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Patterns of prescription and discontinuation of glucagon-like peptide-1 receptor agonists among patients with irritable bowel syndrome

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Abstract

Background Glucagon-like peptide-1 receptor agonists (GLP-1RAs) are associated with gastrointestinal (GI) adverse effects, but real-world evidence about their incidence in patients with functional GI disorders is limited. We examined their prescription and discontinuation patterns in irritable bowel syndrome (IBS) patients.

Methods In this retrospective analysis of GLP-1RAs prescribed to patients with IBS at our institution from 2013-2023, we assessed the association of IBS subtype- and patient-related (age, race, body mass index, insurance, diabetes, gastroesophageal reflux disease) factors on the number and reasons for agent switches throughout the treatment course.

Results Of the 256 patients with IBS prescribed >1 GLP-1RAs, 227 (88.7%) patients trialed 2-3 GLP-1RAs, while 29 (11.3%) trialed ≥4 agents. Mixed-type IBS patients showed the highest rates of switching, followed by constipation- and diarrhea-predominant type IBS (21.7%, 11.7% and 2.2%, respectively; P=0.02). Semaglutide had more discontinuations within 6 months of starting the first GLP-1RA, compared to liraglutide (63.4% vs. 43%; P=0.012). Patients aged ≥65 years were more likely to continue the first agent for >6 months compared to those <65 years (65.8% vs. 44%, P=0.014). In successive lines of therapy, treatment-related discontinuations (injection burden, non-response) remained fairly constant (17%, 14%, 14%) but symptom-related (nausea, vomiting, diarrhea, constipation) discontinuations increased steadily from first to third agent (28%, 30%, 48%, respectively). Patients with Medicare/Medicaid were more likely to switch ≥3 therapies, than those with private/self-pay coverage (23% vs. 7.3%; P=0.006).

Conclusion Our findings highlight the importance of tailoring therapy based on drug-specific and patient-related factors to optimize GLP-1RA use in IBS.

Keywords Irritable bowel syndrome, subtypes, GLP-1 receptor agonists, real-world evidence

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Conflict of Interest: None

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Introduction

Irritable bowel syndrome (IBS) is the most prevalent functional gastrointestinal (GI) disorder, affecting up to 12% of adults in the United States (US), and thereby imposing a significant burden on the healthcare system [1]. It is primarily caused by disturbances of the neural and hormonal function in the GI tract, also known as the brain–gut axis. This complex disorder involves alterations in the sensory, motor, mucosal, immune, and microbial function [2-4]. Several hormones are implicated in IBS pathophysiology; these include glucagon-like peptide 1 (GLP-1), released by the ileal and colonic L-cells in response to food intake [5]. GLP-1 acts on both the central

and peripheral nervous systems to stimulate insulin release and inhibit GI motility [3,6-9]. GLP-1 receptor agonists (RAs) can also influence gut microbiota by increasing the levels of certain bacterial components and neurotransmitters, which may affect gut motility and barrier function [10,11].

In recent years, GLP-1RAs have gained significant prominence, not only in diabetes management, but also for their benefits in cardiovascular risk reduction and weight loss [12]. While these agents offer important therapeutic advantages, they are frequently associated with both upper and lower GI adverse effects (AEs), such as nausea, vomiting, abdominal pain, diarrhea, and constipation [13]. Although the incidence of GI AEs with GLP-1RAs has been well-documented in the general population, real-world evidence remains scant for patients with preexisting functional GI disorders such as IBS [14]. Real-world evidence is particularly important in this subgroup, as clinical trials often exclude patients with complex GI disorders, or may fail to capture their impact. This subgroup is of particular interest, because IBS-related GI disturbances may be exacerbated by the known AEs of GLP-1RAs, thereby introducing unique issues in relation to medication adherence and quality of life. This is complicated further, as IBS is categorized into 3 subgroups, each with its own symptoms and challenges in management. As GLP-1RAs become more popular, it is critical to understand the unique challenges faced by patients with concurrent IBS for guiding prescription patterns, optimizing management strategies and improving long-term treatment outcomes. Additionally, the current literature highlights a substantial gap in our knowledge of the comparative incidence of GI AEs across different GLP-1RA agents in this population. Such data are essential for tailoring treatment approaches that maximize efficacy while minimizing GI AEs, thereby enhancing tolerability and adherence—especially as IBS already constitutes a significant portion of the GI-related healthcare utilization and economic burden.

