

Semaglutide in a real-world outpatient setting: discontinuation patterns and weight maintenance

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Significance

Semaglutide has swiftly emerged as a pivotal treatment modality in obesity management, delivering significant weight loss and cardiometabolic benefits. However, evidence from real-world settings suggests that up to half of patients prematurely discontinue therapy, even when financial barriers are minimized, indicating the multifactorial nature of treatment discontinuation including tolerability, psychosocial factors, and long-term benefit perceptions. This Expert Opinion synthesizes observations from a nonacademic outpatient setting, highlighting key drivers of discontinuation, and advocates for a gradual dose tapering strategy to mitigate rebound weight gain. By understanding patient needs and refining clinical approaches, including flexible titration and comprehensive support, it is possible to enhance adherence and clinical outcomes among users of GLP-1 receptor agonists.

Introduction

Obesity is a chronic, relapsing disease that increasingly demands multidimensional management strategies. Glucagon-like peptide-1 (GLP-1) receptor agonists, specifically semaglutide, have transformed pharmacotherapy for obesity by yielding significant weight loss and favorable metabolic outcomes.¹

However, data derived from nonacademic outpatient settings reveal that up to 50% of patients discontinue treatment prematurely despite financial coverage—highlighting that issues beyond financial barriers drive discontinuation.²

This Expert Opinion integrates real-world observations from a nonacademic setting to elucidate key factors underlying discontinuation and to propose practical strategies, including slow tapering, for maintaining weight loss in patients receiving semaglutide.

Given the small size and observational design of our registry, these findings should be regarded as hypothesis-generating and exploratory rather than conclusive. The observations presented here reflect expert opinion informed by real-world clinical practice and require validation in prospective studies.

Clinical practice experience in a real-world outpatient setting

We observed a total cohort of 76 patients (n = 76) initiating semaglutide therapy.

This was a prospective, observational registry conducted between 2022 and 2024 in a community-based obesity clinic.

Inclusion criteria were adults aged ≥ 18 years with obesity (BMI ≥ 30 kg/m²) who initiated treatment with semaglutide for weight management. Exclusion criteria included presence of diabetes, pregnancy, previous bariatric surgery, or insufficient baseline data. Patients were followed according to a standardized schedule, with visits or teleconsultations every 4-6 weeks during titration and every 8-12 weeks thereafter. Discontinuation was defined as absence of semaglutide prescription refill and/or lack of clinic attendance for more than 12 consecutive weeks. All patients were managed under routine clinical care conditions, and data were prospectively collected in a structured electronic database.

The mean age was 49 years, with a female predominance (68%) and a mean baseline BMI of 37.4 kg/m². Over the 2-year follow-up, we recorded an estimated discontinuation rate of 42%, reflecting the real-world challenges associated with long-term adherence in a nonacademic outpatient population (Table 1).

Nonacademic outpatient clinics are community-based centers not affiliated with a university or tertiary academic medical center. These clinics typically serve diverse patient populations and often operate with limited staffing and specialist support compared to large academic centers.

While our registry is single-center and relatively small, it complements the larger Associazione Medici Diabetologi (AMD) registry, which monitors clinical practice across multiple centers and thus provides a benchmark for real-world management in Italy.

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Table 1. Baseline characteristics and discontinuation in the study cohort.

Characteristic	Value $(n = 76)$
Age, mean (SD), years	49 (±12)
Female sex, n (%)	52 (68%)
Baseline BMI, mean (SD), kg/m ²	$37.4 (\pm 5.2)$
Follow-up duration, months	24 (range 12-24)
Discontinuation rate, n (%)	32 (42%)

Over a 2-year observational period during which semaglutide was administered several observations emerged:

1. Patient selection and expectations

- Patients referred for pharmacotherapy often have extensive histories of failed weight loss attempts through diet and exercise alone.
- Establishing realistic expectations regarding the timeline for weight loss and the potential for gastrointestinal (GI) side effects (eg, nausea, bloating) fosters treatment adherence.

In our clinic, we found that establishing realistic expectations early in the process was critical to fostering long-term adherence. During the initial consultation, patients were informed that average weight loss with semaglutide typically ranged between 10% and 15% of baseline weight over a 12-18-month period, contingent upon adherence and tolerability. We emphasized that results may vary and are not immediate, with the most substantial reductions often occurring after the first 6 months of treatment.

