

The Wild West of GLP-1s: Utilization and Safety among those without FDA Indications

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Presenting on behalf of
IQVIA Government Solutions, Inc.

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Gaps in knowledge about non-indicated users

- **Evidence gap**:
  - Most pivotal trials and many RWE studies focus on patients with diabetes and/or obesity
  - Safety in lower-risk, non-indicated users is less characterized, especially for unexpected, non-cardiometabolic outcomes.
- **Known/expected adverse effects are gastrointestinal (GI)-dominant**
  - Real-world vigilance is increasing around severe pancreatitis warnings and broader GI complications (delayed gastric emptying, gastroparesis-like symptoms, obstruction/ileus signals in some sources).[1,2]
- **Non-indicated populations may differ**
  - Care setting, comorbidity mix, concomitant meds, weight-loss intensity
  - Confounding and surveillance bias more likely in this context, thus requiring designs that **screen first, then confirm** (incident outcomes, SCCS, active comparators)
- **Rare/serious events are hard to study with traditional "single-outcome" designs** because one must pre-specify outcomes; that misses "unknown unknowns."
  - **This is where TreeScan's hypothesis-free scan[3] across ICD-10 hierarchies adds value**

1. MHRA strengthened pancreatitis warning (Jan 2026) GLP-1 receptor agonists and dual GLP-1/GIP receptor agonists: strengthened warnings on acute pancreatitis, including necrotising and fatal cases - GOV.UK
2. GI adverse effects review (2026) | DMSO | Dove Medical Press
3. TreeScan Technical Documentation https://www.treescan.org/techdoc.html

Methods

Motivation & objectives

- To describe population characteristics of "non-indicated" GLP-1 users
- To identify & interpret key signals associated with recent "non-indicated" GLP-1 prescription

Data source & time frame

- IQVIA's Longitudinal Prescription Claims (LRxDx Open Claims, US9-LAAD 202510)
- Study period: 31-Oct-2023 to 31-Oct-2025 (2 years)
- Lookback for GLP-1 product washout: 31-Oct-2022 to 31-Oct-2023 (1-year lookback)
- Lookback for prior FDA indication washout: 3 years before the index date (1st GLP-1 prescription date within the study period) for each patient

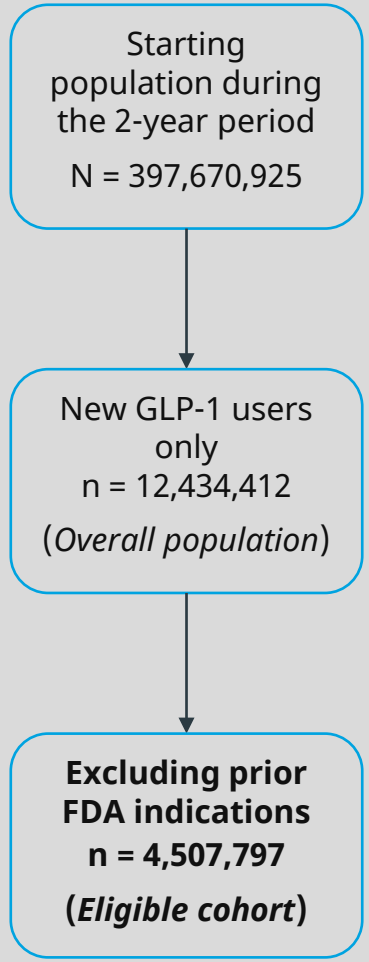
Key definitions

- **'New' GLP-1 users**: 1st GLP-1 prescription during the 2-year study period, and no prior GLP-1 prescription during the previous 1-year lookback
- **Prior FDA indications + common "off label use"**: Excluding prior indications in the past 2 years, using ICD-10-CM diagnosis codes for type 2 diabetes mellitus (**T2DM**), cardiovascular diseases (**CVD**), chronic kidney disease or end-stage renal disease (**CKD/ESRD**), obesity or high body mass index (**BMI**), metabolic dysfunction-associated steatohepatitis (**MASH**) (formerly known as nonalcoholic steatohepatitis [**NASH**]), and obstructive sleep apnea (**OSA**)

