Disclaimer

The following report(s) provides findings from an FDA-initiated query using Sentinel. While Sentinel queries may be undertaken to assess potential medical product safety risks, they may also be initiated for various other reasons. Some examples include determining a rate or count of an identified health outcome of interest, examining medical product use, exploring the feasibility of future, more detailed analyses within Sentinel, and seeking to better understand Sentinel capabilities.

Data obtained through Sentinel are intended to complement other types of evidence such as preclinical studies, clinical trials, postmarket studies, and adverse event reports, all of which are used by FDA to inform regulatory decisions regarding medical product safety. The information contained in this report is provided as part of FDA's commitment to place knowledge acquired from Sentinel in the public domain as soon as possible. Any public health actions taken by FDA regarding products involved in Sentinel queries will continue to be communicated through existing channels.

FDA wants to emphasize that the fact that FDA has initiated a query involving a medical product and is reporting findings related to that query does not mean that FDA is suggesting health care practitioners should change their prescribing practices for the medical product or that patients taking the medical product should stop using it. Patients who have questions about the use of an identified medical product should contact their health care practitioners.

The following report contains a description of the request, request specifications, and results from the modular program run(s).

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Overview for Request: cder_iqp_wp033

Request ID: cder_iqp_wp033

Request Description: In this report, we characterized two cohorts; one indexing on acute Coronavirus Disease (COVID) diagnosis or positive Severe Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) test, and a second cohort indexing on Long COVID. These analyses are intended as an exploration of the FDA's Sentinel Electronic Health Record (EHR) data sources (specifically TriNetX) to capture Long COVID and assess feasability of future Long COVID studies in TriNetX.

Data Source: We ran this query on March 29, 2023. This query contains data from 34 health care organizations (HCOs), provided through the TriNetX Live™ platform in their USA with No Shift Network from January 1, 2021 to February 23, 2023. TriNetX aggregates electronic health record (EHR) systems data from its partner HCOs to create queryable datasets. TriNetX datasets primarily comprise of clinical patient data such as demographics, diagnoses, procedures, labs, and medications. For more information on the TriNetX Live™ platform and the TriNetX data visit their website here: https://trinetx.com/

Study Design: We identified cohorts of individuals with evidence of 1) incident acute COVID-19, and 2) incident Long COVID in the Query Builder module in the TriNetX Live™ platform from January 1, 2021 through August 23, 2022 to allow a full 180-days of follow-up through February 23, 2023. We additionally summarized patients' encounter history using the Summary Statistics module. We further utilized the Analyze Outcomes and Compare Outcomes Analytics modules to determine the number of patients in each cohort with various pre- and post-index characteristics. Finally, we used the Incidence and Prevalence Analytics module to examine incidence and incidence rate of Long COVID in the acute COVID-19 cohort by quarter.

Exposures of Interest: We defined the exposure of interest for cohort 1, acute COVID-19, using International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) diagnosis codes and Logical Observation Identifiers Names and Codes (LOINC) lab codes. The exposure of interest for cohort 2, Long COVID, was defined using ICD-10-CM diagnosis codes. Please see Appendix A for a list of diagnosis codes used to define acute COVID-19 and Long COVID exposures.

Outcomes of Interest: We defined several outcomes in this request, which are described below by the cohort in which they were assessed and the timeframe relative to the index date in which we assessed them. Among patients in the acute COVID-19 cohort only, we assessed COVID-19 related treatments in the 30 days on or after the index date using the Risk section of the Analyze Outcomes module. COVID-19 related treatments were defined using Anatomic Therapeutic Classification (ATC) and RxNorm terminologies and included: antivirals, bamlanivimab, bebtelovimab, casirivimab, corticosteroids, interleukin inhibitors, JAK inhibitors, remdesivir, sarilumab, satralizumab, siltuximab, sotrovimab, tixagevimab, and tocilizumab. We also assessed Long COVID and multisystem inflammatory syndrome (MIS) defined with ICD-10-CM diagnosis codes in the 28-180 and 90-180 days after the index date. Using the Incidence and Prevalence analytics module, we identified the number of patients in the acute COVID-19 cohort with severe COVID-19 in the 30 days on or after the index date by building a separate cohort in Query Builder, then obtaining the count of patients with this outcome by inputting this pseudo-cohort into the Analzye Outcomes module and outputting the number of patients in the cohort on the index date. Among patients in the Long COVID cohort only, we evaluated the top ten most common signs and/or symptoms occuring on the index date using the Risk section of the Analzye Outcomes module. Using that same section, we estimated the average number of ambulatory, emergency, inpatient acute, and inpatient non-acute visits patients had, the number with a COVID-19 vaccination, and the ten most prevalent health conditions and medications in the 180 days on or after the index date. Signs, symptoms, and health conditions were defined using ICD-10-CM diagnosis codes, visits with TriNetX visit terms, and COVID-19 vaccination with International Classification of Diseases, Tenth Revision, Procedure Coding System (ICD-10-PCS), Current Procedural Terminology, Fourth Edition (CPT-4), and Healthcare Common Procedure Coding System (HCPCS) codes. Please see Appendix C for the list of ATC, CPT, HCPCS, ICD-10-PCS, and RxNorm codes to define outcomes in this report.

Cohort Eligibility Criteria: Patients of all ages were included in this report. Patients in both cohorts were required to have at least one visit in the six months prior to index and one visit in the six to twelve months prior to index. Please see Appendix A for the TriNetX curated visit term used to define the visit requirement.

Overview for Request: cder_iqp_wp033

Characteristics: We utilized the Baseline Comparison Statistics section of the Compare Outcomes analytic module to evaluate the following: baseline comorbidities, medications of interest, COVID-19 vaccination, healthcare utilization, Long COVID, multisystem inflammatory syndrome, related diagnoses, and related treatments. We also used the Incidence and Prevalence Analytics module to describe the incidence rate of Long COVID in the acute COVID-19 cohort by quarter. Additionally, we built a cohort in Query Builder that indexed on severe COVID-19, but was treated as an outcome, not a study cohort. We used the Analyze Criteria module to output cohort attrition figures and the Summary Statistics module to output length of patient record. In both cohorts, we output demographics identified on the index date and evidence of COVID-19 vaccination ever before the index date. COVID-19 vaccination was defined using a Vaccine Administered (CVX) code that TrinetX mapped to HCPCS and RxNorm codes. We additionally identified several health conditions in the year prior to the index date in both cohorts. Health conditions assessed included cancer (overall and specifically benign neoplasms, in situ neoplasms, and malignant hematologic neoplasms), chronic kidney disease, liver disease, chronic lower respiratory diseases (overall and specifically asthma), nervous system degeneration, mental disorders due to known physiological conditions, mental and behavioral disorders due to psychoactive substance use, diabetes (type 1 or 2), circulatory system diseases (overall and specifically hypertensive diseases), Human Immunodeficiency Viruses (HIV) infection, disorders involving immune mechanism, mood disorders, schizophrenia, overweight or obese, sickle cell disease, smoking, cerebrovascular disease (overall and specifically cerebral infarction), and tuberculosis. Each was defined using ICD-10-CM diagnosis code hierarchies. Additionally, we evaluated the use of immunosuppressants (defined with ATC codes) in the 30 and 90 days prior to the index date. In the Long COVID cohort only, we evaluated evidence of the following COVID-related medications in the 30 and 90 days prior to the index date using ATC and RxNorm codes: antivirals, bamlanivimab, bebtelovimab, casirivimab, corticosteroids, interleukin inhibitors, JAK inhibitors, remdesivir, sarilumab, satralizumab, siltuximab, sotrovimab, tixagevimab, and tocilizumab. Please see Appendix B for the list of ATC and RxNorm codes to define pre-index characteristics in this report and Appendix F for the Analyze Criteria module specifications.

Please see Appendices D-F for the overall specifications of parameters used in this request.

Limitations: Algorithms used to define exposures, characteristics, pregnancy, and mapping of source data to the data model are imperfect and susceptible to misclassification. In particular, the validity of our algorithm to define long COVID is suboptimal. Additionally, EHR data in the US lacks longitudinality. The information before or after patients' healthcare encounters could be missing, especially if patient care was administered across different HCOs that might not participate in the TriNetX USA network. We are unable to determine if absence of evidence of a condition implies a true absence of a condition or if the condition was not observed in the data. Furthermore, not all HCOs provide brand name information for RxNorm terms or laboratory data. Therefore, data should be interpreted with these limitations in mind. All counts provided through the TriNetX Live™ platform are rounded up to the nearest ten to protect patient privacy. This rounding affects error, especially as sample sizes decrease. Error due to rounding can range from <0.09% when sample sizes are >10,000 to nearly 20% as sample sizes drop. Thus, all estimates should be interpreted as ranges, and small sample sizes should be interpreted with caution. Additionally, percentages are calculated based on these rounded numerators and denominators. Thus, due to rounding, the sum of each value in a category may not total to 100%.

Notes: We ran this query on March 29, 2023. A re-run of this query for the same query period in the future may not yield the same results owing to the dynamic nature of the TriNetX Live™ network.

Please contact the Sentinel Operations Center (info@sentinelsystem.org) for questions and to provide comments/suggestions for future enhancements to this document. For more information on Sentinel's querying in the TriNetX platform, please refer to the Sentinel Website (https://www.sentinelinitiative.org/methods-data-tools/methods/trinetx-rapid-querying).

Sentinel

Table of Contents	

Glossary of Terms for Analyses Using TriNetX Live™ Platform*

Characteristic - A medical fact (e.g., diagnosis, procedure, lab result) that occurred on or before the cohort-defining index event.

Explore Cohort - A description module on the TriNetX platform that presents a clinical profile of patients in a given cohort. Patient counts are rounded up to the nearest 10 before percentages are calculated, so the sum each of the values in one category may not total to 100%.

Date Shifting - A data obfuscation technique that some HCOs use to preserve patient privacy. Date shifting entails assigning each patient a random number of days (eg, -365 to +365 days) and consistently adjusting each of their dates by that number of days, thus maintaining temporal relationships between records within a single patient.

Fact - (Medical Fact) A unit of utilization that represents a medical observation on a patient (e.g., diagnosis, procedure, clinical observation).

Filter - A method of limiting terms included in queries to a specific subset of data. Filters include age at time of event, data source (electronic health record or natural language processing); brand name, route, and strength for medication terms; occurrence (first or most recent) for lab terms; and priority for diagnosis and procedure terms.

Group - A series of codes and terms defined with Boolean logic that are used to create a query cohort. For each group, users have the ability to specified time periods of interest, and the number of instances that the group must occur for cohort entry.

- **Subgroup -** Within a group, additional subgroups can be specified to define temporal relationships between the terms in the subgroup (e.g., terms in subgroup B must occur within 5 days after terms in subgroup A). Users can require that these temporal constraints be applied to the 1) first, 2) last, or 3) any instance of each subgroup.

