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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Request ID: cder_ipq_wp023

Request Description: This query aims to explore the capabilities of the FDA's Sentinel Electronic Health Record (EHR) data from TriNetX, and in particular data derived from natural language processing (NLP), to describe utilization of cannabis and cannabis-derived products, including cannabidiol, Epidiolex, and tetrahydrocannabinol (THC).

Data Source: We ran this query on April 13, 2022. This query contains data from 71 health care organizations (HCOs), provided through the TriNetX Live™ platform in their USA Network from January 1, 2018 to February 28, 2022.

TriNetX aggregates electronic health record (EHR) systems data from its partner HCOs to create queryable datasets. TriNetX datasets are primarily comprised of clinical patient data such as demographics, diagnoses, procedures, labs, and medications. Please see Appendix A for details on the demographic and geographic distribution of patients with any encounter in the USA Network in the prior five years. For more information on the TriNetX Live™ platform and the TriNetX data visit their website here: (https://trinetx.com/).

Study Design: We identified counts of individuals with evidence of cannabis and cannabis-derived product use. This was done using the Query Builder module in the TriNetX Live™ platform. We additionally characterized the demographic and geographic distributions of our cohorts using the Explore Cohort module. We further utilized the Analyze Outcomes analytics module to determine the top ten most frequent International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) diagnosis header codes in the year before and year after the index exposure.

Exposures of Interest: Our exposures of interest for each cohort were as follows:
1) Any cannabis or cannabis-derived product
2) Cannabis or cannabis-derived products, derived from NLP
3) Any cannabidiol
4) Cannabidiol, derived from NLP
5) Known Epidiolex (cannabidiol filtered for brand name Epidiolex)
6) Lab result for positive presence of THC
7) Any cannabis or cannabis-derived product or lab result for positive presence of THC
8) Cannabidiol
9) Cannabidiol AND a lab result for positive presence of THC within +/- two days

We defined exposures using RxNorm medication terms and Logical Observation Identifiers, Names and Codes (LOINC) laboratory codes. Please see Appendix B for the full list of codes used to define exposures in this request.

Outcomes of Interest: We utilized the Explore Outcomes section of the Analyze Outcomes module to identify the ten most frequently occurring ICD-10-CM diagnosis header codes for each cohort in the year following and including the index exposure date. If only convenience samples were available in the Explore Outcomes section, we performed an additional analysis in the Outcomes section of the Analyze Outcomes module; we used the "risk-measure" functionality to obtain patient counts for the identified top ten ICD-10-CM codes among the complete cohort. Please see the Limitations section for more information about convenience sampling in the TriNetX platform.

Cohort Eligibility Criteria: Patients of all ages and sexes were included in the cohorts.

Exclusion Criteria: For cohorts 7-9, we excluded patients with evidence of FDA-approved cannabidiol (Epidiolex) during the query period, using a "cannot have" term for cannabidiol filtered by brand name for Epidiolex.

Baseline Characteristics: We utilized the Characteristics section of the Analyze Outcomes module to identify the ten most frequently occurring ICD-10-CM diagnosis header codes for each cohort in the year prior to the index exposure date. Please note that in some cases the baseline characteristics counts are reported only for a convenience sample of the total cohort due to limitations in the platform. The size of the convenience sample is noted in the tables, when applicable. Please see the limitations section for additional information on convenience samples in the TriNetX platform.

Please see Appendices C-E for additional information on the cannabis and cannabis-derived terms available in the TriNetX network, and for specifications defining parameters used in this request.

Limitations: Algorithms used to define cannabis-derived products and mapping of source data to the data model are imperfect and susceptible to misclassification. 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 may or 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, only 15 out of the 71 contributing HCOs provide data through NLP, and not all HCOs provide brand name information for RxNorm terms. Therefore, data should be interpreted with these limitations in mind.

A subset of HCOs contributing data across the TriNetX Networks date shift between 1 and 365 days in either direction at the level of the patient record. All records for a patient are shifted the same number of days. Data should be interpreted with these limitations in mind, especially when they are relevant to a specific calendar period, like an approval date.

Convenience sampling may occur in the Characteristics and Explore Outcomes Analytic Modules on the TriNetX platform when there are large cohorts. For large cohorts, there can be a long tabulation time to compile the data presented in the platform. To improve performance times, results are limited to approximately 10,000 patients per HCO. This sample is arbitrary; it is not a true random sample.

All counts provided through the TriNetX Live™ platform are rounded up to the nearest 10 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.

Notes: We ran this query on April 13, 2022. 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).

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.

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. Most Frequent Diagnosis Codes Among Patients with Cannabis-derived Product Exposures from July 1, 2018 through February 28, 2022

	All Cannabis-derived Product Users	
	Number	Percent
Total Number of Patients	40,420	100%
Most Frequent Diagnosis ICD-10 Header Codes [-365, -1]*		
R06: Abnormalities of breathing	11,650	30%
Z87: Personal history of other diseases and conditions	11,390	30%
R53: Malaise and fatigue	10,780	28%
M25: Other joint disorder, not elsewhere classified	10,710	28%
M79: Other and unspecified soft tissue disorders, not elsewhere classified	10,630	28%
R10: Abdominal and pelvic pain	10,610	28%
R11: Nausea and vomiting	10,490	27%
R52: Pain, unspecified	10,470	27%
M54: Dorsalgia	10,450	27%
Z79: Long term (current) drug therapy	10,340	27%
Most Frequent Diagnosis ICD-10 Header Codes [0, 365]		
Z87: Personal history of other diseases and conditions	15,570	39%
R06: Abnormalities of breathing	15,450	38%
R53: Malaise and fatigue	14,560	36%
R52: Pain, unspecified	14,370	36%
M79: Other and unspecified soft tissue disorders, not elsewhere classified	14,140	35%
R68: Other general signs and symptoms	14,110	35%
M25: Other joint disorder, not elsewhere classified	14,100	35%
R11: Nausea and vomiting	13,900	34%
R10: Abdominal and pelvic pain	13,510	33%
M54: Dorsalgia	13,430	33%

*Pre-index diagnoses assessed among a convenience sample of 38,350 patients

NOTE: All counts provided through the TriNetX Live™ platform are rounded up to the nearest 10 to protect patient privacy. Thus, all estimates should be interpreted as ranges, with the lower value of the range ≤ 0.09% less than the presented value unless otherwise noted.

Table 2. Most Frequent Diagnosis Codes Among Patients with Cannabis-derived Product Exposures, Derived from Natural Language Processing (NLP) from July 1, 2018 through February 28, 2022

	All Cannabis-derived Product Users, NLP	
	Number	Percent
Total Number of Patients	27,830	100%
Most Frequent Diagnosis ICD-10 Header Codes [-365, -1]*		
Z87: Personal history of other diseases and conditions	10,420	40%
R06: Abnormalities of breathing	10,370	40%
R52: Pain, unspecified	10,140	39%
R53: Malaise and fatigue	9,810	38%
R10: Abdominal and pelvic pain	9,760	38%
R68: Other general signs and symptoms	9,730	38%
M79: Other and unspecified soft tissue disorders, not elsewhere classified	9,660	37%
M25: Other joint disorder, not elsewhere classified	9,620	37%
R11: Nausea and vomiting	9,550	37%
M54: Dorsalgia	9,380	36%
Most Frequent Diagnosis ICD-10 Header Codes [0, 365]		
Z87: Personal history of other diseases and conditions	14,560	52%
R52: Pain, unspecified	14,090	51%
R06: Abnormalities of breathing	14,070	51%
R68: Other general signs and symptoms	13,670	49%
R53: Malaise and fatigue	13,460	48%
R11: Nausea and vomiting	13,040	47%
M79: Other and unspecified soft tissue disorders, not elsewhere classified	12,980	47%
M25: Other joint disorder, not elsewhere classified	12,820	46%
R10: Abdominal and pelvic pain	12,580	45%
R60: Edema, not elsewhere classified	12,540	45%

*Pre-index diagnoses assessed among a convenience sample of 25,840 patients

NOTE: All counts provided through the TriNetX Live™ platform are rounded up to the nearest 10 to protect patient privacy. Thus, all estimates should be interpreted as ranges, with the lower value of the range ≤ 0.09% less than the presented value unless otherwise noted.

Table 3. Most Frequent Diagnosis Codes Among Patients with Cannabidiol Exposures from July 1, 2018 through February 28, 2022

	Cannabidiol Users	
	Number	Percent
Total Number of Patients	37,710	100%
Most Frequent Diagnosis ICD-10 Header Codes [-365, -1]*		
Z87: Personal history of other diseases and conditions	11,110	30%
R06: Abnormalities of breathing	11,040	30%
Z79: Long term (current) drug therapy	10,700	29%
M25: Other joint disorder, not elsewhere classified	10,510	28%
R53: Malaise and fatigue	10,400	28%
M79: Other and unspecified soft tissue disorders, not elsewhere classified	10,290	27%
M54: Dorsalgia	10,190	27%
R10: Abdominal and pelvic pain	10,170	27%
R11: Nausea and vomiting	9,990	27%
I10: Essential (primary) hypertension	9,810	26%
Most Frequent Diagnosis ICD-10 Header Codes [0, 365]		
Z87: Personal history of other diseases and conditions	14,300	38%
R06: Abnormalities of breathing	14,300	38%
R53: Malaise and fatigue	13,530	36%
M25: Other joint disorder, not elsewhere classified	13,190	35%
M79: Other and unspecified soft tissue disorders, not elsewhere classified	13,120	35%
R52: Pain, unspecified	13,030	35%
R68: Other general signs and symptoms	12,890	34%
R11: Nausea and vomiting	12,820	34%
M54: Dorsalgia	12,530	33%
R10: Abdominal and pelvic pain	12,420	33%

*Pre-index diagnoses assessed among a convenience sample of 37,420 patients

NOTE: All counts provided through the TriNetX Live™ platform are rounded up to the nearest 10 to protect patient privacy. Thus, all estimates should be interpreted as ranges, with the lower value of the range ≤ 0.09% less than the presented value unless otherwise noted.

Table 4. Most Frequent Diagnosis Codes Among Patients with Cannabidiol Exposures, Derived from Natural Language Processing (NLP) from July 1, 2018 through February 28, 2022

	Cannbidiol Users, NLP	
	Number	Percent
Total Number of Patients	25,220	100%
Most Frequent Diagnosis ICD-10 Header Codes [-365, -1]*		
Z87: Personal history of other diseases and conditions	9,770	41%
R06: Abnormalities of breathing	9,630	41%
R52: Pain, unspecified	9,330	39%
R53: Malaise and fatigue	9,200	39%
M25: Other joint disorder, not elsewhere classified	9,070	38%
R10: Abdominal and pelvic pain	9,050	38%
M79: Other and unspecified soft tissue disorders, not elsewhere classified	9,040	38%
R68: Other general signs and symptoms	8,980	38%
R11: Nausea and vomiting	8,850	37%
M54: Dorsalgia	8,840	37%
Most Frequent Diagnosis ICD-10 Header Codes [0, 365]		
Z87: Personal history of other diseases and conditions	13,320	53%
R06: Abnormalities of breathing	12,930	51%
R52: Pain, unspecified	12,750	51%
R68: Other general signs and symptoms	12,450	49%
R53: Malaise and fatigue	12,440	49%
M79: Other and unspecified soft tissue disorders, not elsewhere classified	11,980	48%
R11: Nausea and vomiting	11,970	47%
M25: Other joint disorder, not elsewhere classified	11,940	47%
R10: Abdominal and pelvic pain	11,490	46%
R60: Edema, not elsewhere classified	11,370	45%

*Pre-index diagnoses assessed among a convenience sample of 23,630 patients

NOTE: All counts provided through the TriNetX Live™ platform are rounded up to the nearest 10 to protect patient privacy. Thus, all estimates should be interpreted as ranges, with the lower value of the range ≤ 0.09% less than the presented value unless otherwise noted.

