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).

If you are using a web page screen reader and are unable to access this document, please contact the Sentinel Operations Center for assistance at info@sentinelsystem.org.

Overview for Request: cder_iqp_wp039

Request ID: cder_iqp_wp039

Request Description: In this report we aimed to describe clinical characteristics of patients with an incident medication fact record for glucagon-like peptide-1 receptor agonists (GLP-1 RAs) (overall and by drug) between October 1, 2017 to September 30, 2023 in the TriNetX Live™ platform.

Data Source: We ran this query on August 7, 2024. This query contains data from 61 health care organizations (HCOs), provided through the TriNetX Live™ platform in their USA Network Minimal Shift (includes HCOs that shift between 0 and +/- 14 days). This includes all HCOs from the USA Network No Shift.

TriNetX aggregates electronic health record (EHR) systems data from its partner HCOs to create queryable datasets. TriNetX datasets primarily comprise 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: In this retrospective cohort study, we identified counts of individuals with an incident medication fact record for a GLP-1 RA overall and by drug. We built 32 distinct cohorts using the Query Builder module in the TriNetX Live™ platform.

Exposures of Interest: We examined GLP-1 RAs overall and by drug (albiglutide, dulaglutide, exenatide, liraglutide, lixisenatide, semaglutide, and tirzepatide).

We used RxNorm medication terms in the Query Builder module to identify the exposure of interest. In order to be included in a cohort, we required evidence of a prescription, administration, or dispensing of the relevant non-insulin antidiabetic of interest in the time window of interest.

Please see Appendix A for the list of RxNorm medication terms used to define the exposures of interest in this request.

Cohort Eligibility Criteria: Individuals of all ages were included. They were eligible to be an incident user in a given cohort if they had:

1) Evidence of the exposure of interest in the window of interest, and
2) Evidence of a visit from the start of the window of interest to the same day of the exposure of interest, and
3) No evidence of the exposure of interest prior to the window of interest

Windows of interest included: 10/1/17-9/30/23, 10/1/17-9/30/19, 10/1/19-9/30/21, and 10/1/21-9/30/23.

Please see Appendix B for the list of terms used to define inclusion criteria in this request.

Baseline Characteristics: We utilized the Compare Outcomes Analytics module to assess the following clinical characteristics in the 183-days prior to the index date: encounter for Type 2 Diabetes, encounter for Overweight/Obesity, Body Mass Index (BMI) category, BMI measurement present, BMI mean, height measurement present, weight measurement present, prior use of blood glucose lowering drugs, excluding insulins, biguanides, dipeptidyl peptidase 4 inhibitors, sodium-glucose co-transporter 2 inhibitors, and sulfonylureas.

Please see Appendix C for the list of codes used to define characteristics in this request.

Please see Appendix D for specifications defining query builder modules in this request.

Overview for Request: cder_iqp_wp039

Limitations: Algorithms used to define exposures, characteristics, and pregnancy, 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, not all HCOs provide brand name or route 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 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. 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%.

The TriNetX Live™ platform uses RxNorm terms to identify medications, specifically the primary ingredient RxNorm terms.

- In the case of fixed dose combinations/co-packaged medications, the drugs are identified in the platform as the presence of primary ingredient RxNorm terms for all the individual medications on the same day (even if a multiple ingredient RxNorm term is made available by the National Library of Medicine), under the assumption that this refers only to the combined drugs and not two individual drugs prescribed concomitantly.

- A subset of HCOs that contribute to the TriNetX USA Minimal Shift Network may implement date shifting between 0 and 14 days in either direction at the level of the patient record prior to data ingestion at TriNetX as a method to preserve patient privacy. When interpreting the results of an analysis, the impact of date shifting should be considered and readers should exercise caution when extrapolating information related to time.

Notes: We ran this query on August 7, 2024. 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).

Glossary of Terms for Analyses Using TriNetX Live™ Platform*

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 certain laboratory terms, TriNetX aggregates Logical Observation Identifiers Names and Codes (LOINC) laboratory codes 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.

*all terms may not be used in this report

Table 1a. Frequency of Diabetes and Obesity Characteristics Among Incident Glucagon-Like Peptide-1 Receptor Agonist (GLP-1 RA) Medication Users of all Ages in the TriNetX Live™ USA Network Minimal Shift[1] from October 1, 2017 to September 30, 2023, by Time Period of Incident Use

	10/1/17 - 9/30/23		10/1/17 - 9/30/19		10/1/19 - 9/30/21		10/1/21 - 9/30/23	
	Number/ Mean	Percent/ Standard Deviation[2]	Number/ Mean	Percent/ Standard Deviation[2]	Number/ Mean	Percent/ Standard Deviation[2]	Number/ Mean	Percent/ Standard Deviation[2]
Overall								
Total Patients	694,870	100.0%	94,430	100.0%	174,210	100.0%	426,240	100.0%
Diagnosis-Defined Characteristics[3]								
Encounter for Type 2 Diabetes	256,290	36.9%	37,920	40.2%	72,550	41.6%	139,010	32.6%
Encounter for Overweight/Obesity	163,130	23.5%	17,750	18.8%	34,540	19.8%	108,640	25.5%
Body Mass Index (kilograms per square meter)								
19.9 or less	1,090	0.2%	150	0.2%	240	0.1%	690	0.2%
20-29	12,360	1.8%	1,700	1.8%	2,870	1.6%	7,430	1.7%
30-39	60,200	8.7%	6,550	6.9%	11,990	6.9%	40,950	9.6%
40 or greater	55,680	8.0%	5,620	6.0%	11,100	6.4%	38,420	9.0%
Clinical Observation-Defined Characteristics[4]								
Any Body Mass Index Observation	318,850	45.9%	35,130	37.2%	71,110	40.8%	208,180	48.8%
Body Mass Index (kilograms per square meter)	36.5	8.11	36.1	7.97	35.9	8.23	36.8	8.08
Any Height Observation	339,760	48.9%	36,740	38.9%	75,340	43.2%	223,440	52.4%
Any Weight Observation	301,130	43.3%	32,920	34.9%	67,840	38.9%	195,920	46.0%
Prior Medication Use[5]								
Blood glucose lowering drugs, excluding insulins[6]	199,570	28.7%	29,660	31.4%	57,210	32.8%	108,080	25.4%
Biguanides	150,630	21.7%	22,320	23.6%	42,960	24.7%	81,920	19.2%

Table 1a. Frequency of Diabetes and Obesity Characteristics Among Incident Glucagon-Like Peptide-1 Receptor Agonist (GLP-1 RA) Medication Users of all Ages in the TriNetX Live™ USA Network Minimal Shift[1] from October 1, 2017 to September 30, 2023, by Time Period of Incident Use

	10/1/17 - 9/30/23		10/1/17 - 9/30/19		10/1/19 - 9/30/21		10/1/21 - 9/30/23	
	Number/ Mean	Percent/ Standard Deviation[2]	Number/ Mean	Percent/ Standard Deviation[2]	Number/ Mean	Percent/ Standard Deviation[2]	Number/ Mean	Percent/ Standard Deviation[2]
Overall								
Dipeptidyl peptidase 4 inhibitors	31,830	4.6%	6,560	6.9%	10,530	6.0%	13,840	3.2%
Sodium-glucose co-transporter 2 inhibitors	44,440	6.4%	4,680	5.0%	12,070	6.9%	26,820	6.3%
Sulfonylureas	49,770	7.2%	10,050	10.6%	16,680	9.6%	22,860	5.4%

NOTE: All counts provided through the TriNetX Live™ platform are rounded up to the nearest 10 to protect patient privacy. For this reason, number of incident users in each time period may not sum to the number in the overall query period. Percentages were calculated based on the rounded estimates, and are presented here rounded to the tenths position to avoid mischaracterizing the precision of the measurement. Due to rounding, all estimates should be interpreted as ranges, with the lower value of the range ≤ 0.01% less than the presented value unless otherwise noted.

NOTE: TriNetX applies data sanitization to fields such as BMI, sanitizing BMI <0.1 and >50. For patients with BMI >50, these BMI observations are omitted to preserve patient privacy and confidentiality.

[1] A subset of HCOs that contribute to the TriNetX USA network may implement date shifting - between 0 and 14 days in either direction - at the level of the patient record prior to data ingestion at TriNetX as a method to preserve patient privacy. When interpreting the results of an analysis, the impact of date shifting should be considered and readers should exercise caution when extrapolating information related to time.

[2] Percentages in this column are calculated using the count of total incident users of the time period in the column header as the denominator.

[3] Defined using ICD-10-CM codes

[4] Defined using TNX Curated codes. These characteristics are assessed closest to index date.

[5] Each class below is defined using Anatomic Therapeutic Classification (ATC) codes. **Blood glucose lowering drugs, excl. insulins includes**: dulaglutide, semaglutide, liraglutide, exenatide, lixisenatide, albiglutide, metformin, glipizide, glimepiride, chlorpropamide, tolbutamide, acetohexamide, glyburide, tolazamide, gliclazide, empagliflozin, dapagliflozin, canagliflozin, ertugliflozin, sotagliflozin, bexagliflozin, sitagliptin, linagliptin, alogliptin, saxagliptin, vildagliptin, pioglitazone, rosiglitazone, troglitazone, acarbose, miglitol, tirzepatide, repaglinide, nateglinide, guar gum, pramlintide. **Biguanides includes**: metformin. **Dipeptidyl peptidase 4 inhibitors includes**: sitagliptin, linagliptin, alogliptin, saxagliptin, vildagliptin. **Sodium-glucose co-transporter 2 inhibitors includes**: empagliflozin, dapagliflozin, canagliflozin, ertugliflozin, sotagliflozin, bexagliflozin. **Sulfonylureas includes**: glipizide, glimepiride, chlorpropamide, tolbutamide, acetohexamide, glyburide, tolazamide, gliclazide.

[6] Although this ATC category contains the index defining drugs dulaglutide, semaglutide, liraglutide, exenatide, lixisenatide, albiglutide, and tirzepatide, prior use of these medications will not be captured in this row due to incident-cohort design.

