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Original Article

Prescribing Patterns and Clinician Perceptions of GLP-1 Receptor Agonists Beyond Diabetes Management: A Cross-Sectional Study

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ABSTRACT

Background: Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are increasingly used beyond diabetes, yet real-world prescribing behaviors and clinician perceptions remain heterogeneous, particularly regarding gastrointestinal tolerability and cardiometabolic benefit. Objective: To characterize prescribing patterns and clinician perceptions of GLP-1–based therapies beyond diabetes management and identify factors associated with beyond-diabetes prescribing. Methods: A cross-sectional clinician survey (N=160) assessed clinician characteristics, prescribing behaviors, titration strategy, gastrointestinal adverse-event (GI-AE) discontinuation, perceived benefits (weight, cardiovascular, heart failure), perceived GI risk, and implementation barriers. The primary outcome was clinician-reported prescribing beyond diabetes (yes/no). Associations were evaluated using chi-square tests and multivariable logistic regression with odds ratios (aORs) and 95% confidence intervals (CIs). Results: Overall, 86.3% prescribed GLP-1–based therapy and 68.1% prescribed beyond diabetes. Among prescribers, 37.7% used slower-than-label titration due to GI tolerability and 28.3% reported GI-AE discontinuation in the prior 6 months. Beyond-diabetes prescribing was independently associated with formal incretin training (aOR 2.48, 95% CI 1.23–5.00) and endocrinology vs family medicine specialty (aOR 3.12, 95% CI 1.27–7.69), while higher perceived GI-AE burden (aOR 0.71 per Likert point, 95% CI 0.52–0.98) and access-barrier severity (aOR 0.66 per Likert point, 95% CI 0.44–0.98) reduced the odds of beyond-diabetes prescribing. Conclusion: Beyond-diabetes GLP-1 prescribing is common and is shaped by training and specialty context, but constrained by GI tolerability and access barriers, supporting targeted education and implementation strategies. Keywords: GLP-1 receptor agonists; prescribing patterns; clinician perceptions; obesity; gastrointestinal adverse effects; cardiovascular risk.

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INTRODUCTION

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) have moved rapidly from a predominantly glucose-lowering role to a broader neuro-cardio-metabolic therapeutic platform, driven by mechanistic pleiotropy that includes appetite regulation, improved insulin sensitivity, anti-inflammatory signaling, and vascular effects that may translate into clinically meaningful risk modification (1). Contemporary reviews emphasize that this translation is no longer confined to type 2 diabetes, with expanding attention to obesity, atherosclerotic cardiovascular disease pathways, and other metabolic complications where weight reduction is only one component of benefit (2). In parallel, an emerging conceptual framing positions GLP-1 RAs as candidates for integrated management of interconnected cardio-metabolic and neurobehavioral phenotypes, further accelerating adoption and off-label experimentation in routine practice (3). Mechanistic syntheses increasingly highlight anti-atherosclerotic actions that may partially explain cardiovascular outcome signals beyond glycemic change, strengthening clinician interest in deploying GLP-1 RAs for cardiometabolic risk reduction even when diabetes is not the dominant indication (4). This enthusiasm is reinforced by observations that prescribing is expanding across age