Health Care Organization (HCO) - Organizations that contribute electronic healthcare record data to the TriNetX data networks. HCOs include academic institutions and community health provider systems and a single HCO may contain one or more individual sites or facilities.

Index - The first date when a patient meets all of the cohort-defining criteria. In Analytics modules, the index can be defined as the date when a patient meets all of the cohort criteria, or only one specific group's criteria.

Module - A subsection of the TriNetX platform that performs a distinct functionality. Cohorts are created using the Query Builder module. Descriptive modules include Healthcare Organizations, Explore Cohorts, Rate of Arrival, Summary Statistics, and Analyze Criteria. Advanced analytic modules include Analyze Outcomes, Compare Outcomes, Compare Cohorts, Treatment Pathways, and Incidence and Prevalence.

Network - An aggregation of HCOs contributing data to the platform. Multiple networks are available for querying on the platform; the different networks represent subsets of HCOs organized by date-shifting practices or availability of downloadable datasets.

Outcome - A medical fact (e.g., diagnosis, procedure, lab result) that occurred on or after the cohort-defining index event.

Query - In the TriNetX platform, a query is a distinct cohort with a unique set of terms and logic. Query cohorts are created using the Query Builder platform module.

Risk - In Advanced Analytics modules, risk refers to the percentage of patients in each cohort with the specified outcome of interest.

Priority - An indication whether the code was the condition that the provider spent the most time evaluating or treating during a visit. Possible values include primary, secondary, or unknown.

Term - The codes used to specify patient cohort criteria in a query. Code options include diagnoses, procedures, medications, labs, demographics, genomics, and visits. Terms can be linked together using and/or Boolean logic. TriNetX also creates terms that group together multiple medical codes into single clinical concepts.

- **Cannot Have Term -** A category of terms within a query group that patients must not have evidence of to be included in the cohort.
- **Must Have Term -** A category of terms within a query group that patients must have evidence of to be included in the cohort.

Time Constraint - used to define time periods of interest for each group within a query. Time constraints can be defined relative to the date the query was run (e.g., any time before today), or defined based on specific dates (e.g., January 1, 2015 to September 30, 2020).

Treatment Pathway - In Advanced Analytics modules, the Treatment Pathways module returns the order in which patients received treatment and the prevalence of treatments, including combination of medications, following an index event.

TriNetX Codes - For commonly used laboratory terms, TriNetX aggregates Logical Observation Identifiers Names and Codes (LOINC) laboratory codes at a clinically significant level to new queryable TNX:LAB terms.

Glossary of Terms for Analyses Using TriNetX Live™ Platform*

Visit - A type of term used to specify the type of medical encounter or facility where the encounter was recorded. Visit terms are derived by TriNetX from the source data. Visits are recorded separately from the codes or labs that occurred during the encounter; care settings are not attached to individual codes. Values for visit terms include: ambulatory, emergency, field, home health, inpatient encounter, inpatient acute, inpatient non-acute, laboratory, observation, pharmacy, pre-admission, short stay, virtual, and unknown.

*all terms may not be used in this report

Table 1. Characteristics of Patients with Acute COVID-19 and Long COVID in the TriNetX USA "No Date Shifting" Network from January 1, 2021 to August 23, 2022

	Acute COVID-19		Long COVID	
	Number	Percent	Number	Percent
Patient Characteristics				
Unique patients	618,230	100%	17,450	100%
Comorbidities Assessed in the Year Prior to Index				
Neoplasms	99,630	16.1%	3,340	19.1%
Benign neoplasms	52,220	8.4%	1,700	9.7%
In situ neoplasms	4,610	0.7%	160	0.9%
Malignant hematologic neoplasms	8,960	1.4%	350	2.0%
Chronic kidney disease	45,050	7.3%	1,800	10.3%
Chronic lower respiratory diseases	90,290	14.6%	4,040	23.2%
Asthma	60,030	9.7%	2,560	14.7%
Circulatory system diseases	246,880	39.9%	9,120	52.3%
Hypertensive diseases	194,580	31.5%	7,030	40.3%
Cerebrovascular disease	26,200	4.2%	1,140	6.5%
Cerebral infarction	11,590	1.9%	530	3.0%
Diabetes (type 1 or 2)	89,960	14.6%	3,300	18.9%
Disorders involving immune mechanism	16,070	2.6%	820	4.7%
HIV infection	4,570	0.7%	160	0.9%
Liver disease	28,540	4.6%	1,240	7.1%
Mental and behavioral disorders				
Mental disorders due to known physiological conditions	12,570	2.0%	550	3.2%
Mental disorders due to psychoactive substance	50,370	8.1%	1,780	10.2%
Nicotine dependence	33,980	5.5%	1,200	6.9%
Mood disorders	92,150	14.9%	3,730	21.4%
Schizophrenia	2,160	0.3%	60	0.3%
Nervous system degeneration	7,460	1.2%	260	1.5%
Overweight or obese	90,530	14.6%	3,620	20.7%
Sickle cell disease	2,190	0.4%	50	0.3%
Tuberculosis	270	<0.1%	20	0.1%
Medications Assessed in the 30 Days Prior to Index				
Immunosuppressants	6,670	1.1%	380	2.2%
Systemic corticosteriods	N/A		2,480	14.2%
Any interleukin inhibitor	N/A		50	0.3%
Tocilizumab (anti-IL-6 receptor monoclonal antibody)	N/A		40	0.2%
Sarilumab (anti-IL-6 receptor monoclonal antibody)	N/A		10	<0.1%
Satralizumab (anti-IL-6 receptor monoclonal antibody)	N/A		0	0.0%
Siltuximab (anti-IL-6 monoclonal antibody)	N/A		10	<0.1%
JAK inhibitors	N/A		10	<0.1%
Monoclonal antibodies for COVID-19[1]				
bamlanivimab or bamlanivimab/etesevimab	N/A		40	0.2%
bebtelovimab	N/A		40	0.2%
casirivimab/imdevimab	N/A		140	0.8%

Table 1. Characteristics of Patients with Acute COVID-19 and Long COVID in the TriNetX USA "No Date Shifting" Network from January 1, 2021 to August 23, 2022

	Acute COVID-19		Long COVID	
	Number	Percent	Number	Percent
sotrovimab	N/A		40	0.2%
tixagevimab/cilgavimab	N/A		10	<0.1%
Oral antivirals	N/A		960	5.5%
Remdesivir	N/A		490	2.8%
Medications Assessed in the 90 Days Prior to Index				
Immunosuppressants	12,750	2.1%	680	3.9%
Systemic corticosteriods	N/A		4,170	23.9%
Any interleukin inhibitor	N/A		110	0.6%
Tocilizumab (anti-IL-6 receptor monoclonal antibody)	N/A		90	0.5%
Sarilumab (anti-IL-6 receptor monoclonal antibody)	N/A		10	<0.1%
Satralizumab (anti-IL-6 receptor monoclonal antibody)	N/A		0	0.0%
Siltuximab (anti-IL-6 monoclonal antibody)	N/A		10	<0.1%
JAK inhibitors	N/A		10	<0.1%
Monoclonal antibodies for COVID-19[1]				
bamlanivimab or bamlanivimab/etesevimab	N/A		60	0.3%
bebtelovimab	N/A		60	0.3%
casirivimab/imdevimab	N/A		240	1.4%
sotrovimab	N/A		70	0.4%
tixagevimab/cilgavimab	N/A		20	0.1%
Oral antivirals	N/A		1,570	9.0%
Remdesivir	N/A		830	4.8%
Other Characteristics Assessed Ever Prior to Index				
COVID-19 vaccination (no CPT codes)	65,880	10.7%	2,120	12.1%

[1]Emergency use authorization for monoclonal antibodies used to treat COVID-19 expired throughout the duration of this study period: bamlanivimab (EUA valid 11/9/20 - 4/16/21), bamlanivimab and etesevimab (2/9/21 - 1/24/22), bebtelovimab (2/11/22 - 11/30/22), casirivimab and imdevimab (11/21/20 - 1/24/22), sotrovimab (5/26/21 - 4/5/22), tixagevimab and cilgavimab (12/8/21 - 1/26/23).

NOTE: All counts provided through the TriNetX Live™ platform are rounded up to the nearest 10 to protect patient privacy. All percentages were calculated based on the rounded estimates, and are presented here rounded to the tenths position to avoid mischararacterizing the precision of the measurement. Due to rounding, all estimates should be interpreted as ranges, with the lower value of the range ≤ 0.05% less than the presented value unless otherwise noted.

Table 2. Summary of Outcomes for Patients with Acute COVID-19 in the TriNetX USA "No Date Shifting" Network from January 1, 2021 to February 23, 2023

	Acute COVID-19	
	Number	**Percent**
Outcomes		
Unique patients	618,230	100.0%
Outcomes Assessed from 28 Days After through 180 Days After Index		
Long COVID	6,860	1.1%
Multisystem Inflammatory Syndrome	80	<0.1%
Outcomes Assessed from 90 Days After through 180 Days After Index		
Long COVID	3,430	0.6%
Multisystem Inflammatory Syndrome	40	<0.1%
Outcomes Assessed from Index through 30 Days After Index		
Severe COVID-19 Disease	4,810	0.8%
Systemic corticosteriods	108,290	17.5%
Any interleukin inhibitor	2,220	0.4%
Tocilizumab (anti-IL-6 receptor monoclonal antibody)	1,790	0.3%
Sarilumab (anti-IL-6 receptor monoclonal antibody)	60	<0.1%
Satralizumab (anti-IL-6 receptor monoclonal antibody)	0	0.0%
Siltuximab (anti-IL-6 monoclonal antibody)	0	0.0%
JAK inhibitors	130	<0.1%
Monoclonal antibodies for COVID-19[1]		
bamlanivimab or bamlanivimab/etesevimab	4,480	0.7%
bebtelovimab	6,080	1.0%
casirivimab/imdevimab	14,430	2.3%
sotrovimab	3,560	0.6%
tixagevimab/cilgavimab	230	<0.1%
Oral antivirals	60,650	9.8%
Remdesivir	22,890	3.7%

[1]Emergency use authorization for monoclonal antibodies used to treat COVID-19 expired throughout the duration of this study period: bamlanivimab (EUA valid 11/9/20 - 4/16/21), bamlanivimab and etesevimab (2/9/21 - 1/24/22), bebtelovimab (2/11/22 - 11/30/22), casirivimab and imdevimab (11/21/20 - 1/24/22), sotrovimab (5/26/21 - 4/5/22), tixagevimab and cilgavimab (12/8/21 - 1/26/23).

NOTE: All counts provided through the TriNetX Live™ platform are rounded up to the nearest 10 to protect patient privacy. All percentages were calculated based on the rounded estimates, and are presented here rounded to the tenths position to avoid mischararacterizing the precision of the measurement. Due to rounding, all estimates should be interpreted as ranges, with the lower value of the range ≤ 0.05% less than the presented value unless otherwise noted.