Analytic methods & tools

- Data access & queries: Snowflake (SQL-based query)
- Descriptive data analysis: Excel, R
- TreeScan: TreeScan™ software
- Data visualization: Excel, R, LucidChart

Patient count cascade



Results – GLP-1 product by brand over 10 years

Over the past 10 years, the landscape of GLP-1 products underwent major shifts in terms of brand recognition and competitive advantages, which was also corroborated by IQVIA's open claims data

Figure A. GLP-1 product unique patient count by brand by year

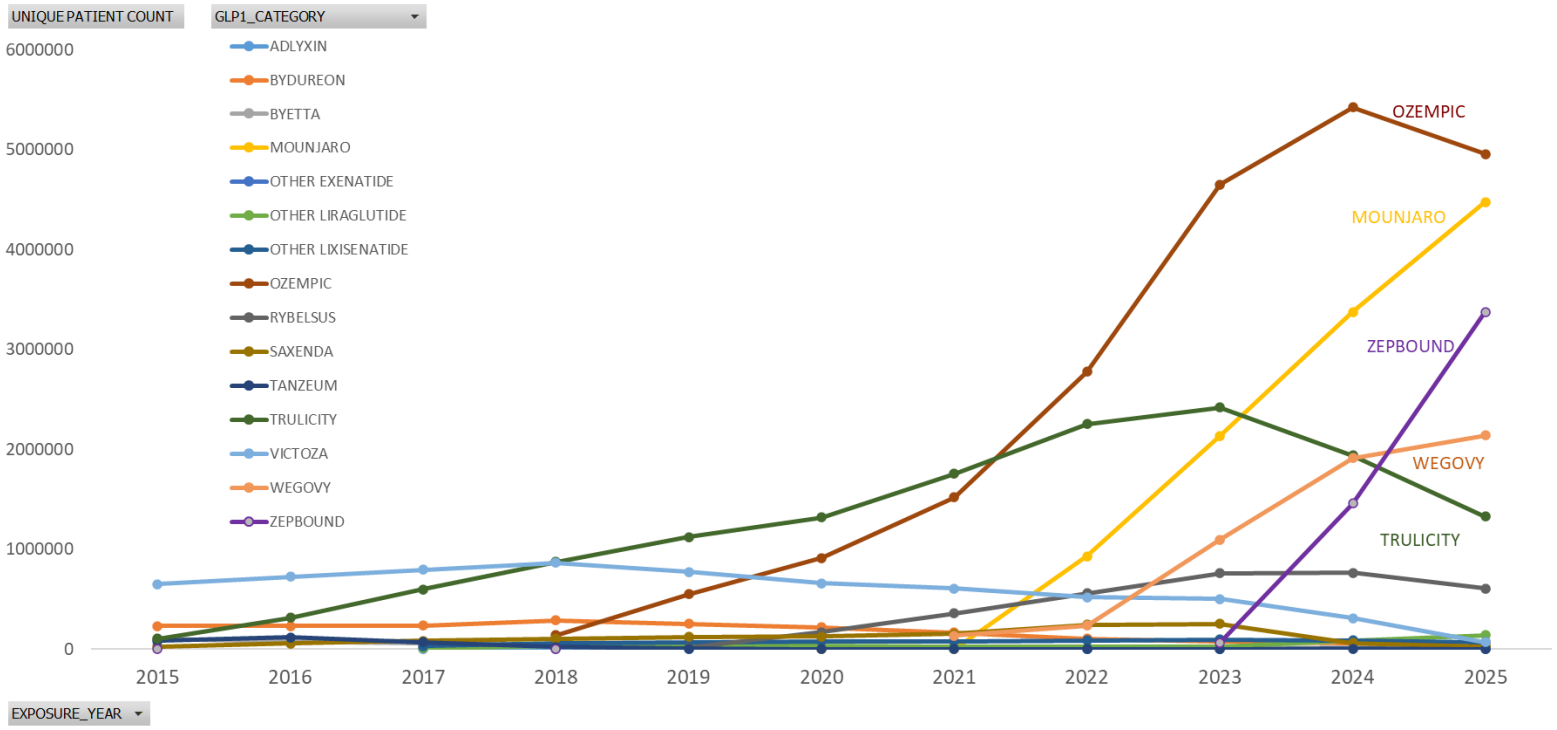
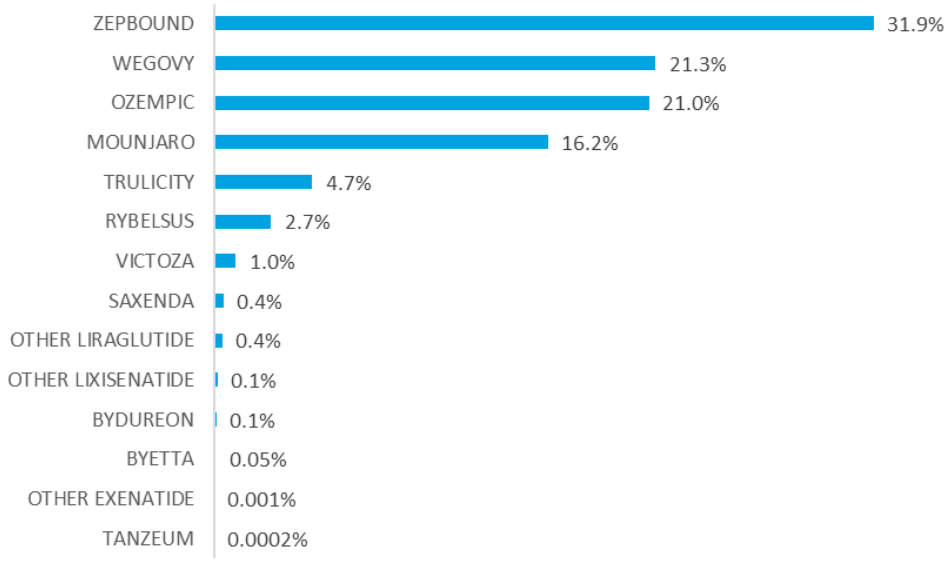