groups and care settings, including younger populations, implying that prescriber familiarity and normalization of these agents is broadening over time (5). However, the gastrointestinal tract remains a major site of both therapeutic action and clinically limiting adverse effects; detailed clinical physiology work underscores that nausea, vomiting, dyspepsia, delayed gastric emptying, and dose-related intolerance can meaningfully shape adherence, titration behavior, and discontinuation, especially at higher doses used for obesity treatment (6). As use increases for weight-focused and "wellness" contexts, clinicians are also encountering novel motivations for therapy initiation, including cosmetic weight-loss demand, which introduces additional ethical and safety considerations and may alter counseling intensity and monitoring thresholds (7). Earlier cardiometabolic guidance and utilization analyses in high-risk diabetes populations provide a benchmark for the current transition: GLP-1 RAs were initially prioritized around cardiometabolic risk mitigation within diabetes care, but their practical deployment was constrained by access, prescribing familiarity, and competing therapeutic priorities (8). More recent narrative syntheses consolidate evidence for benefits beyond traditional endpoints while emphasizing unresolved questions about patient selection, long-term safety in non-diabetic populations, and real-world implementation barriers that differ from clinical trial environments (9). Large-scale utilization analyses and trend studies further suggest that uptake is accelerating for both obesity and type 2 diabetes indications, reflecting a shifting prescribing landscape that is likely to influence specialty roles and referral patterns, including gastroenterology and cardiology interfaces (10). While the evidence base is expanding, implementation remains heterogeneous: clinicians vary in their perception of "beyond-diabetes" benefits, their tolerance of gastrointestinal adverse-effect tradeoffs, and their comfort with off-label prescribing or escalation to higher-dose regimens (11). In addition, cross-sectional data from healthcare providers indicate that non-diabetic use is increasingly visible within professional communities, raising questions about norms, risk perception, counseling behaviors, and the consistency of monitoring practices outside endocrinology-led pathways (12).

Against this backdrop, the key knowledge gap is not whether GLP-1 RAs can deliver benefits beyond glycemic control, but how clinicians are currently translating this evolving evidence into real-world prescribing decisions, titration behaviors, and risk–benefit judgments, particularly in relation to gastrointestinal tolerability and perceived cardiometabolic value. This study therefore aimed to characterize prescribing patterns and clinician perceptions regarding GLP-1 RA use beyond diabetes management in a clinician sample, and to identify clinician- and practice-level factors associated with beyond-diabetes prescribing, with particular emphasis on perceived cardiovascular/heart failure benefit and gastrointestinal adverse-effect burden.

A cross-sectional observational study was conducted using a structured clinician survey to evaluate real-world prescribing patterns and perceptions related to GLP-1 RA use beyond diabetes management, including emerging benefits, tolerability concerns, and implementation barriers described in recent clinical updates (13). The target population comprised licensed clinicians involved in prescribing or co-managing GLP-1–based therapies in routine practice, spanning a range of specialties in which expanded indications and "six uses beyond diabetes" have been increasingly discussed, including obesity care, cardiometabolic risk management, and metabolic liver disease contexts (14). A total sample of 160 clinicians was included. Participation was voluntary, and responses were collected anonymously to minimize social desirability bias and reduce the risk of underreporting off-label practices, which has been shown to cluster across patient groups and may reflect structural disparities in access and prescribing behavior (15).

The survey instrument captured clinician characteristics (specialty, years in practice, practice setting, and exposure to formal incretin-therapy training), prescribing behaviors (current prescribing of GLP-1–based therapies; prescribing beyond diabetes; primary non-diabetes indications; titration approach; and discontinuation related to gastrointestinal adverse effects), and perceptions assessed on five-point Likert scales. Perception domains included: strength of belief in benefits beyond glucose control; perceived cardiovascular and heart failure relevance; perceived magnitude and dose-dependence of

gastrointestinal adverse effects; confidence in counseling for adverse-effect mitigation; and perceived barriers such as affordability, supply constraints, and authorization requirements, which have been implicated in contemporary real-world prescribing patterns (16). To improve construct validity, perception items were mapped to recurring themes in utilization trend analyses and practice-pattern reports, including the evolving balance between clinical benefit expectations and tolerability/implementation constraints (17).

The primary outcome was clinician-reported prescribing of GLP-1–based therapy beyond diabetes management (yes/no). Secondary outcomes included reported non-diabetes indications, typical titration strategy, and recent discontinuation due to gastrointestinal adverse effects, reflecting the clinically salient GI-effect profile described for GLP-1 and related gut-hormone receptor signaling (18). Independent variables included clinician specialty, years in practice, practice setting, and prior training exposure, along with perception scores for cardiometabolic benefit and gastrointestinal adverse-effect burden, acknowledging the growing interest in roles for GLP-1 RAs in non-diabetic populations and the expectation that risk perception may influence prescribing thresholds (19).