Table 3. Summary of Outcomes for Patients with Long COVID in the TriNetX USA "No Date Shifting" Network from January 1, 2021 to February 23, 2023

	Long COVID	
	Number	**Percent**
Outcomes		
Unique patients	17,450	100.0%
10 Most Prevalent Clinical Signs and Symptoms Assessed at Index[1]		
Abnormalities of breathing (R06)	4,120	23.6%
Cough (R05)	3,420	19.6%
Malaise and fatigue (R53)	3,310	19.0%
Pain in throat and chest (R07)	1,450	8.3%
Other symptoms and signs involving circulatory and respiratory system (R09)	1,310	7.5%
Abnormalities of heart beat (R00)	1,230	7.0%
Other symptoms and signs involving cognitive functions and awareness (R41)	900	5.2%
Headache (R51)	790	4.5%
Disturbances in smell and taste (R43)	750	4.3%
Abnormal findings on diagnostic imaging of lung (R91)	760	4.4%
Outcomes Assessed from Index through 180 Days After Index		
Healthcare Utilization (Number of Visits)[2]		
Ambulatory	10.9	13.8
Emergency department	1.7	1.8
Inpatient acute	3.1	5.4
Inpatient non-acute	3.9	5.9
COVID-19 Vaccination		
COVID-19 Vaccination (no CPT codes)	660	3.8%
COVID-19 Vaccination (with CPT codes)	1,090	6.2%
10 Most Prevalent Related Conditions[3]		
Essential (primary) hypertension (I10)	6,120	35.1%
Disorders of lipoprotein metabolism and other lipdemias (E78)	5,280	30.3%
Other anxiety disorders (F41)	3,710	21.3%
Viral agents as the cause of diseases classified elsewhere (B97)	3,570	20.5%
Emergency use of U07 (U07)	3,370	19.3%
Sleep disorders (G47)	3,300	18.9%
Gastro-esophageal reflux disease (K21)	3,170	18.2%
Overweight and obesity (E66)	3,070	17.6%
Type 2 diabetes (E11)	3,040	17.4%
Other joint disorder, not elsewhere classified (M25)	2,970	17.0%
10 Most Prevalent Related Treatments[4]		
Opthalmologicals (S01)	7,410	42.5%
Drugs for obstructive airway diseases (R03)	6,380	36.6%
Corticosteroids, dermatological (D07)	6,140	35.2%
Nasal preparations (R01)	6,020	34.5%
Corticosteroids for systemic use (H02)	5,620	32.2%
Analgesics (N02)	5,540	31.7%
Antibacterials for systemic use (J01)	5,510	31.6%

Table 3. Summary of Outcomes for Patients with Long COVID in the TriNetX USA "No Date Shifting" Network from January 1, 2021 to February 23, 2023

	Long COVID	
	Number	**Percent**
Vasoprotectives (C05)	5,290	30.3%
Stomatological preparations (A01)	5,050	28.9%
Blood substitutes and perfusion solutions (B05)	4,740	27.2%

[1]Signs and symptoms are defined using the 3-digit level of the ICD-10-CM hierarchy in the R* range

[2]In TriNetx Ambulatory was classified as ambulatory, virtual, or home health visit and inpatient was classified as inpatient encounter, observation encounter, and short stay.

[3]Conditions are defined using the 3-digit level of the ICD-10-CM hierarchy excluding codes in the R* and Z* range

[4]Treatments are classfied using the 3-digit level of the Anatomical Therapeutic Chemical (ATC) classification system

NOTE: All counts provided through the TriNetX Live™ platform are rounded up to the nearest 10 to protect patient privacy. All percentages were calculated based on the rounded estimates, and are presented here rounded to the tenths position to avoid mischararacterizing the precision of the measurement. Due to rounding, all estimates should be interpreted as ranges, with the lower value of the range ≤ 0.05% less than the presented value unless otherwise noted.

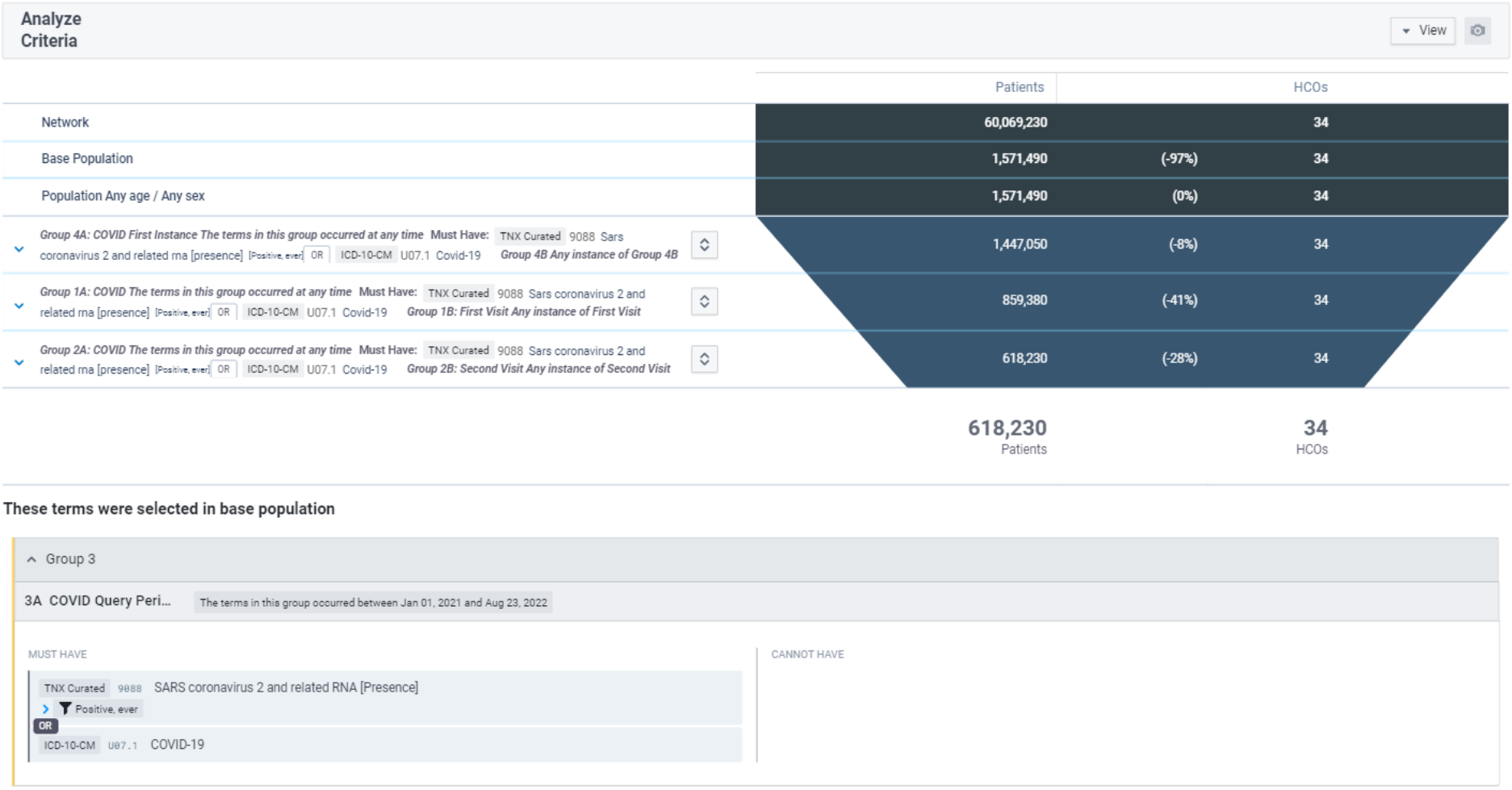
Table 4. Incidence of Long COVID among Patients with Acute COVID-19 in the TriNetX USA "No Date Shifting" Network from January 1, 2021 to February 23, 2023

	January - March 2021	April - June 2021	July - September 2021	October - December 2021
Unique patients in time period	598,870	601,690	600,510	593,430
New Cases	700	740	980	2,660
Incidence Rate per 10,000 person-days	0.13	0.14	0.18	0.50

	January - March 2022	April - June 2022	July - September 2022	October - December 2022
Unique patients in time period	572,400	524,770	482,950	397,320
New Cases	3,960	2,110	1,940	560
Incidence Rate per 10,000 person-days	0.81	0.46	0.47	0.21

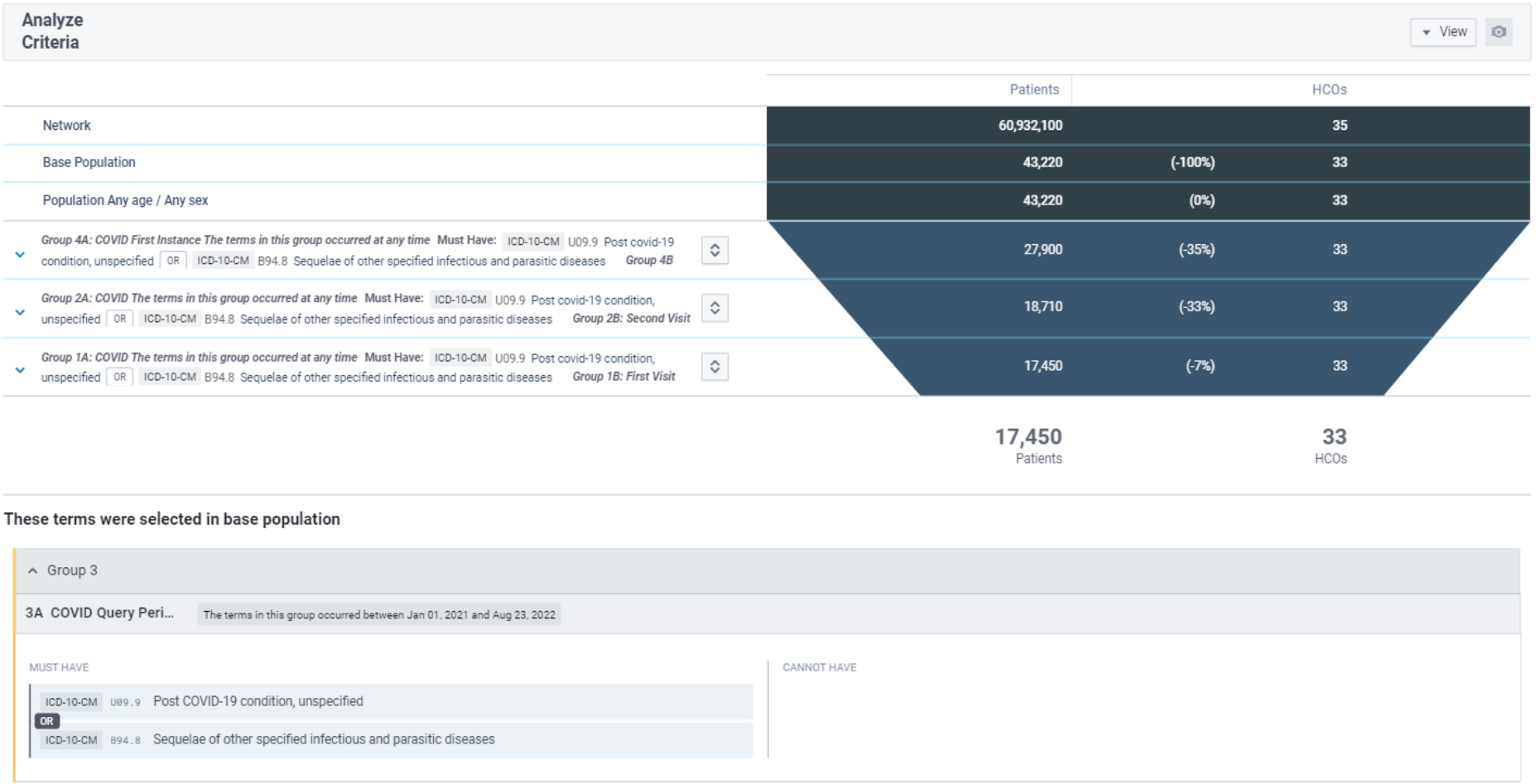
	January 1 - February 23, 2023
Unique patients in time period	197,330
New Cases	150
Incidence Rate per 10,000 person-days	0.18