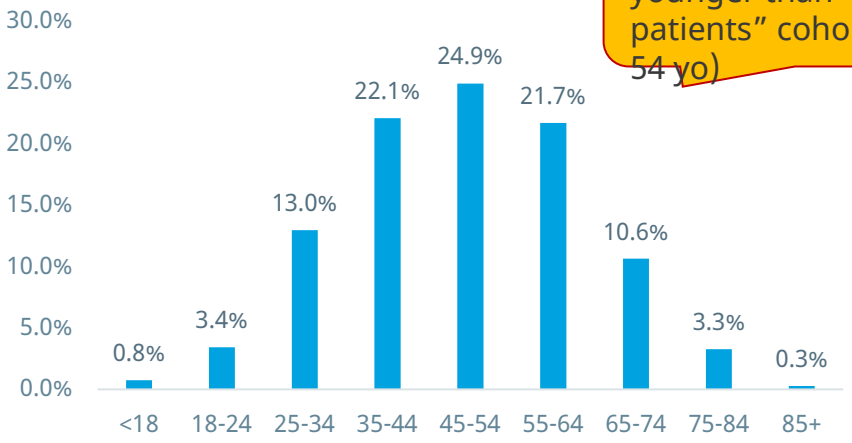
Figure B. GLP-1 product distribution by brand among "eligible cohort"



Results – Sociodemographic distribution (“eligible patients”)

