	13.70	218.99
Anosmia or Loss of smell	191	0	37.13	0.00	0.00	3,688.88
Ageusia or Loss of taste	191	0	37.13	0.00	0.00	3,688.88
Depression	174	7	33.12	211.35	100.76	443.34
Anxiety Disorders	162	25	29.54	846.19	571.78	1,252.30
Post-traumatic Stress Disorder	189	1	36.43	27.45	3.87	194.87
Substance Use Disorders	183	9	34.72	259.25	134.89	498.25
Suicidal behavior and suicide ideation	190	2	36.93	54.16	13.55	216.55
Dizziness on standing (lightheadedness)	180	9	32.82	274.23	142.69	527.06
Pins-and-needles feelings	189	0	36.39	0.00	0.00	3,688.88
Dysautonomia	190	0	36.96	0.00	0.00	3,688.88
Digestive symptoms						
Abdominal pain	168	21	27.43	765.49	499.11	1,174.06
Diarrhea	184	21	32.56	644.99	420.54	989.24
Nausea	182	8	34.47	232.11	116.08	464.12
Constipation	181	17	31.87	533.44	331.62	858.09
Musculoskeletal and Skin						
Arthralgia or joint pain	158	7	29.79	235.00	112.03	492.93
Myalgia or muscle pain	187	3	36.02	83.28	26.86	258.22
Body aches	185	9	34.49	260.93	135.77	501.49
Rash	187	4	36.15	110.66	41.53	294.84
Alopecia	191	0	37.13	0.00	0.00	3,688.88
Hair loss	188	0	36.13	0.00	0.00	3,688.88
Endocrine symptoms						
Diabetes mellitus (Type I & II)	152	22	25.83	851.76	560.84	1,293.58
Diabetic ketoacidosis	191	0	37.13	0.00	0.00	3,688.88
Thyroiditis	189	1	36.59	27.33	3.85	194.01
Hypothyroidism	175	18	31.51	571.30	359.94	906.76
Hyperthyroidism	189	0	36.96	0.00	0.00	3,688.88
Menstrual/period issues	183	2	35.25	56.73	14.19	226.85
Hematologic symptoms						
DVT	188	2	36.56	54.70	13.68	218.71
Pulmonary embolism	190	5	36.08	138.59	57.69	332.98

Table 48. Incidence of Long COVID among Paxlovid Users Hospitalized with COVID-19 by Follow-up Intervals

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Renal symptoms						
Acute kidney injury	187	27	32.48	831.30	570.09	1,212.20
Chronic kidney disease	171	25	28.41	879.87	594.53	1,302.14
Dialysis	191	4	35.75	111.89	42.00	298.13
			>=4 Weeks			
Any below medical condition						
Any below medical condition	14	5	3.18	1,573.00	654.73	3,779.17
Post-COVID syndrome						
Post-COVID syndrome	148	4	34.19	116.99	43.91	311.72
General symptoms						
Fatigue	122	3	27.00	111.12	35.84	344.53
Intermittent fever	143	2	32.64	61.27	15.32	244.98
Post-exertional malaise	143	3	32.20	93.18	30.05	288.90
Multisystem inflammatory syndrome (MIS)	154	1	35.12	28.47	4.01	202.13
Respiratory symptoms						
Dyspnea or Shortness of breath	96	5	20.31	246.22	102.49	591.56
Cough	153	0	35.09	0.00	0.00	3,688.88
Nasal congestion	149	1	33.72	29.66	4.18	210.55
Lung function abnormalities	147	0	32.91	0.00	0.00	3,688.88
Hypoxemia	138	3	30.14	99.53	32.10	308.61
Cardiovascular and cerebrovascular symptoms						
Chest pain	116	5	26.94	185.58	77.24	445.85
Palpitations or Fast-beating or pounding heart	145	3	32.66	91.85	29.62	284.78
Myocarditis	154	0	35.22	0.00	0.00	3,688.88
Pericarditis	154	0	35.22	0.00	0.00	3,688.88
Myocardial infarction	143	1	32.06	31.19	4.39	221.43
Angina	147	0	33.55	0.00	0.00	3,688.88
Atrial fibrillation	139	3	30.44	98.54	31.78	305.53
Atrial flutter	153	0	35.09	0.00	0.00	3,688.88
Sinus tachycardia	140	1	31.50	31.74	4.47	225.34
Sinus bradycardia	139	3	31.80	94.34	30.43	292.51
Heart Failure	135	3	30.49	98.38	31.73	305.03
Stroke	150	0	34.58	0.00	0.00	3,688.88
TIA	151	0	34.86	0.00	0.00	3,688.88
Neurological symptoms						
Headache	154	0	35.22	0.00	0.00	3,688.88
Insomnia	142	2	32.35	61.82	15.46	247.20
Cognitive impairment	135	0	31.32	0.00	0.00	3,688.88
Confusion	152	1	34.55	28.94	4.08	205.46

Table 48. Incidence of Long COVID among Paxlovid Users Hospitalized with COVID-19 by Follow-up Intervals

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Anosmia or Loss of smell	154	0	35.22	0.00	0.00	3,688.88
Ageusia or Loss of taste	154	0	35.22	0.00	0.00	3,688.88
Depression	133	3	31.04	96.64	31.17	299.65
Anxiety Disorders	111	2	27.39	73.02	18.26	291.97
Post-traumatic Stress Disorder	151	0	34.51	0.00	0.00	3,688.88
Substance Use Disorders	139	0	32.66	0.00	0.00	3,688.88
Suicidal behavior and suicide ideation	151	0	34.90	0.00	0.00	3,688.88
Dizziness on standing (lightheadedness)	136	1	30.77	32.50	4.58	230.71
Pins-and-needles feelings	152	0	34.48	0.00	0.00	3,688.88
Dysautonomia	153	0	35.05	0.00	0.00	3,688.88
Digestive symptoms						
Abdominal pain	121	3	25.39	118.14	38.10	366.30
Diarrhea	136	2	30.58	65.39	16.36	261.47
Nausea	140	0	32.47	0.00	0.00	3,688.88
Constipation	135	4	29.93	133.63	50.16	356.05
Musculoskeletal and Skin						
Arthralgia or joint pain	122	4	28.01	142.79	53.59	380.44
Myalgia or muscle pain	149	1	34.14	29.29	4.13	207.95
Body aches	144	1	32.55	30.72	4.33	218.11
Rash	147	0	34.16	0.00	0.00	3,688.88
Alopecia	154	0	35.22	0.00	0.00	3,688.88
Hair loss	151	0	34.22	0.00	0.00	3,688.88
Endocrine symptoms						
Diabetes mellitus (Type I & II)	110	2	24.12	82.91	20.74	331.50
Diabetic ketoacidosis	154	0	35.22	0.00	0.00	3,688.88
Thyroiditis	151	0	34.68	0.00	0.00	3,688.88
Hypothyroidism	129	2	29.49	67.82	16.96	271.18
Hyperthyroidism	153	0	35.12	0.00	0.00	3,688.88
Menstrual/period issues	148	2	33.49	59.72	14.94	238.79
Hematologic symptoms						
DVT	151	1	34.69	28.82	4.06	204.62
Pulmonary embolism	149	0	34.12	0.00	0.00	3,688.88
Renal symptoms						
Acute kidney injury	132	1	30.41	32.88	4.63	233.45
Chronic kidney disease	122	5	26.35	189.74	78.98	455.86
Dialysis	153	3	33.82	88.71	28.61	275.05
			>=12 Weeks			
Any below medical condition						

Table 48. Incidence of Long COVID among Paxlovid Users Hospitalized with COVID-19 by Follow-up Intervals

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Any below medical condition	4	0	2.00	0.00	0.00	3,688.88
Post-COVID syndrome						
Post-COVID syndrome	44	1	19.61	50.99	7.18	361.99
General symptoms						
Fatigue	35	1	14.76	67.76	9.55	481.06
Intermittent fever	41	1	18.20	54.95	7.74	390.09
Post-exertional malaise	41	1	17.71	56.47	7.96	400.89
Multisystem inflammatory syndrome (MIS)	44	0	19.69	0.00	0.00	3,688.88
Respiratory symptoms						
Dyspnea or Shortness of breath	25	0	10.70	0.00	0.00	3,688.88
Cough	44	0	19.69	0.00	0.00	3,688.88
Nasal congestion	42	0	18.66	0.00	0.00	3,688.88
Lung function abnormalities	40	0	17.94	0.00	0.00	3,688.88
Hypoxemia	37	0	15.94	0.00	0.00	3,688.88
Cardiovascular and cerebrovascular symptoms						
Chest pain	34	0	15.55	0.00	0.00	3,688.88
Palpitations or Fast-beating or pounding heart	41	0	18.08	0.00	0.00	3,688.88
Myocarditis	44	0	19.69	0.00	0.00	3,688.88
Pericarditis	44	0	19.69	0.00	0.00	3,688.88
Myocardial infarction	39	0	17.45	0.00	0.00	3,688.88
Angina	41	0	18.61	0.00	0.00	3,688.88
Atrial fibrillation	36	0	15.89	0.00	0.00	3,688.88
Atrial flutter	44	0	19.69	0.00	0.00	3,688.88
Sinus tachycardia	36	0	16.76	0.00	0.00	3,688.88
Sinus bradycardia	40	0	18.04	0.00	0.00	3,688.88
Heart Failure	38	2	16.78	119.19	29.81	476.56
Stroke	44	0	19.69	0.00	0.00	3,688.88
TIA	44	0	19.69	0.00	0.00	3,688.88
Neurological symptoms						
Headache	44	0	19.69	0.00	0.00	3,688.88
Insomnia	39	0	17.97	0.00	0.00	3,688.88
Cognitive impairment	39	0	17.71	0.00	0.00	3,688.88
Confusion	43	1	19.23	51.99	7.32	369.10
Anosmia or Loss of smell	44	0	19.69	0.00	0.00	3,688.88
Ageusia or Loss of taste	44	0	19.69	0.00	0.00	3,688.88
Depression	40	0	17.99	0.00	0.00	3,688.88
Anxiety Disorders	36	0	16.65	0.00	0.00	3,688.88
Post-traumatic Stress Disorder	43	0	19.25	0.00	0.00	3,688.88

Table 48. Incidence of Long COVID among Paxlovid Users Hospitalized with COVID-19 by Follow-up Intervals

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Substance Use Disorders	41	0	18.49	0.00	0.00	3,688.88
Suicidal behavior and suicide ideation	44	0	19.69	0.00	0.00	3,688.88
Dizziness on standing (lightheadedness)	39	0	17.41	0.00	0.00	3,688.88
Pins-and-needles feelings	43	0	19.14	0.00	0.00	3,688.88
Dysautonomia	44	0	19.69	0.00	0.00	3,688.88
Digestive symptoms						
Abdominal pain	25	0	11.85	0.00	0.00	3,688.88
Diarrhea	37	1	16.94	59.04	8.32	419.16
Nausea	42	0	18.82	0.00	0.00	3,688.88
Constipation	37	2	16.23	123.21	30.81	492.64
Musculoskeletal and Skin						
Arthralgia or joint pain	34	0	15.66	0.00	0.00	3,688.88
Myalgia or muscle pain	43	0	19.23	0.00	0.00	3,688.88
Body aches	40	0	17.99	0.00	0.00	3,688.88
Rash	43	0	19.44	0.00	0.00	3,688.88
Alopecia	44	0	19.69	0.00	0.00	3,688.88
Hair loss	43	0	19.07	0.00	0.00	3,688.88
Endocrine symptoms						
Diabetes mellitus (Type I & II)	30	1	12.96	77.15	10.87	547.73
Diabetic ketoacidosis	44	0	19.69	0.00	0.00	3,688.88
Thyroiditis	44	0	19.69	0.00	0.00	3,688.88
Hypothyroidism	37	0	16.74	0.00	0.00	3,688.88
Hyperthyroidism	44	0	19.69	0.00	0.00	3,688.88
Menstrual/period issues	43	1	18.72	53.43	7.53	379.31
Hematologic symptoms						
DVT	43	0	19.42	0.00	0.00	3,688.88
Pulmonary embolism	43	0	19.15	0.00	0.00	3,688.88
Renal symptoms						
Acute kidney injury	39	0	17.44	0.00	0.00	3,688.88
Chronic kidney disease	31	0	13.78	0.00	0.00	3,688.88
Dialysis	41	0	18.02	0.00	0.00	3,688.88
			>=6 months			
Any below medical condition						
Any below medical condition	1	0	0.96	0.00	0.00	3,688.88
Post-COVID syndrome						
Post-COVID syndrome	13	0	8.70	0.00	0.00	3,688.88
General symptoms						
Fatigue	9	0	6.01	0.00	0.00	3,688.88
Intermittent fever	12	0	8.15	0.00	0.00	3,688.88

Table 48. Incidence of Long COVID among Paxlovid Users Hospitalized with COVID-19 by Follow-up Intervals

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Post-exertional malaise	11	0	7.17	0.00	0.00	3,688.88
Multisystem inflammatory syndrome (MIS)	13	0	8.70	0.00	0.00	3,688.88
Respiratory symptoms						
Dyspnea or Shortness of breath	5	0	3.53	0.00	0.00	3,688.88
Cough	13	0	8.70	0.00	0.00	3,688.88
Nasal congestion	12	0	8.08	0.00	0.00	3,688.88
Lung function abnormalities	12	0	8.18	0.00	0.00	3,688.88
Hypoxemia	9	0	6.23	0.00	0.00	3,688.88
Cardiovascular and cerebrovascular symptoms						
Chest pain	12	0	8.17	0.00	0.00	3,688.88
Palpitations or Fast-beating or pounding heart	10	0	7.09	0.00	0.00	3,688.88
Myocarditis	13	0	8.70	0.00	0.00	3,688.88
Pericarditis	13	0	8.70	0.00	0.00	3,688.88
Myocardial infarction	12	0	8.17	0.00	0.00	3,688.88
Angina	12	0	8.17	0.00	0.00	3,688.88
Atrial fibrillation	8	0	5.96	0.00	0.00	3,688.88
Atrial flutter	13	0	8.70	0.00	0.00	3,688.88
Sinus tachycardia	12	0	8.17	0.00	0.00	3,688.88
Sinus bradycardia	12	0	8.08	0.00	0.00	3,688.88
Heart Failure	10	0	7.03	0.00	0.00	3,688.88
Stroke	13	0	8.70	0.00	0.00	3,688.88
TIA	13	0	8.70	0.00	0.00	3,688.88
Neurological symptoms						
Headache	13	0	8.70	0.00	0.00	3,688.88
Insomnia	13	0	8.70	0.00	0.00	3,688.88
Cognitive impairment	12	0	8.17	0.00	0.00	3,688.88
Confusion	13	0	8.70	0.00	0.00	3,688.88
Anosmia or Loss of smell	13	0	8.70	0.00	0.00	3,688.88
Ageusia or Loss of taste	13	0	8.70	0.00	0.00	3,688.88
Depression	13	0	8.70	0.00	0.00	3,688.88
Anxiety Disorders	11	0	7.63	0.00	0.00	3,688.88
Post-traumatic Stress Disorder	13	0	8.70	0.00	0.00	3,688.88
Substance Use Disorders	13	0	8.70	0.00	0.00	3,688.88
Suicidal behavior and suicide ideation	13	0	8.70	0.00	0.00	3,688.88
Dizziness on standing (lightheadedness)	11	0	7.61	0.00	0.00	3,688.88

Table 48. Incidence of Long COVID among Paxlovid Users Hospitalized with COVID-19 by Follow-up Intervals

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Pins-and-needles feelings	12	0	8.15	0.00	0.00	3,688.88
Dysautonomia	13	0	8.70	0.00	0.00	3,688.88
Digestive symptoms						
Abdominal pain	9	0	6.55	0.00	0.00	3,688.88
Diarrhea	13	0	8.70	0.00	0.00	3,688.88
Nausea	12	0	8.08	0.00	0.00	3,688.88
Constipation	11	0	7.26	0.00	0.00	3,688.88
Musculoskeletal and Skin						
Arthralgia or joint pain	11	0	7.55	0.00	0.00	3,688.88
Myalgia or muscle pain	13	0	8.70	0.00	0.00	3,688.88
Body aches	11	0	7.55	0.00	0.00	3,688.88
Rash	13	0	8.70	0.00	0.00	3,688.88
Alopecia	13	0	8.70	0.00	0.00	3,688.88
Hair loss	12	0	8.08	0.00	0.00	3,688.88
Endocrine symptoms						
Diabetes mellitus (Type I & II)	8	0	5.24	0.00	0.00	3,688.88
Diabetic ketoacidosis	13	0	8.70	0.00	0.00	3,688.88
Thyroiditis	13	0	8.70	0.00	0.00	3,688.88
Hypothyroidism	12	0	7.81	0.00	0.00	3,688.88
Hyperthyroidism	13	0	8.70	0.00	0.00	3,688.88
Menstrual/period issues	12	0	7.73	0.00	0.00	3,688.88
Hematologic symptoms						
DVT	13	0	8.70	0.00	0.00	3,688.88
Pulmonary embolism	12	0	8.16	0.00	0.00	3,688.88
Renal symptoms						
Acute kidney injury	11	0	7.64	0.00	0.00	3,688.88
Chronic kidney disease	6	0	4.54	0.00	0.00	3,688.88
Dialysis	12	0	7.81	0.00	0.00	3,688.88

Table 49. Incidence of Long COVID among Paxlovid Users Non-Hospitalized with COVID-19 by Follow-up Intervals

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
			Overall			
Any below medical condition						
Any below medical condition	7,209	1,730	550.76	3,141.13	2,996.55	3,292.69
Post-COVID syndrome						
Post-COVID syndrome	16,355	199	1,902.87	104.58	91.01	120.17
General symptoms						
Fatigue	15,482	501	1,741.59	287.67	263.55	313.99
Intermittent fever	16,231	423	1,857.37	227.74	207.04	250.51

Table 49. Incidence of Long COVID among Paxlovid Users Non-Hospitalized with COVID-19 by Follow-up Intervals

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Post-exertional malaise	16,296	62	1,905.02	32.55	25.37	41.74
Multisystem inflammatory syndrome (MIS)	16,392	0	1,928.81	0.00	0.00	3,688.88
Respiratory symptoms						
Dyspnea or Shortness of breath	15,549	536	1,724.99	310.73	285.51	338.18
Cough	16,339	9	1,910.48	4.71	2.45	9.05
Nasal congestion	16,144	261	1,867.78	139.74	123.77	157.76
Lung function abnormalities	16,312	31	1,910.08	16.23	11.41	23.08
Hypoxemia	16,333	24	1,913.59	12.54	8.41	18.71
Cardiovascular and cerebrovascular symptoms						
Chest pain	15,545	444	1,754.23	253.10	230.62	277.77
Palpitations or Fast-beating or pounding heart	15,976	145	1,855.10	78.16	66.42	91.98
Myocarditis	16,388	2	1,928.27	1.04	0.26	4.15
Pericarditis	16,389	1	1,928.45	0.52	0.07	3.68
Myocardial infarction	16,340	16	1,918.08	8.34	5.11	13.62
Angina	16,203	51	1,888.68	27.00	20.52	35.53
Atrial fibrillation	15,929	93	1,848.67	50.31	41.05	61.64
Atrial flutter	16,351	13	1,920.64	6.77	3.93	11.66
Sinus tachycardia	16,239	97	1,893.13	51.24	41.99	62.52
Sinus bradycardia	16,239	52	1,901.90	27.34	20.83	35.88
Heart Failure	15,975	90	1,852.74	48.58	39.51	59.72
Stroke	16,283	31	1,906.92	16.26	11.43	23.12
TIA	16,333	22	1,915.94	11.48	7.56	17.44
Neurological symptoms						
Headache	16,391	2	1,928.36	1.04	0.26	4.15
Insomnia	15,787	105	1,836.46	57.18	47.22	69.23
Cognitive impairment	16,107	91	1,874.09	48.56	39.54	59.63
Confusion	16,386	3	1,926.58	1.56	0.50	4.83
Anosmia or Loss of smell	16,384	5	1,927.41	2.59	1.08	6.23
Ageusia or Loss of taste	16,382	5	1,926.53	2.60	1.08	6.24
Depression	15,229	196	1,742.73	112.47	97.78	129.37
Anxiety Disorders	14,277	427	1,594.67	267.77	243.54	294.41
Post-traumatic Stress Disorder	16,284	21	1,908.89	11.00	7.17	16.87
Substance Use Disorders	16,173	51	1,895.07	26.91	20.45	35.41
Suicidal behavior and suicide ideation	16,382	4	1,927.20	2.08	0.78	5.53
Dizziness on standing (lightheadedness)	15,942	166	1,842.54	90.09	77.38	104.90
Pins-and-needles feelings	16,210	69	1,898.69	36.34	28.70	46.01

Table 49. Incidence of Long COVID among Paxlovid Users Non-Hospitalized with COVID-19 by Follow-up Intervals

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Dysautonomia	16,359	4	1,923.84	2.08	0.78	5.54
Digestive symptoms						
Abdominal pain	15,393	309	1,750.86	176.49	157.87	197.30
Diarrhea	16,114	145	1,868.56	77.60	65.94	91.32
Nausea	16,153	153	1,875.54	81.58	69.62	95.58
Constipation	16,074	87	1,873.30	46.44	37.64	57.30
Musculoskeletal and Skin						
Arthralgia or joint pain	14,638	497	1,637.48	303.52	277.97	331.41
Myalgia or muscle pain	16,146	122	1,874.94	65.07	54.49	77.70
Body aches	16,265	131	1,894.49	69.15	58.27	82.06
Rash	16,016	130	1,866.21	69.66	58.66	82.73
Alopecia	16,382	0	1,927.70	0.00	0.00	3,688.88
Hair loss	16,287	24	1,912.41	12.55	8.41	18.72
Endocrine symptoms						
Diabetes mellitus (Type I & II)	14,008	243	1,555.80	156.19	137.74	177.12
Diabetic ketoacidosis	16,383	1	1,926.49	0.52	0.07	3.69
Thyroiditis	16,214	26	1,897.87	13.70	9.33	20.12
Hypothyroidism	14,869	255	1,690.02	150.89	133.46	170.59
Hyperthyroidism	16,299	18	1,915.17	9.40	5.92	14.92
Menstrual/period issues	15,823	132	1,843.02	71.62	60.39	84.94
Hematologic symptoms						
DVT	16,318	11	1,914.81	5.74	3.18	10.37
Pulmonary embolism	16,337	18	1,917.41	9.39	5.92	14.90
Renal symptoms						
Acute kidney injury	16,299	45	1,906.80	23.60	17.62	31.61
Chronic kidney disease	15,680	153	1,796.75	85.15	72.68	99.77
Dialysis	16,384	6	1,926.13	3.12	1.40	6.93
			>=4 Weeks			
Any below medical condition						
Any below medical condition	2,775	611	467.16	1,307.89	1,208.19	1,415.82
Post-COVID syndrome						
Post-COVID syndrome	9,181	62	1,736.08	35.71	27.84	45.81
General symptoms						
Fatigue	8,460	179	1,582.66	113.10	97.69	130.95
Intermittent fever	9,011	32	1,697.38	18.85	13.33	26.66
Post-exertional malaise	9,210	32	1,741.85	18.37	12.99	25.98
Multisystem inflammatory syndrome (MIS)	9,308	0	1,765.63	0.00	0.00	3,688.88
Respiratory symptoms						
Dyspnea or Shortness of breath	8,444	174	1,564.50	111.22	95.86	129.03
Cough	9,255	0	1,747.42	0.00	0.00	3,688.88
Nasal congestion	9,025	34	1,706.77	19.92	14.23	27.88

Table 49. Incidence of Long COVID among Paxlovid Users Non-Hospitalized with COVID-19 by Follow-up Intervals