Figure 1a. Cohort Attrition for Patients with Acute COVID-19 in the TriNetX USA "No Date Shifting" Network from January 1, 2021 to August 23, 2022



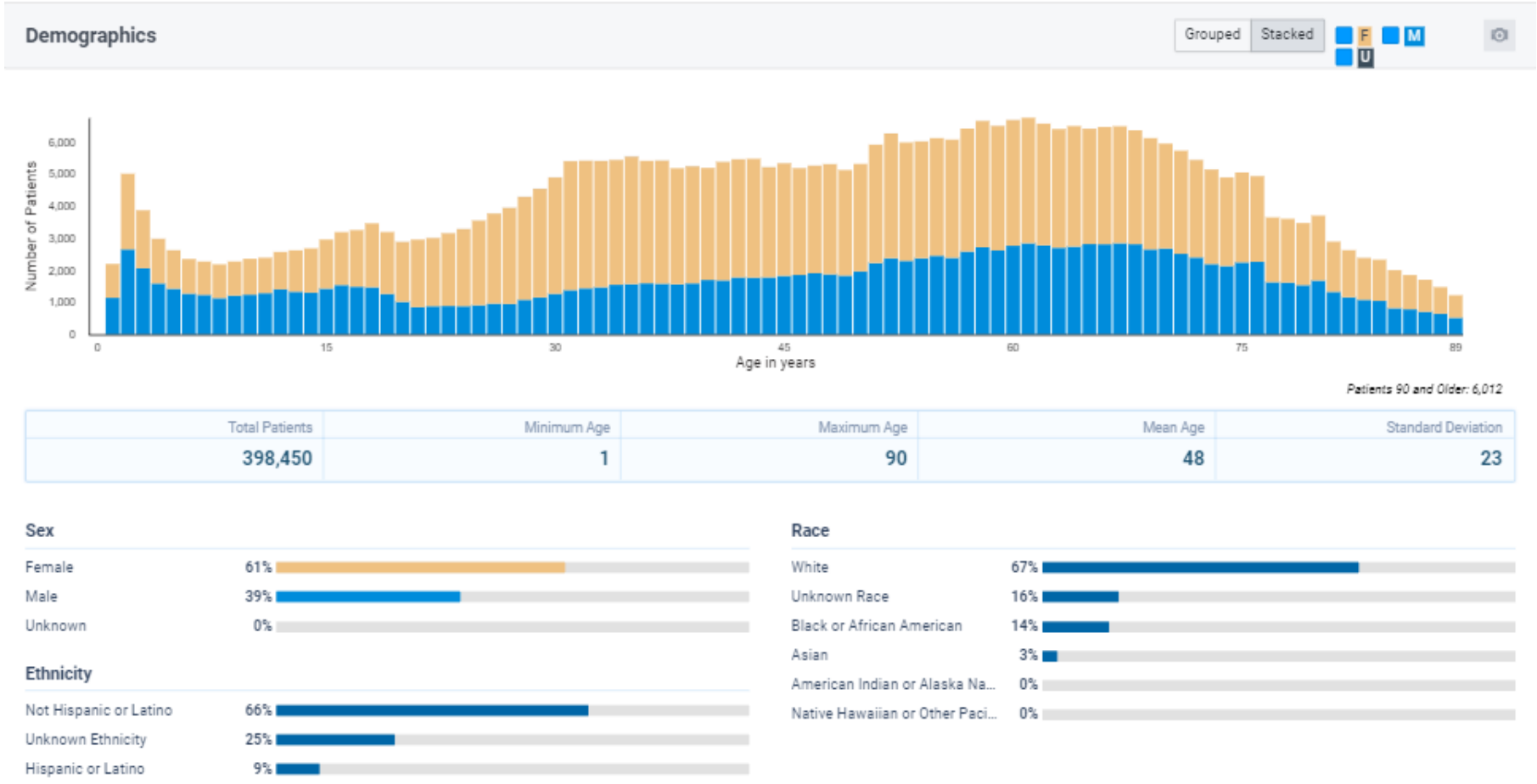
NOTE : All counts on the TriNetX Live™ platform are rounded up to the nearest 10 to protect patient privacy. Thus, all values in this table are in reality ranges (i.e. 10 represents values from 1-10, 20 represents values 11-20, etc.)

Figure 1b. Cohort Attrition for Patients with Long COVID in the TriNetX USA "No Date Shifting" Network from January 1, 2021 to August 23, 2022



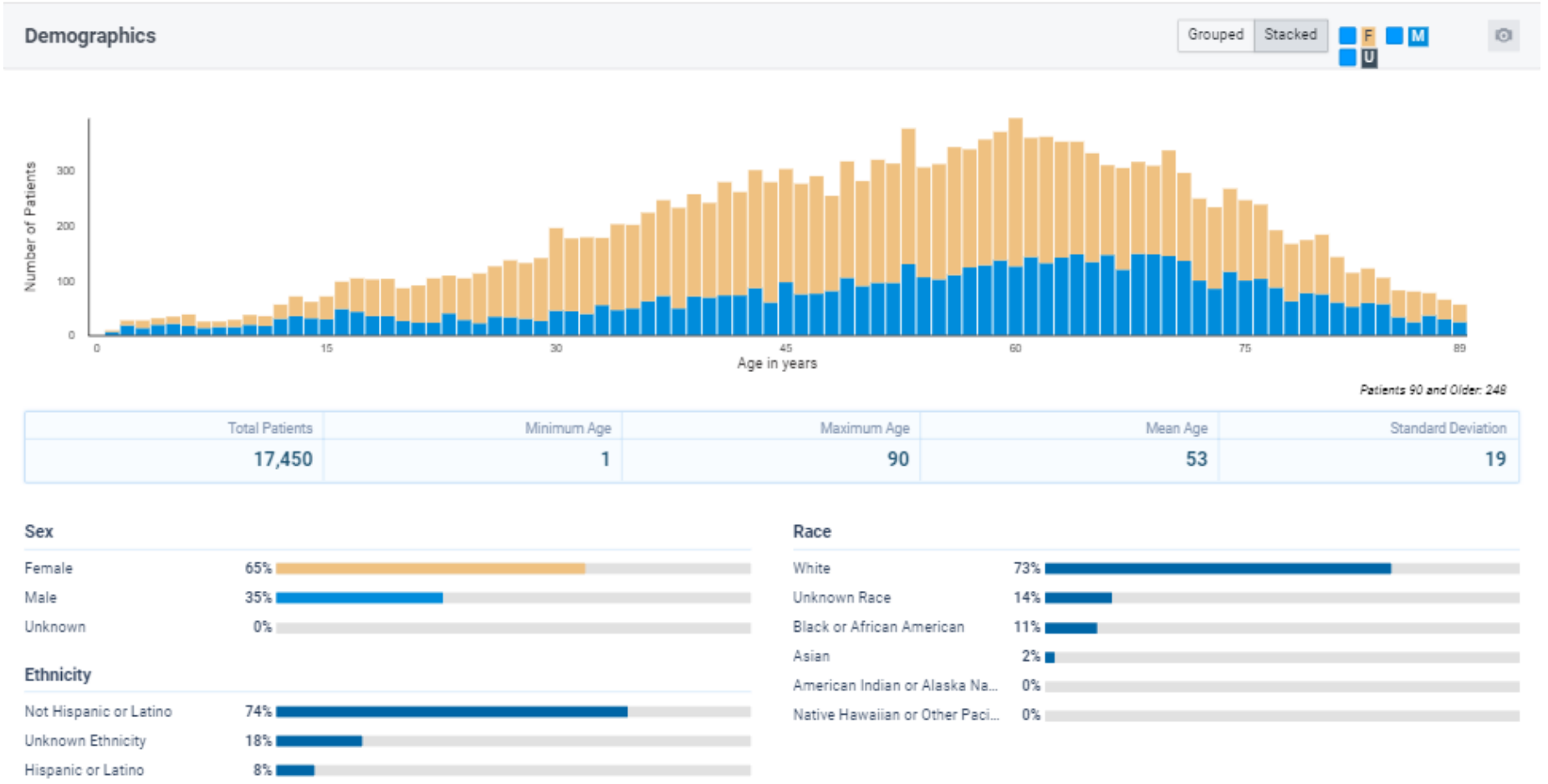
***NOTE** : All counts on the TriNetX Live™ platform are rounded up to the nearest 10 to protect patient privacy. Thus, all values in this table are in reality ranges (i.e. 10 represents values from 1-10, 20 represents values 11-20, etc.)*

Figure 2a. Demographics for Patients with Acute COVID-19 in the TriNetX USA "No Date Shifting" Network from January 1, 2021 to August 23, 2022