This framing helped to align expectations and reduce premature frustration. Many patients expressed relief in knowing that the treatment was not a quick fix but rather part of a broader, sustainable approach. Some also voiced appreciation for the clarity around the likely trajectory of weight loss, which improved trust and engagement with follow-up visits.

Additionally, patients were briefed on the potential for GI side effects—such as nausea or bloating—and were advised that these are often transient and manageable. This preemptive discussion was well-received and reduced anxiety when such symptoms occurred, thereby supporting persistence through the titration phase.

2. Dosing and titration nuances

- Standard titration protocols may prove overly aggressive for some patients, exacerbating GI side effects.
- A more gradual dose escalation, combined with closer follow-up, may improve tolerability, promote persistence, and support adherence to treatment.³

In our clinical experience, we observed that the manufacturer's standard titration schedule—typically escalating from 0.25 to 2.4 mg over 16-20 weeks—was often too rapid for our patient population, particularly among those with a history of GI sensitivity. To address this, we adopted a more individualized and slower titration approach. Specifically, we extended each dose level (eg, 0.25, 0.5, 1.0 mg) to 6-8 weeks, rather than the standard 4 weeks, before advancing to the next step. In some cases, we paused dose escalation entirely for 2-4 additional weeks when patients experienced significant GI symptoms.

This flexible approach improved tolerability and reduced treatment discontinuation during the early phase of therapy. Patients reported fewer severe side effects and showed better adherence when they felt the regimen was being adapted to their individual needs. In follow-up visits, conducted approximately every 4-6 weeks, we reassessed symptom burden, weight loss progress, and readiness to escalate.

3. Comprehensive support

- A multidisciplinary approach that includes nutritional counseling, behavioral therapy, and physical activity planning often yields better clinical outcomes.
- Nonacademic clinics may rely on external referral networks for psychological or dietary support, emphasizing the importance of collaborative care models.

In our clinic, we integrated a structured multidisciplinary support model that combined routine consultations with dietitians, periodic psychological counseling, and individualized physical activity recommendations delivered by trained staff or through coordinated referral networks. Patients who engaged consistently with at least two support modalities (eg, nutrition + behavioral) demonstrated significantly higher rates of treatment persistence and weight loss maintenance. For instance, among patients receiving both pharmacotherapy and nutritional follow-up, the average weight loss at 12 months was 13%, compared to 8% in those who attended pharmacologic follow-up only.

Although this was not a randomized comparison, observational differences within our registry suggest that those without access to or engagement with support services were more likely to discontinue semaglutide due to perceived ineffectiveness or tolerability issues. These patients often lacked strategies for managing hunger, emotional eating, or lifestyle drift following initial weight loss.

Patient impressions and feelings

Patients' subjective experiences frequently serve as a decisive factor in their continued use of semaglutide:

1. Initial enthusiasm

• Early appetite suppression and rapid weight loss provide motivation and reinforce adherence in the initial phase.

2. GI side effects and tolerability

- Occurrences of nausea, bloating, or periodic vomiting can adversely impact quality of life, leading to early discontinuation.⁴
- Proactive management strategies with antiemetics or dose modifications can mitigate adverse effects.

In our clinic, early positive experiences—such as reduced appetite and initial weight loss—were strong motivators that reinforced adherence. However, GI side effects were the most common subjective barrier to continued treatment. Among our cohort, 35% (27 of 76 patients) reported moderate to severe GI symptoms during titration, including nausea, bloating, and occasional vomiting. These adverse effects were most prominent during dose escalations beyond 0.5 mg/week.

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Table 2. Key factors in semaglutide discontinuation and potential solutions.