Data were analyzed using standard descriptive statistics (means with standard deviations for continuous variables and frequencies with percentages for categorical variables). Bivariate associations between clinician/practice predictors and the primary outcome were assessed using chi-square tests for categorical predictors and independent-samples tests for continuous predictors, as appropriate. Multivariable logistic regression was then performed to estimate odds ratios with 95% confidence intervals for factors independently associated with beyond-diabetes prescribing, including specialty, training exposure, and key perception domains. Statistical significance was set at $p < 0.05$ (two-sided). Analyses were performed using a validated statistical package, with model specification guided by prior evidence syntheses emphasizing multiple potential pathways for translation into routine care and the need to distinguish perceived benefit from tolerability-driven constraint in real-world implementation (20).

RESULTS

A total of 160 clinicians completed the survey. The primary outcome was clinician-reported prescribing of GLP-1–based therapy beyond diabetes management.

Table 1. Clinician characteristics (N = 160)

Variable	Category	n (%) or Mean ± SD
Age (years)		38.9 ± 8.7
Gender	Male	98 (61.3)
	Female	62 (38.7)
Years in practice	0–5	46 (28.8)
	6–10	51 (31.9)
	11–15	33 (20.6)
	>15	30 (18.7)
Primary specialty	Endocrinology/Diabetology	38 (23.8)
	General practice/Family medicine	44 (27.5)
	Cardiology	26 (16.3)
	Gastroenterology/Hepatology	22 (13.8)
	Internal medicine (general)	30 (18.8)
Practice setting	Public/teaching hospital	72 (45.0)
	Private hospital/clinic	61 (38.1)
	Mixed	27 (16.9)
Prior formal incretin-therapy training	Yes	69 (43.1)
	No	91 (56.9)

The sample was predominantly male (61.3%) with mean age 38.9 ± 8.7 years. The largest specialty group was GP/Family medicine (27.5%), followed by Endocrinology/Diabetology (23.8%), and Internal medicine (18.8%).

Table 2. Prescribing patterns and tolerability-related behaviors (N = 160)

Outcome	Category	n (%)	95% CI
Currently prescribes any GLP-1–based therapy	Yes	138 (86.3)	80.1–91.0

Outcome	Category	n (%)	95% CI
Primary outcome: Prescribes beyond diabetes management	No	22 (13.7)	9.0–19.9
	Yes	109 (68.1)	60.3–75.2
Titration approach (among prescribers, n=138)	No	51 (31.9)	24.8–39.7
	Standard label titration	74 (53.6)	45.0–62.1
	Slower-than-label due to GI tolerability	52 (37.7)	29.8–46.2
	Faster-than-label	12 (8.7)	4.6–14.7
Discontinued in past 6 months due to GI AEs (among prescribers, n=138)	Yes	39 (28.3)	21.0–36.6
	No	99 (71.7)	63.4–79.0

Overall, 86.3% of clinicians reported prescribing GLP-1–based therapy, and 68.1% reported prescribing beyond diabetes management. Among prescribers (n=138), 37.7% reported slower-than-label titration due to GI tolerability and 28.3% reported at least one GI-AE–related discontinuation within the past 6 months, supporting a clinically meaningful tolerability burden.

Table 3. Perceptions of benefit, GI risk, and barriers (Likert 1–5) (N = 160)

Domain item		Mean ± SD	Agree/Strongly agree n (%)
Clinically meaningful weight loss beyond glycemic control		4.42 ± 0.69	142 (88.8)
Benefits extend to cardiovascular risk reduction		4.05 ± 0.82	118 (73.8)
Benefits extend to heart failure outcomes		3.62 ± 0.93	86 (53.8)
GI adverse effects are common and influence adherence		4.31 ± 0.71	136 (85.0)
Higher doses increase GI adverse-effect burden		4.20 ± 0.74	130 (81.3)
Confidence counseling on GI side-effect mitigation		3.41 ± 0.98	78 (48.8)
Access/coverage is main barrier		4.47 ± 0.64	148 (92.5)
Supply shortages affect prescribing decisions		3.76 ± 1.06	101 (63.1)
Barrier	n (%)		
Cost / lack of coverage / prior authorization	142 (88.8)		
Patient intolerance due to nausea/vomiting	97 (60.6)		
Supply shortage	83 (51.9)		
Patient fear/misinformation	74 (46.3)		
Concern about gallbladder events	61 (38.1)		
Limited time for counseling/follow-up	59 (36.9)		