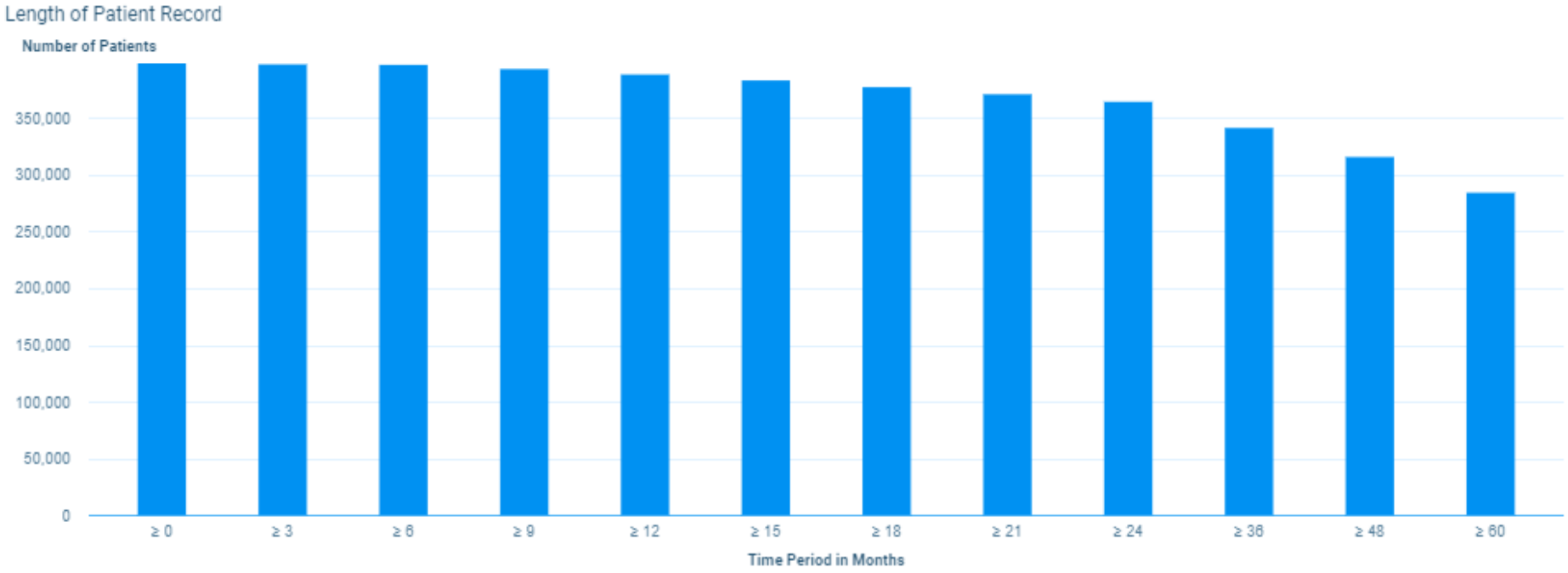
NOTE *: All counts on the TriNetX Live™ platform are rounded up to the nearest 10 to protect patient privacy. Thus, all values in this table are in reality ranges (i.e. 10 represents values from 1-10, 20 represents values 11-20, etc.)*

Figure 2b. Demographics for Patients with Long COVID in the TriNetX USA "No Date Shifting" Network from January 1, 2021 to August 23, 2022



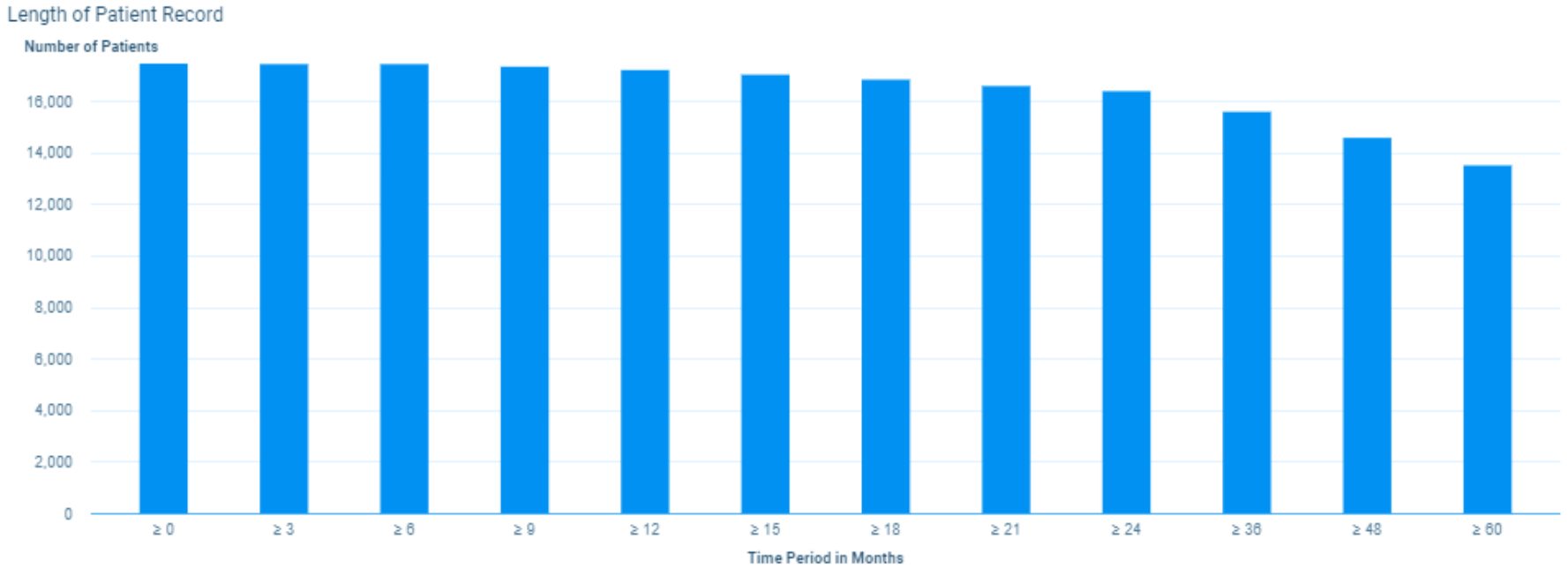
NOTE : All counts on the TriNetX Live™ platform are rounded up to the nearest 10 to protect patient privacy. Thus, all values in this table are in reality ranges (i.e. 10 represents values from 1-10, 20 represents values 11-20, etc.)

Figure 3a. Distribution of Length of Patient Record for Patients with Acute COVID-19 in the TriNetX USA "No Date Shifting" Network from January 1, 2021 to August 23, 2022



NOTE : All counts on the TriNetX Live™ platform are rounded up to the nearest 10 to protect patient privacy. Thus, all values in this table are in reality ranges (i.e. 10 represents values from 1-10, 20 represents values 11-20, etc.)

Figure 3b. Distribution of Length of Patient Record for Patients with Long COVID in the TriNetX USA "No Date Shifting" Network from January 1, 2021 to August 23, 2022



***NOTE** : All counts on the TriNetX Live™ platform are rounded up to the nearest 10 to protect patient privacy. Thus, all values in this table are in reality ranges (i.e. 10 represents values from 1-10, 20 represents values 11-20, etc.)*

Appendix A. List of International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) and TriNetX Curated Codes Used to Define Exposures and Cohort Eligibility in this Request

Code	Description	Code Category	Code Type	Filter
	Acute COVID-19			
U07.1	Covid-19	Diagnosis	ICD-10-CM	n/a
9088	Sars coronavirus 2 and related rna [presence]	Custom TriNetX Code	TNX Curated	Positive
	Long COVID			
U09.9	Post covid-19 condition, unspecified	Diagnosis	ICD-10-CM	
B94.8	Sequelae of other specified infectious and parasitic diseases	Diagnosis	ICD-10-CM	
	Healthcare Visit			
N/A	Visit	Custom TriNetX Code	TNX Curated	

Appendix B. List of Anatomical Therapeutic Chemical (ATC) Classification, International Classification of Diseases, Tenth Revision, Clinical Modfication (ICD-10-CM), RxNorm, and Vaccine Administered (CVX) Codes used to Define Baseline Characteristics in this Request

Code	Description	Code Category	Code Type
H02A	Corticosteroids for systemic use, plain	Medication	ATC
J05	Antivirals for systemic use	Medication	ATC
L01EJ	JAK Inhibitors	Medication	ATC
L04A	Immunosuppressants	Medication	ATC
L04AC	Interleukin inhibitors	Medication	ATC
213	SARS-CoV-2 (COVID-19) Vaccine	Vaccine Administered	CVX
A15-A19	Tuberculosis	Diagnosis	ICD-10-CM
B20	HIV	Diagnosis	ICD-10-CM
C00-D49	Neoplasms	Diagnosis	ICD-10-CM
C81-C96	Malignant hematologic neoplasms	Diagnosis	ICD-10-CM
D00-D09	In situ neoplasms	Diagnosis	ICD-10-CM
D10-D36	Benign neoplasms	Diagnosis	ICD-10-CM
D57	Sickle Cell Disorders	Diagnosis	ICD-10-CM
D80-D89	Disorders Involving Immune Mechanism	Diagnosis	ICD-10-CM
E08-E13	Diabetes mellitus	Diagnosis	ICD-10-CM
E66	Overweight and Obesity	Diagnosis	ICD-10-CM
F01-F09	Mental disorders due to known physiological conditions	Diagnosis	ICD-10-CM
F10-F19	Mental and behavioral disorders due to psychoactive substance use	Diagnosis	ICD-10-CM
F17	Nicotine Dependence	Diagnosis	ICD-10-CM
F20	Schizophrenia	Diagnosis	ICD-10-CM
F30-F39	Mood disorders	Diagnosis	ICD-10-CM
G30-G32	Nervous system degeneration	Diagnosis	ICD-10-CM
I00-I99	Circulatory System Diseases	Diagnosis	ICD-10-CM
I10-I16	Hypertensive diseases	Diagnosis	ICD-10-CM
I60-I69	Cerebrovascular disesae	Diagnosis	ICD-10-CM
I63	Cerebral Infarction	Diagnosis	ICD-10-CM
J40-47	Chronic lower respiratory dseases	Diagnosis	ICD-10-CM
J45	Asthma	Diagnosis	ICD-10-CM
K70-K77	Liver Disease	Diagnosis	ICD-10-CM
N18	Chronic Kidney Disease	Diagnosis	ICD-10-CM
612865	Tocilizumab (anti-IL-6 receptor monoclonal antibody)	Medication	RxNorm
1535218	Siltuximab (anti-IL-6 monoclonal antibody)	Medication	RxNorm
1923319	Sarilumab (anti-IL-6 receptor monoclonal antibody)	Medication	RxNorm
2284718	Remdesivir	Medication	RxNorm
2391541	Satralizumab (anti-IL-6 receptor monoclonal antibody)	Medication	RxNorm
2463114	Bamlanivimab or Bamlanivimab/etesevimab	Medication	RxNorm
2465242	Casirivimab or casirivimab/imdevimab	Medication	RxNorm
2550731	Sotrovimab	Medication	RxNorm
2587300	Tixagevimab or tixagevimab/cilgavimab	Medication	RxNorm
2592360	Bebtelovimab	Medication	RxNorm