Table 5. Most Frequent Diagnosis Codes Among Patients with Known Epidiolex Exposures from July 1, 2018 through February 28, 2022

	Epidiolex Users	
	Number	Percent
Total Number of Patients	3,330	100%
Most Frequent Diagnosis ICD-10 Header Codes [-365, -1]		
G40: Epilepsy and recurrent seizures	2,310	69%
R56: Convulsions, not elsewhere classified	1,050	32%
R62: Lack of expected normal physiological development in childhood and adults	870	26%
G47: Sleep disorders	610	18%
K59: Other functional intestinal disorders	610	18%
R63: Symptoms and signs concerning food and fluid intake	590	18%
Z93: Artificial opening status	540	16%
G93: Other disorders of brain	530	16%
R06: Abnormalities of breathing	520	16%
G80: Cerebral palsy	490	15%
Most Frequent Diagnosis ICD-10 Header Codes [0, 365]		
G40: Epilepsy and recurrent seizures	2,440	73%
R56: Convulsions, not elsewhere classified	1,050	32%
R62: Lack of expected normal physiological development in childhood and adults	920	28%
G47: Sleep disorders	680	20%
K59: Other functional intestinal disorders	650	20%
R63: Symptoms and signs concerning food and fluid intake	640	19%
R06: Abnormalities of breathing	570	17%
Z93: Artificial opening status	560	17%
G80: Cerebral palsy	530	16%
G93: Other disorders of brain	520	16%

NOTE: All counts provided through the TriNetX Live™ platform are rounded up to the nearest 10 to protect patient privacy. Thus, all estimates should be interpreted as ranges, with the lower value of the range ~0.3% less than the presented value.

Table 6. Most Frequent Diagnosis Codes Among Patients with Positive Lab Results for Presence of Tetrahydrocannbinol (THC) from July 1, 2018 through February 28, 2022

	Positive THC Lab Results	
	Number	Percent
Total Number of Patients	32,770	100%
Most Frequent Diagnosis ICD-10 Header Codes [-365, -1]*		
F17: Nicotine dependence	6,280	19%
F41: Other anxiety disorders	5,580	17%
I10: Essential (primary) hypertension	4,780	15%
G89: Pain, not elsewhere classified	4,750	15%
M54: Dorsalgia	4,630	14%
Z68: Body mass index [BMI]	4,500	14%
F32: Depressive episode	4,480	14%
R10: Abdominal and pelvic pain	4,160	13%
M79: Other and unspecified soft tissue disorders, not elsewhere classified	4,050	13%
M25: Other joint disorder, not elsewhere classified	3,760	12%
Most Frequent Diagnosis ICD-10 Header Codes [0, 365]		
F17: Nicotine dependence	8,410	26%
F41: Other anxiety disorders	7,420	23%
F12: Cannabis related disorders	6,690	20%
F32: Depressive episode	6,290	19%
Z68: Body mass index [BMI]	6,290	19%
I10: Essential (primary) hypertension	5,520	17%
G89: Pain, not elsewhere classified	5,460	17%
M54: Dorsalgia	5,100	16%
Z79: Long term (current) drug therapy	4,900	15%
M79: Other and unspecified soft tissue disorders, not elsewhere classified	4,750	14%

*Pre-index diagnoses assessed among a convenience sample of 32,290 patients

NOTE: All counts provided through the TriNetX Live™ platform are rounded up to the nearest 10 to protect patient privacy. Thus, all estimates should be interpreted as ranges, with the lower value of the range ≤ 0.09% less than the presented value unless otherwise noted.

Table 7. Most Frequent Diagnosis Codes Among Patients with Cannabis-derived Product Exposures or Positive Lab Result for Presence of Tetrahydrocannabinol (THC), Excluding Known Epidiolex from July 1, 2018 through February 28, 2022

	Cannabis-derived Product User or Positive THC Lab Result	
	Number	Percent
Total Number of Patients	69,460	100%
Most Frequent Diagnosis ICD-10 Header Codes [-365, -1]*		
M54: Dorsalgia	14,420	22%
R10: Abdominal and pelvic pain	14,160	22%
I10: Essential (primary) hypertension	14,080	21%
M79: Other and unspecified soft tissue disorders, not elsewhere classified	13,950	21%
F41: Other anxiety disorders	13,900	21%
M25: Other joint disorder, not elsewhere classified	13,770	21%
Z87: Personal history of other diseases and conditions	13,310	20%
R06: Abnormalities of breathing	13,210	20%
R11: Nausea and vomiting	13,050	20%
F32: Depressive episode	12,590	19%
Most Frequent Diagnosis ICD-10 Header Codes [0, 365]		
F41: Other anxiety disorders	19,240	28%
Z87: Personal history of other diseases and conditions	18,890	27%
M79: Other and unspecified soft tissue disorders, not elsewhere classified	18,520	26%
M54: Dorsalgia	18,200	26%
M25: Other joint disorder, not elsewhere classified	17,900	26%
R10: Abdominal and pelvic pain	17,810	25%
R06: Abnormalities of breathing	17,740	25%
I10: Essential (primary) hypertension	17,680	25%
F32: Depressive episode	17,510	25%
Z79: Long term (current) drug therapy	16,990	24%

*Pre-index diagnoses assessed among a convenience sample of 65,700 patients

NOTE: All counts provided through the TriNetX Live™ platform are rounded up to the nearest 10 to protect patient privacy. Thus, all estimates should be interpreted as ranges, with the lower value of the range ≤ 0.09% less than the presented value unless otherwise noted.

Table 8. Most Frequent Diagnosis Codes Among Patients with Cannabidiol Exposures, Excluding Known Epidiolex from July 1, 2018 through February 28, 2022

	Cannabidiol Users	
	Number	Percent
Total Number of Patients	37,090	100%
Most Frequent Diagnosis ICD-10 Header Codes [-365, -1]*		
R06: Abnormalities of breathing	11,090	32%
Z87: Personal history of other diseases and conditions	10,860	32%
R53: Malaise and fatigue	10,360	30%
M25: Other joint disorder, not elsewhere classified	10,300	30%
M79: Other and unspecified soft tissue disorders, not elsewhere classified	10,260	30%
R52: Pain, unspecified	10,250	30%
R10: Abdominal and pelvic pain	10,230	30%
M54: Dorsalgia	10,130	30%
R11: Nausea and vomiting	10,030	29%
R68: Other general symptoms and signs	9,940	29%
Most Frequent Diagnosis ICD-10 Header Codes [0, 365]		
Z87: Personal history of other diseases and conditions	15,380	41%
R06: Abnormalities of breathing	15,150	40%
R53: Malaise and fatigue	14,380	38%
R52: Pain, unspecified	14,320	38%
M79: Other and unspecified soft tissue disorders, not elsewhere classified	14,010	37%
R68: Other general symptoms and signs	13,990	37%
M25: Other joint disorder, not elsewhere classified	13,950	37%
R11: Nausea and vomiting	13,720	37%
R10: Abdominal and pelvic pain	13,360	36%
M54: Dorsalgia	13,330	36%

*Pre-index diagnoses assessed among a convenience sample of 34,270 patients

NOTE: All counts provided through the TriNetX Live™ platform are rounded up to the nearest 10 to protect patient privacy. Thus, all estimates should be interpreted as ranges, with the lower value of the range ≤ 0.09% less than the presented value unless otherwise noted.

Table 9. Most Frequent Diagnosis Codes Among Patients with Cannabidiol Exposures and Positive Lab Result for Presence of Tetrahydrocannabinol (THC), Excluding Known Epidiolex from July 1, 2018 through February 28, 2022

	Cannabidiol Users and Positive THC Lab Result	
	Number	Percent
Total Number of Patients	100	100%
Most Frequent Diagnosis ICD-10 Header Codes [-365, -1]		
Z79: Long term (current) drug therapy	70	70%
G89: Pain, not elsewhere classified	70	70%
M79: Other and unspecified soft tissue disorders, not elsewhere classified	70	70%
M25: Other joint disorder, not elsewhere classified	50	50%
Z87: Personal history of other diseases and conditions	50	50%
F32: Depressive episode	50	50%
M54: Dorsalgia	50	50%
conditions other than malignant neoplasm	50	50%
F41: Other anxiety disorders	50	50%
G47: Sleep disorders[1]	40	40%
Most Frequent Diagnosis ICD-10 Header Codes [0, 365]		
G89: Pain, not elsewhere classified	90	90%
Z79: Long term (current) drug therapy	80	80%
M54: Dorsalgia	70	70%
M79: Other and unspecified soft tissue disorders, not elsewhere classified	70	70%
F32: Depressive episode	60	60%
F41: Other anxiety disorders	60	60%
Z87: Personal history of other diseases and conditions	60	60%
M25: Other joint disorder, not elsewhere classified	50	50%
G47: Sleep disorders[2]	40	40%
R10: Abdominal and pelvic pain[2]	40	40%

[1]R10: Abdominal and pelvic pain, I10: Essential (primary) hypertension, and Z98: Other postprocedural states tied for utilization counts with G47

[2]I10: Essential (primary) hypertension, Z68: Body mass index [BMI], and Z86: Personal history of certain other diseases tied for utilization counts with G47 and R10

NOTE: All counts provided through the TriNetX Live™ platform are rounded up to the nearest 10 to protect patient privacy. Thus, all estimates should be interpreted as ranges, with the lower value of the range 9% less than the presented value.

Figure 1. Cohort Demographics for Patients with Cannabis-derived Product Exposures
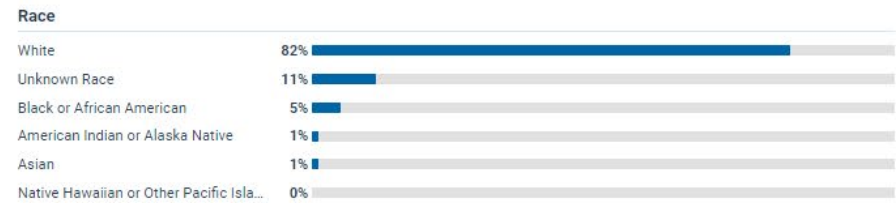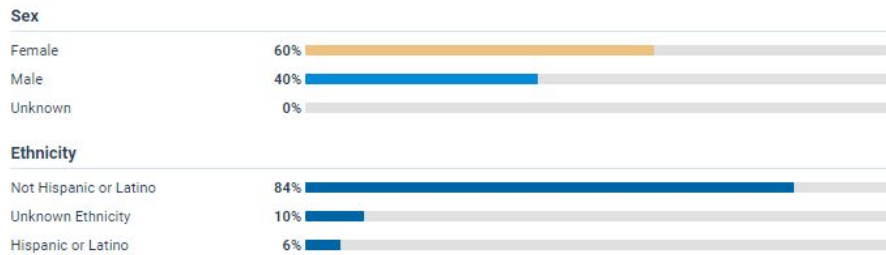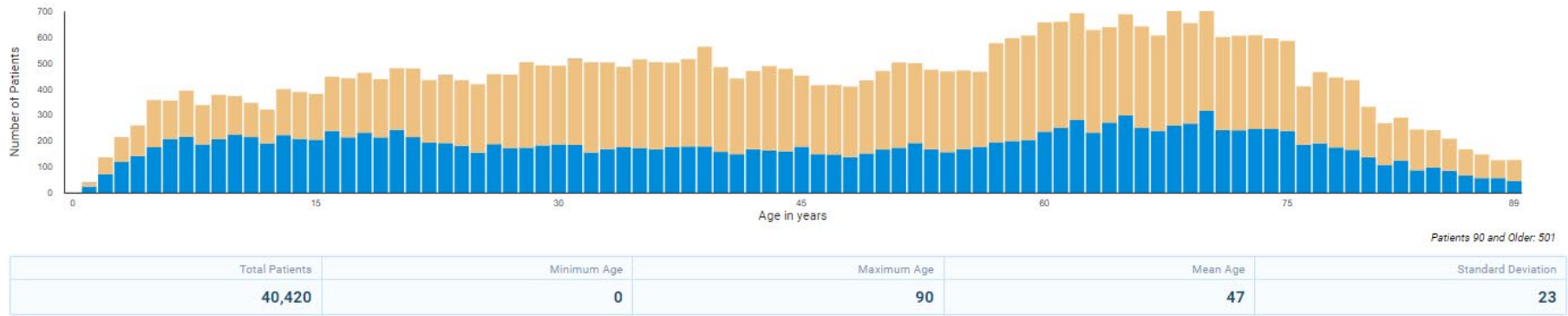
Patients 90 and Older: 501

