Poster Code: B-270

Scan for poster + more

# Impact of Operational Definition Variations on GLP-1 Agonist Treatment Eligibility: An Analysis Using Real-World Data

**Jared Kamauu, BFA[1]; Aimee Harrison, MFA[1]; Scott L. DuVall, PhD[2]; Michael Buck, PhD[1]; Craig Parker, MD, MS[1]; Aaron Kamauu, MD, MS, MPH[1]**

*[1]Navidence Inc., USA; [2]PurpleLab Healthcare Analytics*, USA

**DISCLOSURES:** JK, MB, CP, and AK are employees of Navidence. AH was an employee of Navidence during this work. SLD is an employee of PurpleLab. This analysis was conducted using licensed and publicly available real-world data; no external or industry funding was received. [Confirm all author disclosures before submission.]

**So What?**

For GLP-1 agonist treatment eligibility, each comorbidity has a varying impact on the inclusivity of the cohort; however, the overall inclusion or exclusion of different CV-comorbidities does impact which patients are considered eligible for treatment. Specific and intentional CODef choices for comorbidities can have a critically important impact on GLP-1 treatment eligibility determination in real-world research.

## BACKGROUND

### Context

Glucagon-like peptide-1 (GLP-1) receptor agonists are now widely used for weight management, and demand for real-world evidence on eligibility is growing quickly. Yet complex clinical concepts such as treatment eligibility often lack standardized conceptual and operational definitions (CODefs), creating challenges for comparison and reproducibility. GLP-1 eligibility is a clear example: it depends jointly on age, body mass index, and weight-related comorbidities, each specifiable in several defensible ways.

### The Gap / Problem

A previous analysis of 14 reference sources documented substantial variation in the definitions used to establish eligibility for GLP-1 agonist treatment for weight management.[1] Sources differed on age thresholds, overweight and obesity criteria, and which cardiovascular-related comorbidities qualify. The impact of applying these differing definitions to real-world data (RWD) had not been explored, so it was not known whether this variation was a technical detail or a substantive driver of how many patients are counted as eligible.

### Pharmacoepidemiologic Relevance

Eligible-population estimates derived from RWD inform payer coverage policy, budget-impact models, study feasibility assessments, and the comparability of published findings. When CODefs are undocumented or inconsistently applied, eligible cohorts cannot be reproduced or pooled across studies. Transparent, computable definitions are therefore central to good pharmacoepidemiologic practice and to reporting frameworks such as ENCePP, GPP, and the FDA's real-world evidence guidance.

## OBJECTIVES

### Primary Objective

To quantify the real-world impact of GLP-1 agonist eligibility definitional variations on the size of eligible patient pools in RWD, applying consistent CODefs so that any difference observed is attributable to the comorbidity criteria alone.

### Secondary Objectives

- Compare eligible population size across three progressively broader comorbidity-based cohort definitions in two independent RWD sources.
- Quantify the incremental contribution of cardiovascular disease (CVD) and type 2 diabetes mellitus (T2DM) to the eligible pool.
- Identify which individual comorbidities contribute the most and the fewest unique patients in each data source.
- Assess whether the direction and magnitude of definitional sensitivity are consistent between an administrative claims source and an EHR-derived source.

## LIMITATIONS

Cohorts were defined from diagnosis codes, which reflect billed or documented care rather than verified clinical status, so misclassification is possible. Only narrow BMI thresholds were applied, and BMI is captured differently in claims than in EHR data, which may affect who qualifies as overweight or obese. Only the five most commonly cited comorbidities were assessed, and age criteria — another documented source of definitional variation — were held constant, so the three cohorts represent a subset of the permutations found across reference sources. Unique-patient contribution is reported for the comorbidities with the largest and smallest impact rather than for all five. The analysis quantifies the size of the eligible pool but not its clinical composition. MIMIC-IV is a single-center critical care database, so its estimates are not generalizable to ambulatory populations, and absolute counts are not directly comparable between sources given differences in population, data capture, and time frame.