Table 1b. Frequency of Diabetes and Obesity Characteristics Among Incident Dulaglutide Users of all Ages in the TriNetX Live™ USA Network Minimal Shift[1] from October 1, 2017 to September 30, 2023, by Time Period of Incident Use

	10/1/17 - 9/30/23		10/1/17 - 9/30/19		10/1/19 - 9/30/21		10/1/21 - 9/30/23	
	Number/ Mean	Percent/ Standard Deviation[2]	Number/ Mean	Percent/ Standard Deviation[2]	Number/ Mean	Percent/ Standard Deviation[2]	Number/ Mean	Percent/ Standard Deviation[2]
Dulaglutide								
Total Patients	351,080	100.0%	76,280	100.0%	116,570	100.0%	158,240	100.0%
Diagnosis-Defined Characteristics[3]								
Encounter for Type 2 Diabetes	189,840	54.1%	40,330	52.9%	63,100	54.1%	84,570	53.4%
Encounter for Overweight/Obesity	78,780	22.4%	15,190	19.9%	23,220	19.9%	39,620	25.0%
Body Mass Index (kilograms per square meter)								
19.9 or less	730	0.2%	120	0.2%	230	0.2%	380	0.2%
20-29	7,260	2.1%	1,610	2.1%	2,270	1.9%	3,390	2.1%
30-39	29,110	8.3%	5,740	7.5%	8,610	7.4%	14,690	9.3%
40 or greater	26,370	7.5%	4,690	6.1%	7,520	6.5%	13,990	8.8%
Clinical Observation-Defined Characteristics[4]								
Any Body Mass Index Observation	161,900	46.1%	30,390	39.8%	50,750	43.5%	78,510	49.6%
Body Mass Index (kilograms per square meter)	35.9	8.19	35.9	7.8	35.7	8.11	36	8.38
Any Height Observation	172,090	49.0%	31,870	41.8%	53,910	46.2%	84,230	53.2%
Any Weight Observation	156,790	44.7%	28,550	37.4%	49,580	42.5%	76,400	48.3%
Prior Medication Use[5]								
Blood glucose lowering drugs, excluding insulins[6]	162,930	46.4%	35,420	46.4%	52,510	45.0%	73,860	46.7%
Biguanides	107,050	30.5%	24,490	32.1%	35,900	30.8%	45,760	28.9%

Table 1b. Frequency of Diabetes and Obesity Characteristics Among Incident Dulaglutide Users of all Ages in the TriNetX Live™ USA Network Minimal Shift[1] from October 1, 2017 to September 30, 2023, by Time Period of Incident Use

	10/1/17 - 9/30/23		10/1/17 - 9/30/19		10/1/19 - 9/30/21		10/1/21 - 9/30/23	
	Number/ Mean	Percent/ Standard Deviation[2]	Number/ Mean	Percent/ Standard Deviation[2]	Number/ Mean	Percent/ Standard Deviation[2]	Number/ Mean	Percent/ Standard Deviation[2]
Dulaglutide								
Dipeptidyl peptidase 4 inhibitors	24,630	7.0%	7,160	9.4%	9,050	7.8%	8,160	5.2%
Sodium-glucose co-transporter 2 inhibitors	34,410	9.8%	6,060	7.9%	10,750	9.2%	17,480	11.0%
Sulfonylureas	41,150	11.7%	11,120	14.6%	14,880	12.8%	14,870	9.4%

NOTE: All counts provided through the TriNetX Live™ platform are rounded up to the nearest 10 to protect patient privacy. For this reason, number of incident users in each time period may not sum to the number in the overall query period. Percentages were calculated based on the rounded estimates, and are presented here rounded to the tenths position to avoid mischaracterizing the precision of the measurement. Due to rounding, all estimates should be interpreted as ranges, with the lower value of the range ≤ 0.01% less than the presented value unless otherwise noted.

NOTE: TriNetX applies data sanitization to fields such as BMI, sanitizing BMI <0.1 and >50. For patients with BMI >50, these BMI observations are omitted to preserve patient privacy and confidentiality.

[1] A subset of HCOs that contribute to the TriNetX USA network may implement date shifting - between 0 and 14 days in either direction - at the level of the patient record prior to data ingestion at TriNetX as a method to preserve patient privacy. When interpreting the results of an analysis, the impact of date shifting should be considered and readers should exercise caution when extrapolating information related to time.

[2] Percentages in this column are calculated using the count of total incident users of the time period in the column header as the denominator.

[3] Defined using ICD-10-CM codes

[4] Defined using TNX Curated codes. These characteristics are assessed closest to index date.

[5] Each class below is defined using Anatomic Therapeutic Classification (ATC) codes. **Blood glucose lowering drugs, excl. insulins includes**: dulaglutide, semaglutide, liraglutide, exenatide, lixisenatide, albiglutide, metformin, glipizide, glimepiride, chlorpropamide, tolbutamide, acetohexamide, glyburide, tolazamide, gliclazide, empagliflozin, dapagliflozin, canagliflozin, ertugliflozin, sotagliflozin, bexagliflozin, sitagliptin, linagliptin, alogliptin, saxagliptin, vildagliptin, pioglitazone, rosiglitazone, troglitazone, acarbose, miglitol, tirzepatide, repaglinide, nateglinide, guar gum, pramlintide. **Biguanides includes**: metformin. **Dipeptidyl peptidase 4 inhibitors includes**: sitagliptin, linagliptin, alogliptin, saxagliptin, vildagliptin. **Sodium-glucose co-transporter 2 inhibitors includes**: empagliflozin, dapagliflozin, canagliflozin, ertugliflozin, sotagliflozin, bexagliflozin. **Sulfonylureas includes**: glipizide, glimepiride, chlorpropamide, tolbutamide, acetohexamide, glyburide, tolazamide, gliclazide.

[6] Although this ATC category contains the index defining drug dulaglutide, prior use of this medication will not be captured in this row due to incident-cohort design.

Sentinel

Table 1c. Frequency of Diabetes and Obesity Characteristics Among Incident Liraglutide Users of all Ages in the TriNetX Live™ USA Network Minimal Shift[1] from October 1, 2017 to September 30, 2023, by Time Period of Incident Use

	10/1/17 - 9/30/23		10/1/17 - 9/30/19		10/1/19 - 9/30/21		10/1/21 - 9/30/23	
	Number/ Mean	Percent/ Standard Deviation[2]	Number/ Mean	Percent/ Standard Deviation[2]	Number/ Mean	Percent/ Standard Deviation[2]	Number/ Mean	Percent/ Standard Deviation[2]
Liraglutide								
Total Patients	181,490	100.0%	61,570	100.0%	56,370	100.0%	63,560	100.0%
Diagnosis-Defined Characteristics[3]								
Encounter for Type 2 Diabetes	64,190	35.4%	24,300	39.5%	20,150	35.7%	16,210	25.5%
Encounter for Overweight/Obesity	62,370	34.4%	15,870	25.8%	16,750	29.7%	27,900	43.9%
Body Mass Index (kilograms per square meter)								
19.9 or less	330	0.2%	130	0.2%	90	0.2%	110	0.2%
20-29	3,060	1.7%	870	1.4%	760	1.3%	1,230	1.9%
30-39	20,360	11.2%	4,670	7.6%	5,100	9.0%	9,640	15.2%
40 or greater	20,850	11.5%	4,680	7.6%	5,520	9.8%	9,580	15.1%
Clinical Observation-Defined Characteristics[4]								
Any Body Mass Index Observation	93,210	51.4%	27,690	45.0%	27,230	48.3%	36,920	58.1%
Body Mass Index (kilograms per square meter)	37.9	8.31	37.4	8.16	37.9	8.48	38.3	8.27
Any Height Observation	96,850	53.4%	27,480	44.6%	26,820	47.6%	38,130	60.0%
Any Weight Observation	89,920	49.5%	26,120	42.4%	26,540	47.1%	35,900	56.5%
Prior Medication Use[5]								
Blood glucose lowering drugs, excluding insulins[6]	63,340	34.9%	19,920	32.4%	17,050	30.2%	24,660	38.8%
Biguanides	37,280	20.5%	14,470	23.5%	11,650	20.7%	10,020	15.8%

Table 1c. Frequency of Diabetes and Obesity Characteristics Among Incident Liraglutide Users of all Ages in the TriNetX Live™ USA Network Minimal Shift[1] from October 1, 2017 to September 30, 2023, by Time Period of Incident Use

	10/1/17 - 9/30/23		10/1/17 - 9/30/19		10/1/19 - 9/30/21		10/1/21 - 9/30/23	
	Number/ Mean	Percent/ Standard Deviation[2]	Number/ Mean	Percent/ Standard Deviation[2]	Number/ Mean	Percent/ Standard Deviation[2]	Number/ Mean	Percent/ Standard Deviation[2]
Liraglutide								
Dipeptidyl peptidase 4 inhibitors	6,420	3.5%	3,300	5.4%	1,890	3.4%	920	1.4%
Sodium-glucose co-transporter 2 inhibitors	8,530	4.7%	2,750	4.5%	2,690	4.8%	2,840	4.5%
Sulfonylureas	10,960	6.0%	5,210	8.5%	3,390	6.0%	1,990	3.1%

NOTE: All counts provided through the TriNetX Live™ platform are rounded up to the nearest 10 to protect patient privacy. For this reason, number of incident users in each time period may not sum to the number in the overall query period. Percentages were calculated based on the rounded estimates, and are presented here rounded to the tenths position to avoid mischaracterizing the precision of the measurement. Due to rounding, all estimates should be interpreted as ranges, with the lower value of the range ≤ 0.02% less than the presented value unless otherwise noted.

NOTE: TriNetX applies data sanitization to fields such as BMI, sanitizing BMI <0.1 and >50. For patients with BMI >50, these BMI observations are omitted to preserve patient privacy and confidentiality.

[1] A subset of HCOs that contribute to the TriNetX USA network may implement date shifting - between 0 and 14 days in either direction - at the level of the patient record prior to data ingestion at TriNetX as a method to preserve patient privacy. When interpreting the results of an analysis, the impact of date shifting should be considered and readers should exercise caution when extrapolating information related to time.

[2] Percentages in this column are calculated using the count of total incident users of the time period in the column header as the denominator.

[3] Defined using ICD-10-CM codes

[4] Defined using TNX Curated codes. These characteristics are assessed closest to index date.

[5] Each class below is defined using Anatomic Therapeutic Classification (ATC) codes. **Blood glucose lowering drugs, excl. insulins includes**: dulaglutide, semaglutide, liraglutide, exenatide, lixisenatide, albiglutide, metformin, glipizide, glimepiride, chlorpropamide, tolbutamide, acetohexamide, glyburide, tolazamide, gliclazide, empagliflozin, dapagliflozin, canagliflozin, ertugliflozin, sotagliflozin, bexagliflozin, sitagliptin, linagliptin, alogliptin, saxagliptin, vildagliptin, pioglitazone, rosiglitazone, troglitazone, acarbose, miglitol, tirzepatide, repaglinide, nateglinide, guar gum, pramlintide. **Biguanides includes**: metformin. **Dipeptidyl peptidase 4 inhibitors includes**: sitagliptin, linagliptin, alogliptin, saxagliptin, vildagliptin. **Sodium-glucose co-transporter 2 inhibitors includes**: empagliflozin, dapagliflozin, canagliflozin, ertugliflozin, sotagliflozin, bexagliflozin. **Sulfonylureas includes**: glipizide, glimepiride, chlorpropamide, tolbutamide, acetohexamide, glyburide, tolazamide, gliclazide.