To address this gap, this study aimed to investigate the prescription patterns of GLP-1RAs in patients with IBS, and to explore the factors influencing therapy discontinuation, including drug switching frequency and the duration of medication adherence. By analyzing patient-related factors and outcomes associated with each line of GLP-1RA therapy, we sought to provide actionable insights that could lead to more personalized and effective utilization of GLP-1RAs in patients with IBS, ultimately mitigating the impact of GI AEs on overall treatment adherence and patient outcomes.

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Patients and methods

We retrospectively reviewed patients who were prescribed GLP-1RAs at our academic institution from January 1, 2013, to December 31, 2023, for various indications, including type 2 diabetes, weight management and cardiovascular risk reduction. We extracted all data from the institution's electronic health records following approval by the institutional review board (IRB).

For our study we included individuals with a preexisting diagnosis of IBS, according to the Rome III and IV criteria [15], who were prescribed GLP-1RA. We excluded individuals if their IBS diagnosis was not clearly documented, or if they had incomplete medication records, or if they were <18 years of age at the time of first prescription. We collected baseline characteristics and demographic variables of the individuals, including age, sex, body mass index (BMI), race, type of insurance coverage, indication for GLP-1RA, presence of concurrent gastroesophageal reflux disease (GERD), and subtype of IBS.

Because the primary objective was to characterize switching behavior, we restricted inclusion to patients who underwent at least 1 documented change in GLP-1RA therapy; single-agent courses were therefore excluded. We calculated the time that an individual stayed on the first and each subsequent GLP-1RA, and noted the reason for discontinuation of the therapies and the number of switches throughout the treatment course. We classified the reasons for discontinuation into treatment-related (i.e., injection burden, non-response), symptom-related (i.e., nausea, vomiting, dyspepsia, diarrhea, constipation, malnutrition), and access/coverage-related (i.e., shortage, insurance denial) discontinuations.

For each patient, we recorded the start date of therapy and the duration on each specific GLP-1RA, defined as the time from the initial prescription date until the discontinuation date. The latter was determined by either physician documentation, or the absence of any refills for at least 60 days beyond the anticipated refill date. Similarly, the reasons for discontinuation of therapies and the number of switches throughout the treatment course were obtained from chart documentation. We hypothesized that the duration of each line of therapy would be a marker of drug tolerability.

Statistical analysis

We used univariate analysis to investigate the association between IBS subtype- or patient-related (age, race, BMI, insurance type, presence of diabetes or presence of GERD) factors and the duration of therapy, reasons for switching agents, and number of switches throughout the treatment course. Categorical variables were compared using Fisher's exact test, and continuous variables were compared using the Wilcoxon rank sum test. For continuous variables compared across >2 groups, we applied a Kruskal-Wallis test. If the omnibus test was significant, we performed Dunn all-pairs joint-rank comparisons with the Benjamini-Hochberg adjustment. In

addition to univariate tests, we fitted 4 multivariate-logistic models: (i) capturing the early discontinuation pattern (within 6 months of starting therapy); (ii) ≥3 vs. <3 therapy switches; (iii) median duration on first- and (iv) second-line GLP-1RA therapy. Covariates were age, sex, BMI category, race, insurance type, IBS subtype, presence of diabetes or GERD, and GLP-1RA agent. The model fit was assessed (with likelihood-ratio χ^2, pseudo-R^2, lack-of-fit statistics) and P-values were reported. All analysis was performed using JMP (version 17, SAS Institute Inc.). A P-value of <0.05 was considered statistically significant.

This study was IRB approved and was conducted in accordance with the Declaration of Helsinki.