Total Patients	Minimum Age	Maximum Age	Mean Age	Standard Deviation
40,420	0	90	47	23

Sex

Female	60%
Male	40%
Unknown	0%

Ethnicity

Not Hispanic or Latino	84%
Unknown Ethnicity	10%
Hispanic or Latino	6%

Race

White	82%
Unknown Race	11%
Black or African American	5%
American Indian or Alaska Native	1%
Asian	1%
Native Hawaiian or Other Pacific Isla...	0%

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 2. Cohort Demographics for Patients with Cannabis-derived Product Exposures, Derived from Natural Language Processing
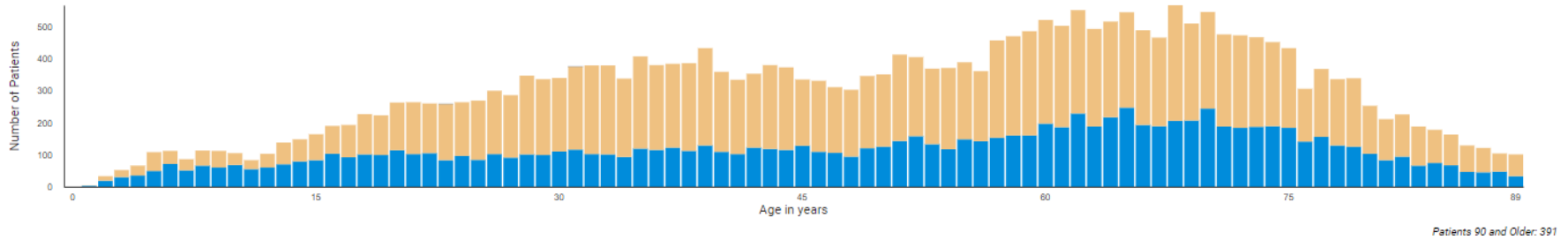
Patients 90 and Older: 391

	Total Patients	Minimum Age	Maximum Age	Mean Age	Standard Deviation
	27,830	1	90	51	21

Sex

Female	62%
Male	38%
Unknown	0%

Ethnicity

Not Hispanic or Latino	90%
Unknown Ethnicity	5%
Hispanic or Latino	5%

Race

White	86%
Unknown Race	7%
Black or African American	5%
American Indian or Alaska Native	1%
Asian	1%
Native Hawaiian or Other Pacific Isla…	0%

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.)
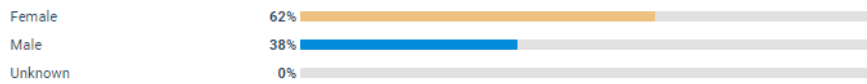
Figure 3. Cohort Demographics for Patients with Cannabidiol Exposures

Patients 90 and Older: 483

	Total Patients	Minimum Age	Maximum Age	Mean Age	Standard Deviation
	37,710	0	90	47	24

Sex

Female	58%	
Male	42%	
Unknown	0%	

Ethnicity

Not Hispanic or Latino	84%	
Unknown Ethnicity	10%	
Hispanic or Latino	6%	

Race

White	82%	
Unknown Race	11%	
Black or African American	5%	
American Indian or Alaska Native	1%	
Asian	1%	
Native Hawaiian or Other Pacific Isla...	0%	

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 4. Cohort Demographics for Patients with Cannabidiol Exposures, Derived from Natural Language Processing

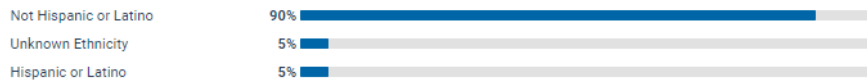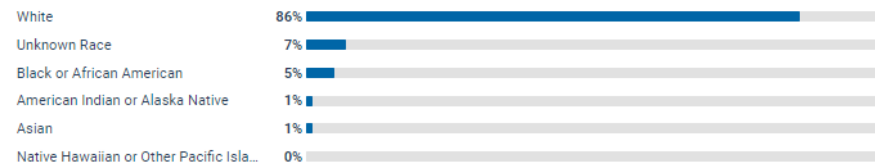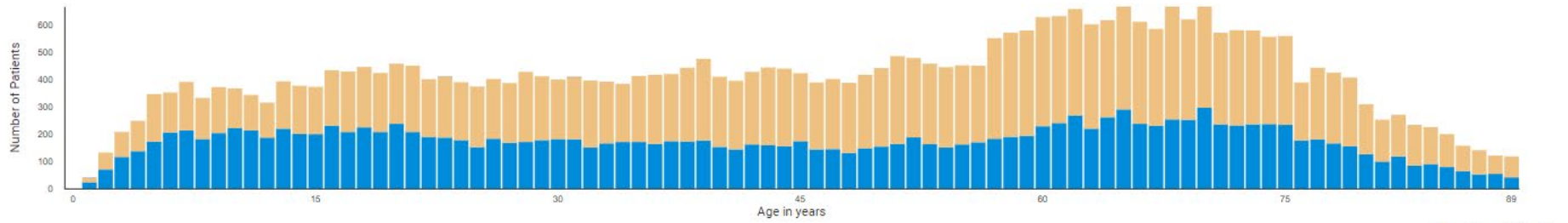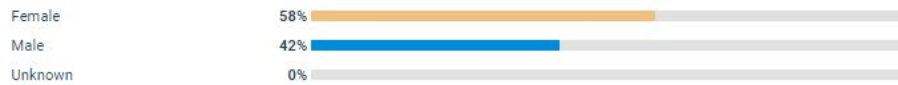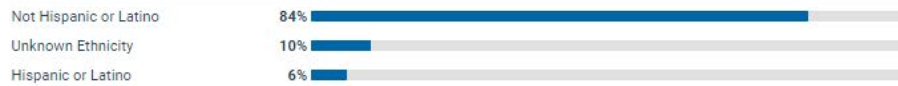*Patients 90 and Older: 375*

	Total Patients	Minimum Age	Maximum Age	Mean Age	Standard Deviation
	25,220	1	90	52	21

Sex
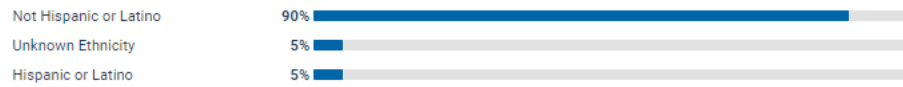
Female	60%	
Male	40%	
Unknown	0%	

Ethnicity

Not Hispanic or Latino	90%	
Unknown Ethnicity	5%	
Hispanic or Latino	5%	

Race

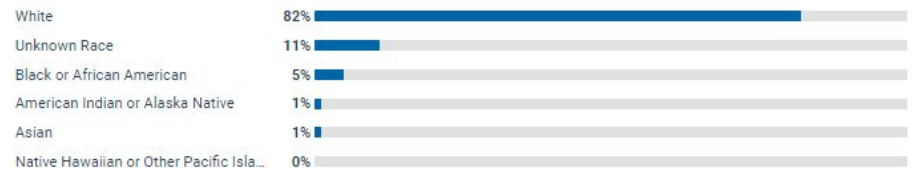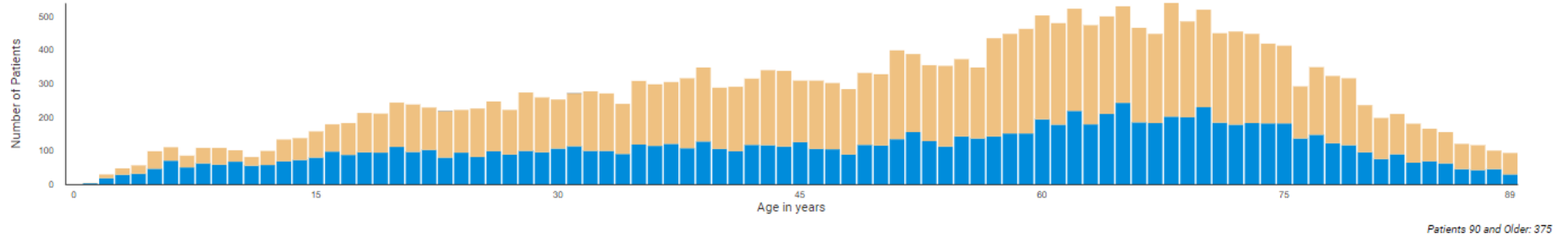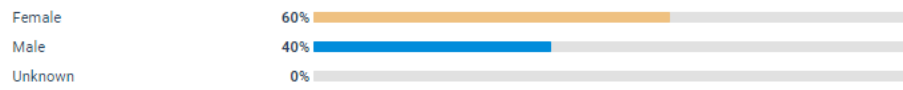|		
White	87%	
Unknown Race	7%	
Black or African American	4%	
Asian	1%	
American Indian or Alaska Native	1%	
Native Hawaiian or Other Pacific Isla…	0%	

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 5. Cohort Demographics for Patients with Known Epidiolex Exposures

Total Patients	Minimum Age	Maximum Age	Mean Age	Standard Deviation
3,330	1	90	23	19

Sex
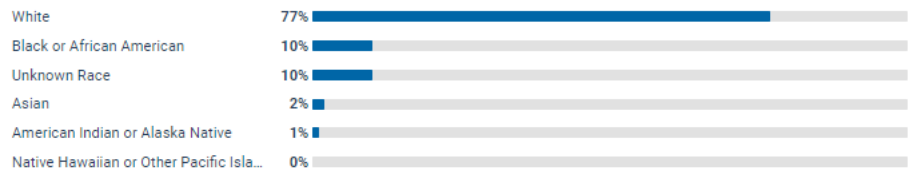
Male	53%	
Female	47%	
Unknown	0%	

Ethnicity

Not Hispanic or Latino	79%	
Hispanic or Latino	17%	
Unknown Ethnicity	4%	

Race

White	77%	
Black or African American	10%	
Unknown Race	10%	
Asian	2%	
American Indian or Alaska Native	1%	
Native Hawaiian or Other Pacific Isla...	0%	

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 6. Cohort Demographics for Patients with Positive Lab Results for Presence of Tetrahydrocannabinol (THC)
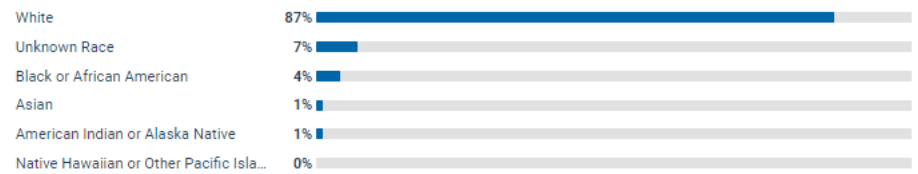