## METHODS

### Study Design & Data Source

Cross-sectional analysis quantifying how variation in eligibility CODefs affects the size of the GLP-1–eligible population. Cohorts were constructed independently in two US real-world data sources: PurpleLab® CLEAR Claims, an all-payer administrative claims database, and MIMIC-IV, a de-identified critical care electronic health record database. Identical CODefs were applied in both sources.

### Study Population

Adults with overweight (BMI 27–29.9 kg/m²) or obesity (BMI ≥ 30 kg/m²), using narrow BMI definitions. Three nested cohorts were defined: (1) dyslipidemia OR hypertension (HTN) OR obstructive sleep apnea (OSA); (2) cohort 1 criteria OR CVD; (3) cohort 2 criteria OR T2DM.

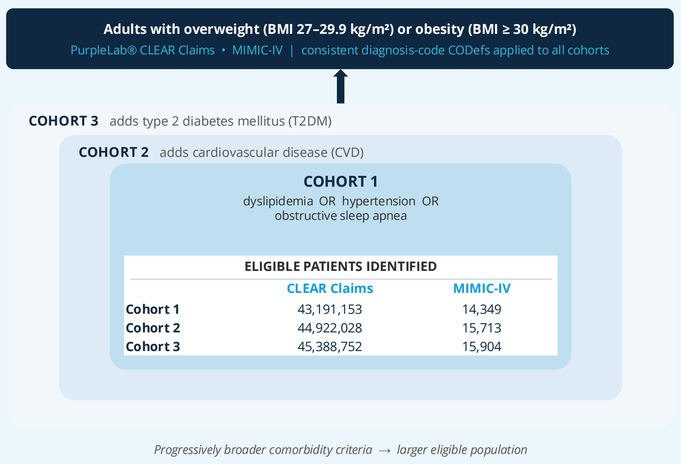



**Figure 1.** Nested GLP-1 eligibility cohort definitions and the resulting eligible patient counts in each data source.

### Exposures & Outcome Measures

The variable of interest was the eligibility definition itself rather than a drug exposure. The five comorbidities most commonly cited across the 14 reference sources were operationalized from diagnosis codes: CVD, dyslipidemia, HTN, OSA, and T2DM. The primary measure was the number of patients meeting each cohort definition; the secondary measure was the number of unique patients contributed by each comorbidity.

### Statistical Analysis

Analyses were descriptive. Cohort sizes were reported as counts, with absolute and relative change calculated against cohort 1. For each comorbidity, unique-patient contribution was the number of patients qualifying through that comorbidity alone. No inferential testing or confounding adjustment was performed, as the analysis compares definitions rather than treatment effects.

**Computable Operational Definitions (CODefs™)**

Study elements — exposures, outcomes, and covariates — were defined using Navidence CODefs™: rigorous, data source-agnostic algorithms that ensure precision and reproducibility across real-world data sources.

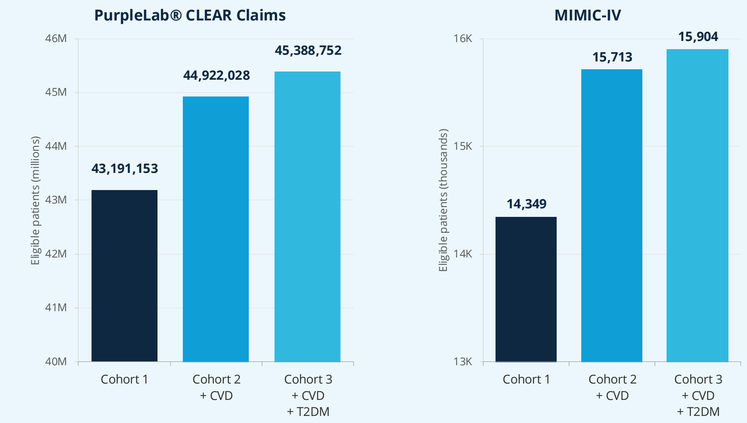
navidence.com

## RESULTS

**45.4M**
Broadest eligible pool CLEAR Claims, cohort 3

**1.7–9.5%**
More patients when CVD is added (cohort 2)

**1.0–9.2%**
More patients when T2DM is added (cohort 3)




Relative to cohort 1, across data sources: **adding CVD gave 1.7–9.5% more patients • adding T2DM gave 1.0–9.2% more patients**