Results

Baseline characteristics

Among the 9581 GLP-1RA prescriptions recorded over the 10-year study period, 820 individuals (8.6%) with IBS were identified. Of these, 256 (31.2%) were prescribed more than 1 GLP-1RA throughout their treatment course and comprised our study cohort.

Overall, the majority of the individuals were women (80.5%), with a mean (± standard deviation) age of 53±11 years. The primary insurance coverage was private or self-pay (64%) for most individuals. The GLP-1RAs were prescribed for weight management and cardiometabolic risk mitigation in 30.8% of patients (n=79), and for type 2 diabetes management in 69% (n=177). Nearly half of the individuals included (49.4%; n=127) had a BMI in the range 25-40 kg/m^2, while the other half (50.4%; n=129) had BMI ≥40 kg/m^2. Of the total, 43% (n=110) had IBS unspecified, 30% (n=77) had IBS constipation-predominant (IBD-C), 18% (n=46) had IBS diarrhea-predominant (IBS-D), and 9% (n=23) had IBS mixed subtype (IBS-M). Additionally, 69.5% (n=178) of the study cohort had preexisting GERD (Table 1).

Table 1 Demographic variables of study cohort

Variables	N (%)
Age in years (mean±SD=53±11)	
<65	218 (85)
≥65	38 (15)
Sex	
Female	206 (80.5)
Male	50 (19.5)
Insurance (primary coverage)	
Medicare/Medicaid	91 (36)
Private/self-pay	165 (64)
BMI (kg/m^2)	
Overweight (25-30)	19 (7.4)
Obesity (30-40)	108 (42)
Severe obesity (≥40)	129 (50.4)
Type 2 diabetes mellitus	
Present	177 (69)
Absent	79 (30.8)
Race	
White	118 (46)
Black	114 (45)
Others	24 (9.4)
IBS subtypes	
Constipation-predominant	77 (30)
Diarrhea-predominant	46 (18)
Mixed	23 (9)
Unspecified	110 (43)
GERD	
Present	78 (30.5)
Absent	178 (69.5)

SD, standard deviation; BMI, body mass index; IBS, irritable bowel syndrome; GERD, gastroesophageal reflux disease

Therapy switches

Overall, 88.7% (n=227) individuals trialed 2-3 GLP-1RAs (i.e., 1-2 therapy switches), while 11.3% (n=29) trialed 4 or more agents (i.e., ≥3 therapy switches). Switching patterns varied by IBS subtype. Specifically, the cohort with IBS-M had the highest proportion of patients with ≥3 therapy switches, followed by IBS-C and IBS-D (21.7%, 11.7% and 2.2%, respectively; P=0.02).

Therapy tolerance varied significantly between agents. While semaglutide was associated with highest rates of discontinuation within 6 months of starting the first GLP-1RA, liraglutide, exenatide and tirzepatide showed longer tolerance, with fewer discontinuations within 6 months of starting the first GLP-1RA (63.4% vs. 43%, 20% and 20%, respectively; P=0.016). Dulaglutide had roughly equal proportions of early and later discontinuations (50% each). Individuals insured with Medicare or Medicaid were more likely to have ≥3 therapy switches, as compared to private or self-pay insurance (23% vs. 7.3%; P=0.006). No significant association was found between BMI or preexisting GERD and the frequency of therapy switches.

Median duration on each therapy line

The median duration of first GLP-1RA therapy for the entire cohort was 5.6 months (interquartile range 1.6-11.5). Elderly individuals (≥65 years) and those with diabetes were more likely to continue the first agent for more than 6 months compared to younger (<65 years) and non-diabetic individuals (65.8% vs. 44%; P=0.014, and 52.5% vs. 35.4%; P=0.019, respectively).