Appendix C. List of Anatomical Therapeutic Chemical (ATC) Classification, Current Procedural Terminology 4th Edition (CPT-4), Healthcare Common Procedure Coding System (HCPCS), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), International Classification of Diseases, Tenth Revision, Procedural Coding System (ICD-10-PCS) Procedure Codes, RxNorm, TriNetX Curated, and Vaccine Administered (CVX) Codes Used to Define Outcomes in this Request

Code	Description	Code Category	Code Type
	Corticosteroids		
H02A	Corticosteroids for systemic use, plain	Medication	ATC
	COVID-19 Vaccination (with CPT codes)		
91300	Pfizer (includes 0001A, 0002A, 0003A, 0004A)	Procedure	CPT
91301	Moderna 100mcg/0.5 ml (includes 0011A, 0012A, 0013A)	Procedure	CPT
91302	AstraZeneca (includes 0021A, 0022A)	Procedure	CPT
91303	Janssen (includes 0031A, 0034A)	Procedure	CPT
91304	Novavax (includes 0041A, 0042A, 0044A)	Procedure	CPT
91305	Pfizer Tris-Sucrose n30 mcg (includes 0051A, 0052A, 0053A, 0054A)	Procedure	CPT
91306	Moderna 50 mcg/0.25 ml (includes 0064A)	Procedure	CPT
91307	Pfizer Tris-Sucrose 10 mcg (includes 0071A, 0072A, 0073A, 0074A)	Procedure	CPT
91308	Pfizer Tris-Sucrose 3 mcg (includes 0081A, 0082A, 0083A)	Procedure	CPT
91309	Moderna 50 mcg/0.5 ml (includes 0091A, 0092A, 0093A, 0094A)	Procedure	CPT
91311	Moderna 25 mcg/0.25 ml (includes 0111A, 0112A, 0113A)	Procedure	CPT
91312	Pfizer Bivalent 30 mcg (includes 0124A, 91313, 0134A)	Procedure	CPT
91314	Moderna Bivalent 25 mcg/0.25 ml (includes 0144A)	Procedure	CPT
91315	Pfizer Bivalent 10 mcg (includes 0154A)	Procedure	CPT
91316	Moderna Bivalent 10 mcg (includes 0164A)	Procedure	CPT
91317	Pfizer Bivalent 3 mcg (includes 0173A)	Procedure	CPT
510	Non-US Vaccine (BIBP, Sinopharm)	Vaccine Adminstered	CVX
511	IV Non-US Vaccine (Coronavac, Sinovac)	Vaccine Adminstered	CVX
213	SARS-CoV-2 (COVID-19) Vaccine	Vaccine Adminstered	CVX
M0201	Home vaccine admin (includes)	Procedure	HCPCS
2468231	SARS-CoV2- (COVID-19) Vaccine, MRNA Spike Protein	Medication	RxNorm
2479831	SARS-CoV2- (COVID-19) Vaccine, Vector non-replicating	Medication	RxNorm
2610328	SARS-CoV2- (COVID-19) Vaccine, MRNA-1273	Medication	RxNorm
2610347	SARS-CoV2- (COVID-19) Vaccine, N-BNT162b2	Medication	RxNorm
	COVID-19 Vaccination (without CPT codes)		
M0201	Home vaccine admin (includes)	Procedure	HCPCS
2468231	SARS-CoV2- (COVID-19) Vaccine, MRNA Spike Protein	Medication	RxNorm
2479831	SARS-CoV2- (COVID-19) Vaccine, Vector non-replicating	Medication	RxNorm
2610328	SARS-CoV2- (COVID-19) Vaccine, MRNA-1273	Medication	RxNorm
2610347	SARS-CoV2- (COVID-19) Vaccine, N-BNT162b2	Medication	RxNorm
213	SARS-CoV-2 (COVID-19) Vaccine	Vaccine Adminstered	CVX
	Ambulatory Visit		
N/A	Visit: Ambulatory	Custom TriNetX Code	TNX Curated
N/A	Visit: Virtual	Custom TriNetX Code	TNX Curated
N/A	Visit: Home Health	Custom TriNetX Code	TNX Curated
	Inpatient Visit		

Appendix C. List of Anatomical Therapeutic Chemical (ATC) Classification, Current Procedural Terminology 4th Edition (CPT-4), Healthcare Common Procedure Coding System (HCPCS), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), International Classification of Diseases, Tenth Revision, Procedural Coding System (ICD-10-PCS) Procedure Codes, RxNorm, TriNetX Curated, and Vaccine Administered (CVX) Codes Used to Define Outcomes in this Request

Code	Description	Code Category	Code Type
N/A	Visit: Inpatient Encounter	Custom TriNetX Code	TNX Curated
N/A	Visit: Observation Encounter	Custom TriNetX Code	TNX Curated
N/A	Visit: Short Stay	Custom TriNetX Code	TNX Curated
	Emergency Visit		
N/A	Visit: Emergency	Custom TriNetX Code	TNX Curated
	Institutional Visit		
N/A	Visit: Inpatient Non-acute	Custom TriNetX Code	TNX Curated
	COVID-related Medications		
J05	Antivirals for systemic use	Medication	ATC
L01EJ	JAK Inhibitors	Medication	ATC
L04AC	Interleukin inhibitors	Medication	ATC
612865	Tocilizumab (anti-IL-6 receptor monoclonal antibody)	Medication	RxNorm
1535218	Siltuximab (anti-IL-6 monoclonal antibody)	Medication	RxNorm
1923319	Sarilumab (anti-IL-6 receptor monoclonal antibody)	Medication	RxNorm
2284718	remdesivir	Medication	RxNorm
2391541	Satralizumab (anti-IL-6 receptor monoclonal antibody)	Medication	RxNorm
2463114	Bamlanivimab or Bamlanivimab/etesevimab	Medication	RxNorm
2465242	Casirivimab or casirivimab/imdevimab	Medication	RxNorm
2550731	Sotrovimab	Medication	RxNorm
2587300	Tixagevimab or tixagevimab/cilgavimab	Medication	RxNorm
2592360	Bebtelovimab	Medication	RxNorm
	Immunosupressants		
L04A	Immunosuppressants	Medication	ATC
	Multisystem inflammatory syndrome		
M35.81	Multisystem inflammatory syndrome	Diagnosis	ICD-10-CM
	Long COVID		
B94.8	Sequelae of other specified infectious and parasitic diseases	Diagnosis	ICD-10-CM
U09.9	Post covid-19 condition, unspecified	Diagnosis	ICD-10-CM
	Severe COVID-19: ECMO		
33946	Extracorporeal membrane oxygenation (ECMO)/extracorporeal life support (ECLS) provided by physician; initiation, veno-venous	Procedure	CPT
33947	Extracorporeal membrane oxygenation (ECMO)/extracorporeal life support (ECLS) provided by physician; initiation, veno-arterial	Procedure	CPT
33948	Extracorporeal membrane oxygenation (ECMO)/extracorporeal life support (ECLS) provided by physician; daily management, each day, veno-venous	Procedure	CPT
33949	Extracorporeal membrane oxygenation (ECMO)/extracorporeal life support (ECLS) provided by physician; daily management, each day, veno-arterial	Procedure	CPT

Appendix C. List of Anatomical Therapeutic Chemical (ATC) Classification, Current Procedural Terminology 4th Edition (CPT-4), Healthcare Common Procedure Coding System (HCPCS), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), International Classification of Diseases, Tenth Revision, Procedural Coding System (ICD-10-PCS) Procedure Codes, RxNorm, TriNetX Curated, and Vaccine Administered (CVX) Codes Used to Define Outcomes in this Request

Code	Description	Code Category	Code Type
33951	Extracorporeal membrane oxygenation (ECMO)/extracorporeal life support (ECLS) provided by physician; insertion of peripheral (arterial and/or venous) cannula(e), percutaneous, birth through 5 years of age (includes fluoroscopic guidance, when performed)	Procedure	CPT
33952	Extracorporeal membrane oxygenation (ECMO)/extracorporeal life support (ECLS) provided by physician; insertion of peripheral (arterial and/or venous) cannula(e), percutaneous, 6 years and older (includes fluoroscopic guidance, when performed)	Procedure	CPT
33953	Extracorporeal membrane oxygenation (ECMO)/extracorporeal life support (ECLS) provided by physician; insertion of peripheral (arterial and/or venous) cannula(e), open, birth through 5 years of age	Procedure	CPT
33954	Extracorporeal membrane oxygenation (ECMO)/extracorporeal life support (ECLS) provided by physician; insertion of peripheral (arterial and/or venous) cannula(e), open, 6 years and older	Procedure	CPT
33955	Extracorporeal membrane oxygenation (ECMO)/extracorporeal life support (ECLS) provided by physician; insertion of central cannula(e) by sternotomy or thoracotomy, birth through 5 years of age	Procedure	CPT
33956	Extracorporeal membrane oxygenation (ECMO)/extracorporeal life support (ECLS) provided by physician; insertion of central cannula(e) by sternotomy or thoracotomy, 6 years and older	Procedure	CPT
33957	Extracorporeal membrane oxygenation (ECMO)/extracorporeal life support (ECLS) provided by physician; reposition peripheral (arterial and/or venous) cannula(e), percutaneous, birth through 5 years of age (includes fluoroscopic guidance, when performed)	Procedure	CPT
33958	Extracorporeal membrane oxygenation (ECMO)/extracorporeal life support (ECLS) provided by physician; reposition peripheral (arterial and/or venous) cannula(e), percutaneous, 6 years and older (includes fluoroscopic guidance, when performed)	Procedure	CPT
33959	Extracorporeal membrane oxygenation (ECMO)/extracorporeal life support (ECLS) provided by physician; reposition peripheral (arterial and/or venous) cannula(e), open, birth through 5 years of age (includes fluoroscopic guidance, when performed)	Procedure	CPT
33962	Extracorporeal membrane oxygenation (ECMO)/extracorporeal life support (ECLS) provided by physician; reposition peripheral (arterial and/or venous) cannula(e), open, 6 years and older (includes fluoroscopic guidance, when performed)	Procedure	CPT

Appendix C. List of Anatomical Therapeutic Chemical (ATC) Classification, Current Procedural Terminology 4th Edition (CPT-4), Healthcare Common Procedure Coding System (HCPCS), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), International Classification of Diseases, Tenth Revision, Procedural Coding System (ICD-10-PCS) Procedure Codes, RxNorm, TriNetX Curated, and Vaccine Administered (CVX) Codes Used to Define Outcomes in this Request

