Playing the weighting game: a targeted literature review of real-world evidence of weight regain after GLP-1 receptor agonist discontinuation and implications for healthcare resource use

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BACKGROUND

GLP-1 receptor agonists (GLP-1 RAs) have transformed obesity management, and prescribing volumes are growing rapidly. In the UK, semaglutide prescriptions rose substantially following its 2023 NHS rollout[1].

However, over half of patients discontinue their GLP-1 therapy within twelve months[2, 3], frequently for non-clinical reasons such as cost, access or tolerability rather than as a planned treatment decision. Studies indicate that weight regain follows discontinuation, with a substantial proportion of the weight lost during treatment returning within twelve months. This often prompts patients to restart therapy and creates a cycle of cessation and re-prescription with direct implications for healthcare resource use (HCRU).

OBJECTIVES

This targeted review aimed to:

1. Characterise post-discontinuation weight regain and treatment reinitiation, and their implications for HCRU.
2. Assess whether the data required to evaluate the cessation and re-prescription cycle economically, including resource use and nutritional variables, are captured in real-world and clinical data.

METHODS

A targeted literature review was conducted in PubMed (January 2021-April 2026), restricted to primary studies in humans, published in English, covering populations in Europe and North America. Studies were eligible for inclusion if they reported on GLP-1 RA therapy in patients with overweight or obesity, and captured data on weight outcomes, nutritional variables, or both. Both randomised controlled trials (RCTs) and observational studies were included.

RESULTS

Study overview

Fourteen studies met the inclusion criteria (**Figure 1**): 8 RCTs and 6 observational studies collectively including over 280,000 participants across Europe and North America, although this total is dominated by two large cohorts. Six studies reported post-discontinuation weight data.

Post-discontinuation weight regain

Weight regain was rapid and substantial regardless of the magnitude of on-treatment weight loss (**Figure 2**).

Discontinuation, weight regain and HCRU

Discontinuation is common and substantially attenuates the weight benefit achieved (**Figure 3**). Among 125,474 US adults initiating a GLP-1 RA, 46.5–64.8% discontinued within twelve months, rising to 64.1–84.4% by two years[3].

In a US electronic health record cohort of 7,881 patients[2], early discontinuers achieved only −3.6% weight loss at 12 months compared with −11.9% in persistent users.

Critically for HCRU, among 41,792 US adults who discontinued a GLP-1 RA[3], 36.3–47.3% reinitiated therapy within twelve months. **Each 1% of post-discontinuation weight gain was associated with a 2.3–2.8% increased hazard of reinitiation**, indicating that weight regain drives further prescribing rather than simply ending an episode of treatment. No study in this review reported the HCRU or costs associated with this cycle.

Capture of nutritional variables

Formal dietary data were captured in only 3 of 14 studies (21%); 8 (57%) captured none at all (**Figure 1**).

Despite dietary intervention being recommended as an essential component of weight management[16,17], no study linked a nutritional variable to post-discontinuation weight trajectory. Where structured support was delivered, including within NHS specialist weight management services[10] and the most intensive dietary intervention of the STEP programme[14], intake was not measured.

The economic evidence gap

No study reported HCRU or costs associated with discontinuation, regain or reinitiation, so the cost of this cycle cannot be quantified.

Post-discontinuation follow-up was limited: six of 14 studies included a dedicated post-cessation follow-up period, with the longest at 104 weeks, leaving the period that drives long-term cost-effectiveness largely unobserved.

Nutritional variables that might modify the trajectory were not linked to post-discontinuation outcomes in any study, so adjunct support cannot be evaluated economically.

FIGURE 1

Study characteristics overview

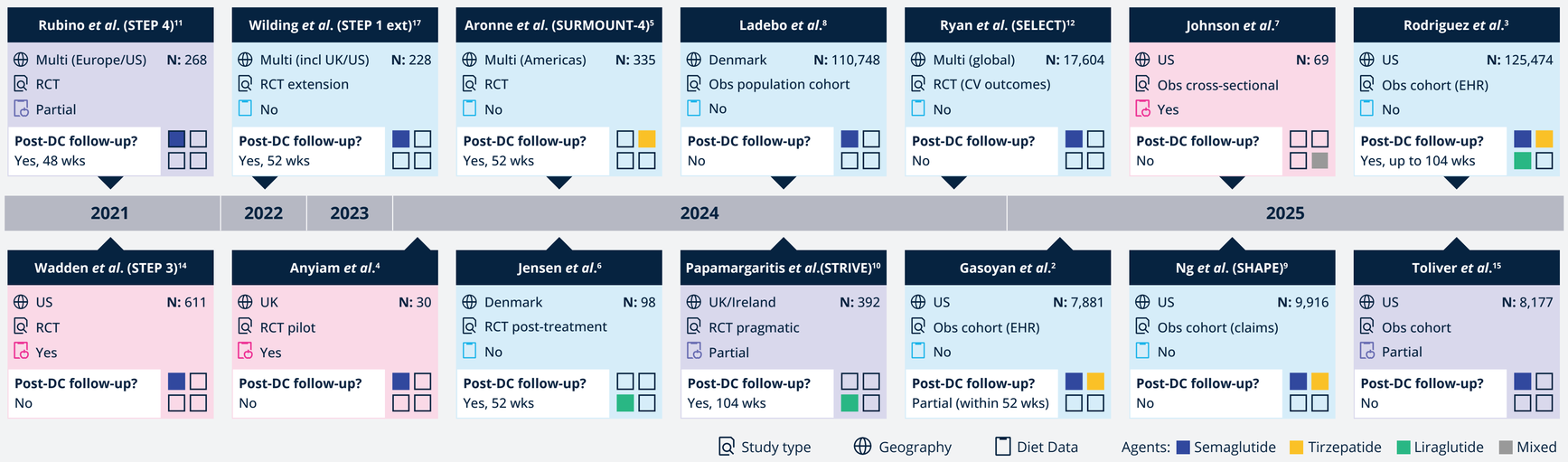
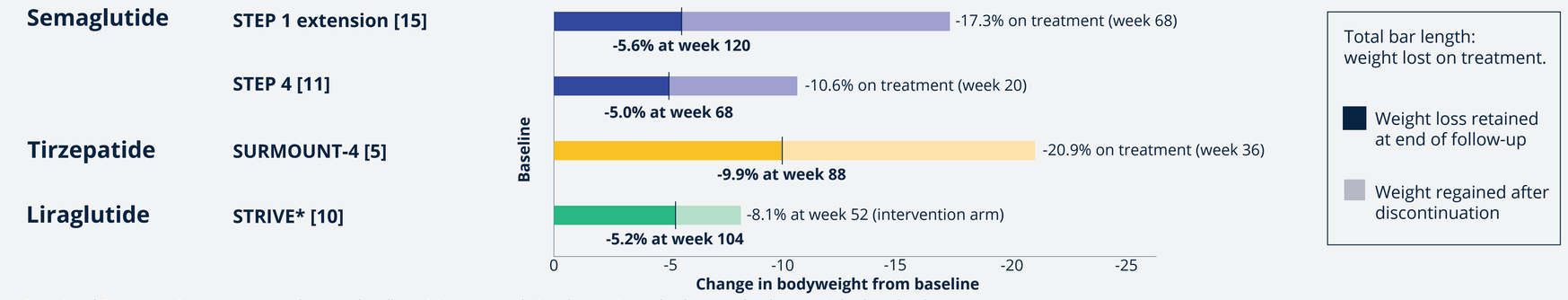