[6] Although this ATC category contains the index defining drug liraglutide, prior use of this medication will not be captured in this row due to incident-cohort design.

Sentinel

Table 1d. Frequency of Diabetes and Obesity Characteristics Among Incident Semaglutide Users of all Ages in the TriNetX Live™ USA Network Minimal Shift[1] from October 1, 2017 to September 30, 2023, by Time Period of Incident Use

	10/1/17 - 9/30/23		10/1/17 - 9/30/19		10/1/19 - 9/30/21		10/1/21 - 9/30/23	
	Number/ Mean	Percent/ Standard Deviation[2]	Number/ Mean	Percent/ Standard Deviation[2]	Number/ Mean	Percent/ Standard Deviation[2]	Number/ Mean	Percent/ Standard Deviation[2]
Semaglutide								
Total Patients	546,930	100.0%	29,000	100.0%	115,820	100.0%	402,120	100.0%
Diagnosis-Defined Characteristics[3]								
Encounter for Type 2 Diabetes	207,720	38.0%	15,970	55.1%	57,270	49.4%	134,030	33.3%
Encounter for Overweight/Obesity	164,140	30.0%	8,790	30.3%	31,870	27.5%	123,260	30.7%
Body Mass Index (kilograms per square meter)								
19.9 or less	960	0.2%	90	0.3%	160	0.1%	710	0.2%
20-29	9,910	1.8%	760	2.6%	2,160	1.9%	7,000	1.7%
30-39	58,870	10.8%	3,240	11.2%	10,630	9.2%	44,980	11.2%
40 or greater	57,690	10.5%	2,800	9.7%	10,330	8.9%	4,490	1.1%
Clinical Observation-Defined Characteristics[4]								
Any Body Mass Index Observation	286,260	52.3%	13,600	46.9%	57,000	49.2%	215,040	53.5%
Body Mass Index (kilograms per square meter)	37.3	8.02	36.8	7.74	36.7	8.17	37.4	8
Any Height Observation	306,720	56.1%	13,210	45.6%	59,950	51.8%	233,030	58.0%
Any Weight Observation	266,700	48.8%	12,370	42.7%	53,000	45.8%	200,710	49.9%
Prior Medication Use[5]								
Blood glucose lowering drugs, excluding insulins[6]	191,860	35.1%	15,920	54.9%	52,750	45.5%	122,870	30.6%
Biguanides	124,560	22.8%	10,390	35.8%	35,930	31.0%	77,990	19.4%

Table 1d. Frequency of Diabetes and Obesity Characteristics Among Incident Semaglutide Users of all Ages in the TriNetX Live™ USA Network Minimal Shift[1] from October 1, 2017 to September 30, 2023, by Time Period of Incident Use

	10/1/17 - 9/30/23		10/1/17 - 9/30/19		10/1/19 - 9/30/21		10/1/21 - 9/30/23	
	Number/ Mean	Percent/ Standard Deviation[2]	Number/ Mean	Percent/ Standard Deviation[2]	Number/ Mean	Percent/ Standard Deviation[2]	Number/ Mean	Percent/ Standard Deviation[2]
Semaglutide								
Dipeptidyl peptidase 4 inhibitors	21,360	3.9%	2,230	7.7%	7,560	6.5%	11,530	2.9%
Sodium-glucose co-transporter 2 inhibitors	42,270	7.7%	3,390	11.7%	12,330	10.6%	26,510	6.6%
Sulfonylureas	34,170	6.2%	3,380	11.7%	11,900	10.3%	19,570	4.9%

NOTE: All counts provided through the TriNetX Live™ platform are rounded up to the nearest 10 to protect patient privacy. For this reason, number of incident users in each time period may not sum to the number in the overall query period. Percentages were calculated based on the rounded estimates, and are presented here rounded to the tenths position to avoid mischaracterizing the precision of the measurement. Due to rounding, all estimates should be interpreted as ranges, with the lower value of the range ≤ 0.03% less than the presented value unless otherwise noted.

NOTE: TriNetX applies data sanitization to fields such as BMI, sanitizing BMI <0.1 and >50. For patients with BMI >50, these BMI observations are omitted to preserve patient privacy and confidentiality.

[1] A subset of HCOs that contribute to the TriNetX USA network may implement date shifting - between 0 and 14 days in either direction - at the level of the patient record prior to data ingestion at TriNetX as a method to preserve patient privacy. When interpreting the results of an analysis, the impact of date shifting should be considered and readers should exercise caution when extrapolating information related to time.

[2] Percentages in this column are calculated using the count of total incident users of the time period in the column header as the denominator.

[3] Defined using ICD-10-CM codes

[4] Defined using TNX Curated codes. These characteristics are assessed closest to index date.

[5] Each class below is defined using Anatomic Therapeutic Classification (ATC) codes. **Blood glucose lowering drugs, excl. insulins includes**: dulaglutide, semaglutide, liraglutide, exenatide, lixisenatide, albiglutide, metformin, glipizide, glimepiride, chlorpropamide, tolbutamide, acetohexamide, glyburide, tolazamide, gliclazide, empagliflozin, dapagliflozin, canagliflozin, ertugliflozin, sotagliflozin, bexagliflozin, sitagliptin, linagliptin, alogliptin, saxagliptin, vildagliptin, pioglitazone, rosiglitazone, troglitazone, acarbose, miglitol, tirzepatide, repaglinide, nateglinide, guar gum, pramlintide. **Biguanides includes**: metformin. **Dipeptidyl peptidase 4 inhibitors includes**: sitagliptin, linagliptin, alogliptin, saxagliptin, vildagliptin. **Sodium-glucose co-transporter 2 inhibitors includes**: empagliflozin, dapagliflozin, canagliflozin, ertugliflozin, sotagliflozin, bexagliflozin. **Sulfonylureas includes**: glipizide, glimepiride, chlorpropamide, tolbutamide, acetohexamide, glyburide, tolazamide, gliclazide.

[6] Although this ATC category contains the index defining drug semaglutide, prior use of this medication will not be captured in this row due to incident-cohort design.

Sentinel

Table 1e. Frequency of Diabetes and Obesity Characteristics Among Incident Albiglutide Users of all Ages in the TriNetX Live™ USA Network Minimal Shift[1] from October 1, 2017 to September 30, 2023, by Time Period of Incident Use

	10/1/17 - 9/30/23		10/1/17 - 9/30/19		10/1/19 - 9/30/21		10/1/21 - 9/30/23	
	Number/ Mean	Percent/ Standard Deviation[2]	Number/ Mean	Percent/ Standard Deviation[2]	Number/ Mean	Percent/ Standard Deviation[2, 7]	Number/ Mean	Percent/ Standard Deviation[2, 8]
Albiglutide								
Total Patients	940	100.0%	850	100.0%	80	100.0%	20	100.0%
Diagnosis-Defined Characteristics[3]								
Encounter for Type 2 Diabetes	400	42.6%	400	47.1%	30	37.5%	10	50.0%
Encounter for Overweight/Obesity	160	17.0%	150	17.6%	20	25.0%	10	50.0%
Body Mass Index (kilograms per square meter)							10	
19.9 or less	0	0.0%	0	0.0%	0	0.0%	0	0.0%
20-29	10	1.1%	10	1.2%	10	12.5%	10	50.0%
30-39	40	4.3%	40	4.7%	10	12.5%	10	50.0%
40 or greater	50	5.3%	50	5.9%	10	12.5%	10	50.0%
Clinical Observation-Defined Characteristics[4]								
Any Body Mass Index Observation	350	37.2%	320	37.6%	30	37.5%	10	50.0%
Body Mass Index (kilograms per square meter)	36	7.64	36	7.53	35.1	7.27	37.5	10.9
Any Height Observation	350	37.2%	310	36.5%	30	37.5%	10	50.0%
Any Weight Observation	340	36.2%	300	35.3%	30	37.5%	10	50.0%
Prior Medication Use[5]								
Blood glucose lowering drugs, excluding insulins[6]	330	35.1%	340	40.0%	40	50.0%	10	50.0%
Biguanides	220	23.4%	220	25.9%	20	25.0%	10	50.0%

Table 1e. Frequency of Diabetes and Obesity Characteristics Among Incident Albiglutide Users of all Ages in the TriNetX Live™ USA Network Minimal Shift[1] from October 1, 2017 to September 30, 2023, by Time Period of Incident Use

	10/1/17 - 9/30/23		10/1/17 - 9/30/19		10/1/19 - 9/30/21		10/1/21 - 9/30/23	
	Number/ Mean	Percent/ Standard Deviation[2]	Number/ Mean	Percent/ Standard Deviation[2]	Number/ Mean	Percent/ Standard Deviation[2, 7]	Number/ Mean	Percent/ Standard Deviation[2, 8]
Albiglutide								
Dipeptidyl peptidase 4 inhibitors	50	5.3%	50	5.9%	10	12.5%	0	0.0%
Sodium-glucose co-transporter 2 inhibitors	60	6.4%	60	7.1%	10	12.5%	10	50.0%
Sulfonylureas	90	9.6%	100	11.8%	10	12.5%	10	50.0%

NOTE: All counts provided through the TriNetX Live™ platform are rounded up to the nearest 10 to protect patient privacy. For this reason, number of incident users in each time period may not sum to the number in the overall query period. Percentages were calculated based on the rounded estimates, and are presented here rounded to the tenths position to avoid mischaracterizing the precision of the measurement. Due to rounding, all estimates should be interpreted as ranges, with the lower value of the range ≤ 1.06% less than the presented value unless otherwise noted.

NOTE: TriNetX applies data sanitization to fields such as BMI, sanitizing BMI <0.1 and >50. For patients with BMI >50, these BMI observations are omitted to preserve patient privacy and confidentiality.

[1] A subset of HCOs that contribute to the TriNetX USA network may implement date shifting - between 0 and 14 days in either direction - at the level of the patient record prior to data ingestion at TriNetX as a method to preserve patient privacy. When interpreting the results of an analysis, the impact of date shifting should be considered and readers should exercise caution when extrapolating information related to time.

[2] Percentages in this column are calculated using the count of total incident users of the time period in the column header as the denominator.

[3] Defined using ICD-10-CM codes

[4] Defined using TNX Curated codes. These characteristics are assessed closest to index date.

[5] Each class below is defined using Anatomic Therapeutic Classification (ATC) codes. **Blood glucose lowering drugs, excl. insulins includes**: dulaglutide, semaglutide, liraglutide, exenatide, lixisenatide, albiglutide, metformin, glipizide, glimepiride, chlorpropamide, tolbutamide, acetohexamide, glyburide, tolazamide, gliclazide, empagliflozin, dapagliflozin, canagliflozin, ertugliflozin, sotagliflozin, bexagliflozin, sitagliptin, linagliptin, alogliptin, saxagliptin, vildagliptin, pioglitazone, rosiglitazone, troglitazone, acarbose, miglitol, tirzepatide, repaglinide, nateglinide, guar gum, pramlintide. **Biguanides includes**: metformin. **Dipeptidyl peptidase 4 inhibitors includes**: sitagliptin, linagliptin, alogliptin, saxagliptin, vildagliptin. **Sodium-glucose co-transporter 2 inhibitors includes**: empagliflozin, dapagliflozin, canagliflozin, ertugliflozin, sotagliflozin, bexagliflozin. **Sulfonylureas includes**: glipizide, glimepiride, chlorpropamide, tolbutamide, acetohexamide, glyburide, tolazamide, gliclazide.

