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RESEARCH LETTER

Why do patients with obesity discontinue glucagon-like peptide 1 analogues?

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1 | BACKGROUND

Obesity medications (OMs) play a growing role in managing the disease of obesity by helping to regulate the homeostatic control of adipocyte mass.[1] Although these medications are becoming increasingly popular and improve health, their long-term weight loss maintenance depends on adherence.[2]

The therapeutic potential of GLP-1 receptor agonists is promising for various non-communicable diseases. However, there is still limited real-world evidence regarding their long-term benefits and potential adverse outcomes in diverse populations. Despite increasing access and popularity, the long-term success of pharmacotherapy for obesity relies heavily on patient adherence.

Extensive database studies on OM usage indicate that adherence, meaning patients consistently taking their medications as directed for more than 90 days, falls to 10%–25%. Improving this short stay time may require adopting chronic disease management models. Lifestyle interventions, including better nutrition and exercise, are cornerstones to improving health in people with the disease of obesity.[3,4]

The terms compliance, adherence and concordance are often confused. Adherence is more specific and collaborative than compliance when discussing how well patients follow their prescribed medication regimens. Concordance emphasizes the relationship between the patient and the prescriber, focusing on a shared understanding where the patient or caregiver takes responsibility for proper medication usage.[5] Medication adherence is evaluated through three key stages. First, initiation occurs when a patient takes the first dose of a prescribed medication. Second, implementation refers to how accurately the patient follows the prescribed dosing schedule from the first to the final dose. Third, persistence indicates the overall duration during which the patient consistently takes the medication until treatment is discontinued.[6] In this study, we examined the duration of OM use and the barriers affecting patient adherence using real-world data.

2 | METHODOLOGY

In January 2025, we reviewed prospectively collected electronic health records from two multidisciplinary obesity outpatient clinics in Ireland for 350 patients who began GLP-1 receptor agonists (GLP-1 RA) between July 2021 and March 2023. These specialized clinics are structured to provide comprehensive obesity care through a team-based model. Each clinic is led by physicians trained in obesity medicine and includes regular input from dietitians, clinical psychologists, bariatric surgeons and specialist nurses. After manual validation, we extracted data on patient demographics, baseline and follow-up anthropometrics and obesity-related complications. Baseline laboratory parameters (e.g., lipids, glycaemic markers and liver function tests) and clinical history (e.g., hypertension, dyslipidaemia, diabetes) were also extracted and summarized in Table 1. Select variables in this table were also reported in a previous publication from the same cohort.[7]

Patients were classified as staying if they were known to be actively using a GLP-1 RA at their last clinic visit within the final 6 months of the study period (July to December 2024). Patients who had stopped using GLP-1 RA medications for more than six consecutive months by their last clinic visit were classified as discontinued. The clinics operate within a mixed public–private healthcare system and follow standardized, evidence-based protocols for initiating and

TABLE 1 Baseline demographics, anthropometrics and clinical characteristics of patients initiating GLP-1 receptor agonist therapy ($n = 350$).

Characteristic	Category/ metric	*n* (%) or Mean (SD)
Gender	Male/female	69 (19.7)/281 (80.3)
Age (years)		48.5 (11.5)
BMI before starting treatment (kg/m^2)		40.7 (7.3)
Weight before starting treatment (kg)		114.7 (22.7)
Ethnicity[a]	White	138 (39.4)
Smoking status[b]	Never/ex/ current	181/132/29 (8.3)
History of hypertension		137 (39.1)
History of dyslipidaemia		109 (31.1)
History of type 2 diabetes		27 (7.7)
HbA1c (%)		5.8 (0.9)
Total cholesterol (mmol/L)		4.7 (1.0)
LDL cholesterol (mmol/L)		2.8 (0.9)
HDL cholesterol (mmol/L)		1.5 (0.4)
Triglycerides (mmol/L)		1.2 (0.4)

Note: Data presented as mean ± SD or *n* (%).
[a]Ethnicity data were missing for 212 patients.
[b]Smoking status missing for 8 patients.

monitoring obesity medications. Clinicians at both clinics adhered to the same prescribing criteria and counselling frameworks, ensuring consistency in patient care and messaging across both sites. However, obesity medications are not covered under the Irish healthcare system. Therefore, all patients in our cohort paid for their medication entirely out of pocket, with an average cost of €150 per month.

Telephone follow-ups were conducted using a semi-structured interview format. Patients were asked open-ended questions and predefined items covering known reasons for medication discontinuation, such as side effects and cost. Interviewers followed a standard script to ensure consistency across respondents.

The primary outcome was the proportion of patients who discontinued medication. Secondary outcomes included the reported reasons for discontinuation and the proportion of patients achieving ≥5%, ≥10% and ≥15% total body weight loss. Continuous variables are reported as mean ± standard error of the mean (SEM). Mann–Whitney U tests were used for group comparisons, and counts, percentages and chi-square tests were applied for categorical variables. Statistical significance was defined as a p-value <0.05. St Vincent's University Hospital provided approval (ref 2024/4216).

3 | RESULTS

The final analysis included 350 patients, with a mean age of 45.7 ± 10.5 years, predominantly female ($n = 283$, 81%). Overall, the average treatment duration across all 350 patients was 707 ± 425 days. Among these, 174 patients (50%) were classified as having discontinued obesity medication based on clinic records. Ultimately, 83 of the 174 patients (48%) responded to telephone follow-up, providing 123 reasons for discontinuation, as some gave multiple reasons. The median stay time was 1028 days for patients on treatment and 394 days for discontinued patients. The total exposure time across the full cohort was 678.2 patient-years, based on the cumulative duration of therapy per individual.