The median duration on the first GLP-1RA therapy varied among agents; individuals who were first prescribed liraglutide (38.2%) switched after a median of 7.3 months, while those who were prescribed exenatide (2%), dulaglutide (18.3%), semaglutide (39.5%) and tirzepatide (2%) switched after a median of 6.8, 5.9, 3.5 and 2.8 months, respectively (P=0.007). A *post hoc* test showed significantly shorter persistence with semaglutide than with liraglutide (adjusted P=0.003); no other pairwise contrasts were significant. Therapy duration did not vary by IBS subtype (P=0.59). The median duration on the

second GLP-1RA therapy before switching to a third therapy was highest for tirzepatide (5%) at 10.3 months, followed by dulaglutide (32.5%) at 9.4, semaglutide (28%) at 6, liraglutide (32.5%) at 5.6, and exenatide (2%) at 2 months. However, these differences did not reach statistical significance (P=0.96; Table 2, Supplementary Table 1).

Reasons for switching

The reasons for switching the GLP-1RA therapies were categorized into treatment-related discontinuations (i.e., injection burden, non-response), symptom-related (i.e., nausea, vomiting, dyspepsia, diarrhea, constipation, malnutrition), and access/coverage-related (shortage, insurance denial).

Of the 256 individuals, 57% (n=145) had documentation giving specific reasons for the discontinuation of their first GLP-1RA. The most common reason was access/coverage-related (55%), followed by symptom-related (28%) and treatment-related (17%). A similar pattern was observed for discontinuations of second-line therapy, with 56% due to access/coverage-related. The proportions of discontinuations due to treatment-related reasons remained fairly constant for the first, second and third lines of therapies (17%, 14% and 14%, respectively). Notably, the proportions of discontinuations due to symptom-related reasons increased steadily for successive lines of therapy (28%, 30% and 48%, respectively). Individuals discontinuing second-line therapy for access/coverage-related reasons made fewer subsequent therapy changes compared to those who switched because of symptom or treatment-related reasons (2 vs. ≥3 switches, 9.1% vs. 29.2% and 36.4%; P=0.03; Fig. 1A).

With respect to specific agents, the treatment-related reasons for discontinuation were reported most frequently with liraglutide (50%), followed by dulaglutide (32%), and semaglutide (18%). However, the difference was not statistically significant (P=0.06). The contribution of the specific agent to the other 2 categories of reasons for discontinuations was not significant (P=0.3; Fig. 1B).

Multivariate logistic models

For the early discontinuation pattern (Model i), the only independent predictor was GLP-1RA agent (overall P=0.02); demographic and clinical covariates were not significant, and the pseudo-R^2 was modest (0.10). For the high-switch outcome (Model ii), IBS subtype was the dominant determinant (overall P=0.004) and the pseudo-R^2 revealed a moderate fit (0.29). Specifically, patients with IBS-D were approximately 87% less likely than those with IBS-M to exhibit ≥3 switches (odds ratio 0.13, 95% confidence interval 0.03-0.55). Race reached marginal significance (P=0.046), while age and public insurance trended toward significance (P=0.05-0.08). For median duration on first-line therapy (Model iii), liraglutide showed a borderline 148-day advantage over dulaglutide (P=0.05). For second-line therapy (Model iv), public insurance predicted a 137-day shorter course compared to private insurance, whereas concomitant GERD prolonged use by 148 days. No covariate significantly influenced the duration of third-line therapy (Table 3).

Discussion

In this retrospective study we identified significant variability in GLP-1RA tolerance and discontinuation patterns among individuals with IBS. These findings substantially enhance our understanding of agent-specific and patient-related characteristics affecting the use of GLP-1RAs in a major population encountered by gastroenterologists in clinics. IBS remains the most common functional GI disorder in the US, and understanding how GLP-1RAs are tolerated in this cohort is vital for optimizing medical management.