[6] Although this ATC category contains the index defining drug albiglutide, prior use of this medication will not be captured in this row due to incident-cohort design.

[7] 10/1/19 - 9/30/21: Due to rounding, all estimates should be interpreted as ranges, with the presented value equivalent to the high end of the range. Due to a small denominator in this column, the lower value of the range is 11.25% less than the presented value.

[8] 10/1/21 - 9/30/23: Due to rounding, all estimates should be interpreted as ranges, with the presented value equivalent to the high end of the range. Due to a small denominator in this column, the lower value of the range is 45% less than the presented value.

Sentinel

Table 1f. Frequency of Diabetes and Obesity Characteristics Among Incident Exenatide Users of all Ages in the TriNetX Live™ USA Network Minimal Shift[1] from October 1, 2017 to September 30, 2023, by Time Period of Incident Use

	10/1/17 - 9/30/23		10/1/17 - 9/30/19		10/1/19 - 9/30/21		10/1/21 - 9/30/23	
	Number/ Mean	Percent/ Standard Deviation[2]	Number/ Mean	Percent/ Standard Deviation[2]	Number/ Mean	Percent/ Standard Deviation[2]	Number/ Mean	Percent/ Standard Deviation[2, 7]
Exenatide								
Total Patients	34,430	100.0%	17,080	100.0%	11,510	100.0%	5,840	100.0%
Diagnosis-Defined Characteristics[3]								
Encounter for Type 2 Diabetes	18,600	54.0%	9,110	53.3%	6,040	52.5%	3,170	54.3%
Encounter for Overweight/Obesity	7,620	22.1%	3,450	20.2%	2,460	21.4%	1,600	27.4%
Body Mass Index (kilograms per square meter)								
19.9 or less	30	0.1%	10	0.1%	10	0.1%	10	0.2%
20-29	660	1.9%	290	1.7%	230	2.0%	140	2.4%
30-39	2,700	7.8%	1,170	6.9%	900	7.8%	620	10.6%
40 or greater	2,640	7.7%	1,130	6.6%	890	7.7%	570	9.8%
Clinical Observation-Defined Characteristics[4]								
Any Body Mass Index Observation	15,910	46.2%	7,790	45.6%	4,730	41.1%	3,010	51.5%
Body Mass Index (kilograms per square meter)	36.5	8.21	36.5	8.07	36.5	8.34	36.4	8.39
Any Height Observation	15,500	45.0%	7,450	43.6%	4,610	40.1%	3,070	52.6%
Any Weight Observation	14,720	42.8%	6,990	40.9%	4,490	39.0%	2,860	49.0%
Prior Medication Use[5]								
Blood glucose lowering drugs, excluding insulins[6]	16,770	48.7%	7,990	46.8%	5,330	46.3%	3,270	56.0%
Biguanides	10,320	30.0%	5,170	30.3%	3,340	29.0%	1,710	29.3%

Table 1f. Frequency of Diabetes and Obesity Characteristics Among Incident Exenatide Users of all Ages in the TriNetX Live™ USA Network Minimal Shift[1] from October 1, 2017 to September 30, 2023, by Time Period of Incident Use

	10/1/17 - 9/30/23		10/1/17 - 9/30/19		10/1/19 - 9/30/21		10/1/21 - 9/30/23	
	Number/ Mean	Percent/ Standard Deviation[2]	Number/ Mean	Percent/ Standard Deviation[2]	Number/ Mean	Percent/ Standard Deviation[2]	Number/ Mean	Percent/ Standard Deviation[2, 7]
Exenatide								
Dipeptidyl peptidase 4 inhibitors	2,400	7.0%	1,430	8.4%	730	6.3%	210	3.6%
Sodium-glucose co-transporter 2 inhibitors	3,320	9.6%	1,370	8.0%	1,230	10.7%	720	12.3%
Sulfonylureas	4,500	13.1%	2,380	13.9%	1,410	12.3%	570	9.8%

NOTE: All counts provided through the TriNetX Live™ platform are rounded up to the nearest 10 to protect patient privacy. For this reason, number of incident users in each time period may not sum to the number in the overall query period. Percentages were calculated based on the rounded estimates, and are presented here rounded to the tenths position to avoid mischaracterizing the precision of the measurement. Due to rounding, all estimates should be interpreted as ranges, with the lower value of the range ≤ 0.08% less than the presented value unless otherwise noted.

NOTE: TriNetX applies data sanitization to fields such as BMI, sanitizing BMI <0.1 and >50. For patients with BMI >50, these BMI observations are omitted to preserve patient privacy and confidentiality.

[1] A subset of HCOs that contribute to the TriNetX USA network may implement date shifting - between 0 and 14 days in either direction - at the level of the patient record prior to data ingestion at TriNetX as a method to preserve patient privacy. When interpreting the results of an analysis, the impact of date shifting should be considered and readers should exercise caution when extrapolating information related to time.

[2] Percentages in this column are calculated using the count of total incident users of the time period in the column header as the denominator.

[3] Defined using ICD-10-CM codes

[4] Defined using TNX Curated codes. These characteristics are assessed closest to index date.

[5] Each class below is defined using Anatomic Therapeutic Classification (ATC) codes. **Blood glucose lowering drugs, excl. insulins includes**: dulaglutide, semaglutide, liraglutide, exenatide, lixisenatide, albiglutide, metformin, glipizide, glimepiride, chlorpropamide, tolbutamide, acetohexamide, glyburide, tolazamide, gliclazide, empagliflozin, dapagliflozin, canagliflozin, ertugliflozin, sotagliflozin, bexagliflozin, sitagliptin, linagliptin, alogliptin, saxagliptin, vildagliptin, pioglitazone, rosiglitazone, troglitazone, acarbose, miglitol, tirzepatide, repaglinide, nateglinide, guar gum, pramlintide. **Biguanides includes**: metformin. **Dipeptidyl peptidase 4 inhibitors includes**: sitagliptin, linagliptin, alogliptin, saxagliptin, vildagliptin. **Sodium-glucose co-transporter 2 inhibitors includes**: empagliflozin, dapagliflozin, canagliflozin, ertugliflozin, sotagliflozin, bexagliflozin. **Sulfonylureas includes**: glipizide, glimepiride, chlorpropamide, tolbutamide, acetohexamide, glyburide, tolazamide, gliclazide.

[6] Although this ATC category contains the index defining drug exenatide, prior use of this medication will not be captured in this row due to incident-cohort design.

[7] 10/1/21 - 9/30/23: Due to rounding, all estimates should be interpreted as ranges, with the presented value equivalent to the high end of the range. Due to a small denominator in this column, the lower value of the range is 0.15% less than the presented value.

Table 1g. Frequency of Diabetes and Obesity Characteristics Among Incident Lixisenatide Users of all Ages in the TriNetX Live™ USA Network Minimal Shift[1] from October 1, 2017 to September 30, 2023, by Time Period of Incident Use

	10/1/17 - 9/30/23		10/1/17 - 9/30/19		10/1/19 - 9/30/21		10/1/21 - 9/30/23	
	Number/ Mean	Percent/ Standard Deviation[2]	Number/ Mean	Percent/ Standard Deviation[2, 7]	Number/ Mean	Percent/ Standard Deviation[2, 8]	Number/ Mean	Percent/ Standard Deviation[2, 9]
Lixisenatide								
Total Patients	10,440	100.0%	3,260	100.0%	3,740	100.0%	3,440	100.0%
Diagnosis-Defined Characteristics[3]								
Encounter for Type 2 Diabetes	5,080	48.7%	1,640	50.3%	1,790	47.9%	1,660	48.3%
Encounter for Overweight/Obesity	1,670	16.0%	550	16.9%	550	14.7%	570	16.6%
Body Mass Index (kilograms per square meter)								
19.9 or less	10	0.1%	10	0.3%	10	0.3%	10	0.3%
20-29	310	3.0%	90	2.8%	130	3.5%	110	3.2%
30-39	920	8.8%	300	9.2%	300	8.0%	320	9.3%
40 or greater	570	5.5%	180	5.5%	210	5.6%	190	5.5%
Clinical Observation-Defined Characteristics[4]								
Any Body Mass Index Observation	4,350	41.7%	1,260	38.7%	1,500	40.1%	1,600	46.5%
Body Mass Index (kilograms per square meter)	34.1	7.54	34.6	7.76	34.2	7.58	33.5	7.28
Any Height Observation	4,550	43.6%	1,270	39.0%	1,600	42.8%	1,690	49.1%
Any Weight Observation	4,220	40.4%	1,190	36.5%	1,470	39.3%	1,570	45.6%
Prior Medication Use[5]								
Blood glucose lowering drugs, excluding insulins[6]	4,440	42.5%	1,490	45.7%	1,460	39.0%	1,470	42.7%
Biguanides	2,710	26.0%	950	29.1%	890	23.8%	870	25.3%

Table 1g. Frequency of Diabetes and Obesity Characteristics Among Incident Lixisenatide Users of all Ages in the TriNetX Live™ USA Network Minimal Shift[1] from October 1, 2017 to September 30, 2023, by Time Period of Incident Use

	10/1/17 - 9/30/23		10/1/17 - 9/30/19		10/1/19 - 9/30/21		10/1/21 - 9/30/23	
	Number/ Mean	Percent/ Standard Deviation[2]	Number/ Mean	Percent/ Standard Deviation[2, 7]	Number/ Mean	Percent/ Standard Deviation[2, 8]	Number/ Mean	Percent/ Standard Deviation[2, 9]
Lixisenatide								
Dipeptidyl peptidase 4 inhibitors	700	6.7%	300	9.2%	220	5.9%	180	5.2%
Sodium-glucose co-transporter 2 inhibitors	1,180	11.3%	340	10.4%	380	10.2%	460	13.4%
Sulfonylureas	1,220	11.7%	440	13.5%	410	11.0%	380	11.0%

NOTE: All counts provided through the TriNetX Live™ platform are rounded up to the nearest 10 to protect patient privacy. For this reason, number of incident users in each time period may not sum to the number in the overall query period. Percentages were calculated based on the rounded estimates, and are presented here rounded to the tenths position to avoid mischaracterizing the precision of the measurement. Due to rounding, all estimates should be interpreted as ranges, with the lower value of the range ≤ 0.09% less than the presented value unless otherwise noted.