Patients 90 and Older: 23

Total Patients	Minimum Age	Maximum Age	Mean Age	Standard Deviation
32,770	0	90	40	15

Sex

Male	56%	
Female	44%	
Unknown	0%	

Race

White	61%	
Black or African American	23%	
Unknown Race	15%	
Asian	1%	
American Indian or Alaska Native	0%	
Native Hawaiian or Other Pacific Isla...	0%	

Ethnicity

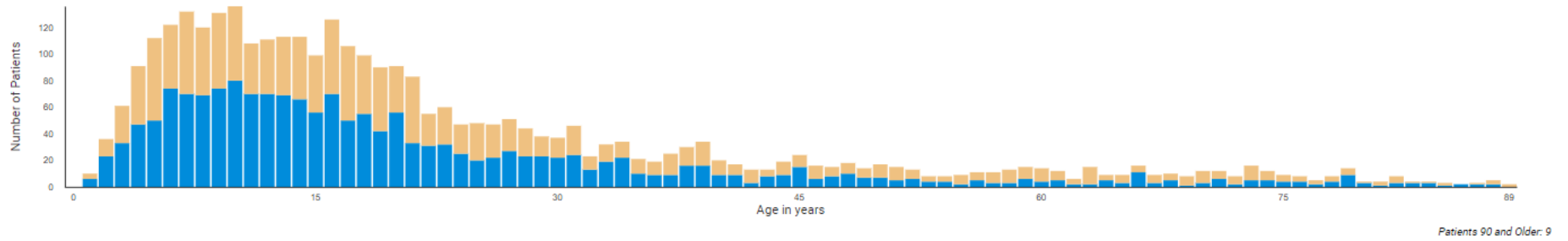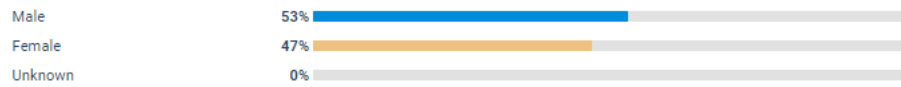|		
Not Hispanic or Latino	56%	
Unknown Ethnicity	37%	
Hispanic or Latino	7%	

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.)

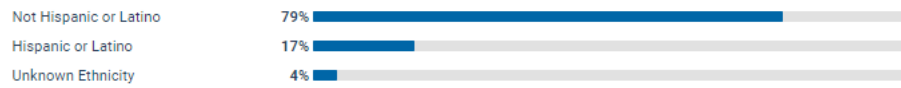**Figure 7. Cohort Demographics for Patients with Cannabis-derived Product Exposures or Positive Lab Result for Presence of Tetrahydrocannabinol (THC), Excluding Known Epidiolex**

Patients 90 and Older: 515
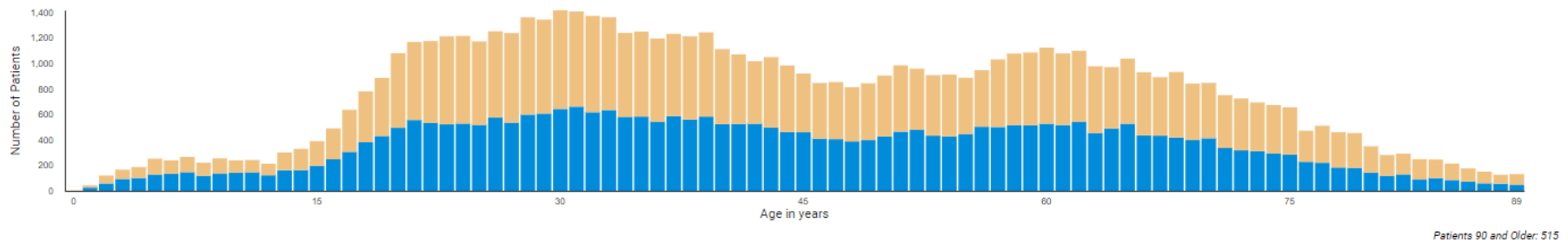
	Total Patients	Minimum Age	Maximum Age	Mean Age	Standard Deviation
	69,490	0	90	45	20

Sex

Female	53%	
Male	47%	
Unknown	0%	

Ethnicity

Not Hispanic or Latino	71%	
Unknown Ethnicity	23%	
Hispanic or Latino	6%	

Race

White	72%	
Black or African American	13%	
Unknown Race	13%	
Asian	1%	
American Indian or Alaska Native	1%	
Native Hawaiian or Other Pacific Isla...	0%	

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 8. Cohort Demographics for Patients with Cannabidiol Exposures, Excluding Epidiolex

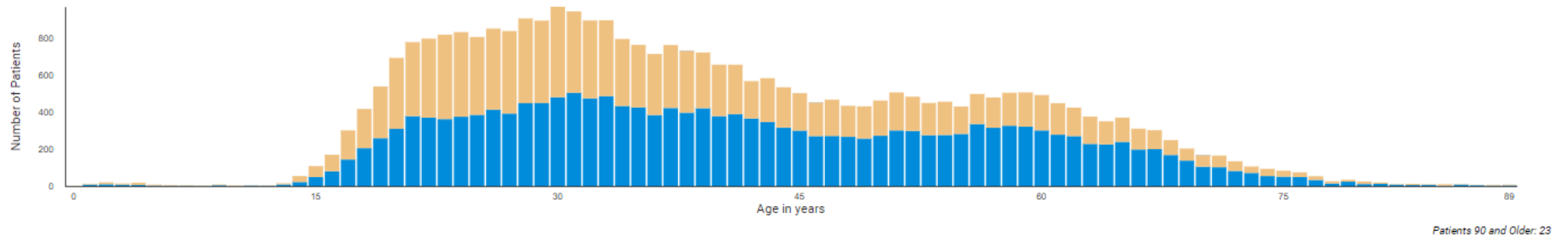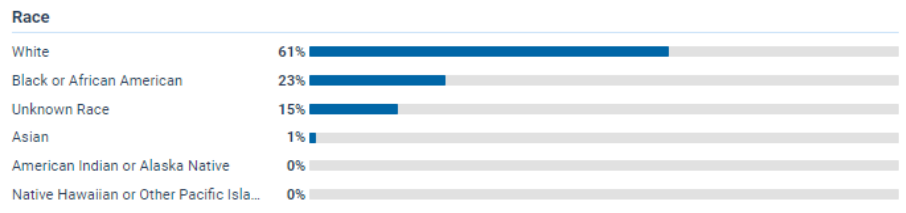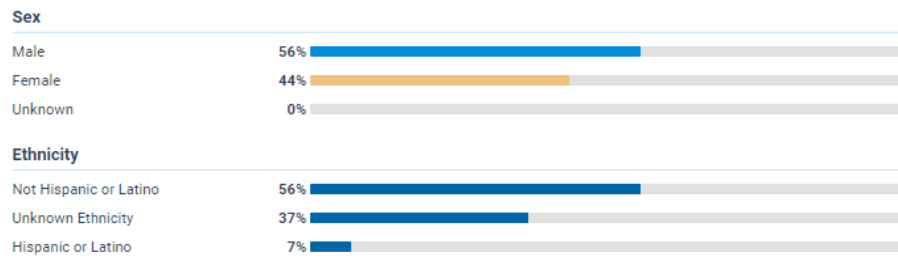|	Total Patients	Minimum Age	Maximum Age	Mean Age	Standard Deviation
	37,090	0	90	49	22

Sex

Female	61%	
Male	39%	
Unknown	0%	

Ethnicity

Not Hispanic or Latino	85%	
Unknown Ethnicity	10%	
Hispanic or Latino	5%	

Race

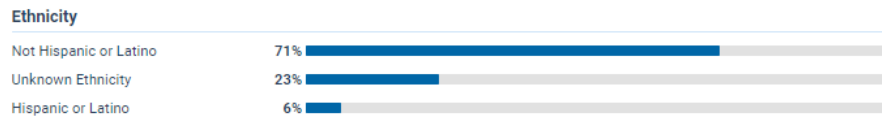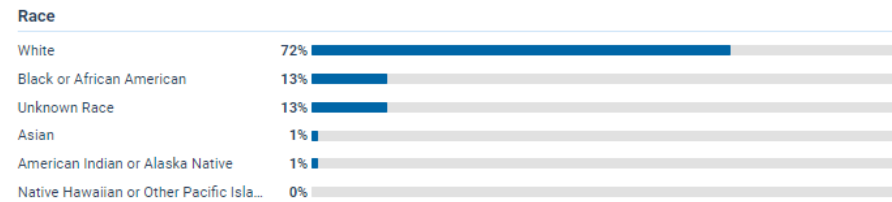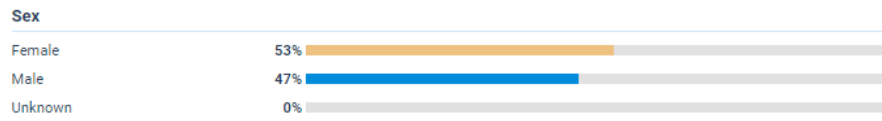|		
White	82%	
Unknown Race	11%	
Black or African American	5%	
American Indian or Alaska Native	1%	
Asian	1%	
Native Hawaiian or Other Pacific Isla...	0%	

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 9. Cohort Demographics for Patients with Cannabidiol Exposures and Positive Lab Result for Presence of Tetrahydrocannabinol (THC), Excluding Known Epidiolex
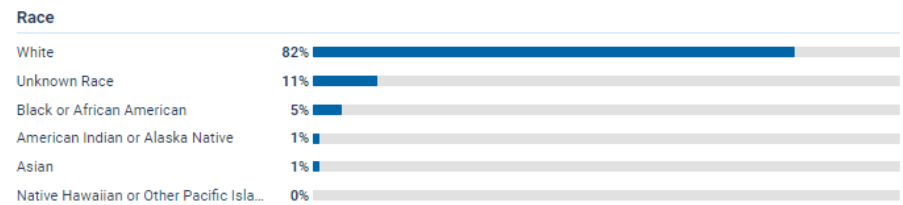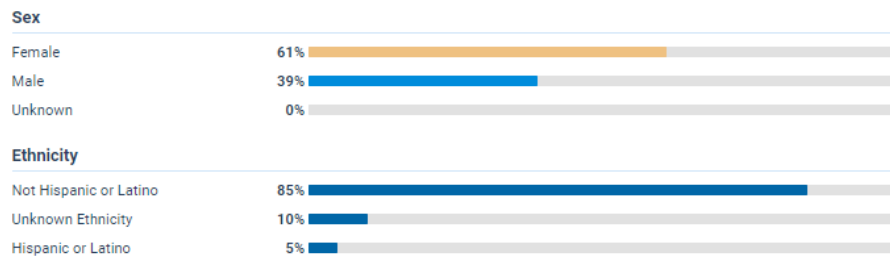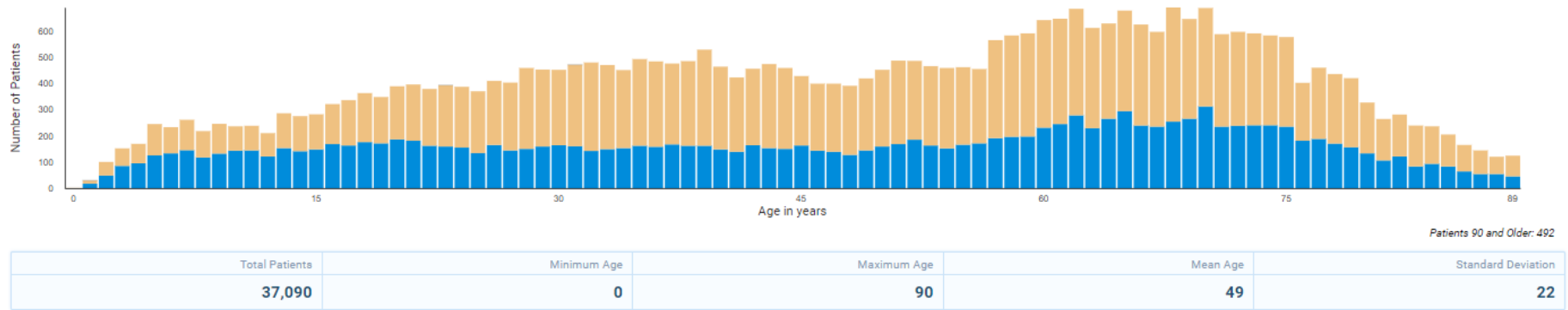