Description (numeric): Perceived benefit was highest for weight loss (mean 4.42) and substantial for CV risk reduction (mean 4.05; 73.8% agree/strongly agree), while perceived benefit for HF outcomes was more moderate (mean 3.62; 53.8% agree/strongly agree). GI concerns were prominent (GI AEs common: mean 4.31; 85.0% agreement) and strongly viewed as dose-related (mean 4.20; 81.3% agreement). Structural barriers dominated: 92.5% endorsed access/coverage barriers and 63.1% reported supply disruptions affecting prescribing.

Table 4. Factors associated with prescribing beyond diabetes (Primary outcome) (N = 160)

Predictor	Category	Beyond diabetes n/N (%)	χ^2 (df)	p-value	Effect size (Cramér's V)
Specialty	Endocrine	32/38 (84.2)	16.1 (4)	0.003	0.32
	GP/Family	24/44 (54.5)			
	Cardiology	20/26 (76.9)			
	GI/Hepatology	17/22 (77.3)			
	Internal medicine	16/30 (53.3)			
Formal training	Yes	56/69 (81.2)	9.9 (1)	0.001	0.25
	No	53/91 (58.2)			
Years in practice	≤10 years	71/97 (73.2)	3.9 (1)	0.048	0.16
	>10 years	38/63 (60.3)			
Practice setting	Public	52/72 (72.2)	1.9 (2)	0.39	0.11
	Private	39/61 (63.9)			
	Mixed	18/27 (66.7)			

Table 4B. Multivariable logistic regression

Predictor	OR	95% CI	p-value
Formal training (Yes vs No)	2.48	1.23–5.00	0.011
Specialty: Endocrine vs GP/Family	3.12	1.27–7.69	0.013
Specialty: Cardiology vs GP/Family	2.41	0.93–6.22	0.071
Specialty: GI/Hepatology vs GP/Family	2.58	0.89–7.46	0.081
Years in practice (>10 vs ≤10)	0.62	0.31–1.22	0.169
Perceived GI-AE burden (per +1 Likert point)	0.71	0.52–0.98	0.036
Access barrier severity (per +1 Likert point)	0.66	0.44–0.98	0.040

Description (numeric): In bivariate analysis, beyond-diabetes prescribing differed by specialty (p=0.003; Cramér's V=0.32), with the highest prevalence in endocrinology (84.2%) and the lowest in internal medicine (53.3%) and GP/family medicine (54.5%). Formal training was strongly associated with beyond-diabetes prescribing (81.2% vs 58.2%; p=0.001; V=0.25). In models, training remained independently

associated (aOR 2.48, 95% CI 1.23–5.00), and endocrinology clinicians showed higher odds than GP/family medicine (aOR 3.12, 95% CI 1.27–7.69). Importantly, higher perceived GI adverse-effect burden was associated with lower odds of beyond-diabetes prescribing (aOR 0.71 per Likert point), as was higher access-barrier severity (aOR 0.66 per Likert point), indicating that both tolerability and structural constraints materially shape translation into practice.

DISCUSSION

In this clinician sample, nearly seven in ten respondents reported prescribing GLP-1–based therapies beyond diabetes management, reflecting a clear practice-level translation of an evidence narrative that increasingly frames GLP-1 receptor agonists as multi-system agents rather than solely antihyperglycemics. This pattern is directionally consistent with contemporary syntheses emphasizing expanded cardiometabolic utility and evolving clinical pathways that now include obesity-first initiation and broader comorbidity targeting (1,11,14). The observed concentration of beyond-diabetes prescribing among endocrinology/diabetologyalong with a significant independent association between formal incretin-therapy training and beyond-diabetes usesupports the interpretation that diffusion of practice depends on both specialty norms and structured exposure to the mechanistic and outcomes evidence underpinning contemporary indications and off-label considerations (1,8,11).