**Figure 2.** Eligible patient population in each data source under the three cohort definitions. Note the differing vertical scales.

| Cohort definition | CLEAR Claims patients | MIMIC-IV patients | More patients vs cohort 1 |
|---|---|---|---|
| **1. Dyslipidemia OR HTN OR OSA** | 43,191,153 | 14,349 | reference |
| **2. Cohort 1 OR CVD** | 44,922,028 | 15,713 | 1.7–9.5% |
| **3. Cohort 2 OR T2DM** | 45,388,752 | 15,904 | 1.0–9.2% |

**Table 1.** Eligible patient counts by cohort definition in each data source. The final column gives the range, across data sources, of the percentage increase relative to cohort 1.

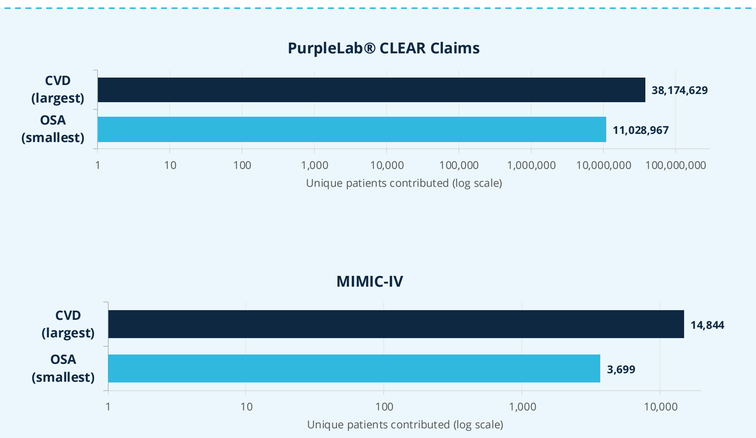



**Figure 3.** Comorbidities contributing the most and the fewest unique patients in each data source (log scale).

## CONCLUSIONS

### Key Findings

- The addition of CVD in cohort 2 resulted in 1.7–9.5% more patients relative to cohort 1; the addition of T2DM in cohort 3 resulted in 1.0–9.2% more patients relative to cohort 1.
- Comorbidities contributed very unequally. Dyslipidemia had the largest impact in CLEAR Claims (4,505,656 unique patients) and CVD the largest in MIMIC-IV (1,182); HTN had the smallest impact in both (6,491 and 1).
- Which comorbidity mattered most differed by data source, so definitional sensitivity is itself data-source dependent.

### Clinical & Policy Implications

Eligible-population estimates are interpretable only alongside the definition that produced them. Coverage decisions, budget-impact estimates, and cross-study comparisons should state the exact comorbidity criteria applied, and definitions should be reported in computable form so that results can be reproduced.

## REFERENCES

1. Kamauu J, Harrison A, DuVall SL, Buck M, Parker C, Kamauu A. Analysis and Characterization of Variations in Conceptual and Operational Definitions for GLP-1 Agonist Treatment Eligibility for Weight Management. Presented at: ISPOR Europe 2025.
2. PurpleLab. CLEAR Claims database. PurpleLab, Inc.
3. Johnson AEW, Bulgarelli L, Shen L, et al. MIMIC-IV, a freely accessible electronic health record dataset. Sci Data. 2023;10(1):1.

## TRANSPARENCY & REPRODUCIBILITY

Protocol and definitions: all cohort definitions — including the diagnosis code lists for each comorbidity and the BMI criteria — are documented as Navidence CODefs™ and are available from the authors on request. Data access: PurpleLab® CLEAR Claims is available under commercial license from PurpleLab; MIMIC-IV is available to credentialed users via PhysioNet. Reporting: results are reported in line with RECORD-PE and STROBE principles for database studies. [Add pre-registration ID and analytic code repository link if applicable.]