Patients 90 and Older: 0

Total Patients	Minimum Age	Maximum Age	Mean Age	Standard Deviation
100	21	85	53	16

Sex
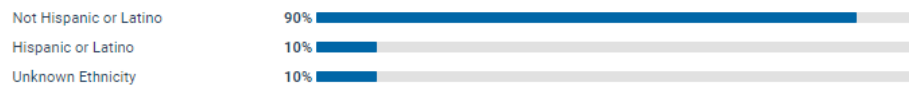
Female	70%	
Male	40%	
Unknown	0%	

Ethnicity

Not Hispanic or Latino	90%	
Hispanic or Latino	10%	
Unknown Ethnicity	10%	

Race

White	100%	
Black or African American	10%	
Unknown Race	10%	
American Indian or Alaska Native	0%	
Asian	0%	
Native Hawaiian or Other Pacific Isla...	0%	

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.)*
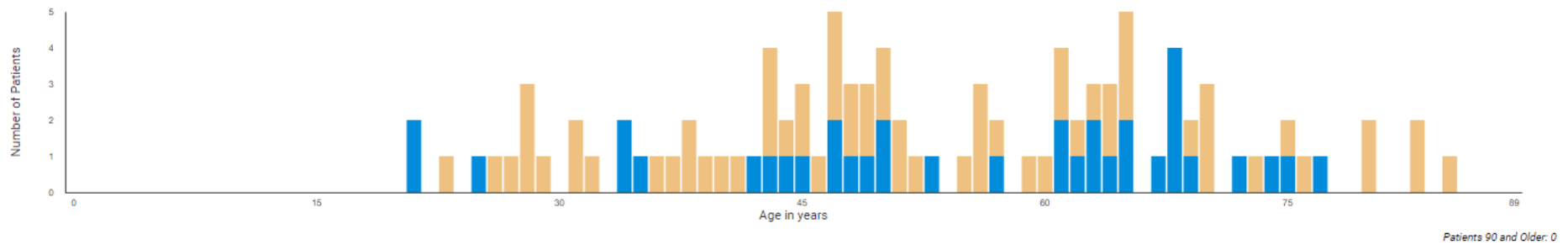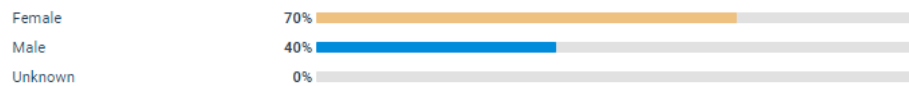
Figure 10. Cohort Geographic Distribution for Patients with Cannabis-derived Product Exposures

US Regions	Regional Patient Count ↓	Regional Network Count	Percentage
Missouri	10	3,491,670	<0.001%
Illinois	60	2,014,890	0.003%
Kentucky	100	1,291,180	0.008%
Vermont	120	877,630	0.014%
Arizona	130	4,917,610	0.003%
New Mexico	140	1,090,210	0.013%
West Virginia	140	2,567,970	0.005%
Louisiana	170	3,830,000	0.004%
Arkansas	200	1,080,150	0.019%
Minnesota	270	3,220,280	0.008%
California	290	2,408,460	0.012%
District of Columbia	330	1,867,480	0.018%
South Carolina	360	1,412,750	0.025%
Alabama	410	1,321,500	0.031%
Massachusetts	570	7,653,050	0.007%
Maryland	600	3,111,710	0.019%
Wisconsin	840	5,246,110	0.016%
North Carolina	850	2,363,890	0.036%
Tennessee	1,020	6,297,710	0.016%
Colorado	1,090	5,663,370	0.019%
Texas	1,330	17,278,450	0.008%
Ohio	1,390	7,405,600	0.019%
Virginia	2,330	6,893,790	0.034%
Pennsylvania	3,100	16,546,350	0.019%
Iowa	3,360	1,372,990	0.245%
New York	9,390	10,911,870	0.086%
Utah	11,920	1,394,930	0.855%

Patient counts can be obfuscated to protect patient privacy ⊙
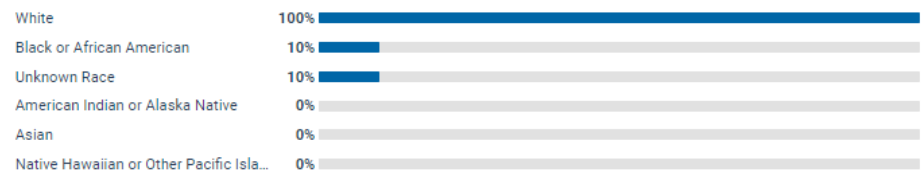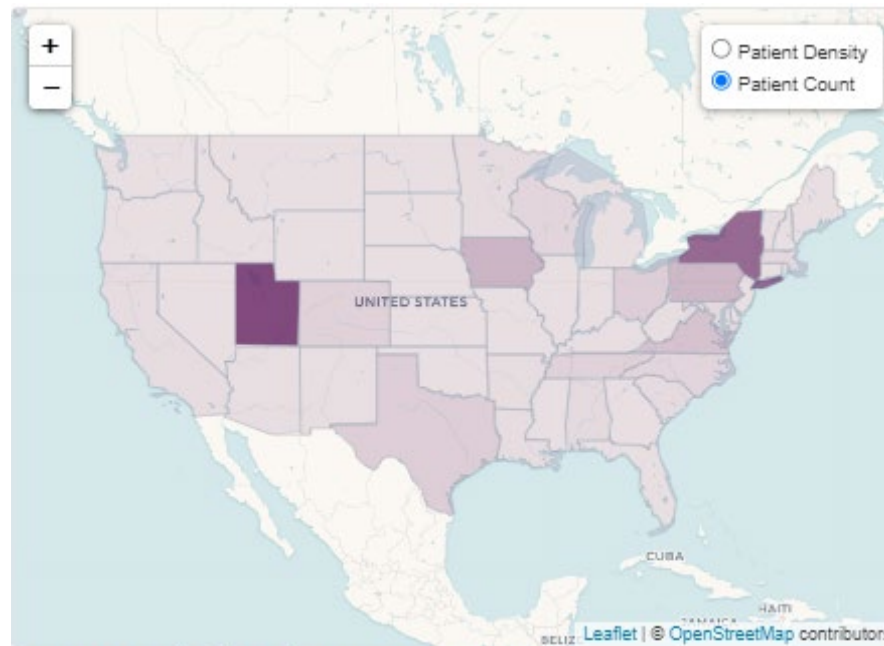
Patient location is determined by location of HCO headquarters

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 11. Cohort Geographic Distribution for Patients with Cannabis-derived Product Exposures, Derived from Natural Language Processing

| US Regions	Regional Patient Count ↓	Regional Network Count	Percentage
Arkansas	20	1,080,150	0.002%
California	90	2,408,460	0.004%
Tennessee	200	6,297,710	0.003%
Ohio	230	7,405,600	0.003%
Massachusetts	410	7,653,050	0.005%
Texas	600	17,278,450	0.003%
North Carolina	830	2,363,890	0.035%
Virginia	2,160	6,893,790	0.031%
Iowa	3,120	1,372,990	0.227%
New York	8,290	10,911,870	0.076%
Utah	11,920	1,394,930	0.855%
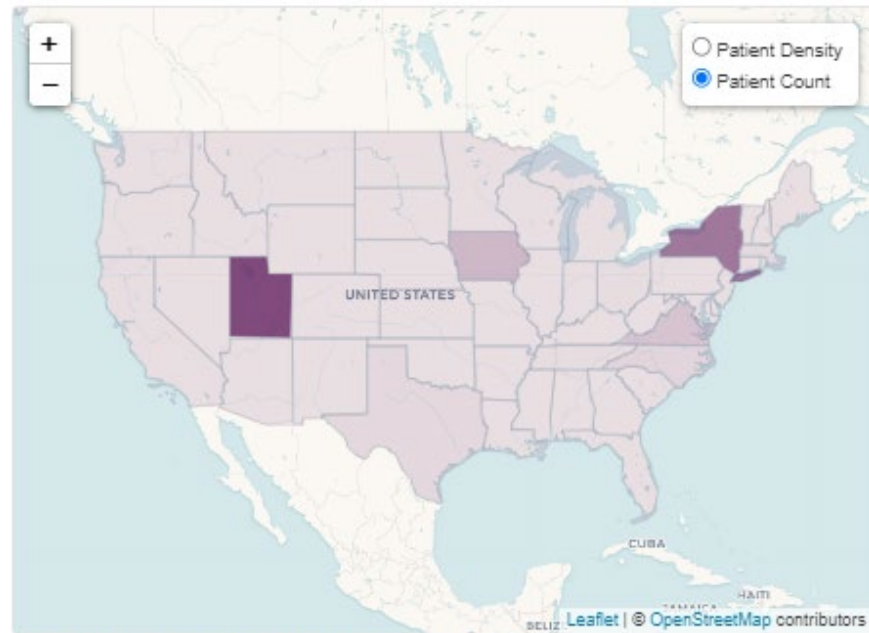
Patient counts can be obfuscated to protect patient privacy ⊙
Patient location is determined by location of HCO headquarters