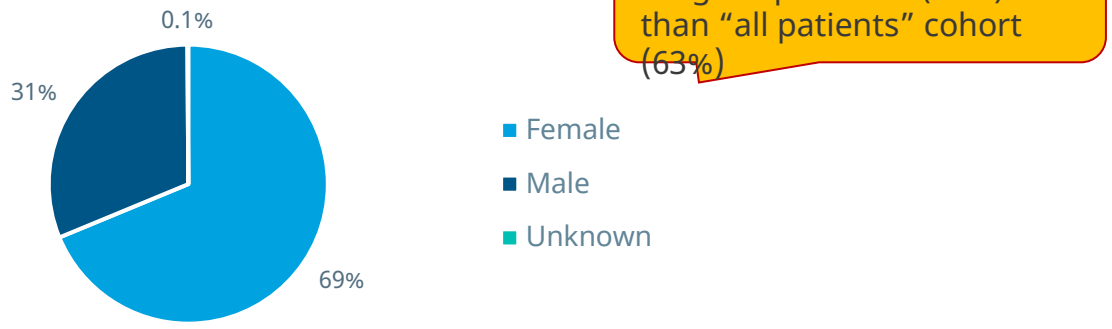
4.5M GLP-1 patients, without prior FDA indications

A) Age distribution (year)



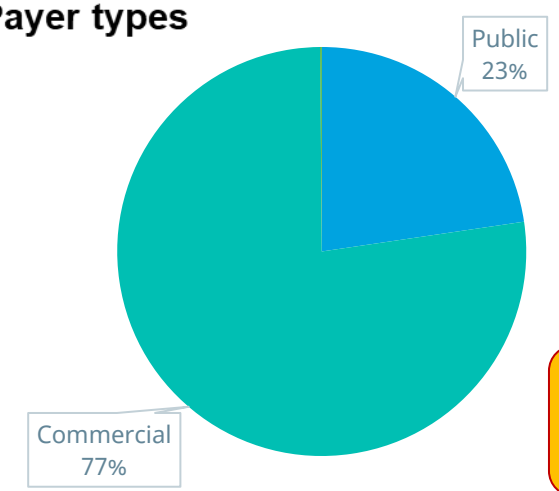
Peak user age group is younger than “all patients” cohort (more 25-54 yo)

B) Sex distribution



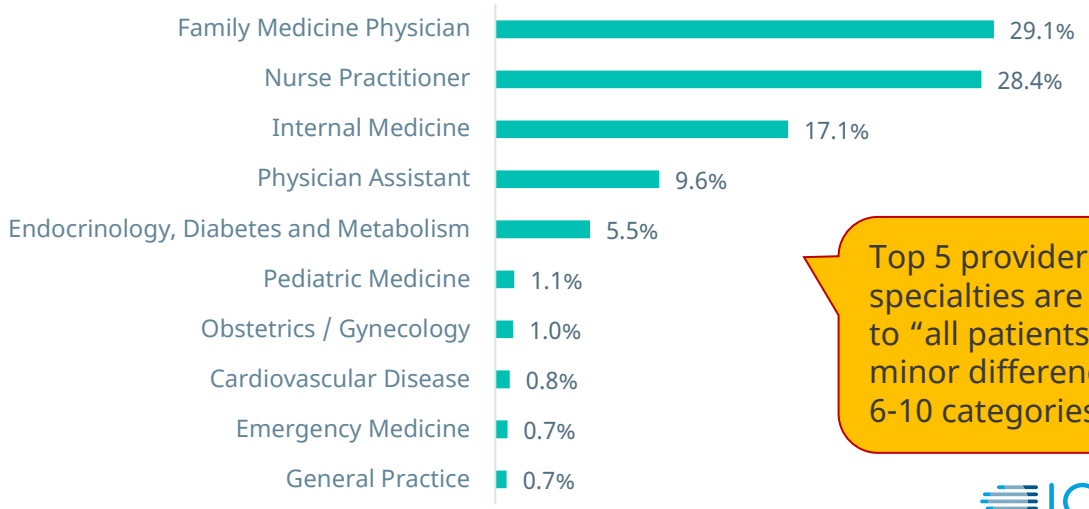
More women among “eligible patients” (69%) than “all patients” cohort (63%)

C) Payer types



Payer type is similar to “all patients” cohort

D) Top 10 GLP-1 Prescribing specialties (% pts)



Top 5 provider specialties are similar to “all patients” cohort; minor difference in top 6-10 categories