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Lung function abnormalities	9,237	18	1,746.97	10.30	6.49	16.35
Hypoxemia	9,253	10	1,750.64	5.71	3.07	10.62
Cardiovascular and cerebrovascular symptoms						
Chest pain	8,552	166	1,595.29	104.06	89.37	121.15
Palpitations or Fast-beating or pounding heart	8,990	79	1,694.43	46.62	37.40	58.13
Myocarditis	9,305	2	1,765.13	1.13	0.28	4.53
Pericarditis	9,306	1	1,765.29	0.57	0.08	4.02
Myocardial infarction	9,266	10	1,755.26	5.70	3.07	10.59
Angina	9,137	27	1,725.98	15.64	10.73	22.81
Atrial fibrillation	8,945	50	1,688.27	29.62	22.45	39.08
Atrial flutter	9,273	6	1,757.78	3.41	1.53	7.60
Sinus tachycardia	9,147	27	1,730.64	15.60	10.70	22.75
Sinus bradycardia	9,185	29	1,739.81	16.67	11.58	23.99
Heart Failure	8,969	57	1,692.14	33.69	25.98	43.67
Stroke	9,222	20	1,744.70	11.46	7.40	17.77
TIA	9,254	10	1,753.00	5.70	3.07	10.60
Neurological symptoms						
Headache	9,306	0	1,765.17	0.00	0.00	3,688.88
Insomnia	8,880	57	1,678.50	33.96	26.19	44.03
Cognitive impairment	9,062	52	1,711.63	30.38	23.15	39.87
Confusion	9,302	3	1,763.40	1.70	0.55	5.28
Anosmia or Loss of smell	9,302	1	1,764.34	0.57	0.08	4.02
Ageusia or Loss of taste	9,298	3	1,763.39	1.70	0.55	5.28
Depression	8,449	83	1,590.31	52.19	42.09	64.72
Anxiety Disorders	7,735	231	1,446.35	159.71	140.39	181.70
Post-traumatic Stress Disorder	9,221	10	1,746.58	5.73	3.08	10.64
Substance Use Disorders	9,146	23	1,733.58	13.27	8.82	19.97
Suicidal behavior and suicide ideation	9,301	2	1,764.05	1.13	0.28	4.53
Dizziness on standing (lightheadedness)	8,943	91	1,682.55	54.08	44.04	66.42
Pins-and-needles feelings	9,164	44	1,736.16	25.34	18.86	34.06
Dysautonomia	9,282	2	1,760.88	1.14	0.28	4.54
Digestive symptoms						
Abdominal pain	8,521	176	1,592.96	110.49	95.31	128.08
Diarrhea	9,046	51	1,706.64	29.88	22.71	39.32
Nausea	9,068	46	1,713.46	26.85	20.11	35.84
Constipation	9,064	53	1,712.30	30.95	23.65	40.52
Musculoskeletal and Skin						
Arthralgia or joint pain	7,970	311	1,485.47	209.36	187.34	233.97
Myalgia or muscle pain	9,065	39	1,713.23	22.76	16.63	31.16

Table 49. Incidence of Long COVID among Paxlovid Users Non-Hospitalized with COVID-19 by Follow-up Intervals

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Body aches	9,149	23	1,732.05	13.28	8.82	19.98
Rash	9,000	71	1,704.30	41.66	33.01	52.57
Alopecia	9,302	0	1,764.66	0.00	0.00	3,688.88
Hair loss	9,230	13	1,749.94	7.43	4.31	12.79
Endocrine symptoms						
Diabetes mellitus (Type I & II)	7,575	108	1,414.04	76.38	63.25	92.23
Diabetic ketoacidosis	9,299	1	1,763.31	0.57	0.08	4.03
Thyroiditis	9,171	17	1,736.03	9.79	6.09	15.75
Hypothyroidism	8,201	125	1,539.33	81.20	68.15	96.76
Hyperthyroidism	9,240	9	1,752.59	5.14	2.67	9.87
Menstrual/period issues	8,903	81	1,684.62	48.08	38.67	59.78
Hematologic symptoms						
DVT	9,247	6	1,751.99	3.42	1.54	7.62
Pulmonary embolism	9,257	11	1,754.31	6.27	3.47	11.32
Renal symptoms						
Acute kidney injury	9,222	25	1,743.81	14.34	9.69	21.22
Chronic kidney disease	8,736	84	1,637.26	51.31	41.43	63.54
Dialysis	9,299	4	1,762.88	2.27	0.85	6.05
			>=12 Weeks			
Any below medical condition						
Any below medical condition	396	96	146.49	655.34	536.53	800.47
Post-COVID syndrome						
Post-COVID syndrome	1,699	5	676.78	7.39	3.08	17.75
General symptoms						
Fatigue	1,525	32	603.76	53.00	37.48	74.95
Intermittent fever	1,645	8	653.62	12.24	6.12	24.47
Post-exertional malaise	1,704	4	678.58	5.89	2.21	15.71
Multisystem inflammatory syndrome (MIS)	1,735	0	691.72	0.00	0.00	3,688.88
Respiratory symptoms						
Dyspnea or Shortness of breath	1,481	31	582.09	53.26	37.45	75.73
Cough	1,701	0	676.38	0.00	0.00	3,688.88
Nasal congestion	1,673	11	665.77	16.52	9.15	29.83
Lung function abnormalities	1,712	5	680.24	7.35	3.06	17.66
Hypoxemia	1,712	0	681.97	0.00	0.00	3,688.88
Cardiovascular and cerebrovascular symptoms						
Chest pain	1,528	23	602.76	38.16	25.36	57.42
Palpitations or Fast-beating or pounding heart	1,653	16	656.17	24.38	14.94	39.80
Myocarditis	1,735	0	691.72	0.00	0.00	3,688.88
Pericarditis	1,735	0	691.72	0.00	0.00	3,688.88

Table 49. Incidence of Long COVID among Paxlovid Users Non-Hospitalized with COVID-19 by Follow-up Intervals

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Myocardial infarction	1,722	1	686.08	1.46	0.21	10.35
Angina	1,686	6	669.36	8.96	4.03	19.95
Atrial fibrillation	1,646	7	654.98	10.69	5.10	22.42
Atrial flutter	1,721	1	686.64	1.46	0.21	10.34
Sinus tachycardia	1,704	6	676.63	8.87	3.98	19.74
Sinus bradycardia	1,704	9	679.26	13.25	6.89	25.47
Heart Failure	1,641	9	653.13	13.78	7.17	26.48
Stroke	1,708	5	679.71	7.36	3.06	17.67
TIA	1,719	2	685.08	2.92	0.73	11.67
Neurological symptoms						
Headache	1,734	0	691.46	0.00	0.00	3,688.88
Insomnia	1,643	11	651.78	16.88	9.35	30.47
Cognitive impairment	1,674	9	664.92	13.54	7.04	26.01
Confusion	1,732	1	689.94	1.45	0.20	10.29
Anosmia or Loss of smell	1,734	0	691.25	0.00	0.00	3,688.88
Ageusia or Loss of taste	1,732	1	690.55	1.45	0.20	10.28
Depression	1,553	10	615.50	16.25	8.74	30.20
Anxiety Disorders	1,401	32	554.38	57.72	40.82	81.62
Post-traumatic Stress Disorder	1,714	3	682.66	4.39	1.42	13.63
Substance Use Disorders	1,709	2	679.04	2.95	0.74	11.78
Suicidal behavior and suicide ideation	1,733	1	690.94	1.45	0.20	10.27
Dizziness on standing (lightheadedness)	1,637	17	648.72	26.21	16.29	42.15
Pins-and-needles feelings	1,702	6	678.14	8.85	3.98	19.69
Dysautonomia	1,730	0	690.00	0.00	0.00	3,688.88
Digestive symptoms						
Abdominal pain	1,543	32	608.05	52.63	37.22	74.42
Diarrhea	1,661	11	660.11	16.66	9.23	30.09
Nausea	1,670	10	665.44	15.03	8.09	27.93
Constipation	1,681	11	665.87	16.52	9.15	29.83
Musculoskeletal and Skin						
Arthralgia or joint pain	1,432	57	566.00	100.71	77.68	130.56
Myalgia or muscle pain	1,677	9	667.30	13.49	7.02	25.92
Body aches	1,698	5	676.50	7.39	3.08	17.76
Rash	1,676	15	666.86	22.49	13.56	37.31
Alopecia	1,735	0	691.72	0.00	0.00	3,688.88
Hair loss	1,719	2	684.80	2.92	0.73	11.68
Endocrine symptoms						
Diabetes mellitus (Type I & II)	1,349	27	531.92	50.76	34.81	74.02
Diabetic ketoacidosis	1,733	0	690.44	0.00	0.00	3,688.88
Thyroiditis	1,703	5	677.29	7.38	3.07	17.74

Table 49. Incidence of Long COVID among Paxlovid Users Non-Hospitalized with COVID-19 by Follow-up Intervals

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Hypothyroidism	1,505	23	596.82	38.54	25.61	57.99
Hyperthyroidism	1,725	1	687.83	1.45	0.21	10.32
Menstrual/period issues	1,662	14	659.62	21.22	12.57	35.84
Hematologic symptoms						
DVT	1,717	1	684.51	1.46	0.21	10.37
Pulmonary embolism	1,722	2	686.76	2.91	0.73	11.64
Renal symptoms						
Acute kidney injury	1,708	9	678.23	13.27	6.91	25.50
Chronic kidney disease	1,578	18	624.50	28.82	18.16	45.75
Dialysis	1,731	2	689.67	2.90	0.73	11.60
			>=6 months			
Any below medical condition						
Any below medical condition	45	0	27.25	0.00	0.00	3,688.88
Post-COVID syndrome						
Post-COVID syndrome	366	0	217.88	0.00	0.00	3,688.88
General symptoms						
Fatigue	314	0	187.47	0.00	0.00	3,688.88
Intermittent fever	351	1	208.85	4.79	0.67	33.99
Post-exertional malaise	366	0	218.15	0.00	0.00	3,688.88
Multisystem inflammatory syndrome (MIS)	374	0	222.61	0.00	0.00	3,688.88
Respiratory symptoms						
Dyspnea or Shortness of breath	298	1	178.03	5.62	0.79	39.88
Cough	365	0	217.02	0.00	0.00	3,688.88
Nasal congestion	358	0	213.62	0.00	0.00	3,688.88
Lung function abnormalities	363	0	215.94	0.00	0.00	3,688.88
Hypoxemia	366	0	218.05	0.00	0.00	3,688.88
Cardiovascular and cerebrovascular symptoms						
Chest pain	324	1	192.20	5.20	0.73	36.94
Palpitations or Fast-beating or pounding heart	352	0	209.45	0.00	0.00	3,688.88
Myocarditis	374	0	222.61	0.00	0.00	3,688.88
Pericarditis	374	0	222.61	0.00	0.00	3,688.88
Myocardial infarction	370	0	220.18	0.00	0.00	3,688.88
Angina	359	0	213.06	0.00	0.00	3,688.88
Atrial fibrillation	345	0	205.32	0.00	0.00	3,688.88
Atrial flutter	371	0	220.86	0.00	0.00	3,688.88
Sinus tachycardia	363	0	215.57	0.00	0.00	3,688.88
Sinus bradycardia	368	0	219.30	0.00	0.00	3,688.88
Heart Failure	351	0	209.19	0.00	0.00	3,688.88
Stroke	365	0	217.30	0.00	0.00	3,688.88
TIA	369	0	219.57	0.00	0.00	3,688.88

Table 49. Incidence of Long COVID among Paxlovid Users Non-Hospitalized with COVID-19 by Follow-up Intervals

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Neurological symptoms						
Headache	374	0	222.61	0.00	0.00	3,688.88
Insomnia	347	0	206.56	0.00	0.00	3,688.88
Cognitive impairment	354	0	210.87	0.00	0.00	3,688.88
Confusion	372	0	221.38	0.00	0.00	3,688.88
Anosmia or Loss of smell	374	0	222.61	0.00	0.00	3,688.88
Ageusia or Loss of taste	374	0	222.61	0.00	0.00	3,688.88
Depression	328	0	194.38	0.00	0.00	3,688.88
Anxiety Disorders	290	0	171.12	0.00	0.00	3,688.88
Post-traumatic Stress Disorder	366	0	218.15	0.00	0.00	3,688.88
Substance Use Disorders	362	0	215.16	0.00	0.00	3,688.88
Suicidal behavior and suicide ideation	374	0	222.61	0.00	0.00	3,688.88
Dizziness on standing (lightheadedness)	340	0	202.95	0.00	0.00	3,688.88
Pins-and-needles feelings	363	1	216.02	4.63	0.65	32.86
Dysautonomia	374	0	222.61	0.00	0.00	3,688.88
Digestive symptoms						
Abdominal pain	306	0	182.57	0.00	0.00	3,688.88
Diarrhea	356	0	211.69	0.00	0.00	3,688.88
Nausea	363	0	216.13	0.00	0.00	3,688.88
Constipation	353	0	209.11	0.00	0.00	3,688.88
Musculoskeletal and Skin						
Arthralgia or joint pain	301	0	179.15	0.00	0.00	3,688.88
Myalgia or muscle pain	359	0	214.08	0.00	0.00	3,688.88
Body aches	366	1	217.58	4.60	0.65	32.63
Rash	354	0	211.44	0.00	0.00	3,688.88
Alopecia	374	0	222.61	0.00	0.00	3,688.88
Hair loss	369	0	219.75	0.00	0.00	3,688.88
Endocrine symptoms						
Diabetes mellitus (Type I & II)	272	0	162.18	0.00	0.00	3,688.88
Diabetic ketoacidosis	373	0	221.69	0.00	0.00	3,688.88
Thyroiditis	360	0	214.68	0.00	0.00	3,688.88
Hypothyroidism	308	0	183.87	0.00	0.00	3,688.88
Hyperthyroidism	371	0	221.06	0.00	0.00	3,688.88
Menstrual/period issues	351	0	208.80	0.00	0.00	3,688.88
Hematologic symptoms						
DVT	368	0	219.26	0.00	0.00	3,688.88
Pulmonary embolism	373	0	222.07	0.00	0.00	3,688.88

Table 49. Incidence of Long COVID among Paxlovid Users Non-Hospitalized with COVID-19 by Follow-up Intervals

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Renal symptoms						
Acute kidney injury	361	0	214.51	0.00	0.00	3,688.88
Chronic kidney disease	328	0	194.83	0.00	0.00	3,688.88
Dialysis	371	0	221.04	0.00	0.00	3,688.88

10.3.1.5. Objective 5: Describe the health equity and demographic and clinical characteristics (e.g. co-morbid conditions, outcomes, treatment patterns, healthcare utilization) among patients treated with Paxlovid

Table 50 summarizes demographics of the Paxlovid cohort. Across all groups, nearly all Paxlovid use occurred in 2022, with prescribing concentrated between May and August 2022. Age distributions show that Paxlovid users were predominantly older adults, especially those aged 65–74 and 75–84, with White users having the highest share of older individuals. Gender distribution varies modestly across groups, with a higher proportion of female users in most groups. Insurance patterns reflect the age distribution, with Medicare being the dominant coverage type across all racial/ethnic categories. Socioeconomic indicators show consistent disparities: Black and Hispanic users were more likely to have lower household incomes, lower educational attainment, whereas White and Asian users more often lived in higher-income households.

Table 50. Demographics of Paxlovid Users

Character-istics	White N	White %	Black N	Black %	Asian N	Asian %	Hispanic N	Hispanic %	Missing N	Missing %	Overall N	Overall %
Cohort Entry Year												
2021	27	0.01	6	0.03	1	0.01	5	0.02	4	0.02	43	0.02
2022	194,833	99.99	19,451	99.97	13,785	99.99	30,155	99.98	17,923	99.98	276,147	99.98
Cohort Month/Year												
Dec-21	27	0.01	6	0.03	1	0.01	5	0.02	4	0.02	43	0.02
Jan-22	1,164	0.60	144	0.74	65	0.47	186	0.62	126	0.70	1,685	0.61
Feb-22	747	0.38	74	0.38	21	0.15	100	0.33	58	0.32	1,000	0.36
Mar-22	542	0.28	31	0.16	34	0.25	42	0.14	51	0.28	700	0.25
Apr-22	4,254	2.18	260	1.34	284	2.06	381	1.26	312	1.74	5,491	1.99
May-22	24,911	12.78	1,778	9.14	1,928	13.99	3,061	10.15	2,076	11.58	33,754	12.22
Jun-22	33,595	17.24	3,254	16.72	2,570	18.64	5,826	19.32	3,145	17.54	48,390	17.52
Jul-22	46,312	23.77	5,476	28.14	3,390	24.59	8,369	27.75	4,511	25.16	68,058	24.64
Aug-22	36,847	18.91	4,231	21.75	2,379	17.26	6,035	20.01	3,431	19.14	52,923	19.16
Sep-22	23,468	12.04	2,313	11.89	1,513	10.97	3,209	10.64	2,118	11.81	32,621	11.81
Oct-22	18,834	9.67	1,518	7.80	1,268	9.20	2,236	7.41	1,665	9.29	25,521	9.24
Nov-22	4,159	2.13	372	1.91	333	2.42	710	2.35	430	2.40	6,004	2.17
Age												
12-17	499	0.26	59	0.30	60	0.44	116	0.38	263	1.47	997	0.36
18-29	4,090	2.10	437	2.25	388	2.81	878	2.91	1,102	6.15	6,895	2.50
30-39	9,582	4.92	1,148	5.90	1,017	7.38	1,897	6.29	1,557	8.69	15,201	5.50

Table 50. Demographics of Paxlovid Users

Characteristics	White		Black		Asian		Hispanic		Missing		Overall	
	N	%	N	%	N	%	N	%	N	%	N	%
40-49	16,590	8.51	2,182	11.21	1,812	13.14	3,416	11.33	1,712	9.55	25,712	9.31
50-59	27,424	14.07	3,085	15.86	2,115	15.34	4,335	14.37	2,137	11.92	39,096	14.16
60-64	18,160	9.32	1,836	9.44	826	5.99	2,260	7.49	1,296	7.23	24,378	8.83
65-74	64,314	33.01	6,278	32.27	4,218	30.60	9,479	31.43	6,180	34.47	90,469	32.76
75-84	42,159	21.64	3,468	17.82	2,742	19.89	5,942	19.70	2,898	16.17	57,209	20.71
85+	12,042	6.18	964	4.95	608	4.41	1,837	6.09	782	4.36	16,233	5.88
Age continuous												
Mean+/- SD	65	14.89	63	15.13	62	16.20	63	16.03	60	17.90	64	15.37
Median, IQR	68	57-75	67	53-74	67	50-74	68	52-75	67	49-73	68	55-75
Gender												
Female	109,099	55.99	12,750	65.53	7,187	52.13	17,747	58.84	10,198	56.89	156,981	56.84
Male	85,761	44.01	6,707	34.47	6,599	47.87	12,413	41.16	7,729	43.11	119,209	43.16
Insurance												
Commercial	78,860	40.47	7,992	41.08	6,564	47.61	12,429	41.21	7,557	42.15	113,402	41.06
Medicare	115,974	59.52	11,463	58.91	7,221	52.38	17,727	58.78	10,368	57.83	162,753	58.93
Missing	26	0.01	2	0.01	1	0.01	4	0.01	2	0.01	35	0.01
Geographic Region												
Northeast	29,870	15.33	1,619	8.32	3,261	23.65	3,071	10.18	2,569	14.33	40,390	14.62
Midwest	48,957	25.12	3,035	15.60	1,538	11.16	1,988	6.59	3,373	18.82	58,891	21.32
South	73,805	37.88	13,574	69.76	4,346	31.52	17,461	57.89	7,243	40.40	116,429	42.16
West	42,089	21.60	1,209	6.21	4,631	33.59	7,611	25.24	4,706	26.25	60,246	21.81
Missing/ Unknown	139	0.07	20	0.10	10	0.07	29	0.10	36	0.20	234	0.08
Education Level												
Less than 12th Grade	109	0.06	18	0.09	41	0.30	501	1.66	5	0.03	674	0.24
High School Diploma	28,597	14.68	7,064	36.31	1,289	9.35	10,071	33.39	657	3.66	47,678	17.26
Less than Bachelor Degree	108,262	55.56	10,119	52.01	5,941	43.09	14,947	49.56	3,025	16.87	142,294	51.52
Bachelor Degree Plus	55,618	28.54	2,010	10.33	6,381	46.29	4,377	14.51	2,037	11.36	70,423	25.50
Missing/ Unknown	2,274	1.17	246	1.26	134	0.97	264	0.88	12,203	68.07	15,121	5.47
Rolled up Housing (Rent/Own)												
Probable Homeowner	167,411	85.91	14,368	73.84	11,390	82.62	23,560	78.12	4,812	26.84	221,541	80.21
Probable Renter	10,840	5.56	2,214	11.38	805	5.84	2,412	8.00	337	1.88	16,608	6.01
Missing/Unknown	16,609	8.52	2,875	14.78	1,591	11.54	4,188	13.89	12,778	71.28	38,041	13.77
Rolled up Household Income												

Table 50. Demographics of Paxlovid Users

Character-istics	White		Black		Asian		Hispanic		Missing		Overall	
	N	%	N	%	N	%	N	%	N	%	N	%
<$40K	30,045	15.42	7,342	37.73	1,254	9.10	7,624	25.28	730	4.07	46,995	17.02
$40K-$49K	11,473	5.89	1,977	10.16	567	4.11	2,922	9.69	276	1.54	17,215	6.23
$50K-$59K	13,813	7.09	1,984	10.20	815	5.91	3,115	10.33	357	1.99	20,084	7.27
$60K-$74K	20,169	10.35	2,108	10.83	1,275	9.25	3,581	11.87	553	3.08	27,686	10.02
$75K-$99K	35,107	18.02	2,419	12.43	2,234	16.20	4,734	15.70	987	5.51	45,481	16.47
$100K+	82,161	42.16	3,281	16.86	7,115	51.61	7,222	23.95	2,660	14.84	102,439	37.09
Missing/ Unknown	2,092	1.07	346	1.78	526	3.82	962	3.19	12,364	68.97	16,290	5.90

Table 51 summarizes Comorbidities and Medical History among Paxlovid cohort. Across all comorbidity categories, Black and Hispanic patients consistently show higher burdens of chronic conditions—especially hypertension, diabetes, obesity, and chronic kidney disease—while Asian patients have the lowest prevalence of most conditions. White patients generally fall in the middle but show the highest rates of hyperlipidemia and cancer. Overall comorbidity burden (Charlson Index) is slightly higher for Black and Hispanic patients, and prior COVID-19 infections were uncommon across all groups (≥92% had no previous infection).