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 12. Cohort Geographic Distribution for Patients with Cannabidiol Exposures

| US Regions	Regional Patient Count ↓	Regional Network Count	Percentage
Missouri	10	3,491,670	<0.001%
Illinois	60	2,014,890	0.003%
Kentucky	100	1,291,180	0.008%
Vermont	120	877,630	0.014%
Arizona	130	4,917,610	0.003%
New Mexico	140	1,090,210	0.013%
West Virginia	140	2,567,970	0.005%
Louisiana	170	3,830,000	0.004%
Arkansas	200	1,080,150	0.019%
Minnesota	270	3,220,280	0.008%
California	280	2,408,460	0.012%
District of Columbia	330	1,867,480	0.018%
South Carolina	360	1,412,750	0.025%
Alabama	410	1,321,500	0.031%
Massachusetts	560	7,653,050	0.007%
Maryland	600	3,111,710	0.019%
North Carolina	810	2,363,890	0.034%
Wisconsin	830	5,246,110	0.016%
Tennessee	980	6,297,710	0.016%
Colorado	1,090	5,663,370	0.019%
Texas	1,290	17,278,450	0.007%
Ohio	1,360	7,405,600	0.018%
Virginia	2,130	6,893,790	0.031%
Pennsylvania	3,080	16,546,350	0.019%
Iowa	3,150	1,372,990	0.229%
New York	8,320	10,911,870	0.076%
Utah	10,900	1,394,930	0.781%
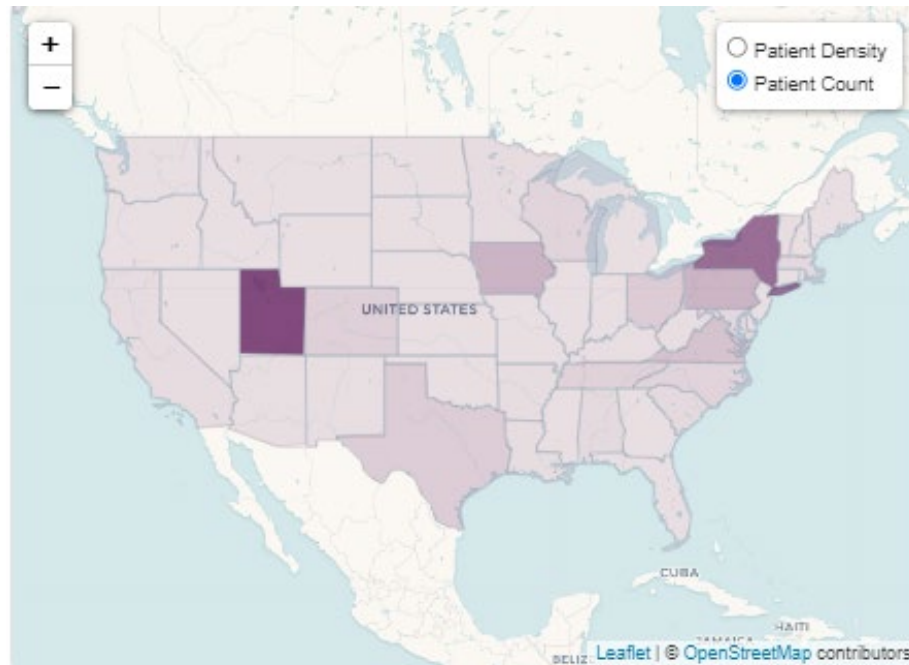
Patient counts can be obfuscated to protect patient privacy ?
Patient location is determined by location of HCO headquarters

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 13. Cohort Geographic Distribution for Patients with Cannabidiol Exposures, Derived from Natural Language Processing

| US Regions	Regional Patient Count ↓	Regional Network Count	Percentage
Arkansas	20	1,080,150	0.002%
California	80	2,408,460	0.003%
Tennessee	160	6,297,710	0.003%
Ohio	210	7,405,600	0.003%
Massachusetts	400	7,653,050	0.005%
Texas	590	17,278,450	0.003%
North Carolina	800	2,363,890	0.034%
Virginia	1,960	6,893,790	0.028%
Iowa	2,920	1,372,990	0.213%
New York	7,220	10,911,870	0.066%
Utah	10,890	1,394,930	0.781%
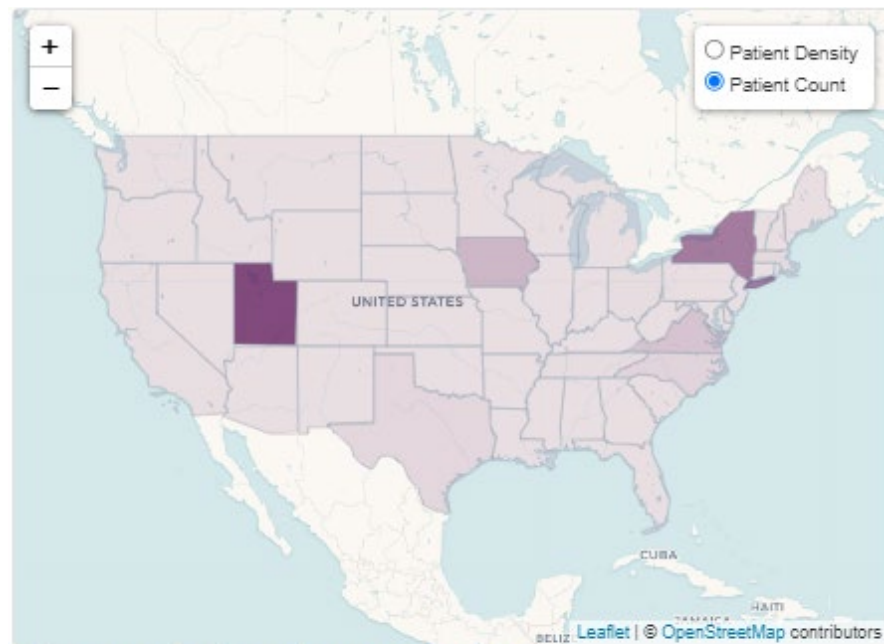
Patient counts can be obfuscated to protect patient privacy ❓

Patient location is determined by location of HCO headquarters

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 14. Cohort Geographic Distribution for Patients with Known Epidiolex Exposures

| US Regions	Regional Patient Count ↓	Regional Network Count	Percentage
Missouri	10	3,491,670	<0.001%
Pennsylvania	10	16,546,350	<0.001%
Tennessee	10	6,297,710	<0.001%
Wisconsin	10	5,246,110	<0.001%
District of Columbia	30	1,867,480	0.002%
North Carolina	40	2,363,890	0.002%
Massachusetts	70	7,653,050	<0.001%
Virginia	90	6,893,790	0.001%
Kentucky	100	1,291,180	0.008%
Minnesota	140	3,220,280	0.004%
Arkansas	180	1,080,150	0.017%
New York	180	10,911,870	0.002%
Colorado	320	5,663,370	0.006%
Alabama	330	1,321,500	0.025%
Ohio	520	7,405,600	0.007%
Maryland	600	3,111,710	0.019%
Texas	750	17,278,450	0.004%
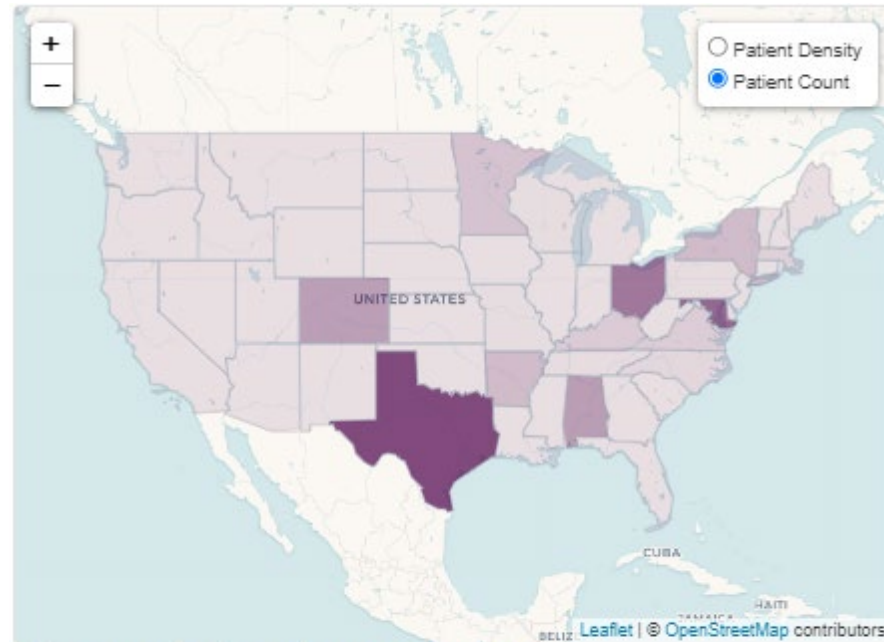
Patient counts can be obfuscated to protect patient privacy ?
Patient location is determined by location of HCO headquarters

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 15. Cohort Geographic Distribution for Patients with Positive Lab Results for Presence of Tetrahydrocannabinol (THC)

| US Regions	Regional Patient Count ↓	Regional Network Count	Percentage
New Hampshire	10	850,670	0.001%
North Carolina	10	2,363,890	<0.001%
Massachusetts	50	7,653,050	<0.001%
Iowa	140	1,372,990	0.010%
Minnesota	140	3,220,280	0.004%
Pennsylvania	260	16,546,350	0.002%
District of Columbia	280	1,867,480	0.015%
Texas	300	17,278,450	0.002%
Arkansas	370	1,080,150	0.034%
New York	520	10,911,870	0.005%
Wisconsin	570	5,246,110	0.011%
Louisiana	750	3,830,000	0.020%
Virginia	800	6,893,790	0.012%
Colorado	1,130	5,663,370	0.020%
West Virginia	1,170	2,567,970	0.046%
Utah	1,900	1,394,930	0.136%
California	6,140	2,408,460	0.255%
Tennessee	8,200	6,297,710	0.130%
Ohio	10,100	7,405,600	0.136%
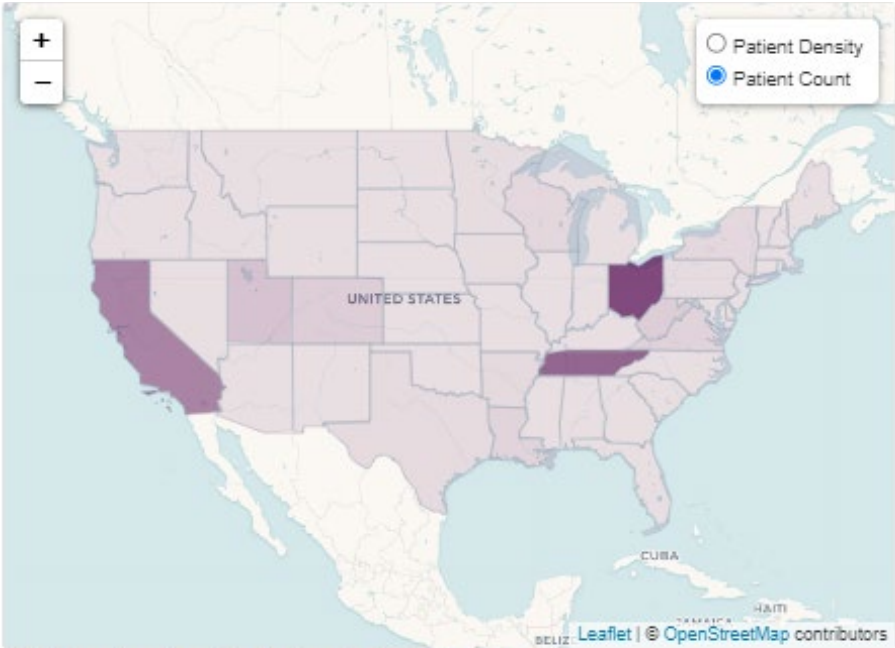
Patient counts can be obfuscated to protect patient privacy ⑦
Patient location is determined by location of HCO headquarters