Substance use disorder within GLP-1 cohort

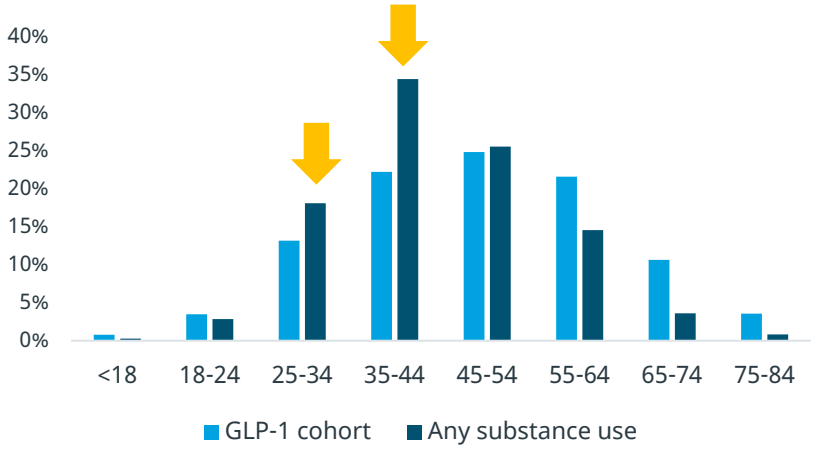
Using IQVIA Open Claims (LRxDx) 2024-25 data range

CATEGORY	Patient count	Percentage
GLP1 cohort (no prior FDA indications)	4,538,790	100%
Any substance use 30 days prior to GLP-1 initiation	16,449	**0.36%**
Substance category (have overlaps)		
Opioid-related disorders	6,964	0.15%
Alcohol-related disorders	4,111	0.09%
Nicotine/tobacco-related disorders	4,066	0.09%
Other stimulant-related disorders	1,260	0.03%
Cannabis-related disorders	1,226	0.03%
Other psychoactive substance-related disorders	691	0.02%
Cocaine-related disorders	586	0.01%
Sedative/hypnotic/anxiolytic-related disorders	375	0.01%
Hallucinogen-related disorders	56	0.001%
Gambling disorder / pathological gambling	45	0.001%
Inhalant-related disorders	14	0.0003%

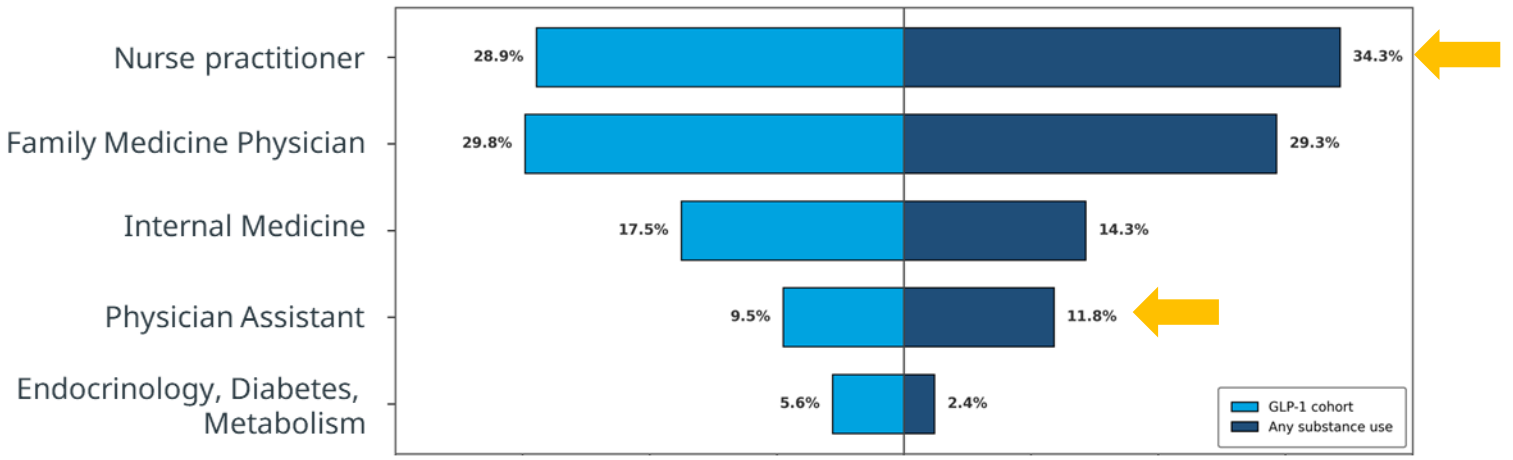
- **Among the GLP-1 cohort without prior FDA indication, <1% had any substance use code within 30 days prior to GLP-1 initiation**
- **Top 3 categories of substance used were opioid, alcohol, and nicotine/tobacco**