Around one third of individuals with IBS switched their initially prescribed GLP-1RA agent. We found that patients

Table 2 Median durations before switching lines of therapies (median, IQR; months)

Median duration before switching to second agent	
Liraglutide (38.2%)	7.3 (3-19)
Semaglutide (39.5%)	3.5 (0.5-10)
Dulaglutide (18.3%)	5.9 (3-10)
Tirzepatide (2%)	2.8 (2-11)
Exenatide (2%)	6.8 (6-10)
Median duration before switching to third agent	
Liraglutide (32.5%)	5.6 (2-12)
Semaglutide (28%)	6 (3-16)
Dulaglutide (32.5%)	9.4 (3-20)
Tirzepatide (5%)	10.3 (7-15)
Exenatide (2%)	2 (0.5-4)

QR, interquartile range

Table 3 Multivariate models for discontinuation patterns and switch burden

Outcome	Model	Independent predictors
Early discontinuation (within 6 months)	P=0.2 (pseudo-R^2≈0.10)	GLP-1RA agent (overall *P*=0.02)
≥3 switches	P=0.03 (pseudo-R^2≈0.29)	IBS subtype overall (overall *P*=0.004; IBS-D vs. IBS-M OR≈0.13, 95%CI 0.03-0.55) Race marginal (P=0.046) Age and public insurance borderline (P≈0.05-0.07)
First-line therapy duration	P=0.9 (pseudo-R^2≈0.15)	Liraglutide+148 days vs. dulaglutide borderline (P=0.051)
Second-line therapy duration	P=0.06 (pseudo-R^2≈0.39)	Public insurance−137 days vs. private (P=0.006) Concomitant GERD+148 days (P=0.01)

GLP-1, glucagon-like peptide 1; IBS, irritable bowel syndrome; GERD, gastroesophageal reflux disease; CI, confidence interval; OR, odds ratio; pseudo-R^2, pseudo-coefficient of determination

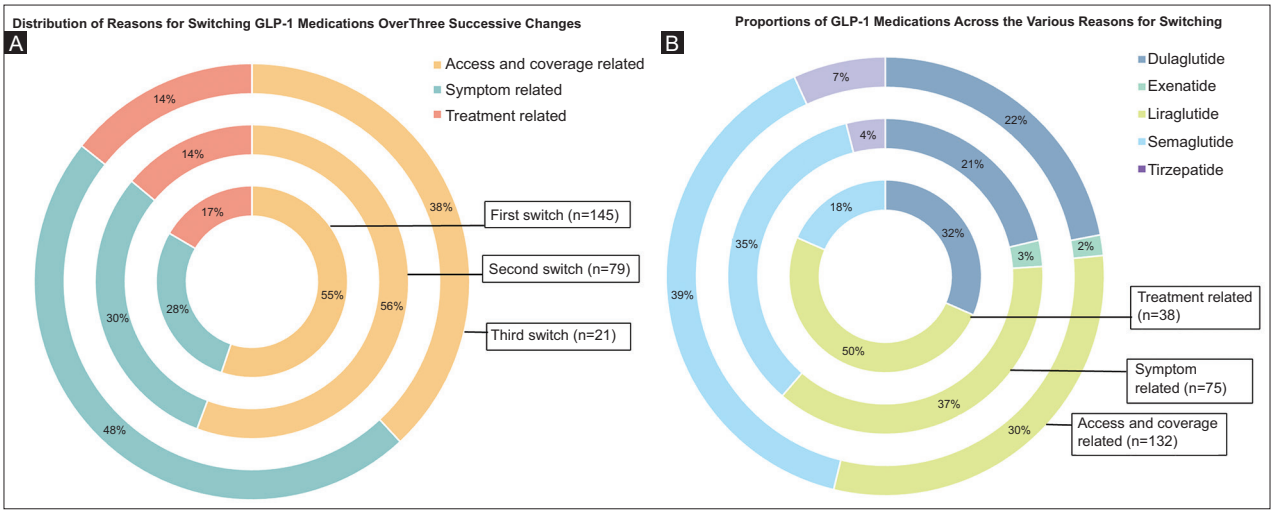

Figure 1 Stacked donut charts depicting reasons for GLP-1RA therapy discontinuation stratified by lines of therapy (A), and contribution of specific agent to the 3 categories of discontinuation reasons (B)
GLP-1, glucagon-like peptide 1