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 16. Cohort Geographic Distribution for Patients with Cannabis-derived Product Exposures or Positive Lab Result for Presence of Tetrahydrocannabinol (THC), Excluding Known Epidiolex

| US Regions	Regional Patient Count ↓	Regional Network Count	Percentage
Maryland	10	3,111,710	<0.001%
New Hampshire	10	850,670	0.001%
Illinois	60	2,014,890	0.003%
Alabama	90	1,321,500	0.007%
Vermont	120	877,630	0.014%
Arizona	130	4,917,610	0.003%
New Mexico	140	1,090,210	0.013%
Minnesota	280	3,220,280	0.009%
South Carolina	360	1,412,750	0.025%
Arkansas	380	1,080,150	0.035%
Massachusetts	550	7,653,050	0.007%
District of Columbia	580	1,867,480	0.031%
North Carolina	820	2,363,890	0.035%
Texas	880	17,278,450	0.005%
Louisiana	920	3,830,000	0.024%
West Virginia	1,300	2,567,970	0.051%
Wisconsin	1,400	5,246,110	0.027%
Colorado	1,890	5,663,370	0.033%
Virginia	3,040	6,893,790	0.044%
Pennsylvania	3,360	16,546,350	0.020%
Iowa	3,480	1,372,990	0.253%
California	6,410	2,408,460	0.266%
Tennessee	9,200	6,297,710	0.146%
New York	9,730	10,911,870	0.089%
Ohio	10,960	7,405,600	0.148%
Utah	13,480	1,394,930	0.966%
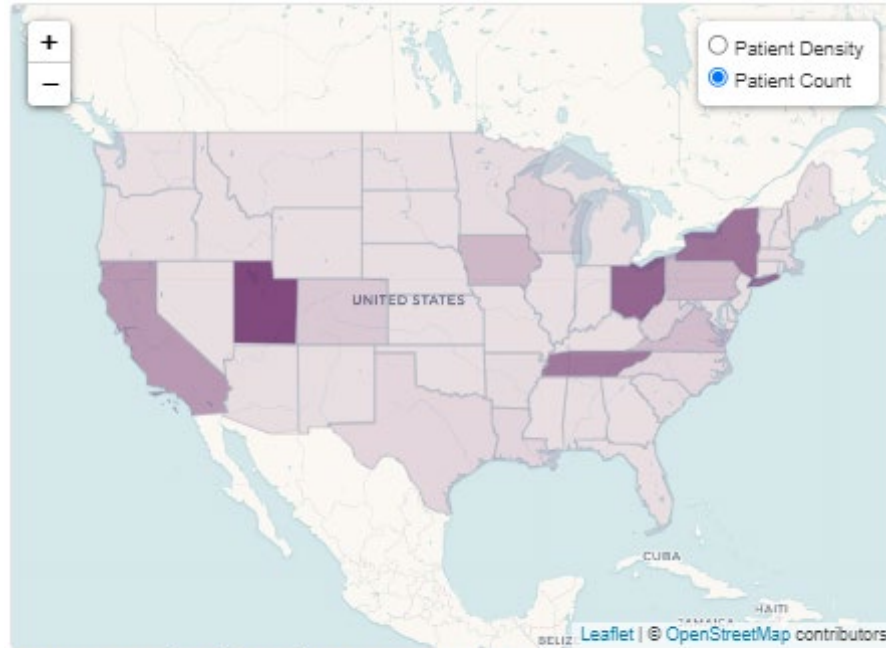
Patient counts can be obfuscated to protect patient privacy ?

Patient location is determined by location of HCO headquarters

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 17. Cohort Geographic Distribution for Patients with Cannabidiol Exposures, Excluding Epidiolex

| US Regions	Regional Patient Count ↓	Regional Network Count	Percentage
Maryland	10	3,111,710	<0.001%
Arkansas	20	1,080,150	0.002%
Illinois	60	2,014,890	0.003%
Alabama	90	1,321,500	0.007%
Vermont	120	877,630	0.014%
Arizona	130	4,917,610	0.003%
Minnesota	140	3,220,280	0.004%
New Mexico	140	1,090,210	0.013%
West Virginia	140	2,567,970	0.005%
Louisiana	170	3,830,000	0.004%
California	290	2,408,460	0.012%
District of Columbia	310	1,867,480	0.017%
South Carolina	360	1,412,750	0.025%
Massachusetts	510	7,653,050	0.007%
Texas	580	17,278,450	0.003%
Colorado	770	5,663,370	0.014%
North Carolina	810	2,363,890	0.034%
Wisconsin	830	5,246,110	0.016%
Ohio	870	7,405,600	0.012%
Tennessee	1,020	6,297,710	0.016%
Virginia	2,240	6,893,790	0.032%
Pennsylvania	3,100	16,546,350	0.019%
Iowa	3,360	1,372,990	0.245%
New York	9,210	10,911,870	0.084%
Utah	11,920	1,394,930	0.855%
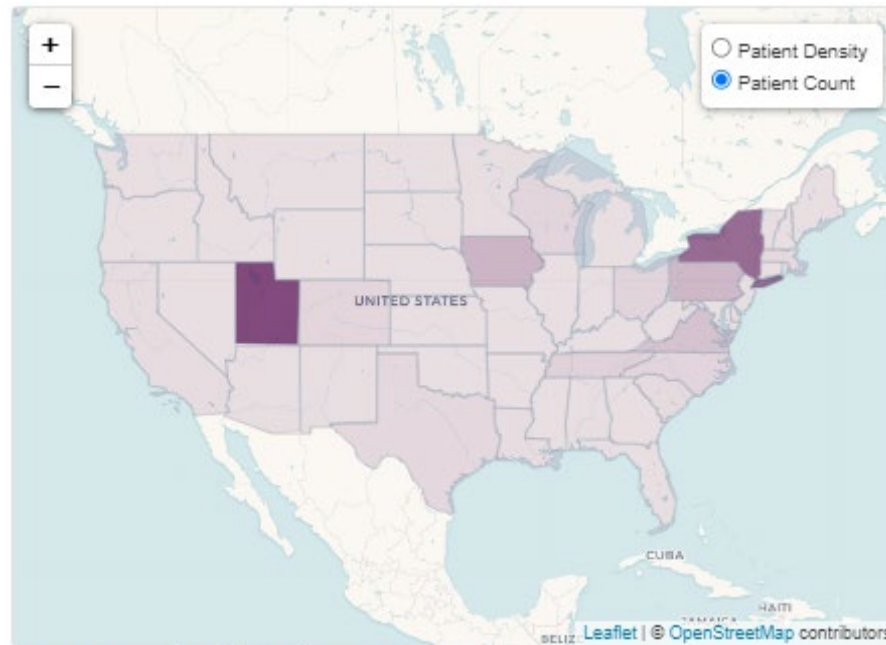
Patient counts can be obfuscated to protect patient privacy ⍰
Patient location is determined by location of HCO headquarters

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 18. Cohort Geographic Distribution for Patients with Cannabidiol Exposures and Positive Lab Result for Presence of Tetrahydrocannabinol (THC), Excluding Known Epidiolex

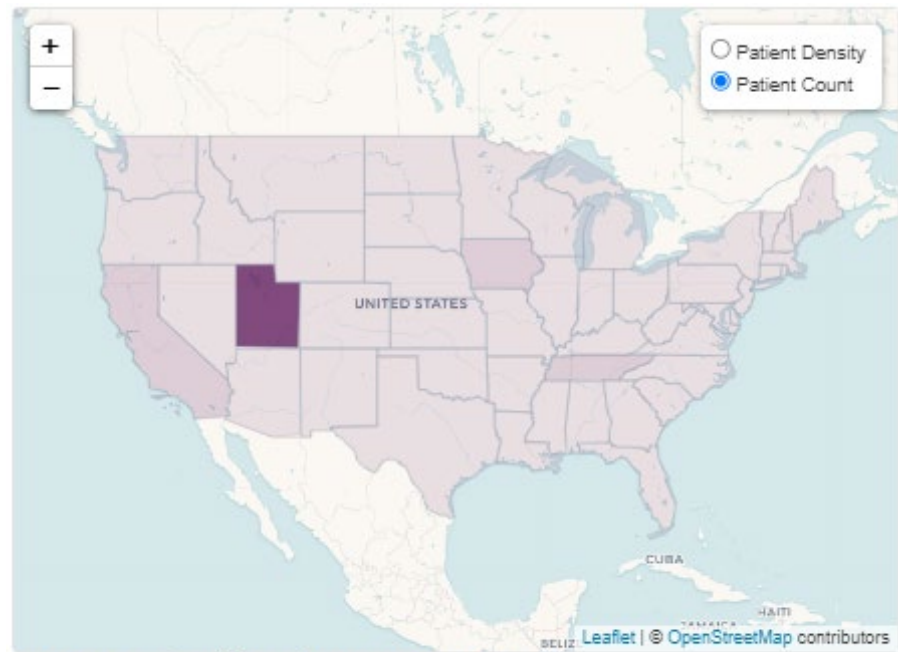| US Regions	Regional Patient Count ↓	Regional Network Count	Percentage
California	10	2,408,460	<0.001%
Iowa	10	1,372,990	<0.001%
Tennessee	10	6,297,710	<0.001%
Utah	90	1,394,930	0.006%

Patient counts can be obfuscated to protect patient privacy ?
Patient location is determined by location of HCO headquarters

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.)
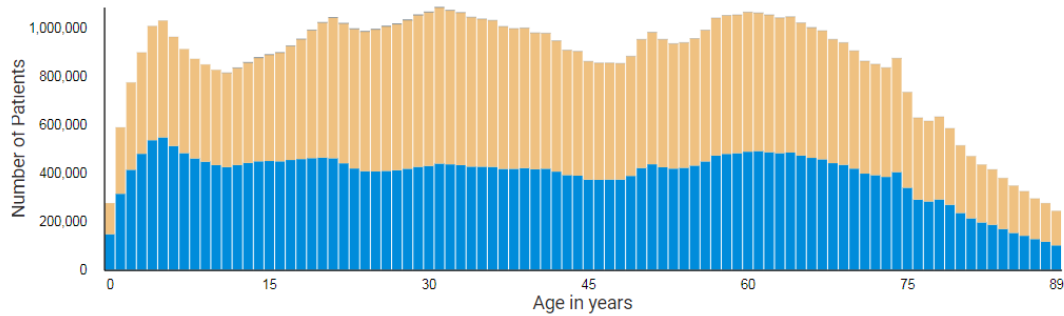
Appendix A. Demographic and Geographic Distribution of Patients in the TriNetX USA Network with Any Encounter in the Past Five Years (2016-2021)

Patients 90 and Older: 1,331,612

Total Patients	Minimum Age	Maximum Age	Mean Age	Standard Deviation
79,170,850	0	90	42	24

Sex
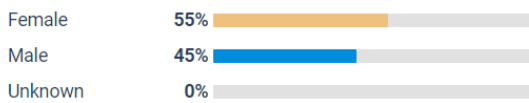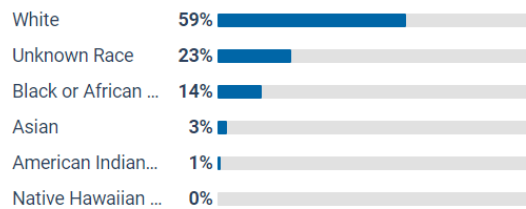
Female	55%	
Male	45%	
Unknown	0%	

Ethnicity

Not Hispanic or ...	60%	
Unknown Ethnici...	30%	
Hispanic or Latino	10%	

Race

White	59%	
Unknown Race	23%	
Black or African ...	14%	
Asian	3%	
American Indian...	1%	
Native Hawaiian ...	0%	

Patient counts can be obfuscated to protect patient privacy ?