Comparisons of patient distribution between GLP-1 full cohort and subset with any substance use

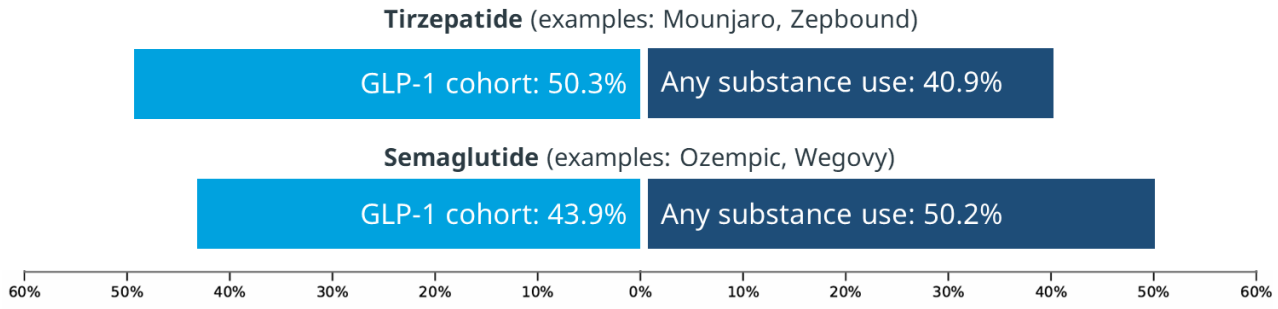
A. Comparison by age group



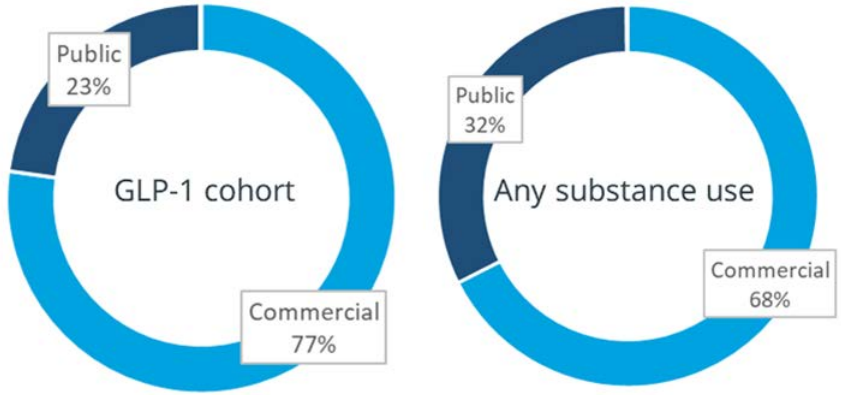
B. Top prescriber types



C. Most prescribed GLP-1 types



D. Payer types





TreeScan results

Results - TreeScan Output (most stringent threshold, p ≤ 0.001)

At the most stringent threshold, signals clustered around mental health, neurobehavioral, female endocrine/reproductive, metabolic-risk-adjacent, pain / musculoskeletal, and dermatologic / cosmetic-adjacent conditions

Mental health, mood, anxiety, & neurobehavioral conditions

Strongest signals:
- Anxiety disorders (F41/F411)
- ADHD (F90*),
- MDD (F33*) dominate frequency at this threshold