Table 51. Comorbidities and Medical History among Paxlovid users

	White		Black		Asian		Hispanic		Missing		Overall	
	N	%	N	%	N	%	N	%	N	%	N	%
Comorbidities & Medical History												
Hypertension	105,543	54.16	12,867	66.13	6,609	47.94	17,313	57.40	8,919	49.75	151,251	54.76
Hyperlipidemia	113,146	58.07	11,468	58.94	8,036	58.29	18,032	59.79	9,486	52.91	160,168	57.99
BMI>=30 or obesity	45,981	23.60	6,862	35.27	1,274	9.24	8,542	28.32	3,946	22.01	66,605	24.12
Diabetes Mellitus	40,026	20.54	6,472	33.26	3,939	28.57	9,805	32.51	4,142	23.10	64,384	23.31
Asthma	19,008	9.75	2,317	11.91	981	7.12	3,024	10.03	1,736	9.68	27,066	9.80
Coronary Heart Disease	27,127	13.92	2,523	12.97	1,384	10.04	3,640	12.07	2,067	11.53	36,741	13.30
Cardiomyopathies	4,482	2.30	564	2.90	168	1.22	638	2.12	393	2.19	6,245	2.26
Cerebrovascular disease or stroke (including Transient Ischemic Attack)	14,400	7.39	1,611	8.28	803	5.82	2,141	7.10	1,174	6.55	20,129	7.29
Chronic Kidney Disease	24,527	12.59	3,267	16.79	1,604	11.63	4,991	16.55	2,224	12.41	36,613	13.26
VTE	4,030	2.07	477	2.45	120	0.87	537	1.78	336	1.87	5,500	1.99

Table 51. Comorbidities and Medical History among Paxlovid users

	White		Black		Asian		Hispanic		Missing		Overall	
	N	%	N	%	N	%	N	%	N	%	N	%
Cancer	40,706	20.89	2,912	14.97	1,333	9.67	3,795	12.58	2,591	14.45	51,337	18.59
Autoimmune diseases	15,453	7.93	1,538	7.90	783	5.68	2,388	7.92	1,297	7.23	21,459	7.77
COPD	20,442	10.49	2,294	11.79	697	5.06	2,914	9.66	1,753	9.78	28,100	10.17
Liver Disease	12,705	6.52	1,297	6.67	1,185	8.60	2,856	9.47	1,245	6.94	19,288	6.98
ILD	3,181	1.63	293	1.51	151	1.10	678	2.25	282	1.57	4,585	1.66
HIV infection	556	0.29	158	0.81	25	0.18	173	0.57	55	0.31	967	0.35
Smoking	30,255	15.53	3,169	16.29	799	5.80	3,166	10.50	2,423	13.52	39,812	14.41
Deyo-Charlson Comorbidity Index Score												
Mean+/- SD	1.52	2.14	1.94	2.40	1.33	1.96	1.91	2.41	1.50	2.17	1.58	2.19
Median, IQR	1	0-2	1	0-3	1	0-2	1	0-3	1	0-2	1	0-2
Past COVID-19												
0	185,209	95.05	18,038	92.71	13,355	96.87	27,745	91.99	16,960	94.61	261,307	94.61
1	8,868	4.55	1,302	6.69	388	2.81	2,171	7.2	885	4.94	13,614	4.93
2+	783	0.4	117	0.6	43	0.31	244	0.81	82	0.46	1,269	0.46

Table 52 summarizes healthcare utilization of Paxlovid users 1 Year Prior to Index. Across all groups, prior-year hospitalization rates were low (about 93% had zero hospitalizations), with only minor variation by group. Emergency room use showed somewhat more variation, with Black patients having the highest proportion with ≥1 ER visit (about 26%), while Asian patients had the lowest (about 14%). Physician office visits were consistently high across all groups, with over 90% of patients having ≥2 visits, though Asian patients had slightly fewer visits on average. COVID-19 vaccination coverage varied substantially, ranging from about 31% in Black patients to 49% in Asian patients, with an overall rate of 38%.

Table 52. Healthcare utilization of Paxlovid users 1 Year Prior to Index

	White		Black		Asian		Hispanic		Missing		Overall	
	N	%	N	%	N	%	N	%	N	%	N	%
Hospitalization												
0	181,119	92.95	17,993	92.48	13,233	95.99	28,121	93.24	16,653	92.89	257,119	93.09
1	9,951	5.11	1,023	5.26	436	3.16	1,491	4.94	955	5.33	13,856	5.02
2+	3,790	1.94	441	2.27	117	0.85	548	1.82	319	1.78	5,215	1.89
Mean+/- SD	0.10	0.46	0.11	0.49	0.05	0.31	0.10	0.43	0.10	0.44	0.10	0.45
Median, IQR	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Length of Stay												
Mean+/- SD	10.8	16.6	11.9	16.9	9.1	13.3	9.9	13.4	10.3	16.2	10.7	16.2
Median, IQR	5	3-11	6	3-12	5	3-9	5	3-10	5	3-10	5	3-11
Emergency Room Visits												
0	153,717	78.89	14,425	74.14	11,922	86.48	23,560	78.12	14,222	79.33	217,846	78.88
1	23,730	12.18	2,644	13.59	1,174	8.52	3,756	12.45	2,059	11.49	33,363	12.08

Table 52. Healthcare utilization of Paxlovid users 1 Year Prior to Index

	White		Black		Asian		Hispanic		Missing		Overall	
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
2+	17,413	8.94	2,388	12.27	690	5.01	2,844	9.43	1,646	9.18	24,981	9.04
Mean+/-SD	0.48	1.76	0.61	1.88	0.28	1.28	0	1.67	0	1.73	0	1.74
Median, IQR	0	0.00	0	0-1	0	0.00	0	0.00	0	0.00	0	0.00
Physician Office Visits												
0	3,647	1.87	352	1.81	607	4.40	962	3.19	630	3.51	6,198	2.24
1	4,524	2.32	414	2.13	561	4.07	935	3.10	654	3.65	7,088	2.57
2+	186,689	95.81	18,691	96.06	12,618	91.53	28,263	93.71	16,643	92.84	262,904	95.19
Mean+/-SD	16.64	15.37	16.76	15.03	12.71	13.31	15	14.30	15	14.90	16	15.14
Median, IQR	12	6-22	13	7-22	9	4-16	11	6-20	11	5-20	12	6-21
COVID-19 vaccination	75,944	38.97	5,982	30.74	6,709	48.67	10,066	33.38	6,383	35.61	105,084	38.05

Table 53 summarizes the Hospitalization among subgroups of patients with COVID-19 by Paxlovid prescription status after PSM. Across all subgroups—White, African American, ≥65 years, <65 years, and vaccinated—Paxlovid consistently shows a substantially lower risk of hospitalization within both 15 and 30 days after COVID-19 diagnosis compared with matched untreated patients. Relative risks in the primary analyses range from 0.11 to 0.19, indicating an 81–89% reduction in hospitalization risk across groups. Sensitivity analyses adjusting for potential misclassification of day-of-diagnosis hospitalizations yield slightly higher—but still very low—risk estimates, and the protective association remains robust, with adjusted relative risks generally between 0.15 and 0.25.

Table 53 shows higher incidence proportion and relative risk of hospitalization among the non-Paxlovid treated group as compared to the Paxlovid treated group across all subgroups, including race, age, and vaccination status. These results are consistent in the 30 day and 15 day post-COVID-19 groups.

Table 53. Hospitalization among subgroups of patients with COVID-19 by nirmatrelvir/ritonavir prescription status after PSM

	Hospitalization Within 30 Days		Hospitalization Within 15 Days	
	Nirmatrelvir/ Ritonavir	**Non-nirmatrelvir/ Ritonavir**	**Nirmatrelvir/ Ritonavir**	**Non-nirmatrelvir/ Ritonavir**
Race				
White[a]				
Patients at risk / events	10,374 / 95	29,825 / 1750	10,374 / 66	29,825 / 1637
Incidence proportion, % (95% CI)	0.92 (0.74, 1.12)	5.87 (5.60, 6.14)	0.64 (0.49, 0.81)	5.49 (5.23, 5.75)
Relative risk (95% CI)	0.16 (0.13, 0.19)	-	0.12 (0.09, 0.15)	-
Sensitivity analysis				
True events, n[b]	92.62	1323.64	63.62	1210.64
Crude relative risk (95% CI)[b]	0.201 (0.163, 0.248)	-	0.151 (0.118, 0.194)	-

Table 53. Hospitalization among subgroups of patients with COVID-19 by nirmatrelvir/ritonavir prescription status after PSM

	Hospitalization Within 30 Days		Hospitalization Within 15 Days	
	Nirmatrelvir/ Ritonavir	Non-nirmatrelvir/ Ritonavir	Nirmatrelvir/ Ritonavir	Non-nirmatrelvir/ Ritonavir
Adjusted relative risk (95% CI)[c]	0.200 (0.163, 0.248)	-	0.150 (0.118, 0.194)	-
African American[d]				
Patients at risk / events	943 / 12	2922 / 217	943 / 10	2922 / 207
Incidence proportion, % (95% CI)	1.27 (0.66, 2.21)	7.43 (6.50, 8.44)	1.06 (0.51, 1.94)	7.08 (6.18, 8.08)
Relative risk (95% CI)	0.19 (0.10, 0.34)	-	0.17 (0.09, 0.31)	-
Sensitivity analysis				
True events, n[b]	11.66	157.50	9.66	147.50
Crude relative risk (95% CI)[b]	0.229 (0.127, 0.414)	-	0.203 (0.106, 0.387)	-
Adjusted relative risk (95% CI)[c]	0.252 (0.139, 0.455)	-	0.224 (0.117, 0.430)	-
Age				
≥65 years[e]				
Patients at risk / events	5172 / 82	14,025 / 1607	5172 / 61	14,025 / 1537
Incidence proportion, % (95% CI)	1.59 (1.26, 1.96)	11.46 (10.94, 12.00)	1.18 (0.90, 1.51)	10.96 (10.45, 11.49)
Relative risk (95% CI)	0.17 (0.13, 0.21)	-	0.13 (0.10, 0.17)	-
Sensitivity analysis				
True events, n[b]	79.96	1190.5	58.96	1120.50
Crude relative risk (95% CI)[b]	0.182 (0.146, 0.228)	-	0.143 (0.110, 0.185)	-
Adjusted relative risk (95% CI)[c]	0.219 (0.176, 0.274)	-	0.173 (0.134, 0.223)	-
<65 years[f]				
Patients at risk / events	7267 / 30	22,465 / 550	7267 / 19	22,465 / 489
Incidence proportion, % (95% CI)	0.41 (0.28, 0.59)	2.45 (2.25, 2.66)	0.26 (0.16, 0.41)	2.18 (1.99, 2.38)
Relative risk (95% CI)	0.16 (0.11, 0.23)	-	0.11 (0.07, 0.18)	-
Sensitivity analysis				
True events, n[b]	29.32	432.36	18.32	371.36
Crude relative risk (95% CI)[b]	0.210 (0.144, 0.304)	-	0.153 (0.095, 0.244)	-
Adjusted relative risk (95% CI)[c]	0.197 (0.135, 0.284)	-	0.143 (0.089, 0.228)	-
Vaccination status				
Vaccinated[g]				
Patients at risk / events	8709 / 71	24,082 / 1123	8709 / 48	24,082 / 1045
Incidence proportion, % (95% CI)	0.82 (0.64, 1.03)	4.66 (4.40, 4.94)	0.55 (0.41, 0.73)	4.34 (4.09, 4.60)
Relative risk (95% CI)	0.17 (0.14, 0.22)	-	0.13 (0.09, 0.17)	-
Sensitivity analysis				
True events, n[b]	69.98	851.34	46.98	773.34
Crude relative risk (95% CI)[b]	0.227 (0.178, 0.290)	-	0.168 (0.125, 0.225)	-
Adjusted relative risk (95% CI)[c]	0.225 (0.178, 0.287)	-	0.167 (0.125, 0.224)	-

Table 53. Hospitalization among subgroups of patients with COVID-19 by nirmatrelvir/ritonavir prescription status after PSM

	Hospitalization Within 30 Days		Hospitalization Within 15 Days	
	Nirmatrelvir/ Ritonavir	Non-nirmatrelvir/ Ritonavir	Nirmatrelvir/ Ritonavir	Non-nirmatrelvir/ Ritonavir

PSM=propensity score matching.
Relative risk and 95% CIs were calculated using modified Poisson regression with a robust error variance.
aThe covariates, including cohort month/year, region, medical history of hyperlipidemia were adjusted in the model among White patients.
bSensitivity analysis to account for hospitalizations on the day of COVID-19 diagnosis. The analysis uses as a positive predictive value of 0.66 to estimate true events (ie, excluding day of diagnosis hospitalizations estimated to be incidental) and associated crude relative risk.
cAdjusted relative accounts for the ratio of the relative risk to the crude relative risk.
dThe covariates, including cohort month/year, region, medical history of hypertension, hyperlipidemia and diabetes, and baseline physician office visits were adjusted in the model among Africa American patients.
eThe covariates, including cohort month/year, age (continuous), ethnicity, region, baseline hyperlimidemia, number of physician office visit and COVID-19 vaccines status were adjusted in the model among ≥65-year-old patients.
fThe covariates, including cohort month/year, age (continuous), Deyo-Charlson Comorbidity Index Score and medical history of hypertension, hyperlipidemia, and diabetes mellitus were adjusted in the model among <65-year-old patients.
gThe covariates, including cohort month/year, ethnicity, region, medical history of hypertension and hyperlipidemia, and baseline telemedicine visits were adjusted in the model among vaccinated patients.

10.3.2. Secondary Objectives

10.3.2.1. Objective 1: Estimate the incidence of oxygen supplementation among COVID-19 patients hospitalized with mechanical ventilation/ECMO

Table 54 shows the incidence of oxygen supplementation among COVID-19 patients hospitalized with mechanical ventilation/ECMO from 1/1/2020-07/20/2022. Across all COVID-19 cohorts, incidence of ICU-level respiratory support (mechanical ventilation/ECMO) was substantially higher among hospitalized patients, with rates ranging from 3,790 to 4,013 per 1,000 person-years across cohorts. Among hospitalized groups, the High-Risk trial-similar cohort showed the highest incidence (about 4,013 per 1,000 person-years), followed by the Standard-Risk cohort (3,962) and the Source cohort (3,790). In contrast, rates among non-hospitalized patients were far lower, ranging from 6.1 to 34.2 per 1,000 person-years, with the Source cohort having the highest and the Standard-Risk cohort the lowest.

Table 54. Incidence of oxygen supplementation among COVID-19 patients hospitalized with mechanical ventilation/ECMO, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate per 1000 person years	95% CI	
Overall						
Source Cohort						
ICU/Mechanical ventilation/ECMO	1,649,617	51,912	122,305.72	424.44	420.81	428.11
High Risk Trial Similar Cohort						
ICU/Mechanical ventilation/ECMO	939,400	30,508	69,907.64	436.40	431.54	441.33
Standard Risk Trial Similar Cohort						
ICU/Mechanical ventilation/ECMO	590,368	10,350	43,740.73	236.62	232.11	241.22
Hospitalized						
Source Cohort						

Table 54. Incidence of oxygen supplementation among COVID-19 patients hospitalized with mechanical ventilation/ECMO, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate per 1000 person years	95% CI	
ICU/Mechanical ventilation/ECMO	205,930	48,159	12,706.04	3,790.25	3,756.55	3,824.25
High Risk Trial Similar Cohort						
ICU/Mechanical ventilation/ECMO	122,308	29,799	7,425.99	4,012.80	3,967.50	4,058.62
Standard Risk Trial Similar Cohort						
ICU/Mechanical ventilation/ECMO	41,456	10,097	2,548.70	3,961.63	3,885.11	4,039.67
Non-Hospitalized						
Source Cohort						
ICU/Mechanical ventilation/ECMO	1,443,687	3,753	109,599.69	34.24	33.17	35.36
High Risk Trial Similar Cohort						
ICU/Mechanical ventilation/ECMO	817,092	709	62,481.65	11.35	10.54	12.21
Standard Risk Trial Similar Cohort						
ICU/Mechanical ventilation/ECMO	548,912	253	41,192.03	6.14	5.43	6.95

Table 55 shows the incidence of oxygen supplementation among COVID-19 patients hospitalized with mechanical ventilation/ECMO from 1/1/2020-10/31/2020 in the Pre-Vaccine period. During the pre-vaccine period, incidence of ICU-level respiratory support (mechanical ventilation/ECMO) was substantially higher among hospitalized patients than non-hospitalized patients across all cohorts. Among hospitalized patients, incidence rates were extremely high, ranging from 4,293 to 4,814 per 1,000 person-years, with the High-Risk trial-similar cohort having the highest rates, followed by the Source and Standard-Risk cohorts. In contrast, among non-hospitalized patients, incidence rates were much lower, ranging from 8.6 to 73.0 per 1,000 person-years, with the Source cohort showing the highest rates and the Standard-Risk cohort the lowest.

Table 55. Incidence of oxygen supplementation among COVID-19 patients hospitalized with mechanical ventilation/ECMO, 1/1/2020-10/31/2020 (Pre-Vaccine Period)

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate per 1000 person years	95% CI	
Overall						
Source Cohort						
ICU/Mechanical ventilation/ECMO	281,751	14,252	21,788.41	654.11	643.46	664.94
High Risk Trial Similar Cohort						
ICU/Mechanical ventilation/ECMO	162,404	8,425	12,542.50	671.72	657.53	686.21
Standard Risk Trial Similar Cohort						
ICU/Mechanical ventilation/ECMO	96,946	2,376	7,715.37	307.96	295.82	320.59
Hospitalized						
Source Cohort						

Table 55. Incidence of oxygen supplementation among COVID-19 patients hospitalized with mechanical ventilation/ECMO, 1/1/2020-10/31/2020 (Pre-Vaccine Period)

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate per 1000 person years	95% CI	
ICU/Mechanical ventilation/ECMO	47,481	12,868	2,838.43	4,533.49	4,455.84	4,612.51
High Risk Trial Similar Cohort						
ICU/Mechanical ventilation/ECMO	29,292	8,247	1,713.03	4,814.27	4,711.48	4,919.30
Standard Risk Trial Similar Cohort						
ICU/Mechanical ventilation/ECMO	8,758	2,314	538.96	4,293.46	4,122.04	4,472.00
Non-Hospitalized						
Source Cohort						
ICU/Mechanical ventilation/ECMO	234,270	1,384	18,949.98	73.03	69.29	76.99
High Risk Trial Similar Cohort						
ICU/Mechanical ventilation/ECMO	133,112	178	10,829.46	16.44	14.19	19.04
Standard Risk Trial Similar Cohort						
ICU/Mechanical ventilation/ECMO	88,188	62	7,176.41	8.64	6.74	11.08

Table 56 shows the incidence of oxygen supplementation among COVID-19 patients hospitalized with mechanical ventilation/ECMO from 12/13/2020-07/20/2022 in the Vaccine period. During the vaccine period, incidence of ICU-level respiratory support (mechanical ventilation/ECMO) remained much higher among hospitalized patients than non-hospitalized patients across all cohorts. Among hospitalized individuals, rates ranged from 3,573 to 3,937 per 1,000 person-years, with the Standard-Risk trial-similar cohort showing the highest rate (~3,937), followed closely by the High-Risk (~3,790) and Source (~3,573) cohorts. In contrast, rates among non-hospitalized patients were far lower, ranging from 5.7 to 26.0 per 1,000 person-years, with the Source cohort having the highest rate and the Standard-Risk cohort the lowest.

Table 56. Incidence of oxygen supplementation among COVID-19 patients hospitalized with mechanical ventilation/ECMO, 12/13/2020-07/20/2022 (Vaccine Period)

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate per 1000 person years	95% CI	
Overall						
Source Cohort						
ICU/Mechanical ventilation/ECMO	1,181,574	31,664	85,793.66	369.07	365.03	373.16
High Risk Trial Similar Cohort						
ICU/Mechanical ventilation/ECMO	666,159	18,339	48,625.17	377.15	371.73	382.65
Standard Risk Trial Similar Cohort						
ICU/Mechanical ventilation/ECMO	429,082	7,000	30,834.61	227.02	221.76	232.40
Hospitalized						
Source Cohort						

Table 56. Incidence of oxygen supplementation among COVID-19 patients hospitalized with mechanical ventilation/ECMO, 12/13/2020-07/20/2022 (Vaccine Period)

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate per 1000 person years	95% CI	
ICU/Mechanical ventilation/ECMO	133,589	29,650	8,298.16	3,573.08	3,532.64	3,613.98
High Risk Trial Similar Cohort						
ICU/Mechanical ventilation/ECMO	77,129	17,889	4,719.99	3,790.05	3,734.91	3,846.00
Standard Risk Trial Similar Cohort						
ICU/Mechanical ventilation/ECMO	28,452	6,833	1,735.57	3,937.03	3,844.78	4,031.49
Non-Hospitalized						
Source Cohort						
ICU/Mechanical ventilation/ECMO	1,047,985	2,014	77,495.50	25.99	24.88	27.15
High Risk Trial Similar Cohort						
ICU/Mechanical ventilation/ECMO	589,030	450	43,905.17	10.25	9.35	11.24
Standard Risk Trial Similar Cohort						
ICU/Mechanical ventilation/ECMO	400,630	167	29,099.04	5.74	4.93	6.68

Table 57 shows the incidence of oxygen supplementation among COVID-19 patients hospitalized with mechanical ventilation/ECMO from 12/15/2021-07/20/2022 in the Omicron period. During the Omicron period, incidence of ICU-level respiratory support (mechanical ventilation/ECMO) remained substantially higher among hospitalized patients than non-hospitalized patients across all cohorts. Among hospitalized individuals, incidence rates ranged from 3,046 to 3,885 per 1,000 person-years, with the Standard-Risk trial-similar cohort showing the highest rate (~3,885), followed by the High-Risk (~3,381) and Source (~3,046) cohorts. In contrast, among non-hospitalized patients, rates were far lower, ranging from 6.0 to 24.0 per 1,000 person-years, with the Source cohort having the highest rate and the Standard-Risk cohort the lowest.

Overall, the incidence rate of oxygen supplementation among COVID-19 patients was highest in the Pre-Vaccine period (Table 55) but decreased in the Vaccine period (Table 56) and further decreased during the Omicron period (Table 57). Incidence rates of oxygen supplementation, varied by setting and period.