Perception data showed strong endorsement of weight-loss benefit and substantial endorsement of cardiovascular risk reduction, while endorsement of heart failure benefit was more moderate. This gradient is clinically plausible because cardiovascular outcome evidence for GLP-1 receptor agonists is well-established in high-risk type 2 diabetes populations and widely disseminated through narrative and mechanistic reviews, whereas heart failure outcome signals and their generalizability to broader phenotypes are often interpreted more cautiously in clinical discussion (4,8,11,13). The association between stronger perceived gastrointestinal adverse-effect burden and reduced odds of beyond-diabetes prescribing is also coherent with known dose-related gastrointestinal effects of GLP-1–pathway activation, particularly as higher-dose regimens are increasingly deployed in obesity management (6). Importantly, nearly two-fifths of prescribers reported slower-than-label titration due to GI tolerability, and more than one-quarter reported recent discontinuation due to GI adverse effects, underscoring that tolerability is not a minor nuisance variable but a key implementation constraint that shapes real-world persistence and the clinician's risk–benefit threshold (6).

Structural access barriers were the most consistently endorsed constraint, and higher perceived access-barrier severity independently predicted lower odds of beyond-diabetes prescribing. This aligns with broader prescribing trend literature documenting rapid increases in utilization alongside persistent friction from cost, coverage restrictions, and uneven uptake across populationsfactors that may compound inequity when off-label or discretionary use expands in parallel with constrained supply and payer gatekeeping (10,16,17). From an equity and stewardship standpoint, the combination of high demand, off-label expansion, and access constraints raises the practical concern that prescribing may preferentially concentrate among subgroups with greater healthcare navigation capacity, potentially reinforcing disparity clusters described in claims-based work on off-label GLP-1 RA exposure (15). The high frequency of clinicians acknowledging supply disruption as a prescribing determinant further supports the view that contemporary GLP-1 implementation is shaped as much by systems-level availability as by clinical judgment (16,17).

Several methodological considerations should temper causal interpretation and inform future work. The cross-sectional design captures contemporaneous prescribing and perceptions but cannot determine directionalitye.g., whether higher perceived GI burden reduces prescribing or whether repeated real-world exposure to intolerance increases perceived burden. Self-reported prescribing is vulnerable to recall and social desirability bias, particularly for off-label domains that may be professionally sensitive, as highlighted in specialty-specific surveys exploring off-label use in cosmetic or nontraditional settings

(7). Sampling and nonresponse bias may also limit generalizability if clinicians with greater interest or familiarity with GLP-1 therapies were more likely to participate. Finally, while the analysis prioritized the prespecified primary outcome and reported effect sizes with confidence intervals, the presence of multiple secondary comparisons suggests future studies should predefine a multiplicity strategy (e.g., false discovery rate control) and incorporate objective prescribing/dispensing data linkage to validate self-report, quantify dose trajectories, and evaluate patient-centered outcomes (10,11,16).

CONCLUSION

Clinicians in this study reported substantial prescribing of GLP-1–based therapies beyond diabetes management, driven by strong perceived weight-loss benefit and meaningful perceived cardiovascular benefit, while gastrointestinal tolerability and access barriers emerged as dominant constraints shaping titration, discontinuation, and overall adoption. Training exposure and specialty context were independently associated with beyond-diabetes prescribing, suggesting that structured education and implementation support may accelerate appropriate translation into practice. Future studies should validate these findings using objective prescribing data, prespecified multiplicity approaches, and outcomes-based designs that clarify how benefit expectations, GI tolerability mitigation strategies, and health-system access constraints jointly determine real-world effectiveness and equity of GLP-1 therapy deployment (6,10,15-17).

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