NOTE: TriNetX applies data sanitization to fields such as BMI, sanitizing BMI <0.1 and >50. For patients with BMI >50, these BMI observations are omitted to preserve patient privacy and confidentiality.

[1] A subset of HCOs that contribute to the TriNetX USA network may implement date shifting - between 0 and 14 days in either direction - at the level of the patient record prior to data ingestion at TriNetX as a method to preserve patient privacy. When interpreting the results of an analysis, the impact of date shifting should be considered and readers should exercise caution when extrapolating information related to time.

[2] Percentages in this column are calculated using the count of total incident users of the time period in the column header as the denominator.

[3] Defined using ICD-10-CM codes

[4] Defined using TNX Curated codes. These characteristics are assessed closest to index date.

[5] Each class below is defined using Anatomic Therapeutic Classification (ATC) codes. **Blood glucose lowering drugs, excl. insulins includes**: dulaglutide, semaglutide, liraglutide, exenatide, lixisenatide, albiglutide, metformin, glipizide, glimepiride, chlorpropamide, tolbutamide, acetohexamide, glyburide, tolazamide, gliclazide, empagliflozin, dapagliflozin, canagliflozin, ertugliflozin, sotagliflozin, bexagliflozin, sitagliptin, linagliptin, alogliptin, saxagliptin, vildagliptin, pioglitazone, rosiglitazone, troglitazone, acarbose, miglitol, tirzepatide, repaglinide, nateglinide, guar gum, pramlintide. **Biguanides includes**: metformin. **Dipeptidyl peptidase 4 inhibitors includes**: sitagliptin, linagliptin, alogliptin, saxagliptin, vildagliptin. **Sodium-glucose co-transporter 2 inhibitors includes**: empagliflozin, dapagliflozin, canagliflozin, ertugliflozin, sotagliflozin, bexagliflozin. **Sulfonylureas includes**: glipizide, glimepiride, chlorpropamide, tolbutamide, acetohexamide, glyburide, tolazamide, gliclazide.

[6] Although this ATC category contains the index defining drug lixisenatide, prior use of this medication will not be captured in this row due to incident-cohort design.

[7] 10/1/17 - 9/30/19: Due to rounding, all estimates should be interpreted as ranges, with the presented value equivalent to the high end of the range. Due to a small denominator in this column, the lower value of the range is 0.28% less than the presented value.

[8] 10/1/19 - 9/30/21: Due to rounding, all estimates should be interpreted as ranges, with the presented value equivalent to the high end of the range. Due to a small denominator in this column, the lower value of the range is 0.24% less than the presented value.

[9] 10/1/21 - 9/30/23: Due to rounding, all estimates should be interpreted as ranges, with the presented value equivalent to the high end of the range. Due to a small denominator in this column, the lower value of the range is 0.26% less than the presented value.

Sentinel

Table 1h. Frequency of Diabetes and Obesity Characteristics Among Incident Tirzepatide Users of all Ages in the TriNetX Live™ USA Network Minimal Shift[1] from October 1, 2017 to September 30, 2023, by Time Period of Incident Use

	10/1/17 - 9/30/23		10/1/17 - 9/30/19		10/1/19 - 9/30/21		10/1/21 - 9/30/23	
	Number/ Mean	Percent/ Standard Deviation[2]	Number/ Mean	Percent/ Standard Deviation[2]	Number/ Mean	Percent/ Standard Deviation[2]	Number/ Mean	Percent/ Standard Deviation[2]
Tirzepatide								
Total Patients	82,220	100.0%	0	100.0%	10	100.0%	82,210	100.0%
Diagnosis-Defined Characteristics[3]								
Encounter for Type 2 Diabetes	32,630	39.7%	N/A	N/A	***	***	32,620	39.7%
Encounter for Overweight/Obesity	27,460	33.4%	N/A	N/A	***	***	27,460	33.4%
Body Mass Index (kilograms per square meter)								
19.9 or less	230	0.3%	N/A	N/A	***	***	230	0.3%
20-29	1,470	1.8%	N/A	N/A	***	***	1,470	1.8%
30-39	10,470	12.7%	N/A	N/A	***	***	10,470	12.7%
40 or greater	11,190	13.6%	N/A	N/A	***	***	11,190	13.6%
Clinical Observation-Defined Characteristics[4]								
Any Body Mass Index Observation	43,280	52.6%	N/A	N/A	***	***	43,280	52.6%
Body Mass Index (kilograms per square meter)	38.3	8.03	N/A	N/A	***	***	38.3	8.03
Any Height Observation	51,160	62.2%	N/A	N/A	***	***	51,160	62.2%
Any Weight Observation	40,100	48.8%	N/A	N/A	***	***	40,100	48.8%
Prior Medication Use[5]								
Blood glucose lowering drugs, excluding insulins[6]	36,530	44.4%	N/A	N/A	***	***	36,530	44.4%
Biguanides	15,480	18.8%	N/A	N/A	***	***	15,480	18.8%

Table 1h. Frequency of Diabetes and Obesity Characteristics Among Incident Tirzepatide Users of all Ages in the TriNetX Live™ USA Network Minimal Shift[1] from October 1, 2017 to September 30, 2023, by Time Period of Incident Use

	10/1/17 - 9/30/23		10/1/17 - 9/30/19		10/1/19 - 9/30/21		10/1/21 - 9/30/23	
	Number/ Mean	Percent/ Standard Deviation[2]	Number/ Mean	Percent/ Standard Deviation[2]	Number/ Mean	Percent/ Standard Deviation[2]	Number/ Mean	Percent/ Standard Deviation[2]
Tirzepatide								
Dipeptidyl peptidase 4 inhibitors	1,570	1.9%	N/A	N/A	***	***	1,570	1.9%
Sodium-glucose co-transporter 2 inhibitors	6,630	8.1%	N/A	N/A	***	***	6,630	8.1%
Sulfonylureas	3,520	4.3%	N/A	N/A	***	***	3,520	4.3%

NOTE: All counts provided through the TriNetX Live™ platform are rounded up to the nearest 10 to protect patient privacy. For this reason, number of incident users in each time period may not sum to the number in the overall query period. Percentages were calculated based on the rounded estimates, and are presented here rounded to the tenths position to avoid mischaracterizing the precision of the measurement. Due to rounding, all estimates should be interpreted as ranges, with the lower value of the range ≤ 0.01% less than the presented value unless otherwise noted.

NOTE: TriNetX applies data sanitization to fields such as BMI, sanitizing BMI <0.1 and >50. For patients with BMI >50, these BMI observations are omitted to preserve patient privacy and confidentiality.

[1] A subset of HCOs that contribute to the TriNetX USA network may implement date shifting - between 0 and 14 days in either direction - at the level of the patient record prior to data ingestion at TriNetX as a method to preserve patient privacy. When interpreting the results of an analysis, the impact of date shifting should be considered and readers should exercise caution when extrapolating information related to time.

[2] Percentages in this column are calculated using the count of total incident users of the time period in the column header as the denominator.

[3] Defined using ICD-10-CM codes

[4] Defined using TNX Curated codes. These characteristics are assessed closest to index date.

[5] Each class below is defined using Anatomic Therapeutic Classification (ATC) codes. **Blood glucose lowering drugs, excl. insulins includes**: dulaglutide, semaglutide, liraglutide, exenatide, lixisenatide, albiglutide, metformin, glipizide, glimepiride, chlorpropamide, tolbutamide, acetohexamide, glyburide, tolazamide, gliclazide, empagliflozin, dapagliflozin, canagliflozin, ertugliflozin, sotagliflozin, bexagliflozin, sitagliptin, linagliptin, alogliptin, saxagliptin, vildagliptin, pioglitazone, rosiglitazone, troglitazone, acarbose, miglitol, tirzepatide, repaglinide, nateglinide, guar gum, pramlintide. **Biguanides includes**: metformin. **Dipeptidyl peptidase 4 inhibitors includes**: sitagliptin, linagliptin, alogliptin, saxagliptin, vildagliptin. **Sodium-glucose co-transporter 2 inhibitors includes**: empagliflozin, dapagliflozin, canagliflozin, ertugliflozin, sotagliflozin, bexagliflozin. **Sulfonylureas includes**: glipizide, glimepiride, chlorpropamide, tolbutamide, acetohexamide, glyburide, tolazamide, gliclazide.

[6] Although this ATC category contains the index defining drug tirzepatide, prior use of this medication will not be captured in this row due to incident-cohort design.

*** Data was not returned in the platform for this cohort given small sample sizes.

N/A" Not available

Appendix A. List of RxNorm Medication Terms Used to Define Exposures in this Request

Code	Code Type	Description	Filter
Glucagon-like peptide-1 Receptor Agonist (GLP-1 RA)			
1534763	RxNorm	albiglutide	Not Applicable
1551291	RxNorm	dulaglutide	Not Applicable
60548	RxNorm	exenatide	Not Applicable
475968	RxNorm	liraglutide	Not Applicable
1440051	RxNorm	lixisenatide	Not Applicable
1991302	RxNorm	semaglutide	Not Applicable
2601723	RxNorm	tirzepatide	Not Applicable

Appendix B. List of Terms Used to Define Inclusion Criteria in this Request

Code	Code Type	Description	Filter
		Visit	
AMB	HL7 V3 Visit Type[1]	Visit: Ambulatory	Not Applicable
EMER	HL7 V3 Visit Type	Visit: Emergency	Not Applicable
HH	HL7 V3 Visit Type	Visit: Home Health	Not Applicable
IMP	HL7 V3 Visit Type	Visit: Inpatient Encounter	Not Applicable
NONAC	HL7 V3 Visit Type	Visit: Inpatient Non-acute	Not Applicable
LAB	HL7 V3 Visit Type	Visit: Laboratory	Not Applicable
OBSENC	HL7 V3 Visit Type	Visit: Observation Encounter	Not Applicable
PHARM	HL7 V3 Visit Type	Visit: Pharmacy	Not Applicable
PRENC	HL7 V3 Visit Type	Visit: Pre-admission	Not Applicable
SS	HL7 V3 Visit Type	Visit: Short Stay	Not Applicable
UNKNOWN	HL7 V3 Visit Type	Visit: Unknown	Not Applicable
VR	HL7 V3 Visit Type	Visit: Virtual	Not Applicable