Table 57. Incidence of oxygen supplementation among COVID-19 patients hospitalized with mechanical ventilation/ECMO, 12/15/2021-07/20/2022 (Omicron Period)

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate per 1000 person years	95% CI	
Overall						
Source Cohort						
ICU/Mechanical ventilation/ECMO	515,000	7,926	33,188.61	238.82	233.62	244.13
High Risk Trial Similar Cohort						

Table 57. Incidence of oxygen supplementation among COVID-19 patients hospitalized with mechanical ventilation/ECMO, 12/15/2021-07/20/2022 (Omicron Period)

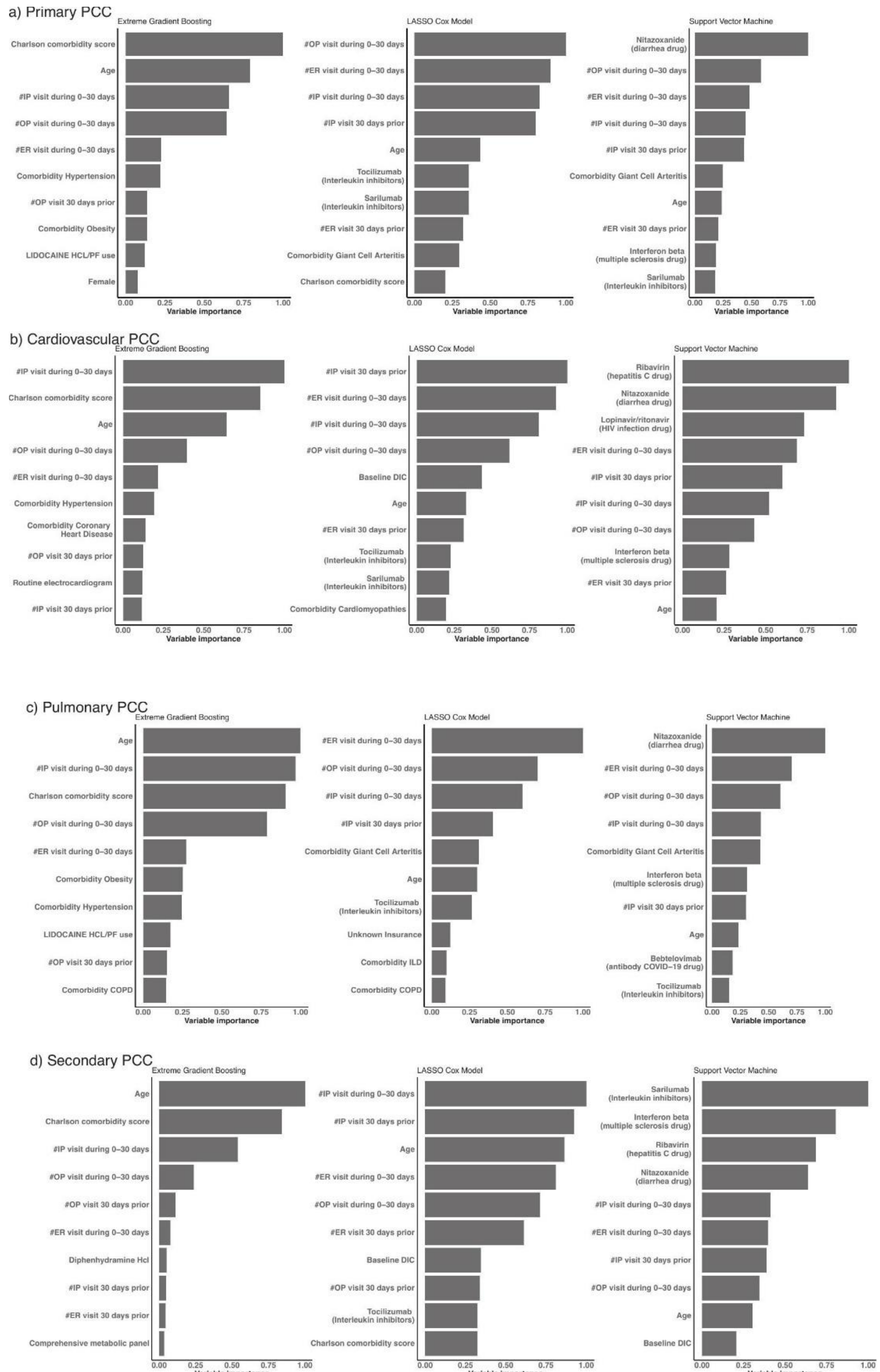
Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate per 1000 person years	95% CI	
ICU/Mechanical ventilation/ECMO	292,998	4,539	19,217.94	236.19	229.41	243.16
Standard Risk Trial Similar Cohort						
ICU/Mechanical ventilation/ECMO	179,319	1,339	10,854.17	123.36	116.93	130.15
Hospitalized						
Source Cohort						
ICU/Mechanical ventilation/ECMO	39,529	7,185	2,359.17	3,045.56	2,975.95	3,116.80
High Risk Trial Similar Cohort						
ICU/Mechanical ventilation/ECMO	21,773	4,287	1,267.93	3,381.10	3,281.39	3,483.84
Standard Risk Trial Similar Cohort						
ICU/Mechanical ventilation/ECMO	6,118	1,276	328.41	3,885.44	3,678.00	4,104.59
Non-Hospitalized						
Source Cohort						
ICU/Mechanical ventilation/ECMO	475,471	741	30,829.44	24.04	22.37	25.83
High Risk Trial Similar Cohort						
ICU/Mechanical ventilation/ECMO	271,225	252	17,950.01	14.04	12.41	15.88
Standard Risk Trial Similar Cohort						
ICU/Mechanical ventilation/ECMO	173,201	63	10,525.77	5.99	4.68	7.66

10.3.3. Exploratory Objectives

10.3.3.1. Objective 1: Identify predictors of COVID-19 severe outcomes/manifestations and Long COVID with machine learning (ML) methods

Figure 6 shows the top 10 predictors (ranked by importance) for developing new primary PCC (a), cardiovascular PCC (b), pulmonary PCC (c), and secondary PCC (d) picked by three different machine learning models —Extreme Gradient Boosting, LASSO Cox, and Support Vector Machine. Across all panels and models, Charlson comorbidity score and recent healthcare utilization variables (for example, outpatient/ER visits within 0–30 days or 31–90 days before infection) rank among the most important predictors across outcome types. In addition, age and baseline comorbidity burden appear prominently, though their relative importance varies by model. For cardiovascular PCC, specific medical history variables (such as coronary disease) are more heavily weighted. For pulmonary PCC, recent respiratory-related utilization (for example, outpatient visits with respiratory diagnoses) shows elevated importance. Secondary PCC models highlight a mix of utilization, comorbidity burden, and baseline symptom indicators.

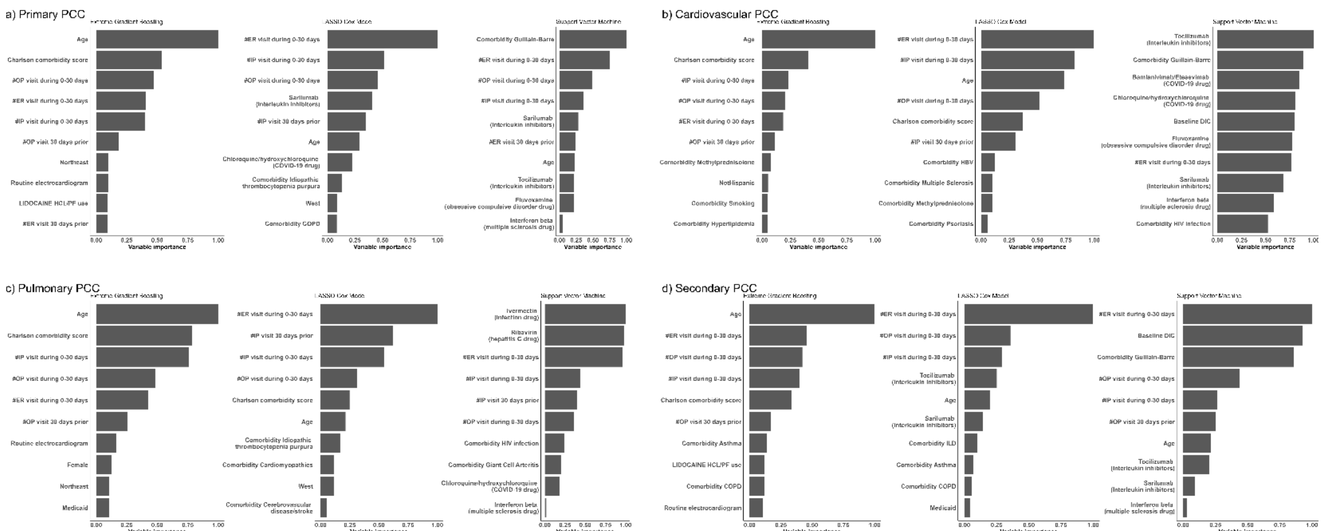
Figure 6. Top 10 predictors (ranked by importance) for developing new primary PCC (a), cardiovascular PCC (b), pulmonary PCC (c), and secondary PCC (d) picked by three different machine learning models



The lengths of horizontal bars represented variable importance, calculated as (absolute value of log hazard ratio for each predictor)/(maximum absolute value of log hazard ratio for all predictors) for LASSO Cox model, (reduction of impurity for each predictor)/(maximum reduction of impurity for all predictors) for XGBoost models, and (absolute value of support vector weight for each predictor)/(maximum absolute value of support vector weight from all predictors) for support vector machine models. COPD, chronic obstructive pulmonary disease; DIC, disseminated intravascular coagulation; ER, emergency room; HIV, human immunodeficiency virus; ILD, interstitial lung disease; IP, inpatient; LASSO, Least Absolute Shrinkage and Selection Operator; Lidocaine HCl/PF, Lidocaine hydrochloride preservative-free; OP, outpatient; PCC, post–COVID-19 conditions; #, number.

Figure 7 shows the top 10 predictors (ranked by importance) for developing new primary PCC (a), cardiovascular PCC (b), pulmonary PCC (c), and secondary PCC (d) in the Omicron era picked by three different machine learning models. Age, Charlson comorbidity score, and healthcare utilization during the first 30 days after COVID-19 infection were consistently identified as the leading risk factors for developing new primary or secondary PCC by three different machine learning models in both the full study period and the Omicron era.

Figure 7. Top 10 predictors (ranked by importance) for developing new primary PCC (a), cardiovascular PCC (b), pulmonary PCC (c), and secondary PCC (d) in the Omicron era picked by three different machine learning models



The lengths of horizontal bars represented variable importance, calculated as (absolute value of log hazard ratio for each predictor)/(maximum absolute value of log hazard ratio for all predictors) for LASSO Cox model, (reduction of impurity for each predictor)/(maximum reduction of impurity for all predictors) for XGBoost models, and (absolute value of support vector weight for each predictor)/(maximum absolute value of support vector weight from all predictors) for support vector machine models. COPD, chronic obstructive pulmonary disease; DIC, disseminated intravascular coagulation; ER, emergency room; HBV, hepatitis B virus, HIV, human immunodeficiency virus; ILD, interstitial lung disease; IP, inpatient; LASSO, Least Absolute Shrinkage and Selection Operator; Lidocaine HCL/PF, Lidocaine hydrochloride preservative-free; OP, outpatient; PCC, post–COVID-19 conditions; XGBoost, Extreme Gradient Boosting; #, number.

10.3.3.2. Objective 2: Predict risk of developing severe outcomes/manifestation and Long COVID with machine learning (ML) methods at the patient level

Figure 8 shows the predicted risk of developing severe outcomes/manifestation and Long COVID with machine learning (ML) methods at the patient level. The probability of remaining free of developing new primary PCC for each patient is shown. Single patients are shown in blue; green, yellow, and red represent increasing amount of overlap (multiple patients in the same location on the graph). PCC, post–COVID-19 condition.

Figure 8. Individual-level risk prediction

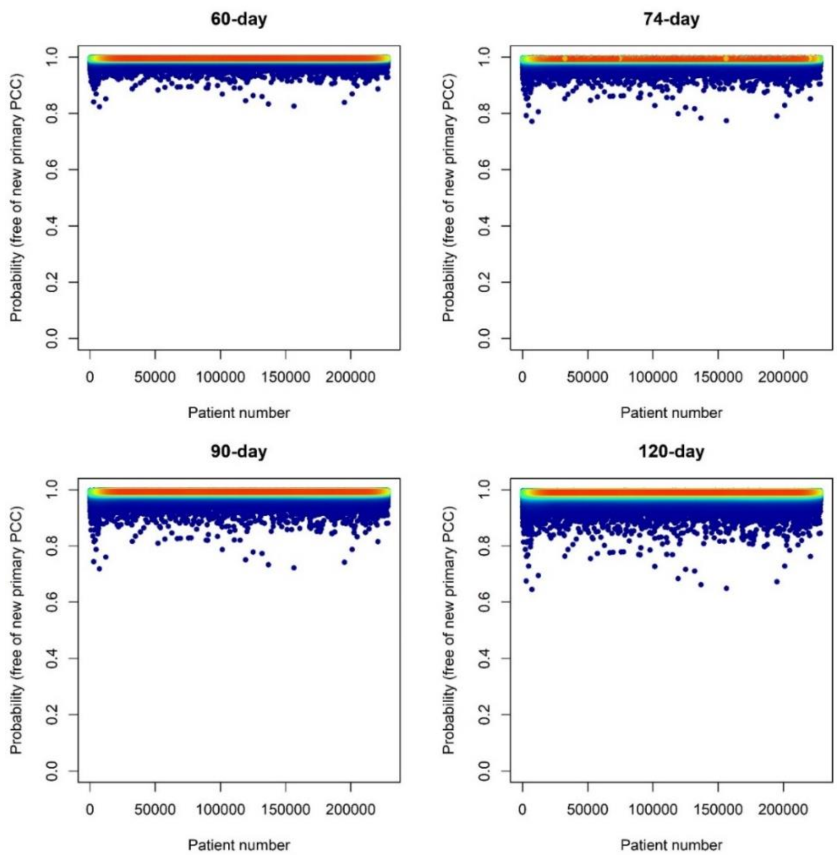


Table 58 shows the AUCs for predicting newly developed primary PCC, cardiovascular PCC, pulmonary PCC, and secondary PCC averaged over 3 independent testing groups. Across all four PCC outcomes, model performance was modest and stable over time, with dynamic AUCs generally in the 0.67–0.74 range for primary, cardiovascular, and pulmonary PCC, and notably higher (0.80–0.82) for secondary PCC. XGBoost consistently achieved the highest AUCs across outcomes and follow-up windows, with LASSO Cox, Survival SVM, and the deep learning models performing similarly but slightly lower. AUCs declined gradually as the follow-up window increased (e.g., day 60 → day 120), though the drop was small, indicating consistent predictive discrimination across time.

Table 58. Dynamic AUCs for predicting newly developed primary PCC, cardiovascular PCC, pulmonary PCC, and secondary PCC averaged over 3 independent testing groups in 3-fold cross validation

	Primary PCC Selected follow-up day				Cardiovascular PCC Selected follow-up day				Pulmonary PCC Selected follow-up day				Secondary PCC Selected follow-up day			
	60	74	90	120	60	74	90	120	60	74	90	120	60	74	90	120
Machine learning																
XGBoost	0.6935	0.6868	0.6840	0.6795	0.7322	0.7252	0.7212	0.7157	0.7029	0.6970	0.6939	0.6901	0.8147	0.8131	0.8089	0.8072
LASSO Cox model	0.6893	0.6819	0.6787	0.6743	0.7245	0.7168	0.7133	0.7082	0.6977	0.6911	0.6877	0.6843	0.8076	0.8058	0.8021	0.7999
Survival Support Vector Machine model	0.6888	0.6816	0.6786	0.6744	0.7237	0.7167	0.7134	0.7088	0.6977	0.6912	0.6881	0.6848	0.8102	0.8081	0.8037	0.8016
Deep learning																
Deep Cox Proportional Hazards model	0.6885	0.6816	0.6780	0.6730	0.7288	0.7213	0.7172	0.7109	0.6980	0.6921	0.6892	0.6854	0.8151	0.8109	0.8062	0.8026
Deep Cox Mixtures model	0.6884	0.6807	0.6777	0.6728	0.7274	0.7206	0.7163	0.7096	0.6966	0.6902	0.6877	0.6838	0.8132	0.8099	0.8030	0.7989
Deep Survival Machine model	0.6884	0.6810	0.6777	0.6730	0.7230	0.7158	0.7118	0.7062	0.6971	0.6912	0.6882	0.6844	0.8110	0.8078	0.8028	0.7999

AUC, area under the receiver operating characteristic curve; LASSO, Least Absolute Shrinkage and Selection Operator; PCC, post–COVID-19 condition; XGBoost, Extreme Gradient Boosting.

Table 59. Dynamic AUCs for predicting newly developed primary PCC, cardiovascular PCC, pulmonary PCC, and secondary PCC averaged over 3 independent testing groups in 3-fold cross validation

	Primary PCC Selected follow-up day				Cardiovascular PCC Selected follow-up day				Pulmonary PCC Selected follow-up day				Secondary PCC Selected follow-up day			
	60	74	90	120	60	74	90	120	60	74	90	120	60	74	90	120
Machine learning																
XGBoost	0.6886	0.6819	0.6752	0.6686	0.6951	0.6923	0.6860	0.6951	0.6845	0.6826	0.6791	0.6747	0.8044	0.7953	0.7871	0.7843
LASSO Cox model	0.6859	0.6807	0.6742	0.6701	0.6946	0.6904	0.6841	0.6946	0.6990	0.6902	0.6851	0.6765	0.7959	0.7907	0.7822	0.7832

Table 59. Dynamic AUCs for predicting newly developed primary PCC, cardiovascular PCC, pulmonary PCC, and secondary PCC averaged over 3 independent testing groups in 3-fold cross validation

	Primary PCC Selected follow-up day				Cardiovascular PCC Selected follow-up day				Pulmonary PCC Selected follow-up day				Secondary PCC Selected follow-up day			
	60	**74**	**90**	**120**	**60**	**74**	**90**	**120**	**60**	**74**	**90**	**120**	**60**	**74**	**90**	**120**
Survival Support Vector Machine model	0.6803	0.6742	0.6696	0.6626	0.6788	0.6761	0.6713	0.6788	0.6910	0.6817	0.6777	0.6697	0.7678	0.7563	0.7532	0.7532
Deep learning																
Deep Cox Proportional Hazards model	0.6878	0.6824	0.6772	0.6685	0.6975	0.6914	0.6837	0.6794	0.6936	0.6868	0.6837	0.6762	0.8058	0.7821	0.7821	0.7788
Deep Cox Mixtures model	0.6845	0.6789	0.6743	0.6654	0.6974	0.6775	0.6820	0.6770	0.6962	0.6876	0.6847	0.6760	0.8066	0.7852	0.7852	0.7828
Deep Survival Machine model	0.6861	0.6809	0.6764	0.6670	0.6890	0.6824	0.6756	0.6723	0.6910	0.6844	0.6816	0.6741	0.7983	0.7740	0.7740	0.7686

AUC, area under the receiver operating characteristic curve; LASSO, Least Absolute Shrinkage and Selection Operator; PCC, post–COVID-19 condition; XGBoost, Extreme Gradient Boosting.

10.3.3.3. Objective 3: Assess the feasibility of Real-world effectiveness of Paxlovid in reducing the COVID-19 related outcomes (eg, hospitalization)

Demographics and baseline clinical characteristics for Paxlovid-treated versus non-Paxlovid COVID-19 cohorts, both before and after PSM, are described in Table 9 and Table 10. Healthcare utilization in the 12 months prior to index comparing both Paxlovid and non-Paxlovid treated cohorts are detailed in Table 16. Hospitalization among patients with COVID-19 patients by treatment status is also described in Table 18.

10.4. Other analyses

Analyses focused on pediatric patients are summarized below.

10.4.1. Primary Objectives

10.4.1.1. Objective 1: Describe the distribution of demographics, co-morbid conditions, medical history, selected biomarkers, and healthcare utilization at baseline for COVID-19 patients (including subpopulation with long COVID)

Due to the small number of pediatric patients, it was not feasible to report propensity score matched results as was done for the entire population in section 10.3.1.1. Exact age is unknown because the Optum® database only reports birth year.

Table 60. Patient demographics and baseline clinical characteristics by Paxlovid use

	Nirmatrelvir/ Ritonavir N=89	Non-nirmatrelvir/ Ritonavir N=11,674	Standardized Difference
Age, years, mean ± SD	15 (1.5)	14 (1.7)	0.401
Age bracket 12-17 (inclusive), n (%)	89 (100.0)	11,674 (100.0)	.
Male sex, n (%)	47 (52.8)	5,688 (48.7)	0.082
Race, n (%)			
Caucasian	63 (70.8)	7,711 (66.1)	0.102
African American	18 (20.2)	1,476 (12.6)	0.206
Asian	3 (3.4)	328 (2.8)	0.032
Other/Unknown	5 (5.6)	2,159 (18.5)	0.403
Ethnicity, n (%)			
Hispanic	12 (13.5)	1,962 (16.8)	0.093
Not Hispanic	61 (68.5)	7,888 (67.6)	0.021
Unknown	16 (18.0)	1,824 (15.6)	0.063
Cohort entry month/year, n (%)			
Dec 2021	.	1,643 (14.1)	.
Jan 2022	10 (11.2)	7,391 (63.3)	1.278
Feb 2022	4 (4.5)	845 (7.2)	0.117
Mar 2022	1 (1.1)	261 (2.2)	0.087
Apr 2022	10 (11.2)	338 (2.9)	0.33
May 2022	49 (55.1)	884 (7.6)	1.192
Jun 2022	15 (16.9)	312 (2.7)	0.492
Insurance type, n (%)			
Commercial	63 (70.8)	7,379 (63.2)	0.162
Medicare	.	63 (0.5)	.
Medicaid	15 (16.9)	2,907 (24.9)	0.199
Other Payor Type	4 (4.5)	421 (3.6)	0.045
Uninsured	.	37 (0.3)	.
Unknown	7 (7.9)	867 (7.4)	0.016
Geographic region, n (%)			
Northeast	30 (33.7)	4,910 (42.1)	0.173
Midwest	26 (29.2)	4,167 (35.7)	0.139
West	7 (7.9)	324 (2.8)	0.228
South	25 (28.1)	1,820 (15.6)	0.306
Other/Unknown	1 (1.1)	453 (3.9)	0.177
Comorbidities, n (%)			
Asthma	30 (33.7)	2,471 (21.2)	0.284
COPD	2 (2.2)	82 (0.7)	0.128
Coronary Heart Disease	.	2 (0.0)	.
Hypertension	2 (2.2)	140 (1.2)	0.081
Chronic Kidney Disease	3 (3.4)	87 (0.7)	0.186
Smoker	23 (25.8)	4,688 (40.2)	0.308
BMI>=30 or obesity	30 (33.7)	4,023 (34.5)	0.016

Table 60. Patient demographics and baseline clinical characteristics by Paxlovid use

	Nirmatrelvir/ Ritonavir N=89	Non-nirmatrelvir/ Ritonavir N=11,674	Standardized Difference
Diabetes Mellitus	4 (4.5)	169 (1.4)	0.18
Cancer	2 (2.2)	52 (0.4)	0.157
Comorbidity index, Mean ± SD	1 (1.1)	0 (0.6)	0.403
Receipt of ≥1 COVID-19 vaccination, n (%)	48 (53.9)	4,132 (35.4)	0.38
Number of previous SARS-CoV-2 infections, n (%)			
0	81 (91.0)	10,744 (92.0)	0.037
1	8 (9.0)	881 (7.5)	0.052
2+	0 (0.0)	49 (0.4)	1.202

Table 61. Healthcare utilization within 12 months before the index date

	Nirmatrelvir/ Ritonavir N=89	Non-nirmatrelvir/ Ritonavir N=11,674	Standardized Difference
Number of hospitalizations			
0	79 (88.8)	11,331 (97.1)	0.328
1	8 (9.0)	268 (2.3)	0.293
2+	2 (2.2)	75 (0.6)	0.135
Mean±SD	0 (0.5)	0 (0.3)	0.276
Length of stay, days			
Mean±SD	7 (7.7)	6 (8.4)	0.08
Emergency room visits			
0	69 (77.5)	8,459 (72.5)	0.117
1	12 (13.5)	1,837 (15.7)	0.064
2+	8 (9.0)	1,378 (11.8)	0.092
Mean±SD	0 (0.9)	0 (1.2)	0.117
Physician office visits			
0	1 (1.1)	861 (7.4)	0.314
1	9 (10.1)	1,380 (11.8)	0.055
2+	79 (88.8)	9,433 (80.8)	0.223
Mean±SD	9 (9.7)	5 (7.0)	0.376
Telemedicine visits			
0	35 (39.3)	5,071 (43.4)	0.084
1	10 (11.2)	1,865 (16.0)	0.139
2+	44 (49.4)	4,738 (40.6)	0.179
Mean±SD	5 (9.6)	2 (6.3)	0.28
Urgent care visits			
0	85 (95.5)	10,292 (88.2)	0.271
1	2 (2.2)	817 (7.0)	0.228
2+	2 (2.2)	565 (4.8)	0.141
Mean±SD	0 (0.4)	0 (0.8)	0.223

10.4.1.2. Objective 2: Describe the time to clinical events (e.g. hospitalization, ICU admission, death)

Due to the small number of pediatric patients, results are not able to contextualized compared to adults or the overall cohort/s.