Code	Description	Code Category	Code Type
33963	Extracorporeal membrane oxygenation (ECMO)/extracorporeal life support (ECLS) provided by physician; reposition of central cannula(e) by sternotomy or thoracotomy, birth through 5 years of age (includes fluoroscopic guidance, when performed)	Procedure	CPT
33964	Extracorporeal membrane oxygenation (ECMO)/extracorporeal life support (ECLS) provided by physician; reposition central cannula(e) by sternotomy or thoracotomy, 6 years and older (includes fluoroscopic guidance, when performed)	Procedure	CPT
33965	Extracorporeal membrane oxygenation (ECMO)/extracorporeal life support (ECLS) provided by physician; removal of peripheral (arterial and/or venous) cannula(e), percutaneous, birth through 5 years of age	Procedure	CPT
33966	Extracorporeal membrane oxygenation (ECMO)/extracorporeal life support (ECLS) provided by physician; removal of peripheral (arterial and/or venous) cannula(e), percutaneous, 6 years and older	Procedure	CPT
33969	Extracorporeal membrane oxygenation (ECMO)/extracorporeal life support (ECLS) provided by physician; removal of peripheral (arterial and/or venous) cannula(e), open, birth through 5 years of age	Procedure	CPT
33984	Extracorporeal membrane oxygenation (ECMO)/extracorporeal life support (ECLS) provided by physician; removal of peripheral (arterial and/or venous) cannula(e), open, 6 years and older	Procedure	CPT
33985	Extracorporeal membrane oxygenation (ECMO)/extracorporeal life support (ECLS) provided by physician; removal of central cannula(e) by sternotomy or thoracotomy, birth through 5 years of age	Procedure	CPT
33986	Extracorporeal membrane oxygenation (ECMO)/extracorporeal life support (ECLS) provided by physician; removal of central cannula(e) by sternotomy or thoracotomy, 6 years and older	Procedure	CPT
33987	Arterial exposure with creation of graft conduit (eg, chimney graft) to facilitate arterial perfusion for ECMO/ECLS (List separately in addition to code for primary procedure)	Procedure	CPT
33988	Insertion of left heart vent by thoracic incision (eg, sternotomy, thoracotomy) for ECMO/ECLS	Procedure	CPT
33989	Removal of left heart vent by thoracic incision (eg, sternotomy, thoracotomy) for ECMO/ECLS	Procedure	CPT
5A15223	Extracorporeal Membrane Oxygenation, Continuous	Procedure	ICD-10-PCS
5A1522F	Extracorporeal Oxygenation, Membrane, Central	Procedure	ICD-10-PCS
5A1522G	Extracorporeal Oxygenation, Membrane, Peripheral Veno-arterial	Procedure	ICD-10-PCS

Appendix C. List of Anatomical Therapeutic Chemical (ATC) Classification, Current Procedural Terminology 4th Edition (CPT-4), Healthcare Common Procedure Coding System (HCPCS), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), International Classification of Diseases, Tenth Revision, Procedural Coding System (ICD-10-PCS) Procedure Codes, RxNorm, TriNetX Curated, and Vaccine Administered (CVX) Codes Used to Define Outcomes in this Request

Code	Description	Code Category	Code Type
5A1522H	Extracorporeal Oxygenation, Membrane, Peripheral Veno-venous	Procedure	ICD-10-PCS
5A15A2F	Extracorporeal Oxygenation, Membrane, Central, Intraoperative	Procedure	ICD-10-PCS
5A15A2G	Extracorporeal Oxygenation, Membrane, Peripheral Veno-arterial, Intraoperative	Procedure	ICD-10-PCS
5A15A2H	Extracorporeal Oxygenation, Membrane, Peripheral Veno-venous, Intraoperative	Procedure	ICD-10-PCS
	Severe COVID-19: ICU		
99291	Critical care, evaluation and management of the critically ill or critically injured patient; first 30-74 minutes	Procedure	CPT
99292	Critical care, evaluation and management of the critically ill or critically injured patient; each additional 30 minutes (List separately in addition to code for primary service)	Procedure	CPT
99466	Critical care face-to-face services, during an interfacility transport of critically ill or critically injured pediatric patient, 24 months of age or younger; first 30-74 minutes of hands-on care during transport	Procedure	CPT
99467	Critical care face-to-face services, during an interfacility transport of critically ill or critically injured pediatric patient, 24 months of age or younger; each additional 30 minutes (List separately in addition to code for primary service)	Procedure	CPT
99468	Initial inpatient neonatal critical care, per day, for the evaluation and management of a critically ill neonate, 28 days of age or younger	Procedure	CPT
99469	Subsequent inpatient neonatal critical care, per day, for the evaluation and management of a critically ill neonate, 28 days of age or younger	Procedure	CPT
99471	Initial inpatient pediatric critical care, per day, for the evaluation and management of a critically ill infant or young child, 29 days through 24 months of age	Procedure	CPT
99472	Subsequent inpatient pediatric critical care, per day, for the evaluation and management of a critically ill infant or young child, 29 days through 24 months of age	Procedure	CPT
99475	Initial inpatient pediatric critical care, per day, for the evaluation and management of a critically ill infant or young child, 2 through 5 years of age	Procedure	CPT
99476	Subsequent inpatient pediatric critical care, per day, for the evaluation and management of a critically ill infant or young child, 2 through 5 years of age	Procedure	CPT
99477	Initial hospital care, per day, for the evaluation and management of the neonate, 28 days of age or younger, who requires intensive observation, frequent interventions, and other intensive care services	Procedure	CPT
99478	Subsequent intensive care, per day, for the evaluation and management of the recovering very low birth weight infant (present body weight less than 1500 grams)	Procedure	CPT

Appendix C. List of Anatomical Therapeutic Chemical (ATC) Classification, Current Procedural Terminology 4th Edition (CPT-4), Healthcare Common Procedure Coding System (HCPCS), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), International Classification of Diseases, Tenth Revision, Procedural Coding System (ICD-10-PCS) Procedure Codes, RxNorm, TriNetX Curated, and Vaccine Administered (CVX) Codes Used to Define Outcomes in this Request

Code	Description	Code Category	Code Type
99479	Subsequent intensive care, per day, for the evaluation and management of the recovering low birth weight infant (present body weight of 1500-2500 grams)	Procedure	CPT
99480	Subsequent intensive care, per day, for the evaluation and management of the recovering infant (present body weight of 2501-5000 grams)	Procedure	CPT
99485	Supervision by a control physician of interfacility transport care of the critically ill or critically injured pediatric patient, 24 months of age or younger, includes two-way communication with transport team before transport, at the referring facility and during the transport, including data interpretation and report; first 30 minutes	Procedure	CPT
99486	Supervision by a control physician of interfacility transport care of the critically ill or critically injured pediatric patient, 24 months of age or younger, includes two-way communication with transport team before transport, at the referring facility and during the transport, including data interpretation and report; each additional 30 minutes (List separately in addition to code for primary procedure)	Procedure	CPT
0188T	Remote real-time interactive video-conferenced critical care, evaluation and management of the critically ill or critically injured patient; first 30-74 minutes	Procedure	CPT
0189T	Remote real-time interactive video-conferenced critical care, evaluation and management of the critically ill or critically injured patient; each additional 30 minutes (List separately in addition to code for primary service)	Procedure	CPT
G0390	Trauma response team associated with hospital critical care service	Procedure	HCPCS
G0508	Telehealth consultation, critical care, initial, physicians typically spend 60 minutes communicating with the patient and providers via telehealth	Procedure	HCPCS
G0509	Telehealth consultation, critical care, subsequent, physicians typically spend 50 minutes communicating with the patient and providers via telehealth	Procedure	HCPCS
	Severe COVID-19: Mechanical Ventilation		
31500	Intubation, endotracheal, emergency procedure	Procedure	CPT
94002	Ventilation assist and management, initiation of pressure or volume preset ventilators for assisted or controlled breathing; hospital inpatient/observation, initial day	Procedure	CPT
94003	Ventilation assist and management, initiation of pressure or volume preset ventilators for assisted or controlled breathing; hospital inpatient/observation, each subsequent day	Procedure	CPT
94004	Ventilation assist and management, initiation of pressure or volume preset ventilators for assisted or controlled breathing; nursing facility, per day	Procedure	CPT

Appendix C. List of Anatomical Therapeutic Chemical (ATC) Classification, Current Procedural Terminology 4th Edition (CPT-4), Healthcare Common Procedure Coding System (HCPCS), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), International Classification of Diseases, Tenth Revision, Procedural Coding System (ICD-10-PCS) Procedure Codes, RxNorm, TriNetX Curated, and Vaccine Administered (CVX) Codes Used to Define Outcomes in this Request

Code	Description	Code Category	Code Type
94662	Continuous negative pressure ventilation (CNP), initiation and management	Procedure	CPT
A0396	ALS specialized service disposable supplies; esophageal intubation	Procedure	HCPCS
A4483	Moisture exchanger, disposable, for use with invasive mechanical ventilation	Procedure	HCPCS
E0481	Intrapulmonary percussive ventilation system and related accessories	Procedure	HCPCS
09HN7BZ	Insertion of Airway into Nasopharynx, Via Natural or Artificial Opening	Procedure	ICD-10-PCS
09HN8BZ	Insertion of Airway into Nasopharynx, Via Natural or Artificial Opening Endoscopic	Procedure	ICD-10-PCS
0BH13EZ	Insertion of Endotracheal Airway into Trachea, Percutaneous Approach	Procedure	ICD-10-PCS
0BH17EZ	Insertion of Endotracheal Airway into Trachea, Via Natural or Artificial Opening	Procedure	ICD-10-PCS
0BH18EZ	Insertion of Endotracheal Airway into Trachea, Via Natural or Artificial Opening Endoscopic	Procedure	ICD-10-PCS
0CHY7BZ	Insertion of Airway into Mouth and Throat, Via Natural or Artificial Opening	Procedure	ICD-10-PCS
0CHY8BZ	Insertion of Airway into Mouth and Throat, Via Natural or Artificial Opening Endoscopic	Procedure	ICD-10-PCS
0DH57BZ	Insertion of Airway into Esophagus, Via Natural or Artificial Opening	Procedure	ICD-10-PCS
0DH58BZ	Insertion of Airway into Esophagus, Via Natural or Artificial Opening Endoscopic	Procedure	ICD-10-PCS
0WHQ73Z	Insertion of Infusion Device into Respiratory Tract, Via Natural or Artificial Opening	Procedure	ICD-10-PCS
0WHQ7YZ	Insertion of Other Device into Respiratory Tract, Via Natural or Artificial Opening	Procedure	ICD-10-PCS
5A09357	Assistance with Respiratory Ventilation, Less than 24 Consecutive Hours, Continuous Positive Airway Pressure	Procedure	ICD-10-PCS
5A09457	Assistance with Respiratory Ventilation, 24-96 Consecutive Hours, Continuous Positive Airway Pressure	Procedure	ICD-10-PCS
5A09557	Assistance with Respiratory Ventilation, Greater than 96 Consecutive Hours, Continuous Positive Airway Pressure	Procedure	ICD-10-PCS
5A1935Z	Respiratory Ventilation, Less than 24 Consecutive Hours	Procedure	ICD-10-PCS
5A1945Z	Respiratory Ventilation, 24-96 Consecutive Hours	Procedure	ICD-10-PCS
5A1955Z	Respiratory Ventilation, Greater than 96 Consecutive Hours	Procedure	ICD-10-PCS
	Clinical Signs and Symptoms		
R06	Abnormalities Breathing	Diagnosis	ICD-10-CM Hierarchy
R05	Cough	Diagnosis	ICD-10-CM Hierarchy
R53	Malaise and Fatigue	Diagnosis	ICD-10-CM Hierarchy