[1]HL7 V3 Visit Type: Health Level 7 (HL7) Vocabulary, Version 3.0

Appendix C. List of Codes Used to Define Characteristics in this Request

Code	Code Type	Characteristic or Outcome	Filter
E11	ICD-10-CM	Encounter for Type 2 Diabetes	Not Applicable
E66	ICD-10-CM	Encounter for Overweight/Obesity	Not Applicable
Z68.1	ICD-10-CM	Underweight (≤19.9 BMI)	Not Applicable
Z68.2	ICD-10-CM	Normal weight (20-29 BMI)	Not Applicable
Z68.3	ICD-10-CM	Overweight (30-39 BMI)	Not Applicable
Z68.4	ICD-10-CM	Obese (40+ BMI)	Not Applicable
9083 [1]	TriNetX curated code	Measurement for BMI present	Not Applicable
9083 [1]	TriNetX curated code	Clinical measurement	Not Applicable
9077 [2]	TriNetX curated code	Measurement for Height present	Not Applicable
9081 [3]	TriNetX curated code	Measurement for Weight present	Not Applicable
A10B [4]	ATC	Blood glucose lowering drugs, excl. insulins	Not Applicable
A10BA [5]	ATC	Biguanides	Not Applicable
A10BB [6]	ATC	Sulfonylureas	Not Applicable
A10BK [7]	ATC	Sodium-glucose co-transporter 2 (sglt2) inhibitors	Not Applicable
A10BH [8]	ATC	Dipeptidyl peptidase 4 (dpp-4) inhibitors	Not Applicable

[1] LOINC 39156-5

[2] LOINC 8308-9, 8301-4, 3137-7, 3138-5, 8302-2

[3] LOINC 29463-7, 8335-2, 3142-7, 3141-9

[4] Includes: dulaglutide, semaglutide, liraglutide, exenatide, lixisenatide, albiglutide, metformin, glipizide, glimepiride, chlorpropamide, tolbutamide, acetohexamide, glyburide, tolazamide, gliclazide, empagliflozin, dapagliflozin, canagliflozin, ertugliflozin, sotagliflozin, bexagliflozin, sitagliptin, linagliptin, alogliptin, saxagliptin, vildagliptin, pioglitazone, rosiglitazone, troglitazone, acarbose, miglitol, tirzepatide, repaglinide, nateglinide, guar gum, pramlintide

[5] Includes: metformin

[6] Includes: glipizide, glimepiride, chlorpropamide, tolbutamide, acetohexamide, glyburide, tolazamide, gliclazide

[7] Includes: empagliflozin, dapagliflozin, canagliflozin, ertugliflozin, sotagliflozin, bexagliflozin

[8] Includes: sitagliptin, linagliptin, alogliptin, saxagliptin, vildagliptin

Appendix D. Specifications Defining Query Builder Modules in this Request

Network:
TriNetX Live™ USA Network Minimal Shift (Includes HCOs that shift between 0 and +/- 14 days) This includes all HCOs in the USA Network No Shift

Cohort 1A (query name: Incident GLP-1 RA 10/1/17 - 9/30/19)

This query was run on the USA Network Minimal Shift 61 HCO(s) queried and 61 HCO(s) responded.

Group 1	*date constraint:*	*The terms in this group occurred between Oct 1, 2017 and Sep 30, 2019* [1]		
Group 1A GLP-1 RA 10/1/17 - 9/30/19[2]				
must have	any of	medication	NLM:RXNORM:1534763	albiglutide
		medication	NLM:RXNORM:1551291	dulaglutide
		medication	NLM:RXNORM:60548	exenatide
		medication	NLM:RXNORM:475968	liraglutide
		medication	NLM:RXNORM:1440051	lixisenatide
		medication	NLM:RXNORM:1991302	semaglutide
		medication	NLM:RXNORM:2601723	tirzepatide
event relationship	Any instance of Group 1B (Any Visit) occurred on or before the first instance of Group 1A (GLP-1 RA 10/1/17 - 9/30/19[2])			
Group 1B Any Visit 10/1/17[3] **- Same Day or Prior to Index**				
must have	any of	visit	UMLS:HL7V3.0:VisitType:AMB	Visit: Ambulatory
		visit	UMLS:HL7V3.0:VisitType:EMER	Visit: Emergency
		visit	UMLS:HL7V3.0:VisitType:HH	Visit: Home Health
		visit	UMLS:HL7V3.0:VisitType:IMP	Visit: Inpatient Encounter
		visit	UMLS:HL7V3.0:VisitType:NONAC	Visit: Inpatient Non-acute
		visit	UMLS:HL7V3.0:VisitType:LAB	Visit: Laboratory
		visit	UMLS:HL7V3.0:VisitType:OBSENC	Visit: Observation Encounter
		visit	UMLS:HL7V3.0:VisitType:PHARM	Visit: Pharmacy
		visit	UMLS:HL7V3.0:VisitType:PRENC	Visit: Pre-admission
		visit	UMLS:HL7V3.0:VisitType:SS	Visit: Short Stay
		visit	UMLS:HL7V3.0:VisitType:UNKNOWN	Visit: Unknown
		visit	UMLS:HL7V3.0:VisitType:VR	Visit: Virtual
Group 2				
Group 2A First GLP-1 RA				
must have	any of	medication	NLM:RXNORM:1534763	albiglutide
		medication	NLM:RXNORM:1551291	dulaglutide
		medication	NLM:RXNORM:60548	exenatide
		medication	NLM:RXNORM:475968	liraglutide
		medication	NLM:RXNORM:1440051	lixisenatide
		medication	NLM:RXNORM:1991302	semaglutide
		medication	NLM:RXNORM:2601723	tirzepatide
event relationship	Any instance of Group 2B (No GLP-1 RA) occurred at least 1 day before the first instance of Group 2A (First GLP-1 RA)			
Group 2B No GLP-1 RA				
cannot have	any of	medication	NLM:RXNORM:1534763	albiglutide
		medication	NLM:RXNORM:1551291	dulaglutide
		medication	NLM:RXNORM:60548	exenatide
		medication	NLM:RXNORM:475968	liraglutide
		medication	NLM:RXNORM:1440051	lixisenatide
		medication	NLM:RXNORM:1991302	semaglutide
		medication	NLM:RXNORM:2601723	tirzepatide
Group 3	*date constraint:*	*The terms in this group occurred between Jan 1, 1900 and Sep 30, 2017* [4]		

Appendix D. Specifications Defining Query Builder Modules in this Request

No GLP-1 RA before 10/1/2017[3]				
cannot have	any of	medication	NLM:RXNORM:1534763	albiglutide
		medication	NLM:RXNORM:1551291	dulaglutide
		medication	NLM:RXNORM:60548	exenatide
		medication	NLM:RXNORM:475968	liraglutide
		medication	NLM:RXNORM:1440051	lixisenatide
		medication	NLM:RXNORM:1991302	semaglutide
		medication	NLM:RXNORM:2601723	tirzepatide

Cohort 1B (query name: Incident GLP-1 RA 10/1/19 - 9/30/21)

The following parameters change from Cohort 1A:

[1] change to: The terms in this group occurred between Oct 1, 2019 and Sep 30, 2021

[2] change to: 10/1/19 - 9/30/21

[3] change to: 10/1/2019

[4] change to: The terms in this group occurred between Jan 1, 1900 and Sep 30, 2019

Cohort 1C (query name: Incident GLP-1 RA 10/1/21 - 9/30/23)

The following parameters change from Cohort 1A:

[1] change to: The terms in this group occurred between Oct 1, 2021 and Sep 30, 2023

[2] change to: 10/1/21 - 9/30/23

[3] change to: 10/1/2021

[4] change to: The terms in this group occurred between Jan 1, 1900 and Sep 30, 2021

Cohort 1D (query name: Incident GLP-1 RA 10/1/17 - 9/30/23)

The following parameters change from Cohort 1A:

[1] change to: The terms in this group occurred between Oct 1, 2017 and Sep 30, 2023

[2] change to: 10/1/17 - 9/30/23

Cohort 2A (query name: Incident Dulaglutide 10/1/17 - 9/30/19)

This query was run on the USA Network Minimal Shift 61 HCO(s) queried and 61 HCO(s) responded.

Group 1	*date constraint:*	*The terms in this group occurred between Oct 1, 2017 and Sep 30, 2019 [1]*		
Group 1A Dulaglutide 10/1/17 - 9/30/19[2]				
must have	any of	medication	NLM:RXNORM:1551291	dulaglutide
event relationship	Any instance of Group 1B (Any Visit) occurred on or before the first instance of Group 1A (Dulaglutide 10/1/17 - 9/30/19[2])			
Group 1B Any Visit 10/1/17[3] - Same Day or Prior to Index				
must have	any of	visit	UMLS:HL7V3.0:VisitType:AMB	Visit: Ambulatory
		visit	UMLS:HL7V3.0:VisitType:EMER	Visit: Emergency
		visit	UMLS:HL7V3.0:VisitType:HH	Visit: Home Health
		visit	UMLS:HL7V3.0:VisitType:IMP	Visit: Inpatient Encounter
		visit	UMLS:HL7V3.0:VisitType:NONAC	Visit: Inpatient Non-acute
		visit	UMLS:HL7V3.0:VisitType:LAB	Visit: Laboratory
		visit	UMLS:HL7V3.0:VisitType:OBSENC	Visit: Observation Encounter
		visit	UMLS:HL7V3.0:VisitType:PHARM	Visit: Pharmacy
		visit	UMLS:HL7V3.0:VisitType:PRENC	Visit: Pre-admission
		visit	UMLS:HL7V3.0:VisitType:SS	Visit: Short Stay
		visit	UMLS:HL7V3.0:VisitType:UNKNOWN	Visit: Unknown
		visit	UMLS:HL7V3.0:VisitType:VR	Visit: Virtual
Group 2				

Appendix D. Specifications Defining Query Builder Modules in this Request

Group 2A First Dulaglutide				
must have	any of	medication	NLM:RXNORM:1551291	dulaglutide
event relationship	Any instance of Group 2B (No Dulaglutide) occurred at least 1 day before the first instance of Group 2A (First Dulaglutide)			
Group 2B No Dulaglutide				
cannot have	any of	medication	NLM:RXNORM:1551291	dulaglutide

Group 3	*date constraint:*	*The terms in this group occurred between Jan 1, 1900 and Sep 30, 2017* [4]		
No Dulaglutide before 10/1/2017[3]				
cannot have	any of	medication	NLM:RXNORM:1551291	dulaglutide

Cohort 2B (query name: Incident Dulaglutide 10/1/19 - 9/30/21)

The following parameters change from Cohort 2A:

[1] change to: The terms in this group occurred between Oct 1, 2019 and Sep 30, 2021

[2] change to: 10/1/19 - 9/30/21

[3] change to: 10/1/2019

[4] change to: The terms in this group occurred between Jan 1, 1900 and Sep 30, 2019

Cohort 2C (query name: Incident Dulaglutide 10/1/21 - 9/30/23)

The following parameters change from Cohort 2A:

[1] change to: The terms in this group occurred between Oct 1, 2021 and Sep 30, 2023

[2] change to: 10/1/21 - 9/30/23

[3] change to: 10/1/2021

[4] change to: The terms in this group occurred between Jan 1, 1900 and Sep 30, 2021

Cohort 2D (query name: Incident Dulaglutide 10/1/17 - 9/30/23)

The following parameters change from Cohort 2A:

[1] change to: The terms in this group occurred between Oct 1, 2017 and Sep 30, 2023

[2] change to: 10/1/17 - 9/30/23

Cohort 3A (query name: Incident Liraglutide 10/1/17 - 9/30/19)

This query was run on the USA Network Minimal Shift 61 HCO(s) queried and 61 HCO(s) responded.