Patients were treated primarily with semaglutide, followed by liraglutide. Of the 50% who continued treatment, 84.5% lost at least 5% of their body weight, 67% lost at least 10% and 39.4% lost at least 15%. In contrast, among those who discontinued treatment, 58% had lost at least 5%, 32% had lost at least 10% and 13% had lost at least 15%. The nadir weight loss at or before 1 year across all participants was 15.2% ± 8.4% (6.8%–23.6%). When stratified by persistence status, those who stayed on treatment achieved significantly greater weight loss at or before 1 year (17.8% ± 7.2%) than those who discontinued (12.6% ± 8.7%; $p = 0.002$). The median duration of treatment was 1028 days (interquartile range [IQR]: 758–1196 days) for patients who stayed on treatment, and 394 days (IQR: 210–582 days) for those who discontinued treatment.

The primary reasons for discontinuation reported by the inactive patients ($n = 83$) were side effects (44 patients, 36%), logistical challenges (29 patients, 24%), such as geographic relocation, inflexible work schedules or limited transportation access, medication cost (28 patients, 23%), supply shortages (14 patients, 11%) and dissatisfaction with weight loss response (9 patients, 7%).

4 | DISCUSSION

The results suggest that clinical factors (e.g., weight loss outcomes and side effects) and non-clinical factors (such as affordability and logistics) limit long-term adherence to GLP-1 RA for obesity treatment. Patients who continued their therapy experienced better weight loss outcomes, averaging 17.8% compared to 12.6% for discontinued patients.

Nearly 40% of patients who remained on treatment achieved more than 15% weight loss. However, treatment persistence was limited overall, with half of all patients discontinuing obesity medication within the first 6 months. This attrition rate, substantially higher than what is typically observed in regulatory trials, highlights the need for robust patient support and adherence strategies to achieve outcomes similar to those seen in controlled settings.[8,9]

Real-world adherence remains suboptimal. The most commonly reported reason for discontinuation was side effects (36%), and although specific categorization was not consistently available, most adverse events were likely gastrointestinal. Additional barriers included logistical challenges (24%) such as geographic relocation, inflexible work schedules, limited transportation access and medication cost (23%) (Figure 1).

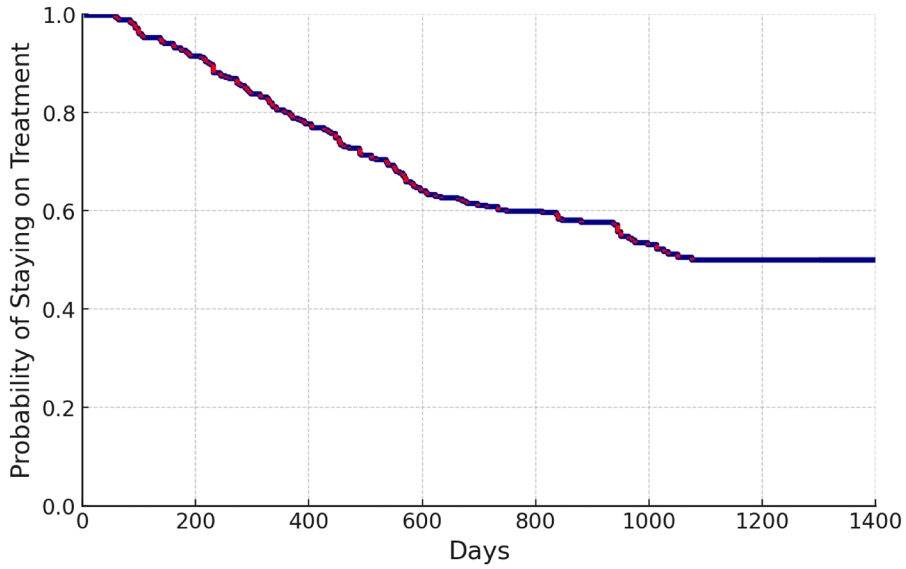

FIGURE 1 Kaplan–Meier curve illustrating the probability of patients remaining on GLP-1 receptor agonist therapy over time.

Although virtual consultations were available, logistical adherence was frequently impacted by the need for in-person visits for medication titration, prescription renewal or clinical monitoring rather than digital barriers. Addressing these challenges, including enhancing telemedicine solutions and reducing the need for physical visits, could significantly improve adherence and long-term outcomes.[10,11]

While long-term use of GLP-1 RA offers functional, metabolic and cardiovascular benefits, addressing early discontinuation remains challenging. Careful dose titration may help reduce gastrointestinal symptoms,[12] while insurance support can improve affordability. Maintaining regular contact with patients through structured follow-up may foster ongoing engagement. Clinical guidelines recommend these strategies, emphasizing personalized patient education, coordinated resources and continued support to optimize obesity management. Although our study did not directly evaluate these interventions, they align with best practice recommendations to enhance adherence.

Despite the insights provided, this study is limited by its modest sample size, single-country setting and retrospective design. Incomplete follow-up, potential selection and responder bias, predominance of female participants and limited data on adverse event specifics may impact generalizability. Future multicentre studies are needed to validate and expand on these findings.

5 | CONCLUSION

Many patients find it challenging to remain on these medications, with half of all patients only averaging 6 months of adherence. Understanding reasons for discontinuation, including side effects, medication costs, logistics, supply shortages and insufficient treatment response, can help healthcare providers better guide patients before starting obesity medications. This approach may improve adherence and support the long-term management of obesity.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

PEER REVIEW

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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