with IBS-M had the highest discontinuation and switching rates, followed by IBS-C and IBS-D. Previous research has demonstrated that GLP-1 exhibits an inhibitory action on GI motility by influencing the migrating myoelectric complex (MMC), vagal afferent fibers and efferent nerves [16]. Furthermore, these complex pathophysiologic mechanisms differ between the subtypes of IBS, contributing to their exclusive symptomatology [17]. For instance, in IBS-C, a lower diurnal amplitude of phase III MMC activity fronts and impaired vagal cholinergic function are more pronounced, whereas in IBS-D repetitive and rapidly propagated bursts of contractions during phase II MMC, a shift toward sympathetic dominance and reduced vagal activity have been demonstrated [18-22]. IBS-M is the manifestation of an even more complex and compounded set of pathophysiologic aberrations. Although prior studies have evaluated the efficacy of GLP-1 analogs in IBS acute pain, and their effect on colon transit, to our knowledge our study is the first to explore the differential real-world tolerance of GLP-1RAs in individuals with IBS and its subtypes [6,23-27]. The extensive distribution of GLP-1 receptors, and their unique pathophysiologic variances in IBS subtypes, may be translating into the variable tolerability profiles and hence discontinuation rates. In addition to these physiological mechanisms, biopsychosocial factors—such as the higher prevalence of central sensitization syndromes and mood disorders among patients with IBS, and particularly IBS-M—may also contribute to the observed differences [28,29]. Although our findings suggested notable variability in discontinuation rates between the IBS subtypes, the smaller subgroup numbers limited our ability to precisely attribute discontinuation to particular GI AEs, or to distinguish their prevalence among IBS subtypes.

Interestingly, elderly and diabetic individuals were more likely to continue the first-line therapy for over 6 months, suggesting either higher motivation to persist with therapy, or potential insurance and clinical management policies that discourage early switching. Although older adults and diabetic patients often experience more GI AEs, the perceived benefits of GLP-1RAs (e.g., glycemic control, cardiometabolic risk reduction) may outweigh discomfort for this group [30,31]. Moreover, specific insurance policies may mandate trial periods before approving a switch, thereby prolonging the use of the initial agent. Contrary to studies suggesting that people with preexisting GERD may experience worsened symptoms, particularly short-acting formulations, we did not find any significant association between symptom-related discontinuation of specific agents and a preexisting diagnosis of GERD [32]. One possibility is that prescribers proactively adjusted treatment regimens or provided supportive care (e.g., acid suppression therapy), mitigating potential exacerbations. Nevertheless, future studies with larger cohorts and granular data on agent dosing or short- vs. long-acting formulations are warranted to clarify this relationship.

Our study revealed disproportionate rates of discontinuation among various GLP-1RAs, with semaglutide being discontinued more frequently compared to liraglutide and other agents within 6 months of starting the first-line therapy. Similarly, the median duration on the first agent prior to switching was longest for liraglutide, followed by dulaglutide and then semaglutide, reinforcing the initial finding of liraglutide being better tolerated in general. Although no significant difference in the incidence of GI AEs was observed, previous data suggest that GI AEs remain a clinically plausible cause for discontinuations [33]. Studies have reported the highest risk for GI AEs with semaglutide, and the lowest risk with dulaglutide [23,34]. Despite their shared mechanism of action, GLP-1RAs differ pharmacologically in terms of their molecular structures (e.g., lipidation or adding lactam bridges), pharmacokinetics (e.g. acylation, PEGylation or fusion), and pharmacodynamics (e.g., biased agonism or affinity toward various intracellular pathways) [35]. Hence, the observed discrepancies are likely to be multifactorial, involving

differences in pharmacology, dose escalation protocols and patient tolerance [23,36].