Appendix C. List of Anatomical Therapeutic Chemical (ATC) Classification, Current Procedural Terminology 4th Edition (CPT-4), Healthcare Common Procedure Coding System (HCPCS), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), International Classification of Diseases, Tenth Revision, Procedural Coding System (ICD-10-PCS) Procedure Codes, RxNorm, TriNetX Curated, and Vaccine Administered (CVX) Codes Used to Define Outcomes in this Request

Code	Description	Code Category	Code Type
R07	Pain in Throat and Chest	Diagnosis	ICD-10-CM Hierarchy
R09	Other symptoms and signs involving circulatory and respiratory system	Diagnosis	ICD-10-CM Hierarchy
R00	Abnormalities of heart beat	Diagnosis	ICD-10-CM Hierarchy
R41	Other symptoms and signs involving cognitive functions and awareness	Diagnosis	ICD-10-CM Hierarchy
R51	Headache	Diagnosis	ICD-10-CM Hierarchy
R43	Disturbances in smell and taste	Diagnosis	ICD-10-CM Hierarchy
R91	Abnormal findings on diagnostic imaging of lung	Diagnosis	ICD-10-CM Hierarchy
	Related Conditions		
I10	Essential (primary) hypertension	Diagnosis	ICD-10-CM Hierarchy
E78	Disorders of lipoprotein metabolism and other lipdemias	Diagnosis	ICD-10-CM Hierarchy
F41	Other anxiety disorders	Diagnosis	ICD-10-CM Hierarchy
B97	Viral agents as the cause of diseases classified elsewhere	Diagnosis	ICD-10-CM Hierarchy
U07	Emergency use of U07	Diagnosis	ICD-10-CM Hierarchy
G47	Sleep disorders	Diagnosis	ICD-10-CM Hierarchy
K21	Gastro-esophageal reflux disease	Diagnosis	ICD-10-CM Hierarchy
E66	Overweight and obesity	Diagnosis	ICD-10-CM Hierarchy
E11	Type 2 diabetes	Diagnosis	ICD-10-CM Hierarchy
M25	Other joint disorder, no elsewhere classified	Diagnosis	ICD-10-CM Hierarchy
	Related Treatments		
S01	Opthalmologicals	Medication	ATC
R03	Drugs for obstructive airway diseases	Medication	ATC
D07	Corticosteroids, dermatological	Medication	ATC
R01	Nasal preparations	Medication	ATC
H02A	Corticosteroids for systemic use	Medication	ATC
N02	Analgesics	Medication	ATC
J01	Antibacterials for systemic use	Medication	ATC
C05	Vasoprotectives	Medication	ATC
A01	Stomatological preparations	Medication	ATC
B05	Blood substitutes and perfusion solutions	Medication	ATC

Appendix D. Specifications Defining Query Builder Modules in this Request

Query (Cohort) 1: Acute COVID-19

Group 1: Visitin within 6 months prior to first COVID

Group 1A COVID		
must have	any of	SARS coronavirus 2 and related RNA [Presence] (labResult: Positive)
		COVID-19
date constraint		The terms in this group occurred at any time
event relationship		Any instance of First Visit occurred within 1 day and 183 days before the first instance of COVID
Group 1B First Visit		
must have		Visit

AND

Group 2: Visit within 6-12 months prior to first COVID

Group 2A COVID		
must have	any of	SARS coronavirus 2 and related RNA [Presence] (labResult: Positive)
		COVID-19
date constraint		The terms in this group occurred at any time
event relationship		Any instance of Second Visit occurred within 365 days and 184 days before the first instance of COVID
Group 2B Second Visit		
must have		Visit

AND

Group 3: COVID 1/1/21 - 8/23/22

COVID Query Period		
must have	any of	SARS coronavirus 2 and related RNA [Presence] (labResult: Positive)
		COVID-19
date constraint		The terms in this group occurred between Jan 1, 2021 and Aug 23, 2022

AND

Group 4: No COVID before first COVID

Group 4A COVID First Instance		
must have	any of	SARS coronavirus 2 and related RNA [Presence] (labResult: Positive)
		COVID-19
date constraint		The terms in this group occurred at any time
event relationship		Any instance of Group 4B occurred at least 1 day before the first instance of COVID First Instance
Group 4B		
cannot have		SARS coronavirus 2 and related RNA [Presence] (labResult: Positive)
	or	COVID-19

Appendix D. Specifications Defining Query Builder Modules in this Request

Query (Cohort) 2: Long COVID		
Group 1: Visitin within 6 months prior to first Long COVID		
Group 1A Long COVID		
must have	any of	Post covid-19 condition, unspecified Sequelae of other specified infectious and parasitic diseases
date constraint		The terms in this group occurred at any time
event relationship		Any instance of First Visit occurred within 1 day and 183 days before the first instance of COVID
Group 1B First Visit		
must have		Visit
AND		
Group 2: Visit within 6-12 months prior to first Long COVID		
Group 2A Long COVID		
must have	any of	Post covid-19 condition, unspecified Sequelae of other specified infectious and parasitic diseases
date constraint		The terms in this group occurred at any time
event relationship		Any instance of Second Visit occurred within 365 days and 184 days before the first instance of PASC
Group 2B Second Visit		
must have		Visit
AND		
Group 3: PASC 1/1/21 - 8/23/22		
PASC Query Period		
must have	any of	Post covid-19 condition, unspecified Sequelae of other specified infectious and parasitic diseases
date constraint		The terms in this group occurred between Jan 1, 2021 and Aug 23, 2022
AND		
Group 4: No Long COVID before first Long COVID		
Group 4A Long COVID First Instance		
must have	any of	Post covid-19 condition, unspecified Sequelae of other specified infectious and parasitic diseases
date constraint		The terms in this group occurred at any time
event relationship		Any instance of Group 4B occurred at least 1 day before the first instance of PASC First Instance
Group 4B		
cannot have		Post covid-19 condition, unspecified
	or	Sequelae of other specified infectious and parasitic diseases

Appendix D. Specifications Defining Query Builder Modules in this Request

Query (Cohort) 3: Severe Acute COVID-19		
Group 1: Visitin within 6 months prior to first COVID		
Group 1A COVID		
must have	any of	SARS coronavirus 2 and related RNA [Presence] (labResult: Positive)
		COVID-19
date constraint		The terms in this group occurred at any time
event relationship		Any instance of First Visit occurred within 6 months before or up to 1 day after the first instance of COVID
Group 1B First Visit		
must have		Visit
AND		
Group 2: Visit within 6-12 months prior to first COVID		
Group 2A COVID		
must have	any of	SARS coronavirus 2 and related RNA [Presence] (labResult: Positive)
		COVID-19
date constraint		The terms in this group occurred at any time
event relationship		Any instance of Second Visit occurred within 365 days and 184 days before the first instance of COVID
Group 2B Second Visit		
must have		Visit
AND		
Group 3: COVID 1/1/21 - 8/23/22		
Group 3A COVID		
must have	any of	SARS coronavirus 2 and related RNA [Presence] (labResult: Positive)
		COVID-19
date constraint		The terms in this group occurred between Jan 1, 2021 and Aug 23, 2022
event relationship		Any instance of Severe markers occurred within 30 days on or after the first instance of COVID
Group 3B Severe markers		
must have	any of	ICU
		ECMO
		Mechanical ventilation
AND		
Group 4: No COVID before first COVID		
Group 4A COVID First Instance		
must have	any of	SARS coronavirus 2 and related RNA [Presence] (labResult: Positive)
		COVID-19

Appendix E. Specifications Defining Analytic Modules in this Request

#	Module	Analysis Type	Cohort(s)	Window	Index Event(s)	Characteristics or Outcomes
1	Compare Outcomes	Baseline Comparison Statistics	1 vs 2	[-365, -1]	All	Comorbidities, Demographics (age at index, female/male, hispanic/latino, and race) output in Figure
2	Compare Outcomes	Baseline Comparison Statistics	1 vs 2	[-30, -1]	All	• Immunosuppresants • COVID-related medications
2	Compare Outcomes	Baseline Comparison Statistics	1 vs 2	[-90, -1]	All	• Immunosuppresants • COVID-related medications
3	Compare Outcomes	Baseline Comparison Statistics	1 vs 2	[-∞, -1]	All	• COVID-19 Vaccination (no CPT codes)
4	Compare Outcomes	Risk	1	[28,180]	All	• Long COVID • Multisystem Inflammatory Syndrome
5	Compare Outcomes	Risk	1	[90,180]	All	• Long COVID • Multisystem Inflammatory Syndrome
6	Compare Outcomes	Risk	2	[0,180]	All	• # of Visits: Ambulatory, ED, IP, IS • COVID-19 Vaccination (w/ and w/o CPT codes) • Related Conditions (10 most common 3 digit ICD-10 terms EXCEPT those in R* and Z*) • Related Treatments (10 most common 3 digit ATC codes)
7	Incidence and Prevelance	Incidence	1	Quarters from 1/1/21 - 2/23/23	All	Long COVID (defined as in Cohort 2 Index Criteria)
8	Analyze Outcomes	Risk	1	[0,30]	All	• Severe COVID • Post-Baseline COVID Treatment
9	Analyze Outcomes	Risk	2	[0,0]	All	Signs and Symptoms of ongoing conditions (10 most common 3 digit ICD-10-CM diagnoses in R* range)
10	Analzye Outcome	Characteristics	3	[0, 0]	All	Demographics (for obtaining the cohort count in Analytics, in case it's different than in Query Builder)

Appendix F. Specifications Defining Analyze Criteria Module in this Request

#	Module	Cohort	Baseline Criteria	Terms for Analysis	Results Screen "View" Selections
1	Analyze Criteria	1	Group 3: COVID Query Period	• Group 1: Any instance of First Visit occurred [-183, -1] before first instance of COVID • Group 2: Any instance of Second Visit occurred [-365, -184] days before first instance of COVID • Group 4: Any instance of No COVID occurred at least one day before first instance of COVID	• Turn "on" the "Exclude HCOs with 0 patients" toggle • Sort criteria by least to most impact
2	Analyze Criteria	2	Group 3: COVID Query Period	• Group 1: Any instance of First Visit occurred [-183, -1] before first instance of COVID • Group 2: Any instance of Second Visit occurred [-365, -184] days before first instance of COVID • Group 4: Any instance of No COVID occurred at least one day before first instance of COVID	• Turn "on" the "Exclude HCOs with 0 patients" toggle • Sort criteria by least to most impact