Female endocrine, reproductive, & hormonal disorders

Strongest signals:
- PCOS# (E282) and menopausal disorders (N95*) are among the most prominent signals

Nutrition, micronutrient, metabolic conditions

Strongest signals:
- Vitamin D deficiency (E55)
- Iron/B-vitamin deficiencies (D50, E53)
- Malabsorption and SIBO-related codes (K90, K63)

Pain, migraine, & musculoskeletal conditions

Strongest signals:
- Migraine (G43*)
- Low-back pain/dorsalgia (M54*) recur across many nodes.

Dermatologic & cosmetic-adjacent conditions

Strongest signals:
- Psoriasis (L40*) and acne (L70*) appear repeatedly.
- Follicular disorders and alopecia

#Polycystic Ovary Syndrome (PCOS) is a very common off-label use

Results - TreeScan Output (all additional signals)

Signal Strength

P-value range	0.001 < p ≤ 0.005	0.005 < p ≤ 0.01	0.01 < p < 0.05
Summary	At this threshold, prior themes persist with expansion into **autoimmune/inflammatory disorders, eating disorders, infertility-related diagnoses, and migraine subtypes**, suggesting broader specialty engagement rather than new etiologic patterns.	Signals broaden to include **immune dysregulation, rare endocrine disorders, autoimmune dermatology, and gynecologic structural disease**, reinforcing the profile of medically complex but non-indicated GLP-1 users.	At the broadest (but still statistically significant) threshold, the signal list becomes **heterogeneous**, dominated by **coding noise**, rare disorders, injuries, procedural follow-up, and low-frequency specialty diagnoses. Interpretability declines, but continued overrepresentation of psychiatric, gynecologic, pain, dermatologic, and metabolic-risk states remains evident.
Key takeaway	Groups remain stable; signal density increases, not diversity.	Signals increasingly correlate with care-seeking behavior rather than direct treatment indications	This level likely reflects high-utilization patients rather than GLP-1–specific correlates.