Group 1	*date constraint:*	*The terms in this group occurred between Oct 1, 2017 and Sep 30, 2019* [1]		
Group 1A Liraglutide 10/1/17 - 9/30/19[2]				
must have	any of	medication	NLM:RXNORM:475968	liraglutide
event relationship	Any instance of Group 1B (Any Visit) occurred on or before the first instance of Group 1A (Liraglutide 10/1/17 - 9/30/19[2])			
Group 1B Any Visit 10/1/17[3] **- Same Day or Prior to Index**				
must have	any of	visit	UMLS:HL7V3.0:VisitType:AMB	Visit: Ambulatory
		visit	UMLS:HL7V3.0:VisitType:EMER	Visit: Emergency
		visit	UMLS:HL7V3.0:VisitType:HH	Visit: Home Health
		visit	UMLS:HL7V3.0:VisitType:IMP	Visit: Inpatient Encounter
		visit	UMLS:HL7V3.0:VisitType:NONAC	Visit: Inpatient Non-acute
		visit	UMLS:HL7V3.0:VisitType:LAB	Visit: Laboratory
		visit	UMLS:HL7V3.0:VisitType:OBSENC	Visit: Observation Encounter

Appendix D. Specifications Defining Query Builder Modules in this Request

		visit	UMLS:HL7V3.0:VisitType:PHARM	Visit: Pharmacy
		visit	UMLS:HL7V3.0:VisitType:PRENC	Visit: Pre-admission
		visit	UMLS:HL7V3.0:VisitType:SS	Visit: Short Stay
		visit	UMLS:HL7V3.0:VisitType:UNKNOWN	Visit: Unknown
		visit	UMLS:HL7V3.0:VisitType:VR	Visit: Virtual
Group 2				
Group 2A First Liraglutide				
must have	any of	medication	NLM:RXNORM:475968	liraglutide
event relationship		Any instance of Group 2B (No Liraglutide) occurred at least 1 day before the first instance of Group 2A (First Liraglutide)		
Group 2B No Liraglutide				
cannot have	any of	medication	NLM:RXNORM:475968	liraglutide
Group 3	*date constraint:*	*The terms in this group occurred between Jan 1, 1900 and Sep 30, 2017* [4]		
No Liraglutide before 10/1/2017[3]				
cannot have	any of	medication	NLM:RXNORM:475968	liraglutide

Cohort 3B (query name: Incident Liraglutide 10/1/19 - 9/30/21)

The following parameters change from Cohort 3A:

[1] change to: The terms in this group occurred between Oct 1, 2019 and Sep 30, 2021

[2] change to: 10/1/19 - 9/30/21

[3] change to: 10/1/2019

[4] change to: The terms in this group occurred between Jan 1, 1900 and Sep 30, 2019

Cohort 3C (query name: Incident Liraglutide 10/1/21 - 9/30/23)

The following parameters change from Cohort 3A:

[1] change to: The terms in this group occurred between Oct 1, 2021 and Sep 30, 2023

[2] change to: 10/1/21 - 9/30/23

[3] change to: 10/1/2021

[4] change to: The terms in this group occurred between Jan 1, 1900 and Sep 30, 2021

Cohort 3D (query name: Incident Liraglutide 10/1/17 - 9/30/23)

The following parameters change from Cohort 3A:

[1] change to: The terms in this group occurred between Oct 1, 2017 and Sep 30, 2023

[2] change to: 10/1/17 - 9/30/23

Cohort 4A (query name: Incident Semaglutide 10/1/17 - 9/30/19)

This query was run on the USA Network Minimal Shift 61 HCO(s) queried and 61 HCO(s) responded.

Group 1	*date constraint:*	*The terms in this group occurred between Oct 1, 2017 and Sep 30, 2019* [1]		
Group 1A Semaglutide 10/1/17 - 9/30/19[2]				
must have	any of	medication	NLM:RXNORM:1991302	semaglutide
event relationship		Any instance of Group 1B (Any Visit) occurred on or before the first instance of Group 1A (Semaglutide 10/1/17 - 9/30/19[2])		
Group 1B Any Visit 10/1/17[3] **- Same Day or Prior to Index**				
must have	any of	visit	UMLS:HL7V3.0:VisitType:AMB	Visit: Ambulatory

Appendix D. Specifications Defining Query Builder Modules in this Request

		visit	UMLS:HL7V3.0:VisitType:EMER	Visit: Emergency
		visit	UMLS:HL7V3.0:VisitType:HH	Visit: Home Health
		visit	UMLS:HL7V3.0:VisitType:IMP	Visit: Inpatient Encounter
		visit	UMLS:HL7V3.0:VisitType:NONAC	Visit: Inpatient Non-acute
		visit	UMLS:HL7V3.0:VisitType:LAB	Visit: Laboratory
		visit	UMLS:HL7V3.0:VisitType:OBSENC	Visit: Observation Encounter
		visit	UMLS:HL7V3.0:VisitType:PHARM	Visit: Pharmacy
		visit	UMLS:HL7V3.0:VisitType:PRENC	Visit: Pre-admission
		visit	UMLS:HL7V3.0:VisitType:SS	Visit: Short Stay
		visit	UMLS:HL7V3.0:VisitType:UNKNOWN	Visit: Unknown
		visit	UMLS:HL7V3.0:VisitType:VR	Visit: Virtual
Group 2				
Group 2A First Semaglutide				
must have	any of	medication	NLM:RXNORM:1991302	semaglutide
event relationship		Any instance of Group 2B (No Semaglutide) occurred at least 1 day before the first instance of Group 2A (First Semaglutide)		
Group 2B No Semaglutide				
cannot have	any of	medication	NLM:RXNORM:1991302	semaglutide
Group 3	*date constraint:*	*The terms in this group occurred between Jan 1, 1900 and Sep 30, 2017* [4]		
No Semaglutide before 10/1/2017[3]				
cannot have	any of	medication	NLM:RXNORM:1991302	semaglutide

Cohort 4B (query name: Incident Semaglutide 10/1/19 - 9/30/21)

The following parameters change from Cohort 4A:

[1] change to: The terms in this group occurred between Oct 1, 2019 and Sep 30, 2021

[2] change to: 10/1/19 - 9/30/21

[3] change to: 10/1/2019

[4] change to: The terms in this group occurred between Jan 1, 1900 and Sep 30, 2019

Cohort 4C (query name: Incident Semaglutide 10/1/21 - 9/30/23)

The following parameters change from Cohort 4A:

[1] change to: The terms in this group occurred between Oct 1, 2021 and Sep 30, 2023

[2] change to: 10/1/21 - 9/30/23

[3] change to: 10/1/2021

[4] change to: The terms in this group occurred between Jan 1, 1900 and Sep 30, 2021

Cohort 4D (query name: Incident Semaglutide 10/1/17 - 9/30/23)

The following parameters change from Cohort 4A:

[1] change to: The terms in this group occurred between Oct 1, 2017 and Sep 30, 2023

[2] change to: 10/1/17 - 9/30/23

Cohort 5A (query name: Incident Albiglutide 10/1/17 - 9/30/19)

This query was run on the USA Network Minimal Shift 61 HCO(s) queried and 61 HCO(s) responded.

Group 1	*date constraint:*	*The terms in this group occurred between Oct 1, 2017 and Sep 30, 2019* [1]		
Group 1A Albiglutide 10/1/17 - 9/30/19[2]				
must have	any of	medication	NLM:RXNORM:1534763	albiglutide

Appendix D. Specifications Defining Query Builder Modules in this Request

event relationship	Any instance of Group 1B (Any Visit) occurred on or before the first instance of Group 1A (Albiglutide 10/1/17 - 9/30/19[2])			
Group 1B Any Visit 10/1/17[3] - Same Day or Prior to Index				
must have	any of	visit	UMLS:HL7V3.0:VisitType:AMB	Visit: Ambulatory
		visit	UMLS:HL7V3.0:VisitType:EMER	Visit: Emergency
		visit	UMLS:HL7V3.0:VisitType:HH	Visit: Home Health
		visit	UMLS:HL7V3.0:VisitType:IMP	Visit: Inpatient Encounter
		visit	UMLS:HL7V3.0:VisitType:NONAC	Visit: Inpatient Non-acute
		visit	UMLS:HL7V3.0:VisitType:LAB	Visit: Laboratory
		visit	UMLS:HL7V3.0:VisitType:OBSENC	Visit: Observation Encounter
		visit	UMLS:HL7V3.0:VisitType:PHARM	Visit: Pharmacy
		visit	UMLS:HL7V3.0:VisitType:PRENC	Visit: Pre-admission
		visit	UMLS:HL7V3.0:VisitType:SS	Visit: Short Stay
		visit	UMLS:HL7V3.0:VisitType:UNKNOWN	Visit: Unknown
		visit	UMLS:HL7V3.0:VisitType:VR	Visit: Virtual
Group 2				
Group 2A First Albiglutide				
must have	any of	medication	NLM:RXNORM:1534763	albiglutide
event relationship	Any instance of Group 2B (No Albiglutide) occurred at least 1 day before the first instance of Group 2A (First Albiglutide)			
Group 2B No Albiglutide				
cannot have	any of	medication	NLM:RXNORM:1534763	albiglutide
Group 3	*date constraint:*	*The terms in this group occurred between Jan 1, 1900 and Sep 30, 2017*[4]		
No Albiglutide before 10/1/2017[3]				
cannot have	any of	medication	NLM:RXNORM:1534763	albiglutide

Cohort 5B (query name: Incident Albiglutide 10/1/19 - 9/30/21)

The following parameters change from Cohort 5A:

[1] change to: The terms in this group occurred between Oct 1, 2019 and Sep 30, 2021

[2] change to: 10/1/19 - 9/30/21

[3] change to: 10/1/2019

[4] change to: The terms in this group occurred between Jan 1, 1900 and Sep 30, 2019

Cohort 5C (query name: Incident Albiglutide 10/1/21 - 9/30/23)

The following parameters change from Cohort 5A:

[1] change to: The terms in this group occurred between Oct 1, 2021 and Sep 30, 2023

[2] change to:
10/1/21 -
9/30/23

[3] change to: 10/1/2021

[4] change to: The terms in this group occurred between Jan 1, 1900 and Sep 30, 2021

Cohort 5D (query name: Incident Albiglutide 10/1/17 - 9/30/23)

The following parameters change from Cohort 5A:

[1] change to: The terms in this group occurred between Oct 1, 2017 and Sep 30, 2023

[2] change to: 10/1/17 - 9/30/23

Cohort 6A (query name: Incident Exenatide 10/1/17 - 9/30/19)

This query was run on the USA Network Minimal Shift 61 HCO(s) queried and 61 HCO(s) responded.