Patient location is determined by location of HCO headquarters

Appendix B. List of RxNorm Medication Terms and Logical Observation Identifiers, Names and Codes (LOINC) Laboratory Codes Used to Define Exposures in this Request

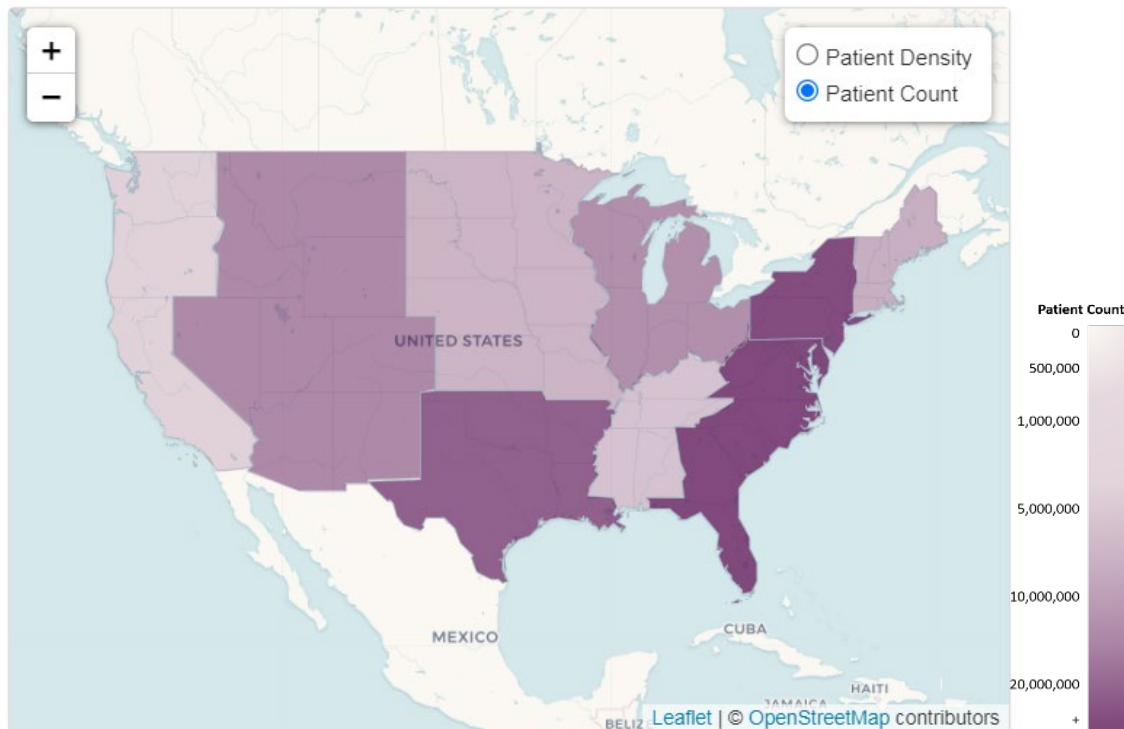| Code	Description	Code Category	Code Type	Filter
All Cannabis and Cannabis-Derived Terms				
2045371	Cannabidiol	Medication	RxNorm	N/A
2464938	Cannabigerol (*note: this term has 0 patients)	Medication	RxNorm	N/A
1976	Cannabinol	Medication	RxNorm	N/A
1788846	Hemp	Medication	RxNorm	N/A
2177094	Cannabis Sativa subsp. Sativa whole extract (*note: this term has 0 NLP patients)	Medication	RxNorm	N/A
1305550	Cannabis sativa seed oil	Medication	RxNorm	N/A
2279519	Cannabigerolate (*note: this term has 0 patients)	Medication	RxNorm	N/A
Cannabidiol				
2045371	Cannabidiol	Medication	RxNorm	N/A
Known Epidiolex				
2045371	Cannabidiol	Medication	RxNorm	Brand Name
THC Presence Lab Test				
19415-9	Tetrahydrocannabinol [presence] in urine by screen method	Laboratory Test	LOINC	Positive result
14312-3	Tetrahydrocannabinol [presence] in urine by screen method >50 ng/ml	Laboratory Test	LOINC	Positive result
3426-4	Tetrahydrocannabinol [presence] in urine	Laboratory Test	LOINC	Positive result
21556-6	Tetrahydrocannabinol [presence] in urine by screen method >20 ng/ml	Laboratory Test	LOINC	Positive result
19416-7	Tetrahydrocannabinol [presence] in urine by confirmatory method	Laboratory Test	LOINC	Positive result
8175-2	Tetrahydrocannabinol [presence] in urine by samhsa screen method	Laboratory Test	LOINC	Positive result
21557-4	Tetrahydrocannabinol [presence] in urine by screen method >100 ng/ml	Laboratory Test	LOINC	Positive result
43834-1	Tetrahydrocannabinol [presence] in specimen	Laboratory Test	LOINC	Positive result
58047-2	Tetrahydrocannabinol [presence] in blood by confirmatory method (*note: 0 positive patients)	Laboratory Test	LOINC	Positive result
3435-5	Carboxy tetrahydrocannabinol [presence] in urine	Laboratory Test	LOINC	Positive result
19381-3	Carboxy tetrahydrocannabinol [presence] in urine by screen method	Laboratory Test	LOINC	Positive result
19382-1	Carboxy tetrahydrocannabinol [presence] in urine by confirmatory method	Laboratory Test	LOINC	Positive result
42492-9	Carboxy tetrahydrocannabinol [presence] in blood	Laboratory Test	LOINC	Positive result
26743-5	Carboxy tetrahydrocannabinol [presence] in serum or plasma	Laboratory Test	LOINC	Positive result
61063-4	Carboxy tetrahydrocannabinol [presence] in specimen	Laboratory Test	LOINC	Positive result
74678-4	Carboxy tetrahydrocannabinol [presence] in saliva (oral fluid) by confirmatory method	Laboratory Test	LOINC	Positive result

Appendix B. List of RxNorm Medication Terms and Logical Observation Identifiers, Names and Codes (LOINC) Laboratory Codes Used to Define Exposures in this Request

Code	Description	Code Category	Code Type	Filter
78754-9	11-hydroxy delta-9 tetrahydrocannabinol [presence] in urine by screen method (*note: 0 positive patients)	Laboratory Test	LOINC	Positive result

Cohort 1: All cannabis and cannabis-derived terms	
Group 1: Cannabis-derived product	**Time Restrictions**
Must Have:	
Cannabis or cannabis-derived product	7/1/2018 - 2/28/2022

Cohort 2: All cannabis and cannabis-derived terms, NLP	
Group 1: Cannabis-derived product	**Time Restrictions**
Must Have:	
Cannabis or cannabis-derived product [FILTER: NLP]	7/1/2018 - 2/28/2022

Cohort 3: All cannabidiol	
Group 1: Cannabidiol	**Time Restrictions**
Must Have:	
Cannabidiol	7/1/2018 - 2/28/2022

Cohort 4: Cannabidiol, NLP	
Group 1: Cannabidiol	**Time Restrictions**
Must Have:	
Cannabidiol [FILTER: NLP]	7/1/2018 - 2/28/2022

Cohort 5: Known Epidiolex	
Group 1: Epidiolex	**Time Restrictions**
Must Have:	
Cannabidiol [FILTER: Epidiolex brand]	7/1/2018 - 2/28/2022

Cohort 6: THC Lab	
Group 1: Positive Presence THC Lab	**Time Restrictions**
Must Have:	
THC Presence Lab Test [FILTER: Positive Result]	7/1/2018 - 2/28/2022

Cohort 7: All cannabis and cannabis-derived terms or lab result for positive presence of THC, excluding known Epidiolex	
Group 1: "Non-approved" Cannabis-derived product exposure	**Time Restrictions**
Must Have:	
Cannabis, cannabis-derived product, or THC presence lab test [FILTER: Positive Result]	7/1/2018 - 2/28/2022
Cannot Have:	
Cannabidiol [FILTER: Epidiolex brand]	7/1/2018 - 2/28/2022

Cohort 8: Cannabidiol, excluding Known Epidiolex	
Group 1: Cannabidiol	**Time Restrictions**
Must Have:	
Cannabidiol	7/1/2018 - 2/28/2022
Cannot Have:	
Cannabidiol [FILTER: Epidiolex brand]	7/1/2018 - 2/28/2022

Cohort 9: CBD and THC Exposure, excluding Known Epidiolex	
Group 1: Cannabidiol	**Time Restrictions**
Must Have:	
Cannabidiol	7/1/2018 - 2/28/2022
Cannot Have:	
Cannabidiol [FILTER: Epidiolex brand]	7/1/2018 - 2/28/2022
Event 2: THC Lab	**Time Restrictions**
Must Have:	
THC Presence Lab Test [FILTER: Positive Result]	within +/- 2 days of Group 1 (CBD)

#	Module	Analysis Type	Cohort(s)	Window	Index Event(s)	Characteristics or Outcomes
1	Analyze Outcomes	Characteristics	Cannabis	[-365, -1]	All Cannabis-related Terms	Top 10 Most Frequent Diagnoses (ICD-10 header code)
2	Analyze Outcomes	Characteristics	NLP_Cannabis	[-365, -1]	All Cannabis-related Terms, NLP-Derived	Top 10 Most Frequent Diagnoses (ICD-10 header code)
3	Analyze Outcomes	Characteristics	Cannabidiol	[-365, -1]	All Cannabidiol	Top 10 Most Frequent Diagnoses (ICD-10 header code)
4	Analyze Outcomes	Characteristics	NLP_Cannabidiol	[-365, -1]	All Cannabidiol, NLP-Derived	Top 10 Most Frequent Diagnoses (ICD-10 header code)
5	Analyze Outcomes	Characteristics	Epidiolex	[-365, -1]	Known Epidiolex	Top 10 Most Frequent Diagnoses (ICD-10 header code)
6	Analyze Outcomes	Characteristics	THC_Lab	[-365, -1]	Positive Lab Value for Presence of THC	Top 10 Most Frequent Diagnoses (ICD-10 header code)
7	Analyze Outcomes	Characteristics	Non-approved	[-365, -1]	All cannabis and cannabis-derived terms or lab result for positive presence of THC, excluding known Epidiolex	Top 10 Most Frequent Diagnoses (ICD-10 header code)
8	Analyze Outcomes	Characteristics	CBD_noEpidiolex	[-365, -1]	Cannabidiol, excluding known Epidiolex	Top 10 Most Frequent Diagnoses (ICD-10 header code)
9	Analyze Outcomes	Characteristics	CBD+THC	[-365, -1]	Cannabidiol, excluding known Epidiolex, AND a lab result for positive presence of THC within 2 days	Top 10 Most Frequent Diagnoses (ICD-10 header code)

#	Module	Analysis Type	Cohort(s)	Window	Index Event(s)	Characteristics or Outcomes
10	Analyze Outcomes	Risk	Cannabis	[0, 365]	All Cannabis-related Terms	Top 10 Most Frequent Diagnoses (ICD-10 header code)
11	Analyze Outcomes	Risk	NLP_Cannabis	[0, 365]	All Cannabis-related Terms, NLP-Derived	Top 10 Most Frequent Diagnoses (ICD-10 header code)
12	Analyze Outcomes	Risk	Cannabidiol	[0, 365]	All Cannabidiol	Top 10 Most Frequent Diagnoses (ICD-10 header code)
13	Analyze Outcomes	Risk	NLP_Cannabidiol	[0, 365]	All Cannabidiol, NLP-Derived	Top 10 Most Frequent Diagnoses (ICD-10 header code)
14	Analyze Outcomes	Explore Outcomes	Epidiolex	[0, 365]	Known Epidiolex	Top 10 Most Frequent Diagnoses (ICD-10 header code)
15	Analyze Outcomes	Risk	THC_Lab	[0, 365]	Positive Lab Value for Presence of THC	Top 10 Most Frequent Diagnoses (ICD-10 header code)
16	Analyze Outcomes	Risk	Non-approved	[0, 365]	All cannabis and cannabis-derived terms or lab result for positive presence of THC, excluding known Epidiolex	Top 10 Most Frequent Diagnoses (ICD-10 header code)
17	Analyze Outcomes	Risk	CBD_noEpidiolex	[0, 365]	Cannabidiol, excluding known Epidiolex	Top 10 Most Frequent Diagnoses (ICD-10 header code)
18	Analyze Outcomes	Explore Outcomes	CBD+THC	[0, 365]	Cannabidiol, excluding known Epidiolex, AND a lab result for positive presence of THC within 2 days	Top 10 Most Frequent Diagnoses (ICD-10 header code)