Insurance coverage, supply dynamics and socioeconomic disparities also play a major role in the discontinuation patterns, as demonstrated by our findings that individuals with Medicare or Medicaid switched agents more often compared to their counterparts with commercial insurance coverage [37,38]. This observation aligns with the existing literature on restricted access due to limited formulary coverage of GLP-1RAs by Medicare or Medicaid compared to commercial insurance providers. However, we found that, while access-related issues were a leading cause of early discontinuation, subsequent switches were frequently attributed to lack of efficacy, injection burden or AEs. Thus, initial insurance hurdles may be resolved with the first or second agent, whereas clinical factors take precedence in driving further therapy changes.

Our multivariate adjusted models confirmed and added to the findings of the univariate analysis. First, they highlighted that the early discontinuation patterns were agent-driven, reflecting idiosyncratic tolerability profiles rather than patient-related factors or social determinants. Second, repeated switching was IBS-driven, with slight modulation by patient-related factors and access. Notably, patients with IBS-D were ~87% less likely than those with IBS-M to have high-switch trajectories, aligning with our hypothesis that diarrhea-predominant physiology may tolerate GLP-1RA-induced motility changes better. Race reached borderline significance, while older age and public insurance trended toward significance, hinting at structural barriers that require confirmation in larger cohorts. Median duration analysis showed that liraglutide had a 148-day persistence advantage over dulaglutide as first-line therapy. These findings confirmed agent-centric tolerability, with liraglutide probably being the best tolerated for the reasons discussed above. Lower rates of discontinuation with private vs. public insurance may be attributed to the coverage churn or cost-sharing issues. As for patients with GERD, they may already be on treatment with acid suppression, allowing for longer persistence. Collectively, these multivariable findings support a 2-step clinical strategy: selecting the agent with the best GI tolerability profile for the individual patient, then anticipating long term persistence issues, chiefly in IBS-M and publicly insured populations (Fig. 2).

Our study serves as a unique pilot investigation into the prescription and discontinuation patterns of GLP-1RAs among IBS patients. We evaluated patient-specific, IBS-related and agent-specific factors and found substantial heterogeneity in real-world practice. These insights could guide clinicians in tailoring therapy for IBS patients to improve adherence and long-term outcomes. Despite these strengths, we acknowledge several limitations. First, the sample size, particularly for specific IBS subtypes, may limit the generalizability of our findings. Second, the lack of granular data on GLP-1RA dosing protocols, severity of IBS or obesity, coexisting central sensitization syndromes and the observational nature of the study limit our ability to infer causality. Further research, incorporating prospective designs, standardized discontinuations and detailed patient-reported outcomes with validated symptom severity assessment scores, could better elucidate the complex relationship between GLP-1RA use and specific side-effects across IBS subtypes—including patients who discontinue therapy without switching.

In conclusion, this retrospective analysis underscores the intricate relationship between IBS subtype, sociodemographic determinants and specific GLP-1RA agents in shaping therapy discontinuation and switching patterns. We found that access/coverage-related barriers can precipitate early therapy switches, whereas subsequent changes are predominantly driven by clinical considerations, such as efficacy and adverse events. Patients with IBS, especially those with the mixed subtype, frequently switch therapies, possibly reflecting the complex physiological interplay between GLP-1 receptor signaling and the gut–brain axis. Additionally, we observed differences in tolerability and persistence within agents, with better persistence on liraglutide compared to semaglutide, particularly among