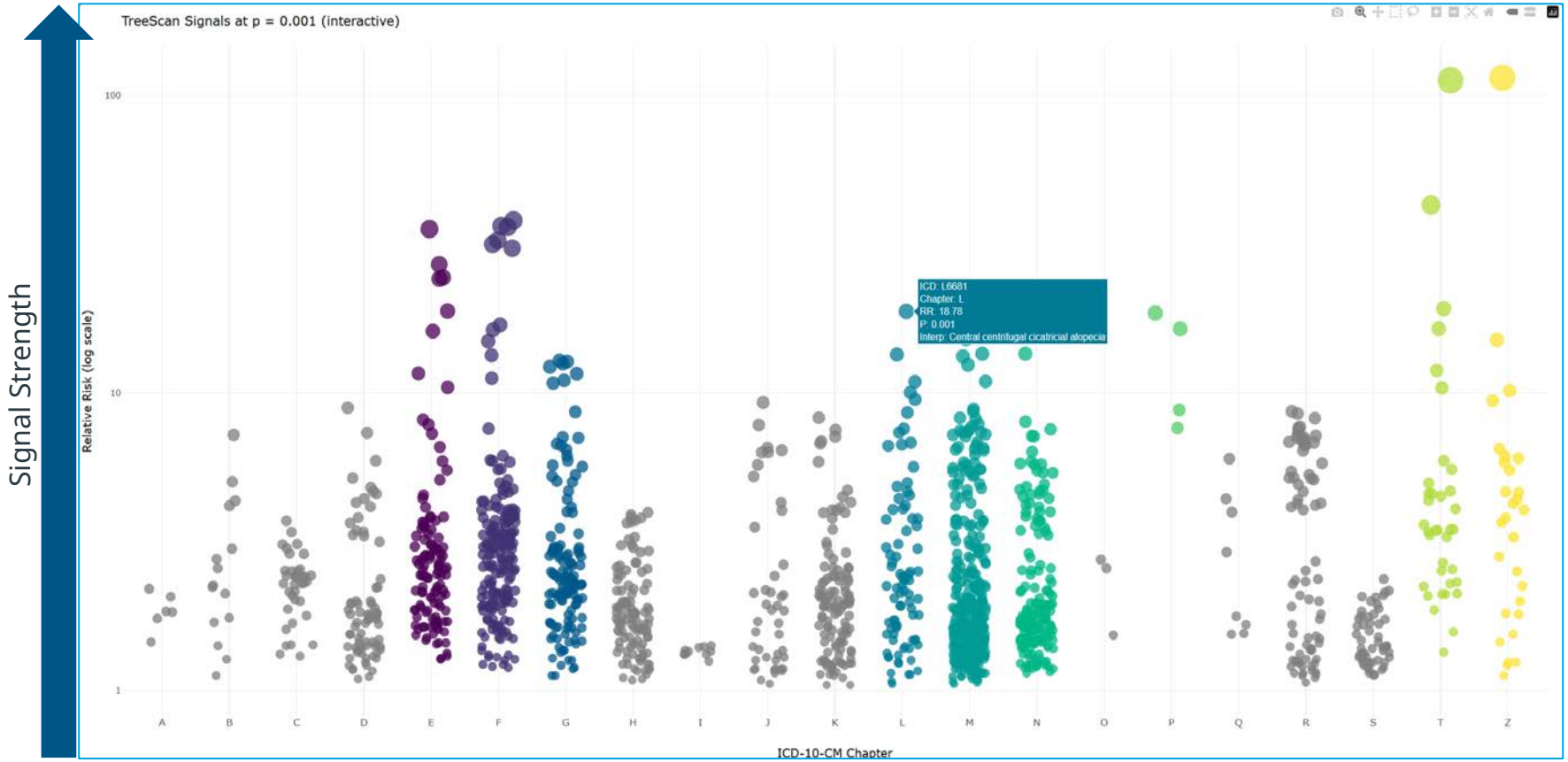
Results - TreeScan Output (Interactive scatterplot)

HTML file location: link

ICD-10-CM chapters:

A00-B99 Certain infectious and parasitic diseases
C00-D49 Neoplasms
D50-D89 Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism
E00-E89 Endocrine, nutritional and metabolic diseases
F01-F99 Mental, Behavioral and Neurodevelopmental disorders
G00-G99 Diseases of the nervous system
H00-H59 Diseases of the eye and adnexa
H60-H95 Diseases of the ear and mastoid process
I00-I99 Diseases of the circulatory system
J00-J99 Diseases of the respiratory system
K00-K95 Diseases of the digestive system
L00-L99 Diseases of the skin and subcutaneous tissue
M00-M99 Diseases of the musculoskeletal system and connective tissue
N00-N99 Diseases of the genitourinary system
O00-O9A Pregnancy, childbirth and the puerperium
P00-P96 Certain conditions originating in the perinatal period
Q00-QA0 Congenital malformations, deformations, chromosomal abnormalities, and genetic disorders
R00-R99 Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified
S00-T88 Injury, poisoning and certain other consequences of external causes
U00-U85 Codes for special purposes
V00-Y99 External causes of morbidity
Z00-Z99 Factors influencing health status and contact with health services

Source: icd10data.com



Results – TreeScan Output (reflections)

Notes/limitations of this preliminary analysis

- At the most stringent threshold, **signal profile in non-indicated population clustered around psychiatric, endocrine, reproductive, nutritional, metabolic, dermatologic, and chronic pain conditions** (*some for conditions where off-label prescribing may be more common*)
- Lacks data on patients who pay with cash
- Many signals at lower cutoff threshold reflect care-seeking intensity, and may not be causal association
- Metabolic codes may reflect early indication, before actual diagnosis
- Specialty clinics may systematically code more diagnoses, amplifying TreeScan signals
- Next steps:
  - Analysis by selected product; incident inpatient/ED codes only
  - Risk categorization by age, sex, co-pay
  - Run self-controlled case series on selected signals

Thank you!

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