Table 62. Time to COVID-19 Complications/interventions since COVID Diagnosis, Age 12 to 17

Study Endpoints	Events	Mean Time	SD	Median Time	IQR
		Overall			
Source Cohort					
Pneumonia	48	4.23	5.21	1	4.5
Kidney failure	28	4.71	7.7	1	3
Thrombotic event	9	6.11	7.06	3	8
ARDS	5	5.2	9.39	1	0
Heart failure	11	5.91	8.69	2	5
Sepsis/septic shock	14	3.93	7.37	1	2
Mechanical ventilation/ECMO	36	4.08	6.26	1	2.5
Hospitalization	181	3.94	6.3	1	1
All-cause mortality	2	7.5	7.78	7.5	11
In hospital death	1	2	.	2	0
Multi-organ dysfunction/failure	77	5.44	7.78	1	5
Vasopressor use	65	9.97	9.67	7	16
Renal impairment	77	80.48	110.9	39	118
Hepatic impairment	29	88.03	111.29	70	109
Dysgeusia	42	31.33	63.14	1	14
Diarrhea	278	83.92	100.06	55.5	110
Hypersensitivity reaction/allergic reaction	1,609	59.08	81.72	28	91
High Risk Trial Similar Cohort					
Pneumonia	42	4.36	5.38	1.5	5
Kidney failure	26	4.58	7.83	1	3
Thrombotic event	7	6.43	7.79	3	10
ARDS	5	5.2	9.39	1	0
Heart failure	11	5.91	8.69	2	5
Sepsis/septic shock	13	4.15	7.63	1	2
Mechanical ventilation/ECMO	34	3.94	6.28	1	2
Hospitalization	174	3.98	6.37	1	1
All-cause mortality	2	7.5	7.78	7.5	11
In hospital death	1	2	.	2	0
Multi-organ dysfunction/failure	71	5.66	7.97	1	7
Vasopressor use	63	10.08	9.78	7	19
Renal impairment	73	77.49	107.8	39	115
Hepatic impairment	28	87.61	113.31	66.5	117.5
Dysgeusia	38	34.53	65.63	1	15
Diarrhea	262	76.92	90.33	51	99
Hypersensitivity reaction/allergic reaction	1,528	57.66	76.94	28.5	91
Standard Risk Trial Similar Cohort					
Pneumonia	7	4.43	4.12	3	8
Kidney failure	2	6.5	7.78	6.5	11
Thrombotic event	2	5	5.66	5	8
ARDS	2	1	0	1	0
Heart failure	0				
Sepsis/septic shock	0				
Mechanical ventilation/ECMO	3	4.67	6.35	1	11
Hospitalization	19	2.53	4.31	1	0
All-cause mortality	0				
In hospital death	0				
Multi-organ dysfunction/failure	10	3.5	5.32	1	0
Vasopressor use	6	10.33	8.8	10	12
Renal impairment	3	125	205.32	12	361
Hepatic impairment	2	136.5	51.62	136.5	73
Dysgeusia	10	23.3	49.03	1	0
Diarrhea	44	115.07	112.59	108.5	174

Table 62. Time to COVID-19 Complications/interventions since COVID Diagnosis, Age 12 to 17

Study Endpoints	Events	Mean Time	SD	Median Time	IQR
Hypersensitivity reaction/allergic reaction	156	79.81	121.27	11	108

Table 63. Time to COVID-19 Complications/interventions since First Paxlovid Prescription, Age 12-17

Study Endpoints	Events	Mean Time	SD	Median Time	IQR
			Overall		
Paxlovid Cohort					
Pneumonia	1	2	.	2	0
Kidney failure	0	.	.	.	.
Thrombotic event	0	.	.	.	.
Heart failure	0	.	.	.	.
Sepsis/septic shock	0	.	.	.	.
Mechanical ventilation/ECMO	0	.	.	.	.
Hospitalization	0	.	.	.	.
All-cause mortality	0	.	.	.	.
In hospital death	0	.	.	.	.
Multi-organ dysfunction/failure	0	.	.	.	.
Vasopressor use	0	.	.	.	.
Renal impairment	1	28	.	28	0
Hepatic impairment	2	19.5	4.95	19.5	7
Dysgeusia	0	.	.	.	.
Diarrhea	0	.	.	.	.
Hypersensitivity reaction/allergic reaction	1	133	.	133	0

10.4.1.3. Objective 3: Estimate background incidence of COVID-19 manifestations/complications and safety outcome of interests following COVID-19 infection or Paxlovid exposure

10.4.1.3.1. Incidence of COVID-19 Complications/Interventions within 30 Days of COVID-19 Infection Among Pediatric Patients

Overall, among pediatric patients in the Source Cohort, the following complications and interventions, pneumonia, ICU/mechanical ventilation/ECMO, hospitalization, multi-organ dysfunction/failure and vasopressor use had the highest incidence rates (Table 64, Table 65, Table 66). It is not possible to ascertain the incidence of COVID-19 complications and interventions among pediatric Paxlovid patients given the low frequency of events (Table 67).

Table 64. Incidence of COVID-19 Complications/Interventions within 30 Days of COVID-19 Infection in the Source Cohort and Trial-similar Cohorts by Hospitalization Status Among Pediatric Patients, Overall, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Overall Person-time	Incidence Rate per 1000 person years	95% CI	
Source Cohort						
Pneumonia	173,143	1,117	13,077.06	85.42	80.55	90.58
Kidney failure	173,713	360	13,169.11	27.34	24.65	30.31
Thrombotic event	173,890	139	13,198.12	10.53	8.92	12.44
ARDS	174,051	96	13,212.80	7.27	5.95	8.88
Heart failure	173,934	187	13,198.28	14.17	12.28	16.35
Sepsis/septic shock	173,922	382	13,183.17	28.98	26.21	32.03
ICU/Mechanical ventilation/ECMO	173,648	690	13,140.31	52.51	48.74	56.58
Hospitalization	171,866	2,828	12,854.28	220.00	212.04	228.26
All-cause mortality	174,063	30	14,295.18	2.10	1.47	3.00
In hospital death	174,063	6	13,220.48	0.45	0.20	1.01
Multi-organ dysfunction/failure	172,710	1,448	13,017.31	111.24	105.65	117.12
Vasopressor use	172,086	1,082	12,998.84	83.24	78.42	88.35
High Risk Trial Similar Cohort						
Pneumonia	66,830	480	5,135.67	93.46	85.47	102.21
Kidney failure	67,197	136	5,185.27	26.23	22.17	31.03
Thrombotic event	67,306	50	5,199.69	9.62	7.29	12.69
ARDS	67,382	44	5,205.93	8.45	6.29	11.36
Heart failure	67,330	69	5,200.59	13.27	10.48	16.80
Sepsis/septic shock	67,334	124	5,196.20	23.86	20.01	28.46
ICU/Mechanical ventilation/ECMO	67,187	264	5,175.62	51.01	45.21	57.55
Hospitalization	66,253	1,073	5,046.24	212.63	200.28	225.75
All-cause mortality	67,387	11	5,534.31	1.99	1.10	3.59
In hospital death	67,387	3	5,209.20	0.58	0.19	1.79
Multi-organ dysfunction/failure	66,690	527	5,120.20	102.93	94.50	112.10
Vasopressor use	66,148	493	5,081.56	97.02	88.82	105.97
Standard Risk Trial Similar Cohort						
Pneumonia	110,139	577	8,232.41	70.09	64.60	76.05
Kidney failure	110,370	165	8,276.91	19.93	17.11	23.22
Thrombotic event	110,378	57	8,284.52	6.88	5.31	8.92
ARDS	110,393	40	8,286.47	4.83	3.54	6.58
Heart failure	110,394	75	8,284.55	9.05	7.22	11.35
Sepsis/septic shock	110,382	182	8,276.03	21.99	19.02	25.43
ICU/Mechanical ventilation/ECMO	110,350	316	8,264.06	38.24	34.25	42.70
Hospitalization	110,116	1,607	8,157.96	196.99	187.59	206.86
All-cause mortality	110,394	15	9,066.39	1.65	1.00	2.74
In hospital death	110,394	3	8,289.33	0.36	0.12	1.12
Multi-organ dysfunction/failure	110,233	724	8,228.37	87.99	81.81	94.64
Vasopressor use	109,837	509	8,215.08	61.96	56.80	67.58

Table 65. Incidence of COVID-19 Complications/Interventions within 30 Days of COVID-19 Infection in the Source Cohort and Trial-similar Cohorts by Hospitalization Status Among Pediatric Patients, Hospitalized, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Hospitalized Person-time	Incidence Rate per 1000 person years	95% CI	
Source Cohort						
Pneumonia	3,188	385	219.82	1,751.39	1,584.90	1,935.38
Kidney failure	3,225	228	233.35	977.09	858.14	1,112.51
Thrombotic event	3,261	86	245.97	349.64	283.03	431.93
ARDS	3,292	69	249.29	276.79	218.61	350.45
Heart failure	3,257	124	243.14	510.00	427.69	608.15
Sepsis/septic shock	3,246	291	230.15	1,264.38	1,127.15	1,418.33
ICU/Mechanical ventilation/ECMO	3,173	612	202.41	3,023.54	2,793.23	3,272.83
Hospitalization	2,828	2,828	23.98	117,954.44	113,686.24	122,382.87
All-cause mortality	3,296	19	269.67	70.46	44.94	110.46
In hospital death	3,296	6	254.42	23.58	10.60	52.49
Multi-organ dysfunction/failure	3,004	927	167.37	5,538.53	5,193.23	5,906.79
Vasopressor use	3,138	330	220.79	1,494.66	1,341.79	1,664.95
High Risk Trial Similar Cohort						
Pneumonia	1,234	165	85.85	1,921.94	1,649.96	2,238.75
Kidney failure	1,254	90	92.27	975.42	793.35	1,199.26
Thrombotic event	1,278	30	98.21	305.47	213.58	436.89
ARDS	1,285	32	98.68	324.27	229.32	458.54
Heart failure	1,277	56	96.74	578.84	445.47	752.16
Sepsis/septic shock	1,274	107	92.16	1,161.00	960.61	1,403.21
ICU/Mechanical ventilation/ECMO	1,233	252	79.37	3,174.99	2,806.22	3,592.22
Hospitalization	1,073	1,073	10.71	100,182.32	94,363.82	106,359.60
All-cause mortality	1,286	8	105.21	76.04	38.03	152.05
In hospital death	1,286	3	100.90	29.73	9.59	92.18
Multi-organ dysfunction/failure	1,156	358	66.41	5,390.37	4,859.94	5,978.69
Vasopressor use	1,216	111	87.97	1,261.83	1,047.64	1,519.83
Standard Risk Trial Similar Cohort						
Pneumonia	1,624	181	110.03	1,645.07	1,422.05	1,903.06
Kidney failure	1,635	117	115.61	1,012.04	844.31	1,213.08
Thrombotic event	1,636	40	120.87	330.94	242.75	451.17
ARDS	1,636	29	121.46	238.76	165.92	343.58
Heart failure	1,637	59	119.58	493.40	382.28	636.82
Sepsis/septic shock	1,636	152	112.86	1,346.77	1,148.82	1,578.83
ICU/Mechanical ventilation/ECMO	1,629	296	102.39	2,890.98	2,579.71	3,239.82
Hospitalization	1,607	1,607	11.35	141,640.14	134,881.60	148,737.34
All-cause mortality	1,637	11	133.80	82.21	45.53	148.46
In hospital death	1,637	3	123.53	24.29	7.83	75.30
Multi-organ dysfunction/failure	1,621	498	88.04	5,656.45	5,180.85	6,175.72
Vasopressor use	1,622	176	111.13	1,583.70	1,366.19	1,835.84

Table 66. Incidence of COVID-19 Complications/Interventions within 30 Days of COVID-19 Infection in the Source Cohort and Trial-similar Cohorts by Hospitalization Status Among Pediatric Patients, Non-Hospitalized, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Non-Hospitalized Person-time	Incidence Rate per 1000 person years	95% CI	
Source Cohort						
Pneumonia	169,955	732	12,857.23	56.93	52.95	61.21
Kidney failure	170,488	132	12,935.76	10.20	8.60	12.10
Thrombotic event	170,629	53	12,952.16	4.09	3.13	5.36
ARDS	170,759	27	12,963.51	2.08	1.43	3.04
Heart failure	170,677	63	12,955.15	4.86	3.80	6.23
Sepsis/septic shock	170,676	91	12,953.02	7.03	5.72	8.63
ICU/Mechanical ventilation/ECMO	170,475	78	12,937.90	6.03	4.83	7.53
Hospitalization	169,038	0	12,830.31	0.00	0.00	3,688.88
All-cause mortality	170,767	11	14,025.52	0.78	0.43	1.42
In hospital death	170,767	0	12,966.06	0.00	0.00	3,688.88
Multi-organ dysfunction/failure	169,706	521	12,849.93	40.54	37.21	44.18
Vasopressor use	168,948	752	12,778.05	58.85	54.79	63.21
High Risk Trial Similar Cohort						
Pneumonia	65,596	315	5,049.82	62.38	55.86	69.66
Kidney failure	65,943	46	5,093.00	9.03	6.77	12.06
Thrombotic event	66,028	20	5,101.48	3.92	2.53	6.08
ARDS	66,097	12	5,107.24	2.35	1.33	4.14
Heart failure	66,053	13	5,103.85	2.55	1.48	4.39
Sepsis/septic shock	66,060	17	5,104.04	3.33	2.07	5.36
ICU/Mechanical ventilation/ECMO	65,954	12	5,096.25	2.35	1.34	4.15
Hospitalization	65,180	0	5,035.53	0.00	0.00	3,688.88
All-cause mortality	66,101	3	5,429.10	0.55	0.18	1.71
In hospital death	66,101	0	5,108.30	0.00	0.00	3,688.88
Multi-organ dysfunction/failure	65,534	169	5,053.79	33.44	28.76	38.88
Vasopressor use	64,932	382	4,993.59	76.50	69.20	84.57
Standard Risk Trial Similar Cohort						
Pneumonia	108,515	396	8,122.38	48.75	44.18	53.80
Kidney failure	108,735	48	8,161.30	5.88	4.43	7.80
Thrombotic event	108,742	17	8,163.66	2.08	1.30	3.35
ARDS	108,757	11	8,165.01	1.35	0.75	2.43
Heart failure	108,757	16	8,164.97	1.96	1.20	3.20
Sepsis/septic shock	108,746	30	8,163.16	3.68	2.57	5.26
ICU/Mechanical ventilation/ECMO	108,721	20	8,161.68	2.45	1.58	3.80
Hospitalization	108,509	0	8,146.61	0.00	0.00	3,688.88
All-cause mortality	108,757	4	8,932.60	0.45	0.17	1.19
In hospital death	108,757	0	8,165.81	0.00	0.00	3,688.88
Multi-organ dysfunction/failure	108,612	226	8,140.33	27.76	24.37	31.63
Vasopressor use	108,215	333	8,103.95	41.09	36.91	45.75

Table 67. Incidence of COVID-19 Complications/Interventions within 30 Days of index date among Paxlovid Cohort with age<18 by Hospitalization Status

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate per 1000 person years	95% CI	
			Overall			
Paxlovid Cohort						
Pneumonia	115	1	6.48	154.44	21.76	1,096.38
Kidney failure	115	0	6.55	0.00	0.00	3,688.88
Thrombotic event	113	0	6.43	0.00	0.00	3,688.88
ARDS	115	0	6.56	0.00	0.00	3,688.88
Heart failure	116	0	6.63	0.00	0.00	3,688.88
Sepsis/septic shock	116	0	6.63	0.00	0.00	3,688.88
ICU/Mechanical ventilation/ECMO	116	0	6.63	0.00	0.00	3,688.88
Hospitalization	109	0	6.06	0.00	0.00	3,688.88
All-cause mortality	116	0	9.53	0.00	0.00	3,688.88
In hospital death	116	0	6.63	0.00	0.00	3,688.88
Multi-organ dysfunction/failure	113	2	6.27	318.86	79.75	1,274.93
Vasopressor use	109	2	6.06	330.24	82.59	1,320.46
			Hospitalized			
Paxlovid Cohort						
Pneumonia	0	.	.	0.00	0.00	3,688.88
Kidney failure	0	.	.	0.00	0.00	3,688.88
Thrombotic event	0	.	.	0.00	0.00	3,688.88
ARDS	0	.	.	0.00	0.00	3,688.88
Heart failure	0	.	.	0.00	0.00	3,688.88
Sepsis/septic shock	0	.	.	0.00	0.00	3,688.88
ICU/Mechanical ventilation/ECMO	0	.	.	0.00	0.00	3,688.88
Hospitalization	0	.	.	0.00	0.00	3,688.88
All-cause mortality	0	.	.	0.00	0.00	3,688.88
In hospital death	0	.	.	0.00	0.00	3,688.88
Multi-organ dysfunction/failure	0	.	.	0.00	0.00	3,688.88
Vasopressor use	0	.	.	0.00	0.00	3,688.88
			Non-Hospitalized			
Paxlovid Cohort						
Pneumonia	115	1	6.48	154.44	21.76	1,096.38
Kidney failure	115	0	6.55	0.00	0.00	3,688.88
Thrombotic event	113	0	6.43	0.00	0.00	3,688.88
ARDS	115	0	6.56	0.00	0.00	3,688.88
Heart failure	116	0	6.63	0.00	0.00	3,688.88
Sepsis/septic shock	116	0	6.63	0.00	0.00	3,688.88
ICU/Mechanical ventilation/ECMO	116	0	6.63	0.00	0.00	3,688.88
Hospitalization	109	0	6.06	0.00	0.00	3,688.88
All-cause mortality	116	0	9.53	0.00	0.00	3,688.88
In hospital death	116	0	6.63	0.00	0.00	3,688.88
Multi-organ dysfunction/failure	113	2	6.27	318.86	79.75	1,274.93
Vasopressor use	109	2	6.06	330.24	82.59	1,320.46

10.4.1.3.2. Incidence of Potential Safety Endpoints Among Pediatric Patients

Due to the low uptake of Paxlovid among pediatric patients and the limited sample size compared to adult patients, caution should be taken when interpreting the results below. Overall, among pediatric patients in the Source Cohort, Hypersensitivity reaction/allergic reaction and diarrhea had the highest incidence rates among health outcomes (Table 68). It is not possible to ascertain the incidence of COVID-19 complications and interventions among pediatric Paxlovid patients given the low frequency of events (Table 69).

Table 68. Incidence of Potential Safety Endpoints in the Source Cohort and Trial-similar Cohorts by Hospitalization Status among Pediatric Patients, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate per 1000 person years	95% CI	
			Overall			
Source Cohort						
Renal impairment	173,278	1,093	116,287.05	9.40	8.86	9.97
Hepatic impairment	173,767	478	117,070.18	4.08	3.73	4.47
Dysgeusia	173,931	1,204	116,286.25	10.35	9.79	10.96
Diarrhea	171,387	4,943	112,971.33	43.75	42.55	44.99
Hypersensitivity reaction/allergic reaction	163,347	11,367	103,896.75	109.41	107.41	111.44
High Risk Trial Similar Cohort						
Renal impairment	66,892	497	46,837.47	10.61	9.72	11.59
Hepatic impairment	67,387	218	47,408.16	4.60	4.03	5.25
Dysgeusia	67,316	566	46,924.57	12.06	11.11	13.10
Diarrhea	65,817	2,409	45,085.19	53.43	51.34	55.61
Hypersensitivity reaction/allergic reaction	57,868	5,636	37,540.44	150.13	146.26	154.10
Standard Risk Trial Similar Cohort						
Renal impairment	110,370	461	72,200.28	6.39	5.83	7.00
Hepatic impairment	110,394	135	72,423.26	1.86	1.58	2.21
Dysgeusia	110,328	699	71,726.39	9.75	9.05	10.50
Diarrhea	109,329	2,505	70,405.54	35.58	34.21	37.00
Hypersensitivity reaction/allergic reaction	109,754	5,823	69,233.63	84.11	81.97	86.30
			Hospitalized			
Source Cohort						
Renal impairment	3,173	375	2,128.57	176.17	159.22	194.94
Hepatic impairment	3,260	126	2,400.09	52.50	44.09	62.51
Dysgeusia	3,296	10	2,517.08	3.97	2.14	7.38
Diarrhea	3,201	318	2,202.22	144.40	129.37	161.18

Table 68. Incidence of Potential Safety Endpoints in the Source Cohort and Trial-similar Cohorts by Hospitalization Status among Pediatric Patients, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate per 1000 person years	95% CI	
Hypersensitivity reaction/allergic reaction	2,953	553	1,823.22	303.31	279.06	329.67
High Risk Trial Similar Cohort						
Renal impairment	1,235	151	885.42	170.54	145.40	200.03
Hepatic impairment	1,286	49	1,010.65	48.48	36.64	64.15
Dysgeusia	1,286	8	1,048.92	7.63	3.81	15.25
Diarrhea	1,246	129	907.91	142.08	119.56	168.85
Hypersensitivity reaction/allergic reaction	1,047	238	658.42	361.47	318.35	410.44
Standard Risk Trial Similar Cohort						
Renal impairment	1,635	170	1,020.98	166.51	143.27	193.52
Hepatic impairment	1,637	51	1,118.80	45.58	34.64	59.98
Dysgeusia	1,637	2	1,149.86	1.74	0.44	6.96
Diarrhea	1,626	137	1,045.84	131.00	110.80	154.87
Hypersensitivity reaction/allergic reaction	1,627	283	956.16	295.97	263.42	332.55
			Non-Hospitalized			
Source Cohort						
Renal impairment	170,105	718	114,158.48	6.29	5.85	6.77
Hepatic impairment	170,507	352	114,670.10	3.07	2.77	3.41
Dysgeusia	170,635	1,194	113,769.17	10.49	9.92	11.11
Diarrhea	168,186	4,625	110,769.11	41.75	40.57	42.97
Hypersensitivity reaction/allergic reaction	160,394	10,814	102,073.54	105.94	103.97	107.96
High Risk Trial Similar Cohort						
Renal impairment	65,657	346	45,952.05	7.53	6.78	8.37
Hepatic impairment	66,101	169	46,397.51	3.64	3.13	4.24
Dysgeusia	66,030	558	45,875.65	12.16	11.20	13.22
Diarrhea	64,571	2,280	44,177.28	51.61	49.54	53.77
Hypersensitivity reaction/allergic reaction	56,821	5,398	36,882.02	146.36	142.51	150.32
Standard Risk Trial Similar Cohort						
Renal impairment	108,735	291	71,179.30	4.09	3.65	4.59
Hepatic impairment	108,757	84	71,304.46	1.18	0.95	1.46
Dysgeusia	108,691	697	70,576.53	9.88	9.17	10.64
Diarrhea	107,703	2,368	69,359.70	34.14	32.79	35.54
Hypersensitivity reaction/allergic reaction	108,127	5,540	68,277.46	81.14	79.03	83.31

Table 69. Incidence of Potential Safety Endpoints among the Paxlovid Cohort with age<18 by Hospitalization Status

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate per 1000 person years	95% CI	
			Overall			
Renal impairment	113	0	16.21	0.00	0.00	3,688.88
Hepatic impairment	116	0	17.10	0.00	0.00	3,688.88
Dysgeusia	116	0	17.10	0.00	0.00	3,688.88
Diarrhea	115	1	16.65	60.07	8.46	426.47
Hypersensitivity reaction/allergic reaction	93	5	10.91	458.28	190.75	1,101.03
			Hospitalized			
Renal impairment	0	.	.	0.00	0.00	3,688.88
Hepatic impairment	0	.	.	0.00	0.00	3,688.88
Dysgeusia	0	.	.	0.00	0.00	3,688.88
Diarrhea	0	.	.	0.00	0.00	3,688.88
Hypersensitivity reaction/allergic reaction	0	.	.	0.00	0.00	3,688.88
			Non-Hospitalized			
Renal impairment	113	0	16.21	0.00	0.00	3,688.88
Hepatic impairment	116	0	17.10	0.00	0.00	3,688.88
Dysgeusia	116	0	17.10	0.00	0.00	3,688.88
Diarrhea	115	1	16.65	60.07	8.46	426.47
Hypersensitivity reaction/allergic reaction	93	5	10.91	458.28	190.75	1,101.03

10.4.1.4. Objective 4: Estimate incidence of long COVID-19 or post-acute sequalae SARS CoV-2 (PASC) and assess health effects of Long COVID.