Key observation	Suggested solution	Evidence level
Gastrointestinal side effects	Slower, individualized dose titration; allow pauses or temporary de-escalation; patient education on meal timing and tolerance strategies	Expert opinion; observational data
Psychosocial barriers (stigma, self-blame, perceived "unworthiness" of therapy)	Use person-first, non-stigmatizing language; validate obesity as a chronic disease; provide motivational or cognitive-behavioral support	Observational data; narrative review
Fear of long-term use/dependence	Early counseling on chronic nature of obesity; emphasize safety data; tapering only under supervision	Expert opinion; narrative review
Mismatch between patient and clinician goals ("expectation effect")	Shared decision-making; visual progress tracking; reinforce non-weight outcomes (eg, metabolic improvements)	Observational studies; narrative review
Lifestyle drift and loss of structure over time	Regular follow-up (in-person or telehealth); behavioral reinforcement via dietitian/psychologist support	Published trials; expert consensus
Medication fatigue/treatment burden	Simplify dosing schedules; use reminders or digital adherence tools; discuss early fatigue risk	Narrative review
Administrative and cost barriers	Simplify reimbursement procedures; assist with prescription renewals	Expert opinion; policy analyses
Limited multidisciplinary resources in community settings	Establish referral networks (dietitians, psychologists, physiotherapists); leverage telemedicine	Narrative review; real-world evidence

To mitigate these issues, we implemented proactive management strategies for patients reporting early signs of GI intolerance. These included the following:

- Slowing the titration schedule, by extending each dose step to 6-8 weeks.
- Temporary dose de-escalation (eg, returning from 1.0 to 0.5 mg for 2-4 weeks) when symptoms became unmanageable.
- Antiemetic therapy, primarily using metoclopramide or ondansetron on an as-needed basis.
- Dietary counseling focused on meal timing, smaller portion sizes, and minimizing high-fat or high-fiber foods during periods of heightened sensitivity.

A total of 18 patients (24%) required at least one of these targeted interventions. In most cases, these measures were sufficient to allow continuation of therapy without permanent discontinuation. Importantly, patients expressed appreciation when side effects were acknowledged and addressed proactively, which fostered trust and increased willingness to persist with treatment.

3. Psychosocial considerations

- Stigma surrounding injectable therapies, fear of "lifelong dependency," and underlying mental health conditions (eg, depression, anxiety) influence adherence.
- Tailored psychosocial support helps patients navigate these concerns.

In our cohort, concerns about becoming "dependent" on semaglutide were expressed by 22% of patients (n = 17), particularly after the first 6-8 months of treatment, when weight loss plateaued and discussions about long-term continuation arose. Patients voiced fears about "never being able to stop" the medication or equated ongoing use with personal failure to manage weight independently.

To address these concerns, we implemented several communication strategies:

 We reframed obesity as a chronic, relapsing condition similar to hypertension or type 2 diabetes—where

- long-term pharmacologic support may be necessary for sustained control.
- We emphasized that needing medication was not a sign of weakness or failure, but rather a medically appropriate tool, especially when combined with lifestyle interventions.
- We introduced the concept of "planned tapering" as a clinical option, helping patients understand that continuation and discontinuation could both be valid and individualized paths, rather than fixed endpoints.
- For patients struggling emotionally with the concept of long-term treatment, we offered additional psychological counseling or motivational interviewing sessions.

These strategies were generally well received. Patients who felt that their concerns were normalized and discussed openly were more likely to continue treatment and participate in follow-up. Moreover, presenting pharmacotherapy as part of a broader self-management plan—rather than a permanent crutch—helped reduce the perceived stigma of ongoing use.

It should be noted that these insights reflect clinician observations and patient feedback during routine consultations, rather than findings from structured qualitative surveys or formal interviews.

4. Cost and administrative challenges

- Even with reimbursement, administrative hurdles or lack of clarity about eligibility can contribute to therapy discontinuation.
- Some patients experience guilt about relying on a potentially expensive medication, fueling discontinuation.

5. Lifestyle drift

- Following significant weight loss, motivation to maintain dietary patterns and activity changes can wane.
- As lifestyle commitments recede, patients may perceive diminishing benefits from continued semaglutide.

Why are discontinuation rates so high?

Despite semaglutide's robust efficacy, the observed real-world discontinuation rates remain strikingly high. Although the

underlying reasons vary among individuals, key factors include GI side effects, insufficient patient education, psychosocial barriers, and ambiguity regarding the long-term management of pharmacotherapy.⁵ These key factors are summarized in Table 2.