FIGURE 2

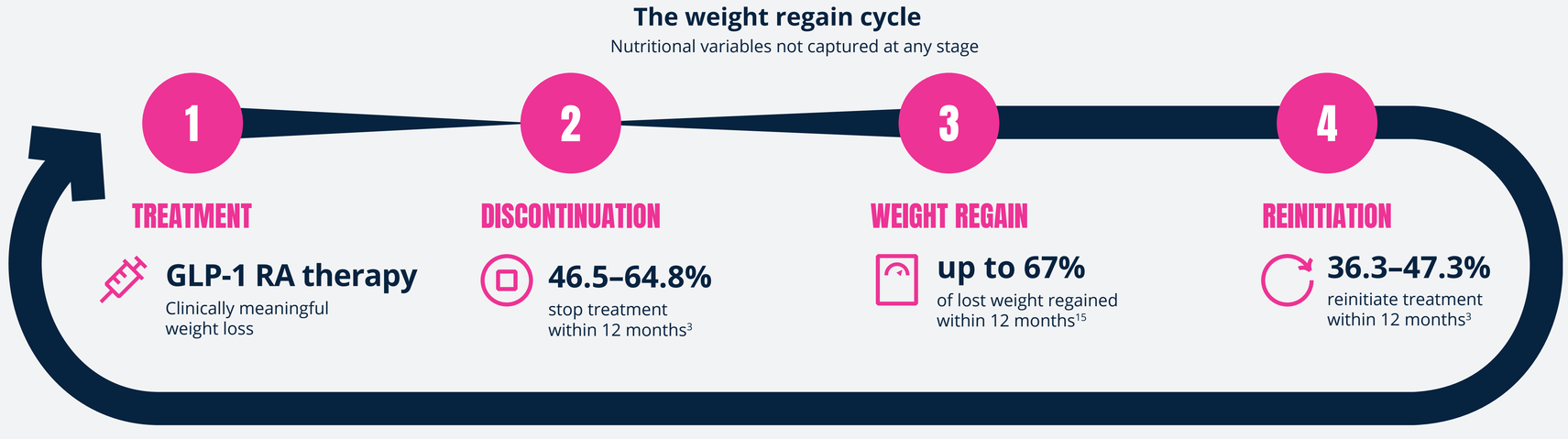
Change in body weight (%) from baseline:on treatment and after discontinuation



Step-4 and Surmount-4: on treatment values are for all participants completing the run-in; end-values are for those switched to placebo.
*STRIVE was a pragmatic trial with stopping rules; not a withdrawal trial. Participants stopped Liraglutide at 16, 32 orr 52 weeks if they did not reach the weight loss targets; 20.8% met all three and continued treatment in year 2. Values are intervention-arm means, so the change from week 52 to 104 reflects a mix of discontinuation and continued treatment

FIGURE 3

Discontinuation, weight regain and treatment reinitiation: a self-perpetuating cycle with implications for HCRU.



CONCLUSIONS

Discontinuation of GLP-1 RA therapy is common, substantially attenuates the weight benefit achieved, and is followed by rapid weight regain.

Weight regain drives treatment reinitiation, creating a cycle of cessation and re-prescription with direct implications for HCRU, yet no study reported the costs associated with it.

Routine incorporation of HCRU and nutritional variables into trial and real-world data collection is essential to enable economic evaluation of weight maintenance strategies and to inform payer decision-making.

RECOMMENDATIONS

To enable health economic evaluation, future studies on GLP-1 RA therapy should capture:

- → **Resource use:** healthcare contacts, prescribing and costs following discontinuation, regain and reinitiation.
- → **Post-discontinuation follow-up:** extended beyond twelve months, to observe rather than model the period that drives cost-effectiveness.
- → **Nutritional variables:** dietary intake, protein intake, programme participation, and dietary behaviour after discontinuation.

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