Group 1	*date constraint:*	*The terms in this group occurred between Oct 1, 2017 and Sep 30, 2019* [1]		
Group 1A Exenatide 10/1/17 - 9/30/19[2]				
must have	any of	medication	NLM:RXNORM:60548	exenatide
event relationship	Any instance of Group 1B (Any Visit) occurred on or before the first instance of Group 1A (Exenatide 10/1/17 - 9/30/19[2])			
Group 1B Any Visit 10/1/17[3] **- Same Day or Prior to Index**				
must have	any of	visit	UMLS:HL7V3.0:VisitType:AMB	Visit: Ambulatory
		visit	UMLS:HL7V3.0:VisitType:EMER	Visit: Emergency
		visit	UMLS:HL7V3.0:VisitType:HH	Visit: Home Health
		visit	UMLS:HL7V3.0:VisitType:IMP	Visit: Inpatient Encounter
		visit	UMLS:HL7V3.0:VisitType:NONAC	Visit: Inpatient Non-acute
		visit	UMLS:HL7V3.0:VisitType:LAB	Visit: Laboratory
		visit	UMLS:HL7V3.0:VisitType:OBSENC	Visit: Observation Encounter
		visit	UMLS:HL7V3.0:VisitType:PHARM	Visit: Pharmacy
		visit	UMLS:HL7V3.0:VisitType:PRENC	Visit: Pre-admission
		visit	UMLS:HL7V3.0:VisitType:SS	Visit: Short Stay
		visit	UMLS:HL7V3.0:VisitType:UNKNOWN	Visit: Unknown
		visit	UMLS:HL7V3.0:VisitType:VR	Visit: Virtual
Group 2				
Group 2A First Exenatide				
must have	any of	medication	NLM:RXNORM:60548	exenatide
event relationship	Any instance of Group 2B (No Exenatide) occurred at least 1 day before the first instance of Group 2A (First Exenatide)			
Group 2B No Exenatide				
cannot have	any of	medication	NLM:RXNORM:60548	exenatide
Group 3	*date constraint:*	*The terms in this group occurred between Jan 1, 1900 and Sep 30, 2017* [4]		
No Exenatide before 10/1/2017[3]				
cannot have	any of	medication	NLM:RXNORM:60548	exenatide

Cohort 6B (query name: Incident Exenatide 10/1/19 - 9/30/21)

The following parameters change from Cohort 6A:

[1] change to: The terms in this group occurred between Oct 1, 2019 and Sep 30, 2021

[2] change to: 10/1/19 - 9/30/21

[3] change to: 10/1/2019

[4] change to: The terms in this group occurred between Jan 1, 1900 and Sep 30, 2019

Cohort 6C (query name: Incident Exenatide 10/1/21 - 9/30/23)

The following parameters change from Cohort 6A:

[1] change to: The terms in this group occurred between Oct 1, 2021 and Sep 30, 2023

[2] change to: 10/1/21 - 9/30/23

Appendix D. Specifications Defining Query Builder Modules in this Request

[3] change to: 10/1/2021

[4] change to: The terms in this group occurred between Jan 1, 1900 and Sep 30, 2021

Cohort 6D (query name: Incident Exenatide 10/1/17 - 9/30/23)

The following parameters change from Cohort 6A:

[1] change to: The terms in this group occurred between Oct 1, 2017 and Sep 30, 2023

[2] change to: 10/1/17 - 9/30/23

Cohort 7A (query name: Incident Lixisenatide 10/1/17 - 9/30/19)

This query was run on the USA Network Minimal Shift 61 HCO(s) queried and 61 HCO(s) responded.

Group 1	*date constraint:*		*The terms in this group occurred between Oct 1, 2017 and Sep 30, 2019* [1]	
Group 1A Lixisenatide 10/1/17 - 9/30/19[2]				
must have	any of	medication	NLM:RXNORM:1440051	lixisenatide
event relationship	Any instance of Group 1B (Any Visit) occurred on or before the first instance of Group 1A (Lixisenatide 10/1/17 - 9/30/19[2])			
Group 1B Any Visit 10/1/17[3] **- Same Day or Prior to Index**				
must have	any of	visit	UMLS:HL7V3.0:VisitType:AMB	Visit: Ambulatory
		visit	UMLS:HL7V3.0:VisitType:EMER	Visit: Emergency
		visit	UMLS:HL7V3.0:VisitType:HH	Visit: Home Health
		visit	UMLS:HL7V3.0:VisitType:IMP	Visit: Inpatient Encounter
		visit	UMLS:HL7V3.0:VisitType:NONAC	Visit: Inpatient Non-acute
		visit	UMLS:HL7V3.0:VisitType:LAB	Visit: Laboratory
		visit	UMLS:HL7V3.0:VisitType:OBSENC	Visit: Observation Encounter
		visit	UMLS:HL7V3.0:VisitType:PHARM	Visit: Pharmacy
		visit	UMLS:HL7V3.0:VisitType:PRENC	Visit: Pre-admission
		visit	UMLS:HL7V3.0:VisitType:SS	Visit: Short Stay
		visit	UMLS:HL7V3.0:VisitType:UNKNOWN	Visit: Unknown
		visit	UMLS:HL7V3.0:VisitType:VR	Visit: Virtual
Group 2				
Group 2A First Lixisenatide				
must have	any of	medication	NLM:RXNORM:1440051	lixisenatide
event relationship	Any instance of Group 2B (No Lixisenatide) occurred at least 1 day before the first instance of Group 2A (First Lixisenatide)			
Group 2B No Lixisenatide				
cannot have	any of	medication	NLM:RXNORM:1440051	lixisenatide
Group 3	*date constraint:*		*The terms in this group occurred between Jan 1, 1900 and Sep 30, 2017* [4]	
No Lixisenatide before 10/1/2017[3]				
cannot have	any of	medication	NLM:RXNORM:1440051	lixisenatide

Cohort 7B (query name: Incident Lixisenatide 10/1/19 - 9/30/21)

The following parameters change from Cohort 7A:

[1] change to: The terms in this group occurred between Oct 1, 2019 and Sep 30, 2021

[2] change to: 10/1/19 - 9/30/21

[3] change to: 10/1/2019

Appendix D. Specifications Defining Query Builder Modules in this Request

[4] change to: The terms in this group occurred between Jan 1, 1900 and Sep 30, 2019

Cohort 7C (query name: Incident Lixisenatide 10/1/21 - 9/30/23)

The following parameters change from Cohort 7A:

[1] change to: The terms in this group occurred between Oct 1, 2021 and Sep 30, 2023

[2] change to: 10/1/21 - 9/30/23

[3] change to: 10/1/2021

[4] change to: The terms in this group occurred between Jan 1, 1900 and Sep 30, 2021

Cohort 7D (query name: Incident Lixisenatide 10/1/17 - 9/30/23)

The following parameters change from Cohort 7A:

[1] change to: The terms in this group occurred between Oct 1, 2017 and Sep 30, 2023

[2] change to: 10/1/17 - 9/30/23

Cohort 8A (query name: Incident Tirzepatide 10/1/17 - 9/30/19)

This query was run on the USA Network Minimal Shift 61 HCO(s) queried and 61 HCO(s) responded.

Group 1	*date constraint:*		*The terms in this group occurred between Oct 1, 2017 and Sep 30, 2019* [1]	
Group 1A Tirzepatide 10/1/17 - 9/30/19[2]				
must have	any of	medication	NLM:RXNORM:2601723	tirzepatide
event relationship	Any instance of Group 1B (Any Visit) occurred on or before the first instance of Group 1A (Tirzepatide 10/1/17 - 9/30/19[2])			
Group 1B Any Visit 10/1/17[3] **- Same Day or Prior to Index**				
must have	any of	visit	UMLS:HL7V3.0:VisitType:AMB	Visit: Ambulatory
		visit	UMLS:HL7V3.0:VisitType:EMER	Visit: Emergency
		visit	UMLS:HL7V3.0:VisitType:HH	Visit: Home Health
		visit	UMLS:HL7V3.0:VisitType:IMP	Visit: Inpatient Encounter
		visit	UMLS:HL7V3.0:VisitType:NONAC	Visit: Inpatient Non-acute
		visit	UMLS:HL7V3.0:VisitType:LAB	Visit: Laboratory
		visit	UMLS:HL7V3.0:VisitType:OBSENC	Visit: Observation Encounter
		visit	UMLS:HL7V3.0:VisitType:PHARM	Visit: Pharmacy
		visit	UMLS:HL7V3.0:VisitType:PRENC	Visit: Pre-admission
		visit	UMLS:HL7V3.0:VisitType:SS	Visit: Short Stay
		visit	UMLS:HL7V3.0:VisitType:UNKNOWN	Visit: Unknown
		visit	UMLS:HL7V3.0:VisitType:VR	Visit: Virtual
Group 2				
Group 2A First Tirzepatide				
must have	any of	medication	NLM:RXNORM:2601723	tirzepatide
event relationship	Any instance of Group 2B (No Tirzepatide) occurred at least 1 day before the first instance of Group 2A (First Tirzepatide)			
Group 2B No Tirzepatide				
cannot have	any of	medication	NLM:RXNORM:2601723	tirzepatide
Group 3	*date constraint:*		*The terms in this group occurred between Jan 1, 1900 and Sep 30, 2017* [4]	
No Tirzepatide before 10/1/2017[3]				
cannot have	any of	medication	NLM:RXNORM:2601723	tirzepatide

Cohort 8B (query name: Incident Tirzepatide 10/1/19 - 9/30/21)

Appendix D. Specifications Defining Query Builder Modules in this Request

The following parameters change from Cohort 8A:

[1] change to: The terms in this group occurred between Oct 1, 2019 and Sep 30, 2021

[2] change to: 10/1/19 - 9/30/21

[3] change to: 10/1/2019

[4] change to: The terms in this group occurred between Jan 1, 1900 and Sep 30, 2019

Cohort 8C (query name: Incident Tirzepatide 10/1/21 - 9/30/23)

The following parameters change from Cohort 8A:

[1] change to: The terms in this group occurred between Oct 1, 2021 and Sep 30, 2023

[2] change to: 10/1/21 - 9/30/23

[3] change to: 10/1/2021

[4] change to: The terms in this group occurred between Jan 1, 1900 and Sep 30, 2021

Cohort 8D (query name: Incident Tirzepatide 10/1/17 - 9/30/23)

The following parameters change from Cohort 8A:

[1] change to: The terms in this group occurred between Oct 1, 2017 and Sep 30, 2023

[2] change to: 10/1/17 - 9/30/23