Maintaining weight loss with slow tapering

Obesity is often a lifelong condition warranting a sustained pharmacological intervention, potentially on an indefinite basis. Nonetheless, some patients discontinue or reduce their semaglutide regimen following the attainment of targeted weight loss or due to intolerable side effects. A strategy of gradual tapering may help sustain weight loss:

1. Gradual dose reduction

 Decreasing the dose stepwise every 4-6 weeks allows metabolic adaptation and may reduce rebound weight gain.

For example, a typical tapering protocol may begin with reducing the weekly dose from 2.4 to 1.7 mg for 4-6 weeks, while monitoring for early signs of weight regain or appetite rebound. If stable, the dose may then be reduced to 1.0 mg for another 4-6 weeks, followed by a further reduction to 0.5 mg, and eventually to discontinuation only if clinical stability is maintained. The timing of each dose reduction can be adjusted based on individualized clinical criteria, including weight trend (eg, less than 2% regain), patient-reported hunger and satiety levels, adherence to lifestyle measures, and absence of significant metabolic deterioration. Regular follow-ups every 4-6 weeks are essential during this period to ensure that the tapering process supports long-term weight maintenance.

2. Enhanced lifestyle interventions

 Amplifying dietary, exercise, and behavioral support is crucial during tapering to compensate for diminished pharmacological appetite suppression.⁶

3. Close monitoring and follow-up

Regular follow-up consultations, systematic weight assessments, and periodic laboratory evaluations (eg, monitoring glycemic control) facilitate the prompt detection of weight regain.

4. Alternative or adjunct therapies

- In cases of persistent intolerance, clinicians may consider transitioning to an alternative anti-obesity medication (AOM) or employing combination therapy.
- Furthermore, therapy should be individualized, guided by patient preferences, comorbidities, and overall treatment goals.

Conclusions and future directions

In summary, semaglutide provides a powerful avenue for achieving significant weight reduction and improving cardiometabolic outcomes. Nevertheless, the high discontinuation rates in real-world settings underscore the need for a more holistic and patient-centered approach, especially regarding tolerability and psychosocial challenges. By adopting more flexible dosing and titration protocols, addressing patient concerns,

and emphasizing sustained lifestyle modifications, clinicians may reduce dropout and boost clinical outcomes.⁸

Adherence and continuation rates with AOMs like semaglutide may differ substantially between academic vs. community-based (real-world) settings due to differences in infrastructure, staffing, and available patient support services.

Academic centers often have access to multidisciplinary teams—including endocrinologists, obesity medicine specialists, dietitians, behavioral psychologists, and pharmacists—who can collaboratively address the multifactorial needs of patients. These centers may also benefit from tighter clinical integration, standardized care pathways, and more frequent patient monitoring, all of which contribute to improved adherence and lower discontinuation rates.

In contrast, nonacademic outpatient clinics may operate with limited personnel and time resources and sometimes lack embedded behavioral or nutritional support. This can hinder timely management of side effects or psychosocial barriers, thereby increasing the risk of treatment dropout.

Our observed discontinuation rate of 42% is markedly higher than that reported in academic clinical trial cohorts. For example, in the STEP 5 trial, discontinuation rates were approximately 5% over 2 years, while other STEP program extensions have reported rates in the 5%-10% range. 8,9 This contrast highlights the role of structured follow-up, multidisciplinary teams, and rigorous trial conditions in supporting long-term adherence. In contrast, community-based outpatient clinics often lack these resources, which may contribute to higher attrition. Notably, emerging real-world reports outside academic centers have described discontinuation rates closer to 20%-60% within the first year of treatment, ¹⁰⁻¹³ suggesting that our findings are within the spectrum of variability observed in routine practice. These differences underscore the importance of contextualizing discontinuation data according to care setting and support infrastructure.

Based on both clinical experience and published literature, a discontinuation rate below 25% may be a realistic and acceptable target in well-supported environments.

To improve continuation rates in nonacademic settings, we propose the following practical strategies:

- Protocolized, flexible titration schedules that accommodate individual tolerability, supported by clear clinical decision pathways.
- Structured education tools (eg, pre-initiation handouts, visual timelines of expected outcomes) to manage expectations and promote engagement.
- Telehealth or group-based support models, which can extend multidisciplinary care without overburdening staff.
- Task-shifting to trained allied professionals, such as nurses or clinical assistants, to perform symptom checkins or reinforce lifestyle advice during follow-ups.
- Integration with community resources (eg, referral to local dietitians or weight management programs) when onsite services are unavailable.