Due to the low uptake of Paxlovid among pediatric patients and the limited sample size compared to adult patients, caution should be taken when interpreting the results below. Among the Source Cohort, while there were a high frequency of events for any symptom, there were relatively few with post-COVID syndrome and thus a fairly low incidence rate in the pediatric population (Table 70). Furthermore, in the pediatric Paxlovid cohort, the incidence rate of any symptom was less than one third of that in the Source Cohort and only one event of Post-COVID syndrome, which made it difficult to ascertain a precise incidence rate (Table 71). Due to the small sample size and low frequency of events, it is difficult to determine precise incidence estimates for Long Covid among Pediatric patients using Paxlovid (Table 71).

Table 70. Incidence of Long COVID in the Source Cohort by Follow-up Intervals among Pediatric Patients, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
			Overall			
Any below medical condition						
Any below medical condition	128,592	53,078	52,895.52	1,003.45	994.95	1,012.02
Post-COVID syndrome						
Post-COVID syndrome	174,046	438	117,465.88	3.73	3.40	4.10
General symptoms						
Fatigue	171,985	5,982	112,221.60	53.31	51.97	54.67
Intermittent fever	163,954	26,035	96,543.03	269.67	266.42	272.97
Post-exertional malaise	173,923	591	117,076.16	5.05	4.66	5.47
Multisystem inflammatory syndrome (MIS)	174,028	373	117,321.59	3.18	2.87	3.52
Respiratory symptoms						
Dyspnea or Shortness of breath	171,510	6,356	111,966.37	56.77	55.39	58.18
Cough	165,923	12,408	99,423.99	124.80	122.62	127.01
Nasal congestion	169,350	9,335	109,060.49	85.59	83.88	87.35
Lung function abnormalities	173,201	949	116,668.32	8.13	7.63	8.67
Hypoxemia	173,761	707	116,934.66	6.05	5.62	6.51
Cardiovascular and cerebrovascular symptoms						
Chest pain	171,604	6,000	112,621.61	53.28	51.95	54.64
Palpitations or Fast-beating or pounding heart	173,822	785	116,984.10	6.71	6.26	7.20
Myocarditis	174,055	122	117,507.08	1.04	0.87	1.24
Pericarditis	174,056	17	117,597.12	0.14	0.09	0.23
Myocardial infarction	174,059	5	117,608.01	0.04	0.02	0.10
Angina	174,062	9	117,608.28	0.08	0.04	0.15
Atrial fibrillation	174,059	15	117,598.55	0.13	0.08	0.21
Atrial flutter	174,059	11	117,604.99	0.09	0.05	0.17
Sinus tachycardia	173,074	2,909	115,177.10	25.26	24.36	26.19
Sinus bradycardia	173,915	487	117,173.04	4.16	3.80	4.54
Heart Failure	173,934	305	117,257.49	2.60	2.33	2.91
Stroke	174,035	43	117,560.48	0.37	0.27	0.49
TIA	174,058	6	117,604.93	0.05	0.02	0.11
Neurological symptoms						
Headache	173,400	476	116,020.75	4.10	3.75	4.49
Insomnia	173,348	944	116,474.66	8.10	7.60	8.64
Cognitive impairment	173,021	1,667	115,944.41	14.38	13.70	15.09
Confusion	174,054	25	117,584.58	0.21	0.14	0.32
Anosmia or Loss of smell	173,968	1,241	116,269.84	10.67	10.10	11.28
Ageusia or Loss of taste	173,931	1,204	116,286.25	10.35	9.79	10.96
Depression	170,738	3,170	112,624.29	28.15	27.18	29.14
Anxiety Disorders	168,050	6,431	109,125.05	58.93	57.51	60.39

Table 70. Incidence of Long COVID in the Source Cohort by Follow-up Intervals among Pediatric Patients, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Post-traumatic Stress Disorder	173,546	606	116,796.39	5.19	4.79	5.62
Substance Use Disorders	173,701	743	116,889.20	6.36	5.92	6.83
Suicidal behavior and suicide ideation	173,283	1,385	116,170.02	11.92	11.31	12.57
Dizziness on standing (lightheadedness)	173,048	2,210	115,657.11	19.11	18.33	19.92
Pins-and-needles feelings	173,942	275	117,355.23	2.34	2.08	2.64
Dysautonomia	173,983	108	117,475.59	0.92	0.76	1.11
Digestive symptoms						
Abdominal pain	168,348	10,443	108,100.24	96.60	94.77	98.48
Diarrhea	171,387	4,943	112,971.33	43.75	42.55	44.99
Nausea	172,588	3,378	114,567.12	29.48	28.51	30.50
Constipation	169,277	5,547	111,314.41	49.83	48.54	51.16
Musculoskeletal and Skin						
Arthralgia or joint pain	169,575	6,895	110,744.22	62.26	60.81	63.75
Myalgia or muscle pain	173,573	1,698	116,129.57	14.62	13.94	15.33
Body aches	173,286	2,643	115,242.32	22.93	22.08	23.83
Rash	169,196	6,074	111,022.97	54.71	53.35	56.10
Alopecia	174,013	45	117,553.63	0.38	0.29	0.51
Hair loss	173,908	368	117,289.67	3.14	2.83	3.48
Endocrine symptoms						
Diabetes mellitus (Type I & II)	173,425	451	116,797.08	3.86	3.52	4.24
Diabetic ketoacidosis	173,996	179	117,424.55	1.52	1.32	1.77
Thyroiditis	173,831	151	117,327.50	1.29	1.10	1.51
Hypothyroidism	173,659	346	117,042.95	2.96	2.66	3.29
Hyperthyroidism	174,006	62	117,530.02	0.53	0.41	0.68
Menstrual/period issues	172,425	2,252	114,914.00	19.60	18.80	20.42
Hematologic symptoms						
DVT	174,038	50	117,557.08	0.43	0.32	0.56
Pulmonary embolism	174,054	36	117,577.57	0.31	0.22	0.42
Renal symptoms						
Acute kidney injury	173,820	651	116,992.04	5.56	5.15	6.01
Chronic kidney disease	173,454	587	116,765.85	5.03	4.64	5.45
Dialysis	173,993	148	117,441.46	1.26	1.07	1.48
			>=4 Weeks			
Any below medical condition						
Any below medical condition	83,751	21,404	52,207.41	409.98	404.52	415.51
Post-COVID syndrome						
Post-COVID syndrome	152,644	219	116,793.13	1.88	1.64	2.14
General symptoms						

Table 70. Incidence of Long COVID in the Source Cohort by Follow-up Intervals among Pediatric Patients, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Fatigue	148,447	3,241	111,537.48	29.06	28.07	30.08
Intermittent fever	129,393	8,803	95,868.05	91.82	89.93	93.76
Post-exertional malaise	152,430	278	116,404.74	2.39	2.12	2.69
Multisystem inflammatory syndrome (MIS)	152,552	94	116,651.21	0.81	0.66	0.99
Respiratory symptoms						
Dyspnea or Shortness of breath	147,511	3,019	111,275.77	27.13	26.18	28.12
Cough	135,770	3,028	98,717.92	30.67	29.60	31.79
Nasal congestion	144,254	4,503	108,385.26	41.55	40.35	42.78
Lung function abnormalities	151,747	592	115,999.44	5.10	4.71	5.53
Hypoxemia	152,150	251	116,264.59	2.16	1.91	2.44
Cardiovascular and cerebrovascular symptoms						
Chest pain	148,399	3,449	111,939.36	30.81	29.80	31.86
Palpitations or Fast-beating or pounding heart	152,439	589	116,311.75	5.06	4.67	5.49
Myocarditis	152,748	31	116,838.09	0.27	0.19	0.38
Pericarditis	152,827	5	116,928.87	0.04	0.02	0.10
Myocardial infarction	152,839	3	116,939.79	0.03	0.01	0.08
Angina	152,840	6	116,940.02	0.05	0.02	0.11
Atrial fibrillation	152,834	7	116,930.29	0.06	0.03	0.13
Atrial flutter	152,838	9	116,936.75	0.08	0.04	0.15
Sinus tachycardia	150,528	1,253	114,503.53	10.94	10.35	11.57
Sinus bradycardia	152,480	247	116,501.89	2.12	1.87	2.40
Heart Failure	152,558	124	116,587.96	1.06	0.89	1.27
Stroke	152,809	31	116,892.24	0.27	0.19	0.38
TIA	152,838	5	116,936.70	0.04	0.02	0.10
Neurological symptoms						
Headache	151,784	58	115,351.69	0.50	0.39	0.65
Insomnia	152,012	781	115,803.46	6.74	6.29	7.23
Cognitive impairment	151,573	1,330	115,273.04	11.54	10.93	12.18
Confusion	152,822	10	116,915.99	0.09	0.05	0.16
Anosmia or Loss of smell	151,681	149	115,598.10	1.29	1.10	1.51
Ageusia or Loss of taste	151,698	168	115,614.72	1.45	1.25	1.69
Depression	148,918	2,357	111,947.03	21.05	20.22	21.92
Anxiety Disorders	145,992	5,133	108,440.82	47.33	46.06	48.65
Post-traumatic Stress Disorder	152,181	425	116,125.64	3.66	3.33	4.03
Substance Use Disorders	152,328	538	116,220.49	4.63	4.25	5.04
Suicidal behavior and suicide ideation	151,639	822	115,500.77	7.12	6.65	7.62

Table 70. Incidence of Long COVID in the Source Cohort by Follow-up Intervals among Pediatric Patients, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Dizziness on standing (lightheadedness)	151,388	1,623	114,982.86	14.12	13.45	14.82
Pins-and-needles feelings	152,689	231	116,686.32	1.98	1.74	2.25
Dysautonomia	152,735	73	116,806.98	0.62	0.50	0.79
Digestive symptoms						
Abdominal pain	145,156	7,627	107,412.04	71.01	69.43	72.62
Diarrhea	148,733	3,078	112,296.00	27.41	26.46	28.40
Nausea	150,427	2,180	113,892.49	19.14	18.35	19.96
Constipation	147,479	4,440	110,634.61	40.13	38.97	41.33
Musculoskeletal and Skin						
Arthralgia or joint pain	148,021	6,150	110,064.20	55.88	54.50	57.29
Myalgia or muscle pain	151,500	691	115,458.97	5.98	5.56	6.45
Body aches	150,799	1,172	114,569.96	10.23	9.66	10.83
Rash	147,108	4,664	110,340.35	42.27	41.07	43.50
Alopecia	152,793	41	116,885.23	0.35	0.26	0.48
Hair loss	152,677	343	116,620.98	2.94	2.65	3.27
Endocrine symptoms						
Diabetes mellitus (Type I & II)	152,014	209	116,128.13	1.80	1.57	2.06
Diabetic ketoacidosis	152,670	62	116,755.96	0.53	0.41	0.68
Thyroiditis	152,589	118	116,658.91	1.01	0.85	1.21
Hypothyroidism	152,351	234	116,373.79	2.01	1.77	2.29
Hyperthyroidism	152,772	45	116,861.37	0.39	0.29	0.52
Menstrual/period issues	151,068	2,010	114,241.02	17.59	16.84	18.38
Hematologic symptoms						
DVT	152,801	31	116,888.66	0.27	0.19	0.38
Pulmonary embolism	152,813	14	116,909.17	0.12	0.07	0.20
Renal symptoms						
Acute kidney injury	152,324	317	116,322.37	2.73	2.44	3.04
Chronic kidney disease	152,111	407	116,096.61	3.51	3.18	3.86
Dialysis	152,706	72	116,772.12	0.62	0.49	0.78
			>=12 Weeks			
Any below medical condition						
Any below medical condition	66,467	15,291	49,653.29	307.96	303.11	312.88
Post-COVID syndrome						
Post-COVID syndrome	133,493	111	113,945.59	0.97	0.81	1.17
General symptoms						
Fatigue	129,028	2,482	108,649.90	22.84	21.96	23.76
Intermittent fever	111,538	6,814	93,209.42	73.10	71.39	74.86
Post-exertional malaise	133,297	202	113,558.48	1.78	1.55	2.04
Multisystem inflammatory syndrome (MIS)	133,430	41	113,808.00	0.36	0.27	0.49

Table 70. Incidence of Long COVID in the Source Cohort by Follow-up Intervals among Pediatric Patients, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Respiratory symptoms						
Dyspnea or Shortness of breath	128,206	2,186	108,406.75	20.16	19.34	21.03
Cough	116,703	2,423	95,885.63	25.27	24.28	26.30
Nasal congestion	125,258	3,513	105,558.94	33.28	32.20	34.40
Lung function abnormalities	132,639	408	113,157.33	3.61	3.27	3.97
Hypoxemia	133,059	170	113,425.00	1.50	1.29	1.74
Cardiovascular and cerebrovascular symptoms						
Chest pain	128,993	2,566	109,054.83	23.53	22.64	24.46
Palpitations or Fast-beating or pounding heart	133,262	449	113,458.38	3.96	3.61	4.34
Myocarditis	133,647	20	113,996.32	0.18	0.11	0.27
Pericarditis	133,730	4	114,087.42	0.04	0.01	0.09
Myocardial infarction	133,741	1	114,098.32	0.01	0.00	0.06
Angina	133,743	5	114,098.73	0.04	0.02	0.11
Atrial fibrillation	133,737	7	114,088.90	0.06	0.03	0.13
Atrial flutter	133,739	7	114,095.18	0.06	0.03	0.13
Sinus tachycardia	131,415	922	111,662.69	8.26	7.74	8.81
Sinus bradycardia	133,348	183	113,655.80	1.61	1.39	1.86
Heart Failure	133,436	84	113,743.55	0.74	0.60	0.92
Stroke	133,704	21	114,049.51	0.18	0.12	0.28
TIA	133,741	4	114,095.42	0.04	0.01	0.09
Neurological symptoms						
Headache	132,673	29	112,507.97	0.26	0.18	0.37
Insomnia	132,759	553	112,939.61	4.90	4.51	5.32
Cognitive impairment	132,287	1,012	112,403.55	9.00	8.47	9.58
Confusion	133,720	4	114,073.90	0.04	0.01	0.09
Anosmia or Loss of smell	132,585	120	112,756.92	1.06	0.89	1.27
Ageusia or Loss of taste	132,597	128	112,772.80	1.14	0.95	1.35
Depression	129,440	1,679	109,046.40	15.40	14.68	16.15
Anxiety Disorders	126,139	3,754	105,488.99	35.59	34.47	36.74
Post-traumatic Stress Disorder	133,020	306	113,273.48	2.70	2.42	3.02
Substance Use Disorders	133,168	418	113,368.68	3.69	3.35	4.06
Suicidal behavior and suicide ideation	132,476	618	112,651.12	5.49	5.07	5.94
Dizziness on standing (lightheadedness)	132,124	1,281	112,116.81	11.43	10.82	12.07
Pins-and-needles feelings	133,564	186	113,841.01	1.63	1.42	1.89
Dysautonomia	133,632	61	113,964.76	0.54	0.42	0.69
Digestive symptoms						
Abdominal pain	125,328	5,818	104,463.10	55.69	54.28	57.14
Diarrhea	129,335	2,281	109,408.78	20.85	20.01	21.72

Table 70. Incidence of Long COVID in the Source Cohort by Follow-up Intervals among Pediatric Patients, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Nausea	131,091	1,668	111,018.10	15.02	14.32	15.76
Constipation	127,832	3,206	107,712.70	29.76	28.75	30.81
Musculoskeletal and Skin						
Arthralgia or joint pain	128,120	4,759	107,104.51	44.43	43.19	45.71
Myalgia or muscle pain	132,396	542	112,616.06	4.81	4.42	5.24
Body aches	131,639	930	111,718.26	8.32	7.81	8.88
Rash	127,624	3,514	107,445.00	32.71	31.64	33.81
Alopecia	133,688	28	114,042.46	0.25	0.17	0.36
Hair loss	133,531	271	113,772.37	2.38	2.12	2.68
Endocrine symptoms						
Diabetes mellitus (Type I & II)	132,938	158	113,290.18	1.39	1.19	1.63
Diabetic ketoacidosis	133,575	52	113,914.88	0.46	0.35	0.60
Thyroiditis	133,484	85	113,816.43	0.75	0.60	0.92
Hypothyroidism	133,245	165	113,531.20	1.45	1.25	1.69
Hyperthyroidism	133,674	37	114,019.92	0.32	0.24	0.45
Menstrual/period issues	131,644	1,555	111,349.06	13.97	13.29	14.68
Hematologic symptoms						
DVT	133,697	22	114,046.30	0.19	0.13	0.29
Pulmonary embolism	133,712	9	114,067.26	0.08	0.04	0.15
Renal symptoms						
Acute kidney injury	133,193	231	113,476.57	2.04	1.79	2.32
Chronic kidney disease	132,974	299	113,249.28	2.64	2.36	2.96
Dialysis	133,604	56	113,930.67	0.49	0.38	0.64
			>=6 months			
Any below medical condition						
Any below medical condition	38,758	7,737	39,272.38	197.01	192.67	201.45
Post-COVID syndrome						
Post-COVID syndrome	88,988	64	96,682.23	0.66	0.52	0.85
General symptoms						
Fatigue	84,970	1,462	91,599.93	15.96	15.16	16.80
Intermittent fever	72,987	3,665	78,408.84	46.74	45.25	48.28
Post-exertional malaise	88,684	112	96,254.80	1.16	0.97	1.40
Multisystem inflammatory syndrome (MIS)	88,869	32	96,520.01	0.33	0.23	0.47
Respiratory symptoms						
Dyspnea or Shortness of breath	84,700	1,183	91,579.83	12.92	12.20	13.68
Cough	74,939	1,342	79,780.26	16.82	15.95	17.75
Nasal congestion	82,486	1,963	89,040.38	22.05	21.09	23.04
Lung function abnormalities	88,380	210	95,998.32	2.19	1.91	2.50
Hypoxemia	88,566	90	96,169.71	0.94	0.76	1.15

Table 70. Incidence of Long COVID in the Source Cohort by Follow-up Intervals among Pediatric Patients, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Cardiovascular and cerebrovascular symptoms						
Chest pain	85,352	1,554	92,164.24	16.86	16.04	17.72
Palpitations or Fast-beating or pounding heart	88,665	298	96,161.50	3.10	2.77	3.47
Myocarditis	89,020	8	96,683.23	0.08	0.04	0.17
Pericarditis	89,097	3	96,772.22	0.03	0.01	0.10
Myocardial infarction	89,105	1	96,781.84	0.01	0.00	0.07
Angina	89,105	3	96,781.38	0.03	0.01	0.10
Atrial fibrillation	89,099	5	96,771.52	0.05	0.02	0.12
Atrial flutter	89,104	6	96,778.98	0.06	0.03	0.14
Sinus tachycardia	87,251	527	94,544.45	5.57	5.12	6.07
Sinus bradycardia	88,772	113	96,365.14	1.17	0.98	1.41
Heart Failure	88,843	44	96,447.58	0.46	0.34	0.61
Stroke	89,065	7	96,732.03	0.07	0.03	0.15
TIA	89,102	2	96,777.72	0.02	0.01	0.08
Neurological symptoms						
Headache	88,048	9	95,196.28	0.09	0.05	0.18
Insomnia	88,204	299	95,667.34	3.13	2.79	3.50
Cognitive impairment	87,775	569	95,157.00	5.98	5.51	6.49
Confusion	89,085	3	96,757.72	0.03	0.01	0.10
Anosmia or Loss of smell	88,068	73	95,490.50	0.76	0.61	0.96
Ageusia or Loss of taste	88,070	60	95,502.46	0.63	0.49	0.81
Depression	85,260	945	91,940.45	10.28	9.64	10.96
Anxiety Disorders	82,540	2,154	88,652.02	24.30	23.29	25.35
Post-traumatic Stress Disorder	88,481	182	95,999.67	1.90	1.64	2.19
Substance Use Disorders	88,573	283	96,073.58	2.95	2.62	3.31
Suicidal behavior and suicide ideation	88,012	371	95,411.23	3.89	3.51	4.31
Dizziness on standing (lightheadedness)	87,610	781	94,867.48	8.23	7.68	8.83
Pins-and-needles feelings	88,911	110	96,520.92	1.14	0.95	1.37
Dysautonomia	89,005	32	96,654.18	0.33	0.23	0.47
Digestive symptoms						
Abdominal pain	81,827	3,405	87,682.28	38.83	37.55	40.16
Diarrhea	85,474	1,278	92,440.60	13.83	13.09	14.60
Nausea	86,748	966	93,846.29	10.29	9.66	10.96
Constipation	84,171	1,722	90,846.92	18.95	18.08	19.87
Musculoskeletal and Skin						
Arthralgia or joint pain	83,889	2,869	90,010.83	31.87	30.73	33.06
Myalgia or muscle pain	88,001	352	95,400.70	3.69	3.32	4.10

Table 70. Incidence of Long COVID in the Source Cohort by Follow-up Intervals among Pediatric Patients, 1/1/2020-07/20/2022

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Body aches	87,290	575	94,527.14	6.08	5.61	6.60
Rash	84,081	1,902	90,612.57	20.99	20.07	21.96
Alopecia	89,063	15	96,730.36	0.16	0.09	0.26
Hair loss	88,840	130	96,441.65	1.35	1.14	1.60
Endocrine symptoms						
Diabetes mellitus (Type I & II)	88,477	110	96,045.85	1.15	0.95	1.38
Diabetic ketoacidosis	88,966	37	96,609.86	0.38	0.28	0.53
Thyroiditis	88,886	46	96,518.25	0.48	0.36	0.64
Hypothyroidism	88,673	88	96,243.59	0.91	0.74	1.13
Hyperthyroidism	89,046	24	96,706.84	0.25	0.17	0.37
Menstrual/period issues	87,060	903	94,080.51	9.60	8.99	10.25
Hematologic symptoms						
DVT	89,068	12	96,732.67	0.12	0.07	0.22
Pulmonary embolism	89,079	5	96,752.39	0.05	0.02	0.12
Renal symptoms						
Acute kidney injury	88,636	133	96,195.38	1.38	1.17	1.64
Chronic kidney disease	88,470	182	95,991.29	1.90	1.64	2.19
Dialysis	88,986	34	96,622.22	0.35	0.25	0.49

Table 71. Incidence of Long COVID among Paxlovid Users (Age<18) by Follow-up Intervals

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
			Overall			
Any below medical condition						
Any below medical condition	68	16	5.83	2,746.24	1,682.44	4,482.69
Post-COVID syndrome						
Post-COVID syndrome	116	1	16.97	58.93	8.30	418.35
General symptoms						
Fatigue	113	4	14.80	270.21	101.41	719.94
Intermittent fever	111	4	14.59	274.21	102.92	730.61
Post-exertional malaise	116	1	17.02	58.75	8.28	417.07
Multisystem inflammatory syndrome (MIS)	116	0	17.10	0.00	0.00	3,688.88
Respiratory symptoms						
Dyspnea or Shortness of breath	114	4	15.53	257.49	96.64	686.06
Cough	116	0	17.10	0.00	0.00	3,688.88
Nasal congestion	112	1	16.60	60.23	8.49	427.60
Lung function abnormalities	116	0	17.10	0.00	0.00	3,688.88
Hypoxemia	116	0	17.10	0.00	0.00	3,688.88

Table 71. Incidence of Long COVID among Paxlovid Users (Age<18) by Follow-up Intervals