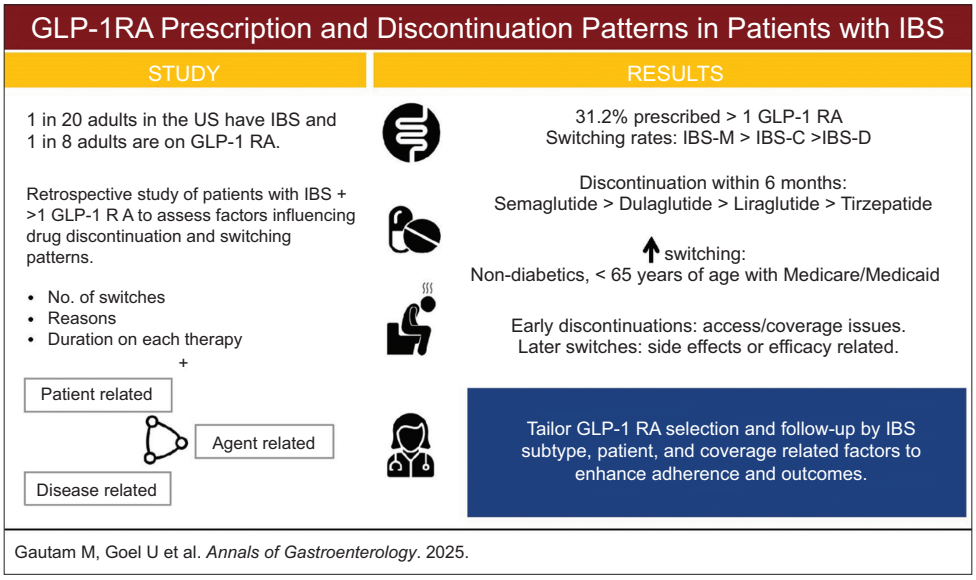

Figure 2 Graphical abstract
GLP-1, glucagon-like peptide 1; IBS, irritable bowel syndrome

older individuals with type 2 diabetes, suggesting that patient motivation and perceived benefits may outweigh common AEs in certain subgroups. In essence, barriers to access determine the initial discontinuation, agent-specific pharmacology plays a crucial role in maintaining adherence, while the underlying IBS physiology predicts the long-term switching trajectory. By understanding the role of each of these facets, clinicians can carefully tailor GLP-1RA treatment strategies in IBS to optimize safety, adherence and long-term outcomes. Future prospective research with larger, more diverse cohorts is warranted to validate these findings and to explore targeted interventions that could enhance the tolerability and effectiveness of GLP-1RA therapy for individuals with IBS.

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Summary Box

What is already known:

- Irritable bowel syndrome (IBS) has 3 subtypes, including constipation-predominant, diarrhea-predominant and mixed, each with distinct pathophysiology
- Glucagon-like peptide-1 receptor agonists (GLP-1RAs) are increasingly prescribed for diabetes, obesity and cardiometabolic risk, but are often associated with gastrointestinal side-effects, influencing treatment adherence
- Real-world data on how patients with IBS tolerate GLP-1RAs are scarce

What the new findings are:

- One-third of IBS patients prescribed GLP-1RAs for different indications switched from their initial agent, suggesting potential challenges in terms of tolerability or efficacy
- IBS-M showed the highest GLP-1RA discontinuation and switching rates in real-world practice
- Liraglutide was associated with better tolerance compared to semaglutide, with early discontinuations driven by coverage-related issues, while later discontinuations owing to side-effects or non-response
- In individualized GLP-1RA therapy, accounting for IBS subtype, patient-related factors are crucial for better adherence and outcomes

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Supplementary material

Supplementary Table 1 Median persistence on GLP-1RA therapy: Kruskal-Wallis omnibus results and Dunn pairwise comparison across 5 GLP-1RA agents and 3 IBS subtypes

Outcome	Kruskal-Wallis χ^2 (df)	Omnibus P-value	Dunn *post hoc* (BH-adjusted)	Interpretation
Median time on first-line therapy				
GLP-1RA (5 agents)	14.1 (df=4)	0.0069	Semaglutide vs. liraglutide Δrank=−37.8, P(adj)=0.003	Semaglutide persistence is significantly shorter than liraglutide; no other pair differs
IBS (3 subtypes)	1.03 (df=2)	0.59	-	No subtype effect
Median time on second-line therapy				
GLP-1RA (5 agents)	0.1 (df=4)	0.96	-	No subtype effect
IBS (3 subtypes)	2 (df=2)	0.97	-	No subtype effect.

GLP-1, glucagon-like peptide 1; IBS, irritable bowel syndrome; BH, Benjamini-Hochberg; df, degrees of freedom; Δrank, rank-difference estimate from Dunn test; P(adj), adjusted P-value