In our own clinic, applying some of these low-resource adaptations—especially prolonged titration schedules and proactive patient counseling—has already improved treatment persistence and patient satisfaction.

Weight stigma remains a pervasive barrier to sustained treatment engagement, often leading patients to internalize negative stereotypes that undermine self-efficacy and perpetuate cycles

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of disengagement. Body image dissatisfaction, even in the context of significant weight loss, can fuel emotional distress and ambivalence toward continuing treatment. These challenges are particularly salient among individuals with a history of weight-based teasing or prior negative healthcare experiences.

Targeted, patient-centered interventions are essential to address these issues. Approaches such as cognitive-behavioral therapy can help patients reframe maladaptive thoughts related to body image and self-worth. Incorporating body neutrality or body functionality discussions into counseling sessions may shift the focus away from appearance and toward overall well-being. Additionally, clinicians should employ non-stigmatizing language, acknowledge the psychosocial burden of obesity, and foster a therapeutic alliance based on empathy and shared decision-making.

Such strategies are supported by prior research emphasizing the role of psychosocial dynamics in obesity care¹⁴ and the importance of targeted behavioral support in sustaining long-term weight management.¹⁵

Gradual dose reduction, or pharmacologic tapering, represents a promising approach to minimize rebound weight gain after semaglutide discontinuation. While this strategy is not yet validated through large-scale prospective trials, our clinical observations suggest that it can mitigate abrupt physiologic and psychological disruptions often associated with sudden cessation.

In our practice, patients who tapered their dose over 8-12 weeks—stepping down incrementally to lower weekly doses (eg, from 2.4 to 1.0 mg, then to 0.5 mg)—tended to experience more stable appetite regulation and less anxiety about losing pharmacologic support.

It is important to emphasize that our tapering approach is based on clinical experience and remains anecdotal, rather than supported by randomized controlled trials. As such, it should be regarded as hypothesis-generating and speculative, requiring validation in prospective studies before being considered an evidence-based strategy.

Current guideline statements, including those from the American Association of Clinical Endocrinology¹⁶ and the American Diabetes Association,¹⁷ do not provide formal recommendations for tapering protocols with GLP-1 receptor agonists. Instead, these guidelines emphasize the chronic and relapsing nature of obesity, the need for long-term pharmacotherapy in many patients, and the importance of individualized care. Our proposed tapering framework aligns with the principle of personalization but diverges from existing guidelines in offering a structured step-down approach. This underscores the need for multicenter prospective trials to establish whether tapering can mitigate rebound weight gain and support sustained weight maintenance.

The long-term sustainability of this strategy depends on several factors:

- Patient adherence to nonpharmacologic supports during and after tapering (eg, diet, exercise, behavioral therapy).
- Clinician capacity to provide close follow-up and individualized counseling during the tapering process.
- Ongoing psychosocial support to manage expectations and prevent relapse.

From a broader implementation perspective, gradual dose reduction is feasible in both academic and nonacademic settings if guided by structured protocols and supported by patient education. Sustainability may be enhanced by incorporating tapering discussions into long-term care planning from the outset, allowing patients to psychologically prepare and engage more actively in the transition.

Future research should focus on several key priorities:

- Prospective trials investigating tapering protocols, to establish evidence-based strategies that minimize rebound weight gain and optimize long-term maintenance.
- Identification of clinical, behavioral, and psychosocial predictors of successful discontinuation/low dose maintenance, to enable individualized treatment planning and risk stratification.
- Comparative studies between academic and nonacademic settings, to evaluate differences in adherence, treatment outcomes, and barriers to continuation, thereby informing context-specific care models.
- Development of standardized frameworks for multidisciplinary support, especially in resource-limited settings, to enhance the scalability and accessibility of obesity pharmacotherapy.

Ultimately, coordinated efforts among clinicians, patients, and payers can help ensure that the advantages of semaglutide endure well beyond the initial weight loss phase.

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Conflicts of interest

None declared.

Data availability

No new data were generated or analyzed in this Expert Opinion. Further inquiries can be directed to the corresponding author.

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