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Cardiovascular and cerebrovascular symptoms						
Chest pain	113	9	14.23	632.53	329.11	1,215.67
Palpitations or Fast-beating or pounding heart	116	1	17.07	58.59	8.25	415.94
Myocarditis	116	0	17.10	0.00	0.00	3,688.88
Pericarditis	116	0	17.10	0.00	0.00	3,688.88
Myocardial infarction	116	0	17.10	0.00	0.00	3,688.88
Angina	116	0	17.10	0.00	0.00	3,688.88
Atrial fibrillation	116	0	17.10	0.00	0.00	3,688.88
Atrial flutter	116	0	17.10	0.00	0.00	3,688.88
Sinus tachycardia	115	1	16.76	59.68	8.41	423.68
Sinus bradycardia	116	0	17.10	0.00	0.00	3,688.88
Heart Failure	116	0	17.10	0.00	0.00	3,688.88
Stroke	116	0	17.10	0.00	0.00	3,688.88
TIA	116	0	17.10	0.00	0.00	3,688.88
Neurological symptoms						
Headache	116	0	17.10	0.00	0.00	3,688.88
Insomnia	115	0	17.02	0.00	0.00	3,688.88
Cognitive impairment	116	1	16.86	59.30	8.35	421.00
Confusion	116	0	17.10	0.00	0.00	3,688.88
Anosmia or Loss of smell	116	0	17.10	0.00	0.00	3,688.88
Ageusia or Loss of taste	116	0	17.10	0.00	0.00	3,688.88
Depression	111	3	15.85	189.22	61.03	586.68
Anxiety Disorders	101	4	14.46	276.55	103.79	736.84
Post-traumatic Stress Disorder	116	1	16.98	58.90	8.30	418.15
Substance Use Disorders	116	0	17.10	0.00	0.00	3,688.88
Suicidal behavior and suicide ideation	114	0	16.76	0.00	0.00	3,688.88
Dizziness on standing (lightheadedness)	114	1	16.85	59.36	8.36	421.41
Pins-and-needles feelings	116	0	17.10	0.00	0.00	3,688.88
Dysautonomia	115	0	16.94	0.00	0.00	3,688.88
Digestive symptoms						
Abdominal pain	109	3	15.25	196.69	63.44	609.85
Diarrhea	115	1	16.65	60.07	8.46	426.47
Nausea	115	2	16.84	118.76	29.70	474.86
Constipation	110	2	16.10	124.23	31.07	496.75
Musculoskeletal and Skin						
Arthralgia or joint pain	111	0	16.19	0.00	0.00	3,688.88
Myalgia or muscle pain	116	1	17.01	58.79	8.28	417.34
Body aches	115	0	17.00	0.00	0.00	3,688.88
Rash	116	1	17.09	58.51	8.24	415.34

Table 71. Incidence of Long COVID among Paxlovid Users (Age<18) by Follow-up Intervals

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Alopecia	116	0	17.10	0.00	0.00	3,688.88
Hair loss	116	0	17.10	0.00	0.00	3,688.88
Endocrine symptoms						
Diabetes mellitus (Type I & II)	111	2	15.63	127.96	32.00	511.62
Diabetic ketoacidosis	116	0	17.10	0.00	0.00	3,688.88
Thyroiditis	115	0	16.92	0.00	0.00	3,688.88
Hypothyroidism	115	1	16.31	61.31	8.64	435.28
Hyperthyroidism	116	0	17.10	0.00	0.00	3,688.88
Menstrual/period issues	109	3	15.07	199.01	64.19	617.05
Hematologic symptoms						
DVT	115	0	17.06	0.00	0.00	3,688.88
Pulmonary embolism	116	0	17.10	0.00	0.00	3,688.88
Renal symptoms						
Acute kidney injury	116	0	17.10	0.00	0.00	3,688.88
Chronic kidney disease	113	0	16.21	0.00	0.00	3,688.88
Dialysis	116	0	17.10	0.00	0.00	3,688.88
			>=4 Weeks			
Any below medical condition						
Any below medical condition	25	4	5.18	772.20	289.82	2,057.45
Post-COVID syndrome						
Post-COVID syndrome	67	1	15.84	63.14	8.89	448.22
General symptoms						
Fatigue	64	4	13.67	292.55	109.80	779.48
Intermittent fever	60	1	13.43	74.43	10.49	528.42
Post-exertional malaise	67	1	15.89	62.93	8.87	446.75
Multisystem inflammatory syndrome (MIS)	67	0	15.97	0.00	0.00	3,688.88
Respiratory symptoms						
Dyspnea or Shortness of breath	62	0	14.36	0.00	0.00	3,688.88
Cough	67	0	15.97	0.00	0.00	3,688.88
Nasal congestion	65	0	15.57	0.00	0.00	3,688.88
Lung function abnormalities	67	0	15.97	0.00	0.00	3,688.88
Hypoxemia	67	0	15.97	0.00	0.00	3,688.88
Cardiovascular and cerebrovascular symptoms						
Chest pain	59	0	13.07	0.00	0.00	3,688.88
Palpitations or Fast-beating or pounding heart	67	0	15.97	0.00	0.00	3,688.88
Myocarditis	67	0	15.97	0.00	0.00	3,688.88
Pericarditis	67	0	15.97	0.00	0.00	3,688.88
Myocardial infarction	67	0	15.97	0.00	0.00	3,688.88
Angina	67	0	15.97	0.00	0.00	3,688.88

Table 71. Incidence of Long COVID among Paxlovid Users (Age<18) by Follow-up Intervals

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Atrial fibrillation	67	0	15.97	0.00	0.00	3,688.88
Atrial flutter	67	0	15.97	0.00	0.00	3,688.88
Sinus tachycardia	65	0	15.62	0.00	0.00	3,688.88
Sinus bradycardia	67	0	15.97	0.00	0.00	3,688.88
Heart Failure	67	0	15.97	0.00	0.00	3,688.88
Stroke	67	0	15.97	0.00	0.00	3,688.88
TIA	67	0	15.97	0.00	0.00	3,688.88
Neurological symptoms						
Headache	67	0	15.97	0.00	0.00	3,688.88
Insomnia	67	0	15.97	0.00	0.00	3,688.88
Cognitive impairment	66	0	15.67	0.00	0.00	3,688.88
Confusion	67	0	15.97	0.00	0.00	3,688.88
Anosmia or Loss of smell	67	0	15.97	0.00	0.00	3,688.88
Ageusia or Loss of taste	67	0	15.97	0.00	0.00	3,688.88
Depression	63	2	14.87	134.48	33.63	537.71
Anxiety Disorders	56	3	13.52	221.86	71.55	687.88
Post-traumatic Stress Disorder	67	1	15.85	63.10	8.89	447.99
Substance Use Disorders	67	0	15.97	0.00	0.00	3,688.88
Suicidal behavior and suicide ideation	65	0	15.63	0.00	0.00	3,688.88
Dizziness on standing (lightheadedness)	66	0	15.79	0.00	0.00	3,688.88
Pins-and-needles feelings	67	0	15.97	0.00	0.00	3,688.88
Dysautonomia	66	0	15.81	0.00	0.00	3,688.88
Digestive symptoms						
Abdominal pain	59	2	14.09	141.98	35.51	567.71
Diarrhea	66	1	15.52	64.45	9.08	457.55
Nausea	66	2	15.71	127.31	31.84	509.04
Constipation	60	1	14.90	67.10	9.45	476.38
Musculoskeletal and Skin						
Arthralgia or joint pain	63	0	15.07	0.00	0.00	3,688.88
Myalgia or muscle pain	67	1	15.88	62.97	8.87	447.06
Body aches	66	0	15.87	0.00	0.00	3,688.88
Rash	67	1	15.96	62.65	8.83	444.76
Alopecia	67	0	15.97	0.00	0.00	3,688.88
Hair loss	67	0	15.97	0.00	0.00	3,688.88
Endocrine symptoms						
Diabetes mellitus (Type I & II)	62	1	14.54	68.80	9.69	488.40
Diabetic ketoacidosis	67	0	15.97	0.00	0.00	3,688.88
Thyroiditis	66	0	15.79	0.00	0.00	3,688.88
Hypothyroidism	65	0	15.12	0.00	0.00	3,688.88
Hyperthyroidism	67	0	15.97	0.00	0.00	3,688.88

Table 71. Incidence of Long COVID among Paxlovid Users (Age<18) by Follow-up Intervals

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Menstrual/period issues	62	2	14.03	142.56	35.66	570.04
Hematologic symptoms						
DVT	67	0	15.97	0.00	0.00	3,688.88
Pulmonary embolism	67	0	15.97	0.00	0.00	3,688.88
Renal symptoms						
Acute kidney injury	67	0	15.97	0.00	0.00	3,688.88
Chronic kidney disease	64	0	15.07	0.00	0.00	3,688.88
Dialysis	67	0	15.97	0.00	0.00	3,688.88
			>=12 Weeks			
Any below medical condition						
Any below medical condition	7	1	2.77	360.92	50.84	2,562.19
Post-COVID syndrome						
Post-COVID syndrome	21	0	9.16	0.00	0.00	3,688.88
General symptoms						
Fatigue	17	0	6.97	0.00	0.00	3,688.88
Intermittent fever	17	0	7.31	0.00	0.00	3,688.88
Post-exertional malaise	22	0	9.40	0.00	0.00	3,688.88
Multisystem inflammatory syndrome (MIS)	22	0	9.40	0.00	0.00	3,688.88
Respiratory symptoms						
Dyspnea or Shortness of breath	20	0	8.17	0.00	0.00	3,688.88
Cough	22	0	9.40	0.00	0.00	3,688.88
Nasal congestion	22	0	9.40	0.00	0.00	3,688.88
Lung function abnormalities	22	0	9.40	0.00	0.00	3,688.88
Hypoxemia	22	0	9.40	0.00	0.00	3,688.88
Cardiovascular and cerebrovascular symptoms						
Chest pain	18	0	7.15	0.00	0.00	3,688.88
Palpitations or Fast-beating or pounding heart	22	0	9.40	0.00	0.00	3,688.88
Myocarditis	22	0	9.40	0.00	0.00	3,688.88
Pericarditis	22	0	9.40	0.00	0.00	3,688.88
Myocardial infarction	22	0	9.40	0.00	0.00	3,688.88
Angina	22	0	9.40	0.00	0.00	3,688.88
Atrial fibrillation	22	0	9.40	0.00	0.00	3,688.88
Atrial flutter	22	0	9.40	0.00	0.00	3,688.88
Sinus tachycardia	22	0	9.40	0.00	0.00	3,688.88
Sinus bradycardia	22	0	9.40	0.00	0.00	3,688.88
Heart Failure	22	0	9.40	0.00	0.00	3,688.88
Stroke	22	0	9.40	0.00	0.00	3,688.88
TIA	22	0	9.40	0.00	0.00	3,688.88
Neurological symptoms						

Table 71. Incidence of Long COVID among Paxlovid Users (Age<18) by Follow-up Intervals

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Headache	22	0	9.40	0.00	0.00	3,688.88
Insomnia	22	0	9.40	0.00	0.00	3,688.88
Cognitive impairment	21	0	9.10	0.00	0.00	3,688.88
Confusion	22	0	9.40	0.00	0.00	3,688.88
Anosmia or Loss of smell	22	0	9.40	0.00	0.00	3,688.88
Ageusia or Loss of taste	22	0	9.40	0.00	0.00	3,688.88
Depression	21	0	8.84	0.00	0.00	3,688.88
Anxiety Disorders	19	0	8.41	0.00	0.00	3,688.88
Post-traumatic Stress Disorder	21	0	9.10	0.00	0.00	3,688.88
Substance Use Disorders	22	0	9.40	0.00	0.00	3,688.88
Suicidal behavior and suicide ideation	22	0	9.40	0.00	0.00	3,688.88
Dizziness on standing (lightheadedness)	22	0	9.40	0.00	0.00	3,688.88
Pins-and-needles feelings	22	0	9.40	0.00	0.00	3,688.88
Dysautonomia	22	0	9.40	0.00	0.00	3,688.88
Digestive symptoms						
Abdominal pain	20	2	8.34	239.67	59.94	958.29
Diarrhea	21	1	8.94	111.80	15.75	793.68
Nausea	22	1	9.30	107.58	15.16	763.75
Constipation	22	1	9.34	107.05	15.08	759.95
Musculoskeletal and Skin						
Arthralgia or joint pain	21	0	8.98	0.00	0.00	3,688.88
Myalgia or muscle pain	22	1	9.31	107.43	15.13	762.63
Body aches	22	0	9.40	0.00	0.00	3,688.88
Rash	22	0	9.40	0.00	0.00	3,688.88
Alopecia	22	0	9.40	0.00	0.00	3,688.88
Hair loss	22	0	9.40	0.00	0.00	3,688.88
Endocrine symptoms						
Diabetes mellitus (Type I & II)	20	0	8.55	0.00	0.00	3,688.88
Diabetic ketoacidosis	22	0	9.40	0.00	0.00	3,688.88
Thyroiditis	22	0	9.40	0.00	0.00	3,688.88
Hypothyroidism	20	0	8.55	0.00	0.00	3,688.88
Hyperthyroidism	22	0	9.40	0.00	0.00	3,688.88
Menstrual/period issues	19	0	7.79	0.00	0.00	3,688.88
Hematologic symptoms						
DVT	22	0	9.40	0.00	0.00	3,688.88
Pulmonary embolism	22	0	9.40	0.00	0.00	3,688.88
Renal symptoms						
Acute kidney injury	22	0	9.40	0.00	0.00	3,688.88

Table 71. Incidence of Long COVID among Paxlovid Users (Age<18) by Follow-up Intervals

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Chronic kidney disease	20	0	8.66	0.00	0.00	3,688.88
Dialysis	22	0	9.40	0.00	0.00	3,688.88
			>=6 months			
Any below medical condition						
Any below medical condition	0	.	.	0.00	0.00	3,688.88
Post-COVID syndrome						
Post-COVID syndrome	3	0	2.09	0.00	0.00	3,688.88
General symptoms						
Fatigue	1	0	0.60	0.00	0.00	3,688.88
Intermittent fever	2	0	1.54	0.00	0.00	3,688.88
Post-exertional malaise	3	0	2.09	0.00	0.00	3,688.88
Multisystem inflammatory syndrome (MIS)	3	0	2.09	0.00	0.00	3,688.88
Respiratory symptoms						
Dyspnea or Shortness of breath	2	0	1.15	0.00	0.00	3,688.88
Cough	3	0	2.09	0.00	0.00	3,688.88
Nasal congestion	3	0	2.09	0.00	0.00	3,688.88
Lung function abnormalities	3	0	2.09	0.00	0.00	3,688.88
Hypoxemia	3	0	2.09	0.00	0.00	3,688.88
Cardiovascular and cerebrovascular symptoms						
Chest pain	1	0	0.60	0.00	0.00	3,688.88
Palpitations or Fast-beating or pounding heart	3	0	2.09	0.00	0.00	3,688.88
Myocarditis	3	0	2.09	0.00	0.00	3,688.88
Pericarditis	3	0	2.09	0.00	0.00	3,688.88
Myocardial infarction	3	0	2.09	0.00	0.00	3,688.88
Angina	3	0	2.09	0.00	0.00	3,688.88
Atrial fibrillation	3	0	2.09	0.00	0.00	3,688.88
Atrial flutter	3	0	2.09	0.00	0.00	3,688.88
Sinus tachycardia	3	0	2.09	0.00	0.00	3,688.88
Sinus bradycardia	3	0	2.09	0.00	0.00	3,688.88
Heart Failure	3	0	2.09	0.00	0.00	3,688.88
Stroke	3	0	2.09	0.00	0.00	3,688.88
TIA	3	0	2.09	0.00	0.00	3,688.88
Neurological symptoms						
Headache	3	0	2.09	0.00	0.00	3,688.88
Insomnia	3	0	2.09	0.00	0.00	3,688.88
Cognitive impairment	3	0	2.09	0.00	0.00	3,688.88
Confusion	3	0	2.09	0.00	0.00	3,688.88
Anosmia or Loss of smell	3	0	2.09	0.00	0.00	3,688.88

Table 71. Incidence of Long COVID among Paxlovid Users (Age<18) by Follow-up Intervals

Study Endpoints	Patients at Risk	Events	Person-time	Incidence Rate	95% CI	
Ageusia or Loss of taste	3	0	2.09	0.00	0.00	3,688.88
Depression	2	0	1.54	0.00	0.00	3,688.88
Anxiety Disorders	3	0	2.09	0.00	0.00	3,688.88
Post-traumatic Stress Disorder	3	0	2.09	0.00	0.00	3,688.88
Substance Use Disorders	3	0	2.09	0.00	0.00	3,688.88
Suicidal behavior and suicide ideation	3	0	2.09	0.00	0.00	3,688.88
Dizziness on standing (lightheadedness)	3	0	2.09	0.00	0.00	3,688.88
Pins-and-needles feelings	3	0	2.09	0.00	0.00	3,688.88
Dysautonomia	3	0	2.09	0.00	0.00	3,688.88
Digestive symptoms						
Abdominal pain	2	0	1.49	0.00	0.00	3,688.88
Diarrhea	3	0	2.09	0.00	0.00	3,688.88
Nausea	3	0	2.09	0.00	0.00	3,688.88
Constipation	3	0	2.09	0.00	0.00	3,688.88
Musculoskeletal and Skin						
Arthralgia or joint pain	3	0	2.09	0.00	0.00	3,688.88
Myalgia or muscle pain	3	0	2.09	0.00	0.00	3,688.88
Body aches	3	0	2.09	0.00	0.00	3,688.88
Rash	3	0	2.09	0.00	0.00	3,688.88
Alopecia	3	0	2.09	0.00	0.00	3,688.88
Hair loss	3	0	2.09	0.00	0.00	3,688.88
Endocrine symptoms						
Diabetes mellitus (Type I & II)	3	0	2.09	0.00	0.00	3,688.88
Diabetic ketoacidosis	3	0	2.09	0.00	0.00	3,688.88
Thyroiditis	3	0	2.09	0.00	0.00	3,688.88
Hypothyroidism	2	0	1.54	0.00	0.00	3,688.88
Hyperthyroidism	3	0	2.09	0.00	0.00	3,688.88
Menstrual/period issues	2	0	1.15	0.00	0.00	3,688.88
Hematologic symptoms						
DVT	3	0	2.09	0.00	0.00	3,688.88
Pulmonary embolism	3	0	2.09	0.00	0.00	3,688.88
Renal symptoms						
Acute kidney injury	3	0	2.09	0.00	0.00	3,688.88
Chronic kidney disease	3	0	2.09	0.00	0.00	3,688.88
Dialysis	3	0	2.09	0.00	0.00	3,688.88

10.4.1.5. Objective 5: Describe the health equity and demographic and clinical characteristics (e.g. co-morbid conditions, outcomes, treatment patterns, healthcare utilization) among patients treated with Paxlovid

Pediatric Paxlovid users were more likely to be White compared to other racial and ethnic groups and from the South compared to other geographic areas (Table 72). Across all groups, pediatric Paxlovid users did not have prior COVID-19 infections (Table 73).

Table 72. Demographics of Paxlovid Users, Optum® SES Database

Characteristics	White		Black		Asian		Hispanic		Missing		Overall	
	N	%	N	%	N	%	N	%	N	%	N	%
Cohort Entry Year												
2021	0	0	0	0	0	0	0	0	1	0.38	1	0.1
2022	499	100	59	100	60	100	116	100	262	99.62	996	99.9
Cohort Month/Year												
Dec-21	0	0	0	0	0	0	0	0	1	0.38	1	0.1
Jan-22	7	1.4	0	0	0	0	2	1.72	1	0.38	10	1
Feb-22	2	0.4	0	0	0	0	1	0.86	0	0	3	0.3
Mar-22	2	0.4	0	0	1	1.67	0	0	2	0.76	5	0.5
Apr-22	15	3.01	0	0	3	5	3	2.59	8	3.04	29	2.91
May-22	71	14.23	13	22.03	11	18.33	10	8.62	37	14.07	142	14.24
Jun-22	74	14.83	4	6.78	9	15	23	19.83	26	9.89	136	13.64
Jul-22	130	26.05	12	20.34	15	25	33	28.45	60	22.81	250	25.08
Aug-22	109	21.84	19	32.2	10	16.67	22	18.97	55	20.91	215	21.56
Sep-22	44	8.82	7	11.86	7	11.67	9	7.76	39	14.83	106	10.63
Oct-22	32	6.41	2	3.39	2	3.33	5	4.31	20	7.6	61	6.12
Nov-22	13	2.61	2	3.39	2	3.33	8	6.9	14	5.32	39	3.91
Age												
12-17	499	50	59	5.9	60	6.0	116	11.6	263	26.3	997	100
Age continuous												
Mean+/- SD	15	1.59	15	1.5	15	1.56	15	1.37	15	1.55	15	1.55
Median, IQR	15	14 - 17	16	14 - 17	15	14 - 16	15	14 - 17	15	14 - 16	15	14 - 17
Gender												
Female	248	49.7	30	50.85	29	48.33	54	46.55	136	51.71	497	49.85
Male	251	50.3	29	49.15	31	51.67	62	53.45	127	48.29	500	50.15
Insurance												
Commercial	499	100	59	100	60	100	116	100	263	100	997	100
Medicare	0	0	0	0	0	0	0	0	0	0	0	0
Missing	0	0	0	0	0	0	0	0	0	0	0	0
Geographic Region												
Northeast	48	9.62	2	3.39	4	6.67	3	2.59	33	12.55	90	9.03
Midwest	112	22.44	16	27.12	5	8.33	7	6.03	44	16.73	184	18.46
South	235	47.09	38	64.41	24	40	77	66.38	136	51.71	510	51.15
West	103	20.64	2	3.39	27	45	29	25	50	19.01	211	21.16
Missing/ Unknown	1	0.2	1	1.69	0	0	0	0	0	0	2	0.2
Education Level												
Less than 12th Grade	2	0.4	0	0	0	0	2	1.72	0	0	4	0.4
High School Diploma	57	11.42	8	13.56	6	10	34	29.31	1	0.38	106	10.63
Less than Bachelor Degree	249	49.9	40	67.8	23	38.33	63	54.31	16	6.08	391	39.22
Bachelor Degree Plus	188	37.68	10	16.95	31	51.67	16	13.79	11	4.18	256	25.68
Missing/ Unknown	3	0.6	1	1.69	0	0	1	0.86	235	89.35	240	24.07
Rolled up Housing (Rent/Own)												

Table 72. Demographics of Paxlovid Users, Optum® SES Database

Characteristics	White N	White %	Black N	Black %	Asian N	Asian %	Hispanic N	Hispanic %	Missing N	Missing %	Overall N	Overall %
Probable Homeowner	390	78.16	29	49.15	40	66.67	75	64.66	18	6.84	552	55.37
Probable Renter	20	4.01	13	22.03	5	8.33	12	10.34	2	0.76	52	5.22
Missing/Unknown	89	17.84	17	28.81	15	25	29	25	243	92.4	393	39.42
Rolled up Household Income												
<$40K	26	5.21	17	28.81	2	3.33	17	14.66	3	1.14	65	6.52
$40K-$49K	20	4.01	5	8.47	0	0	4	3.45	1	0.38	30	3.01
$50K-$59K	12	2.4	2	3.39	4	6.67	5	4.31	0	0	23	2.31
$60K-$74K	25	5.01	1	1.69	7	11.67	8	6.9	2	0.76	43	4.31
$75K-$99K	55	11.02	8	13.56	3	5	23	19.83	1	0.38	90	9.03
$100K+	293	58.72	15	25.42	34	56.67	38	32.76	15	5.7	395	39.62
Missing/ Unknown	68	13.63	11	18.64	10	16.67	21	18.1	241	91.63	351	35.21

Table 73. Comorbidities and Medical History among Paxlovid users, Optum® SES Database

	White N	White %	Black N	Black %	Asian N	Asian %	Hispanic N	Hispanic %	Missing N	Missing %	Overall N	Overall %
Comorbidities & Medical History												
Hypertension	12	2.4	1	1.69	0	0	1	0.86	5	1.9	19	1.91
Hyperlipidemia	11	2.2	4	6.78	0	0	6	5.17	7	2.66	28	2.81
BMI>=30 or obesity	36	7.21	5	8.47	2	3.33	11	9.48	21	7.98	75	7.52
Diabetes Mellitus	24	4.81	1	1.69	0	0	3	2.59	14	5.32	42	4.21
Asthma	107	21.44	10	16.95	5	8.33	20	17.24	45	17.11	187	18.76
Coronary Heart Disease	0	0	0	0	0	0	0	0	1	0.38	1	0.1
Cardiomyopathies	1	0.2	0	0	0	0	0	0	1	0.38	2	0.2
Cerebrovascular disease or stroke (including Transient Ischemic Attack)	4	0.8	0	0	0	0	1	0.86	0	0	5	0.5
Chronic Kidney Disease	11	2.2	1	1.69	0	0	0	0	5	1.9	17	1.71
VTE	3	0.6	0	0	0	0	0	0	1	0.38	4	0.4
Cancer	6	1.2	0	0	1	1.67	1	0.86	1	0.38	9	0.9
Autoimmune diseases	20	4.01	1	1.69	0	0	2	1.72	15	5.7	38	3.81
COPD	16	3.21	1	1.69	0	0	2	1.72	7	2.66	26	2.61
Liver Disease	5	1	1	1.69	0	0	1	0.86	5	1.9	12	1.2
ILD	3	0.6	0	0	0	0	0	0	1	0.38	4	0.4
HIV infection	0	0	0	0	0	0	0	0	0	0	0	0
Smoking	4	0.8	0	0	0	0	0	0	1	0.38	5	0.5
Deyo-Charlson Comorbidity Index Score												
Mean+/- SD	0.36	0.73	0.22	0.42	0.12	0.37	0.28	0.55	0.33	0.65	0.32	0.66
Median, IQR	0	0 - 1	0	0 - 0	0	0 - 0	0	0 - 0	0	0 - 1	0	0 - 1
Past COVID-19												
0	462	92.59	54	91.53	59	98.33	109	93.97	247	93.92	931	93.38
1	36	7.21	5	8.47	1	1.67	5	4.31	15	5.7	62	6.22
2+	1	0.2	0	0	0	0	2	1.72	1	0.38	4	0.4

10.4.2. Secondary Objectives

10.4.2.1. Objective 1: Estimate the incidence of oxygen supplementation among COVID-19 patients hospitalized with mechanical ventilation/ECMO

The incidence of oxygen supplementation in pediatric COVID-19 patients was highest in the High Risk TSC Cohort, compared to the Standard Risk TSC Cohort. The Paxlovid Cohort did not report any events and thus it was not possible to calculate incidence rates (Table 74).

Table 74. Incidence of Oxygen Supplementation Among Pediatric COVID-19 Patients, 1/1/2020-07/20/2022

			Overall			
Study Endpoints	**Patients at Risk**	**Events**	**Person-time**	**Incidence Rate per 1000 person years**	**95% CI**	
Source Cohort						
ICU/Mechanical ventilation/ECMO	173,648	690	13,140.31	52.51	48.735	56.578
High Risk Trial Similar Cohort						
ICU/Mechanical ventilation/ECMO	67,187	264	5,175.62	51.01	45.212	57.548
Standard Risk Trial Similar Cohort						
ICU/Mechanical ventilation/ECMO	110,350	316	8,264.06	38.24	34.246	42.695
Paxlovid Cohort						
ICU/Mechanical ventilation/ECMO	116	0	6.63	0	0	3,688.88

10.5. Adverse events/adverse reactions

10.5.1. Primary and Secondary Objectives

This study involved data that exist as structured data. In these data sources, it was not possible to link (i.e. identify a potential association between) a particular product and medical event for any individual. Thus, the minimum criteria for reporting an AE (i.e., identifiable patient, identifiable reporter, a suspect product, and event) could not be met.

10.5.2. Exploratory Objectives

This study involved data that exist as structured data. In these data sources, it was not possible to link (i.e. identify a potential association between) a particular product and medical event for any individual. Thus, the minimum criteria for reporting an AE (i.e., identifiable patient, identifiable reporter, a suspect product, and event) could not be met.

This study also involved human review of patient-level unstructured data; unstructured data refers to verbatim medical data, including text-based descriptions such as medical records, images of physician notes, neurological scans, x-rays, or narrative fields in a database.The reviewers were obligated to report AEs with explicit attribution to any Pfizer drug that appeared in the reviewed information (defined per the patient population and study period specified in the protocol). Explicit attribution was not inferred by a temporal relationship between drug administration and an AE but must have been based on a definite statement of causality by a healthcare provider linking drug administration to the AE.

The requirements for reporting safety events on the NIS adverse event monitoring (AEM) Report Form to Pfizer Safety were as follows:

- All serious and non-serious AEs with explicit attribution to **any Pfizer drug** that appeared in the reviewed information must be recorded on the data collection tool (e.g., chart abstraction form) and reported, within 24 hours of awareness, to Pfizer Safety using the NIS AEM Report Form.

- Scenarios involving drug exposure, including exposure during pregnancy, exposure during breast feeding, medication error, overdose, misuse, extravasation, lack of efficacy, and occupational exposure associated with the use of a Pfizer product must be reported, within 24 hours of awareness, to Pfizer Safety using the NIS AEM Report Form.

- For exposure during pregnancy in studies of pregnant women, data on the exposure to “PF-07321332” during pregnancy, were not reportable unless associated with serious or non-serious AEs.

- For these AEs with an explicit attribution or scenarios involving exposure to a Pfizer product, the safety information identified in the unstructured data reviewed was captured in the Event Narrative section of the report form, and constituted all clinical information known regarding these AEs. No follow-up on related AEs was conducted.

All the demographic fields on the NIS AEM Report Form may not necessarily be completed, as the form designates, since not all elements were available due to privacy concerns with the use of secondary data sources. While not all demographic fields were completed, at the very least, at least one patient identifier (e.g., gender, age as captured in the narrative field of the form) was reported on the NIS AEM Report Form, thus allowing the report to be considered a valid one in accordance with pharmacovigilance legislation. All identifiers were limited to generalities, such as the statement "A 35-year-old female..." or "An elderly male..." Other identifiers were removed.

Additionally, the onset/start dates and stop dates for "Illness," "Study Drug," and "Drug Name" may be documented in month/year (mmm/yyyy) format rather than identifying the actual date of occurrence within the month/year of occurrence in the day/month/year (DD/MMM/YYYY) format.

All research staff members completed the following Pfizer training requirements:

- "Your Reporting Responsibilities (YRR) with Supplemental Topics."

These trainings were completed by research staff members prior to the start of data collection. All trainings included a "Confirmation of Training Statement" (for signature by the trainee) as a record of completion of the training, which is kept in a retrievable format. Copies of all signed training statements were provided to Pfizer.

11. DISCUSSION

11.1. Key results

11.1.1. Primary and Secondary Objectives

When examining baseline characteristics, patient profiles differed by cohort and treatment status. In the Overall Source Cohort, demographic and clinical heterogeneity was exhibited with substantial chronic disease burden and high rates of acute complications occurring within one day of diagnosis. The Overall Source Cohort included the broadest population, spanning a wide age, comorbidity, and socioeconomic range, with intermediate incidence of clinical complications. Clinical severity varied across risk strata, with the High-Risk Trial Similar Cohort showing the highest incidence of hospitalization, pneumonia, multi-organ dysfunction, and other acute events. The High-Risk Trial Similar Cohort was older and more comorbid, consistently showing the highest incidence rates of complications—including hospitalization, pneumonia, organ failure, and mortality—across all periods and time windows. Meanwhile the Standard-Risk patients consistently had the lowest complication rates, as this cohort was younger and healthier, with the lowest complication and healthcare-utilization rates among the risk-stratified groups. Prior to propensity score matching (PSM), Paxlovid-treated patients were older, more comorbid, more frequently Medicare-insured, ad more often vaccinated with slightly lower pre-index healthcare utilization than untreated comparators, aligning with higher baseline risk. After propensity score matching, demographic, clinical, and healthcare utilization characteristics were well balanced, enabling rigorous assessment of treatment effects. After PSM, Paxlovid treated and untreated groups were well-aligned as all pre-treatment utilization differences dropped to ≤0.04 standardized difference, which indicated that the matching was effective in equalizing baseline demographic and clinical characteristics between Paxlovid users and non-users.

Next, when examining clinical event timing and early outcomes, results showed that COVID-19 patients treated with Paxlovid had markedly lower short-term risks of severe outcomes. In propensity-matched analysis, the 30-day hospitalization rate in Paxlovid-treated patients was 0.90% versus 5.91% in comparable untreated patients. Similarly, 15-day hospitalization incidence was 0.64% with Paxlovid compared to 5.55% without treatment. These differences correspond to relative risk (RR) reductions on the order of 80–88% (RR ~0.17 at 30 days; ~0.12 at 15 days). This pronounced early benefit of Paxlovid was consistent across subgroups: for example, risk ratios for 30-day hospitalization remained well below 1 for all categories (e.g., ~0.16 in patients <65 years; ~0.19 in Black patients), indicating a substantially lower likelihood of progression to severe COVID-19 in the Paxlovid treated group. In summary, Paxlovid treatment was associated with substantially lower 15- and 30-day hospitalization risk, consistent reductions across age, race, and vaccination subgroups, and lower incidence of acute complications, safety events, and long-COVID outcomes compared with matched untreated patients.

For acute COVID-19 complications and health outcomes, the study found that acute COVID-19 complications were common, especially in high-risk patients and during hospitalization. Within 30 days of infection, major complications (e.g. pneumonia, organ failure, sepsis) occurred frequently across cohorts, with incidence rates for leading events ranging from hundreds to over 1,000 per 1,000 person-years. For example, pneumonia occurred at roughly 1,100 per 1,000 person-years in the overall Source cohort, 1,200 in the High-Risk trial-similar cohort, and 640 in the Standard-Risk cohort. The 30-day hospitalization rate was similarly elevated in higher-risk patients (approximately 1,800 per 1,000 in the High-Risk group vs roughly 1,675 in the Source cohort and 998 in Standard-Risk). Among individuals treated with Paxlovid, rates of acute complications and safety outcomes (such as acute kidney injury, hepatic impairment, and allergic reactions) were substantially higher in those who were hospitalized during their acute COVID-19 illness compared with those who were not hospitalized. In contrast, when compared with matched individuals who did not receive Paxlovid, Paxlovid users consistently experienced lower rates of hospitalization and COVID-19–related complications. Despite differences in magnitude, the spectrum of common complications was similar across cohorts, with respiratory (pneumonia, respiratory failure), cardiovascular, and systemic events (sepsis, multi-organ dysfunction) dominating the early post-infection period.

Long COVID, as defined by post-covid conditions (PCC), patients who developed the condition tended to have higher baseline risk profiles. In the 31–120 days after infection, ~3.3% of patients had a newly diagnosed primary post–COVID condition (PCC, "long COVID"), with slightly lower risk (3.1%) for those infected during the Omicron wave. Newly diagnosed pulmonary and cardiovascular PCCs occurred in approximately 2–3% and 1.4–1.5% of patients, respectively, while secondary (more severe) PCC manifestations were rare (0.3–0.4%). Among patients who developed PCC, symptom onset was typically 2–3 months post-infection – for example, the median time to first PCC diagnosis was approximately 65–67 days (with interquartile range up to roughly 90 days) across primary, cardiovascular, and pulmonary PCC outcomes. Patients who went on to experience long COVID had notably different profiles: they were older (e.g. approximately 27% were age ≥65 vs 16% among those without PCC) and carried a higher burden of comorbidities – for instance, 35% had pre-existing hypertension (vs 21% without PCC), and 16% had diabetes (vs ~10% without). During acute infection, they also required more intensive therapies and care, such as higher utilization of corticosteroids (about 10% received dexamethasone vs 5% of those without PCC) and therapeutic anticoagulation (9% vs 4%), in line with more severe initial illness.

Paxlovid uptake was concentrated in older age groups and varied by race/ethnicity, with differences in comorbid profiles suggesting potential health disparities. Nearly all Paxlovid prescriptions occurred during 2022 (after its Emergency Use Authorization), peaking in mid-2022. Treated patients skewed older (mean age approximately 64 years, median 68 years), roughly 60% were ≥65 years old and only 2.5% were under 30. Over 70% of recipients were White, while roughly 7% were Black, 5% Asian, 11% Hispanic (broadly reflecting the COVID patient population). Notably, there were socio-demographic disparities: Black and Hispanic individuals on Paxlovid were more likely to have lower household incomes, whereas White and Asian recipients more often reported higher incomes (e.g. 62% of White vs 16% of Black patients resided in high-income households). Clinical profiles differed by race as well – for example, Black and Hispanic patients had higher rates of obesity and diabetes (e.g. diabetes in 33% of Black and 32% of Hispanic Paxlovid users vs ~20% of White users) and were less likely to be vaccinated against COVID-19 prior to treatment (vaccination in approximately 30% of Black patients vs 49% in Asian patients). Overall, these findings highlight that Paxlovid was primarily used in older, comorbidity-burdened patients, and they underscore the need to address racial and socioeconomic gaps in COVID-19 therapy access.

When examining oxygen supplementation usage, results illustrate that the need for intensive respiratory support in COVID-19 declined over time. Among hospitalized COVID-19 patients requiring mechanical ventilation and/or ECMO, the incidence of ICU-level oxygen support was extremely high in the early (pre-vaccine) pandemic: on the order of 4,300–4,800 per 1,000 person-years in late 2020. With widespread vaccination, these rates fell to roughly 3,600–3,960 per 1,000 in 2021, and during the Omicron wave (2022) further to about 3,050–3,900 per 1,000 (a 15–30% relative drop compared to the pre-vaccine period). Differences across patient populations were modest: the High-Risk and Source cohorts had similar overall mechanical ventilation rates (~370–424 per 1,000), whereas the Standard-Risk cohort's rate was lower (~227 per 1,000). By contrast, non-hospitalized patients rarely required advanced oxygen support (only 6–34 per 1,000 across cohorts), underscoring that this severe outcome was concentrated in the sickest (hospitalized) segment of patients.

11.1.2. Exploratory Objectives

Real-world Paxlovid effectiveness against hospitalization during Omicron predominance among COVID-19 patients at high risk of severe disease supports demonstrated clinical trial efficacy. [18] While effectiveness was high and similar across all racial subgroups, uptake of Paxlovid among Black patients was lower compared to White patients. Multiple machine learning and deep learning models identified the Charlson comorbidity score, age, and frequency of healthcare utilization, which may help predict the occurrence of incident long COVID (defined by PCCs) and demonstrated the utility of the models for individualized risk prediction. [19]

11.2. Limitations

11.2.1. Primary and Secondary Objectives

COVID-19 was new disease during the early part of this study, with evolving diagnostic mechanisms and care. A COVID-19 diagnosis code was established on 01 April 2020, months after the initial identification of cases and circulation in the US. The spectrum of clinical manifestations of SARS-CoV-2 is still not fully described. [20] Many infected persons were thought to have mild to unrecognizable symptoms and may therefore not present for care, testing or diagnosis. [20] These infections were likely not be identifiable in the datasets. This may overestimate the incidence of severe disease in relation to overall SARS-CoV-2 infection.

Similarly, patients with chronic diseases or in inpatient settings, the elderly, or other risk groups may be more likely to be under ongoing care or thought to be at higher risk and therefore may be more likely to seek care or be referred for testing. [21, 22] Differences among at-risk subpopulations may arise from access to care/health care seeking behaviors rather than true differences in risk. Generalizability may be further limited as SARS-CoV-2 testing patterns and treatment are evolving over time.

Other limitations are similar to those from observational studies in general, including the inability to obtain detailed clinical information on disease severity and activity due to the nature of secondary databases. [23, 24] In addition, EHR data only offer the prescribed drug information which does not indicate that the medication was consumed or that it was taken as prescribed. Misclassification in diagnosis data is unavoidable in RWD. Some conditions used to assess long-term health effects (eg, Dysgeusia, Diarrhea, Myalgia etc.) may not be well captured in the database if the patient is not seen by a health care provider to report these types of events. We use the data from the IDN that manages end-to- end healthcare facilities of one or more healthcare centers in a defined geographical location and aims at providing full spectrum service of inpatient and outpatient for a patient to help reduce the concern of the discontinuity in patient service. We used the linked data to Claims as sensitivity (or additional) analyses when needed to expand the analyses by adding additional patients or patient records beyond EHR via close or open claims. Lastly, we would also like to note that there is a lack of complete similarity between the Trial Similar Cohort and the clinical trial patients.

11.2.2. Exploratory Objectives

In addition to the limitations outlined above, Optum® data are encounter-based and do not cover all COVID-19 treatment and prescribing sites (e.g., retail pharmacy, telehealth, public health departments). Thus, study patients in both groups can be sicker than the general population and a slower uptake of Paxlovid was observed than expected. However, we expect that our cohort likely reflects the target population who are at higher risk of severe COVID-19 outcomes. The database does not completely collect vaccination data, which precluded assessing effectiveness in the unvaccinated patient subgroup.

Use of hospitalization as a proxy of COVID-19-attributed hospitalization could result in outcome misclassification due to inclusion of admission and encounters for conditions other than COVID-19 in patients hospitalized after the COVID-19 diagnosis date or Paxlovid prescription date. [25, 26] However, we used the 15-day risk window, as adopted in other real-world studies to help reduce potential effects of misclassification due to longer risk windows. [18] We also undertook an additional analysis estimating true COVID-19-attributed hospitalization events. Hospitalizations occurring outside of IDNs would not be captured in the database, leading to potential underestimation of hospitalization in both groups. The EHR data source lacked the specific date of COVID-19 symptom onset, although this likely occurred ≤14 days from diagnosis for most cases.

Paxlovid effectiveness may also be underestimated because of incomplete treatment initiation, nonadherence, and undocumented Paxlovid receipt in the nonprescribed group. Although death was included as a censoring event to define follow-up end date via an algorithm, mortality was not included as an endpoint because of concern of increased outcome misclassification. The study started when Paxlovid was granted EUA; its use has since expanded rapidly, and earlier results may not reflect current use.

Finally, results may lack generalizability to patients not at high risk of severe disease, to other countries with different healthcare systems, in non-US populations, and in pediatric patients. Although the study included patients from 12 years of age, the low number of patients <18 years of age precluded a sub-analysis in this age group. Future research should aim to confirm these early real-world results, expand generalizability, and address limitations. We believe our findings, showing reduced COVID-19-associated hospitalization among those at high risk of severe disease, particularly Black patients, will assist prescribers and decision-makers to prioritize Paxlovid in vulnerable patient groups.

Further limitations include the inability to draw causal conclusions because of the observational nature of the EHR data, particularly around insurance status. [23, 24] While the Optum COVID-19 EHR is a provider-sourced and payer-agnostic EHR dataset that is derived from IDNs, hospitals, and ambulatory practices across the US with inclusion is driven by care delivery at participating providers, not by insurance enrollment, insurance status is not always recorded correctly as it is recorded at a single point-in-time during an encounter. As a result, uninsured individuals are systematically under-represented relative to what is observed in the US population, while privately insured patients are over-represented compared with the uninsured or Medicaid populations. [23, 24]

Longitudinal completeness varies substantially by site and patient engagement with contributing systems. Further, EHR data can be biased toward patients who are more likely to use healthcare systems (e.g., young patients were less likely to seek care than older patients and, hence, might be under-represented in EHR data), or to those with more severe symptoms. We were unable to include patients who did not test for COVID-19 early in the pandemic due to the requirement for a positive COVID-19 test and an index date in our models. The relatively lower vaccination rates in the early pandemic era may also limit the statistical power to detect the potential protective effects of COVID-19 vaccines on PCC in the follow-up periods. [19]

Lastly, because of general limitations in EHR data and the ICD coding system, we were unable to determine whether patients with pre-existing PCC symptoms 1 year before their COVID-19 infection experienced an improvement or a worsening of those symptoms in the follow-up period after their COVID-19 infection. Therefore, we excluded patients with pre-existing PCC symptoms 1 year before their index COVID-19 infection for cleaner endpoints and focused on incidence PCC. [19] These excluded patients were generally in worse health than study participants and therefore conclusions may not be generalizable to the full US population.

11.3. Interpretation

11.3.1. Primary and Secondary Objectives

The contemporaneous and historical background incidence rates for health outcomes of interest produced for the primary and secondary objectives are important to contextualize events in each cohort. The results of this study illustrate that after propensity score matching, baseline characteristics between Paxlovid-treated and untreated patients with COVID-19 could be balanced, enabling valid comparisons. Paxlovid treatment was associated with a substantial reduction in short-term hospitalization risk: 30-day hospitalization rates were 0.90% in treated patients versus 5.91% in untreated, and 15-day rates were 0.64% versus 5.55%, corresponding to relative risk reductions of 80–88%. These benefits were consistent across demographic subgroups. Acute complications such as pneumonia, sepsis, and multi-organ dysfunction were common, were more common among hospitalized and high-risk patients, and patients treated with Paxlovid experienced lower rates of these complications compared to non-treated counterparts. These findings underscore the real-world effectiveness of Paxlovid in reducing severe COVID-19 outcomes and highlight persistent disparities in treatment access and disease burden.

The need for mechanical ventilation (MV) or extracorporeal membrane oxygenation (ECMO) declined over time, from 4,300–4,800 per 1,000 person-years in the pre-vaccine period to 3,050–3,900 during the Omicron wave, and these rates of MV/ECMO and their decline from pre-vaccine to Omicron periods are consistent with the COVID-19 literature in both direction and relative magnitude with the caveat that often proportions are reported in literature rather than rates. [27, 28]

Long COVID in this study was defined by post–COVID-19 conditions (PCC) where approximately 3.3% of patients within 31–120 days post-infection exhibited PCCs, with slightly lower rates during the Omicron wave. [13] Those who developed PCC were more likely to be older and have pre-existing conditions such as hypertension and diabetes, and they required more intensive treatment during acute COVID-19 illness.

Examining health disparities can be challenging as not all social determinants of health are fully captured in any one data source, this study found that Paxlovid uptake was concentrated among older, high-risk individuals, with notable racial and socioeconomic disparities: Black and Hispanic patients had higher comorbidity burdens and lower vaccination rates, and were underrepresented among Paxlovid recipients.

11.3.2. Exploratory Objectives

Real-world Paxlovid effectiveness against hospitalization during Omicron predominance among COVID-19 patients at high risk of severe disease exhibited similar rates as the pivotal clinical trial. While effectiveness was high and similar across all racial subgroups, uptake of Paxlovid among Black patients was lower compared to White patients.

The risk factors identified for Long COVID include histories of heart conditions as well as prior recent healthcare utilization, suggesting that patients may have had predisposing risk factors that contributed to the development of myocarditis across all three settings assessed.

11.4. Generalizability

This study analyses Optum® EHR data from the US and thus generalizability may be limited geographically. Differences among at-risk subpopulations may arise from access to care/health care seeking behaviors rather than true differences in risk. Generalizability may be further limited as SARS-CoV-2 testing patterns and treatment are evolving over time. External validity may be limited by various inclusion criteria requiring additional clinical encounters and documentation for SARS-CoV-2 validation or symptoms and prior database activity, which may result in underrepresentation of individuals with less healthcare engagement or incomplete records.

12. OTHER INFORMATION

Not Applicable

13. CONCLUSIONS

In this study, among COVID-19 patients, hospitalized patients and patients in the high-risk cohort experienced the greatest incidence of complications, interventions, health outcomes and Long COVID symptoms. The Paxlovid treated patients had lower incidence rates of hospitalization, complications, health outcomes and Long COVID symptoms, as compared to patients who did not receive Paxlovid. Real-world Paxlovid effectiveness against hospitalization during Omicron predominance among COVID-19 patients at high risk of severe disease supports demonstrated clinical trial efficacy. [18] While effectiveness was high and similar across all racial subgroups, uptake of Paxlovid among Black patients was lower compared to White patients. [18] Multiple machine learning and deep learning models identified a higher Charlson comorbidity score, older age, and more frequent of healthcare utilization, which may help predict the occurrence of new PCC to identify Long COVID and demonstrate the utility of the models for individualized risk prediction. [19]

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15. LIST OF SOURCE TABLES AND FIGURES

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