



Obesity Care After GLP-1 Discontinuation: Building a Maintenance Pathway Instead of a Cliff Edge

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Abstract

That weight is regained after incretin-based treatment stops is established. What services should do about it is not. Up to 65 per cent of people starting these agents for obesity discontinue within a year, most often for reasons unrelated to whether the drug worked, and roughly two thirds of the weight lost is regained within a year of stopping. Against that, no randomised trial has evaluated any specific tapering, transition or maintenance regimen following withdrawal, so every proposed pathway is inference from other settings. The available evidence is small and uncontrolled: in a digital clinic cohort, 353 people who wished to stop after reaching target were tapered to zero over nine weeks with coaching, 240 completed the taper, and among 85 followed for a further 26 weeks weight remained stable. Switching to older anti-obesity agents after a year of treatment has been reported to maintain weight loss over two years. This review examines what a maintenance pathway could consist of and how thin its evidence is.

Keywords: GLP-1 receptor agonists; Discontinuation; Weight maintenance; Tapering; Service design

Introduction

Incretin-based agents produce weight reduction of 10 to 30 per cent, a magnitude rarely achieved by earlier pharmacotherapy [1,2,3,32,33]. Guidelines across jurisdictions now position pharmacotherapy as a component of long-term obesity care [17,18,31]. Randomised withdrawal designs have established that stopping is followed by substantial regain, and that reversal of cardiometabolic improvement accompanies it [4,5,6].

That question, what happens on stopping, is settled well enough for practical purposes. A different question is not. Services prescribing these agents will have patients who stop, for reasons that are frequently outside anyone's clinical control, and there is no established pathway for what care those patients should receive next [7,8,27]. Persistence with these medicines in routine practice is low, and weight and glycated haemoglobin change accordingly by discontinuation status [9,28].

This review concerns the design of that pathway rather than the magnitude of regain. It examines who stops and why, what maintenance strategies have been proposed, what evidence supports each, and where the gaps are.

Material and Methods

Search strategy: PubMed and the archives of the major obesity, endocrinology and general medical journals were searched for studies of care following discontinuation of incretin-based obesity treatment. Search terms combined GLP-1 receptor agonist and semaglutide with discontinuation, tapering, maintenance, step-down and weight regain. Reference lists of the principal review [7] were screened by hand for primary sources.

Eligibility: Studies were included if they described or evaluated a strategy intended to preserve weight loss after these agents are reduced or stopped, or reported who discontinues and why. Withdrawal trials are cited to establish the problem and are identified as such; the magnitude of regain is not the subject of

this review and is treated as background.

Data extraction and handling: Design, population, the strategy examined and the reported outcome were extracted as published. The evidence level is stated alongside every strategy, distinguishing randomised evidence, observational cohorts, congress-presented abstracts and expert proposal, because these are mixed freely in this literature and the distinction is the central point. This review reports published findings and does not constitute guidance on prescribing, tapering or stopping any medicine. No pooling or re-analysis was performed. Figures 1 to 6 and Tables 1 to 3 reproduce published values only. This is a narrative synthesis and was not registered as a systematic review.

Results

How many stop: Real-world data show that up to 65 per cent of people using these agents discontinue within a year of initiation (Figure 1), with other cohorts reporting around half [7,9,10]. Randomised evidence indicates that roughly two thirds of the weight lost is regained within a year of stopping [4,7].

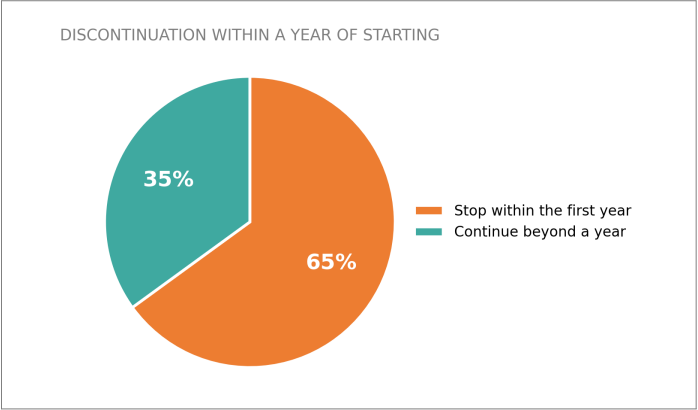


Figure 1: Discontinuation within a year of starting treatment [7,9]

Why they stop: Reported reasons include change in cost or insurance coverage, supply constraints affecting a particular molecule or dose, side effects that did not become tolerable, pregnancy planning, a planned pause for surgery or other treatment, and reaching an agreed target (Figure 2) [7,11]. Only the last of these is an elective stop that can be scheduled, which bears directly on how a maintenance pathway must be designed.

Switching agents: Switching to older anti-obesity medications after twelve months of incretin-based therapy has been reported to maintain weight loss over two years [15]. The agents described in that context are already licensed and considerably less expensive, which matters given that cost is among the commonest reasons for stopping [7,11,16].

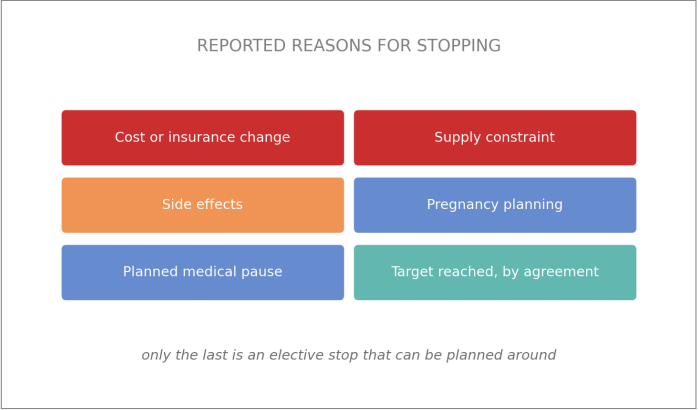


Figure 2: Reported reasons for stopping treatment [7,11]

What has been proposed: A review of this question sets out a hierarchical framework progressing from lifestyle and behavioural intervention through pharmacological approaches to procedural options, with a hybrid phase combining pharmacological tapering and continued behavioural support (Figure 5) [7]. The proposed maintenance phase combines low-dose pharmacotherapy, scheduled behavioural review and continued dietetic oversight, and is explicitly modelled on step-down approaches used in diabetes and hypertension, where treatment intensity is reduced as control improves [7,12].

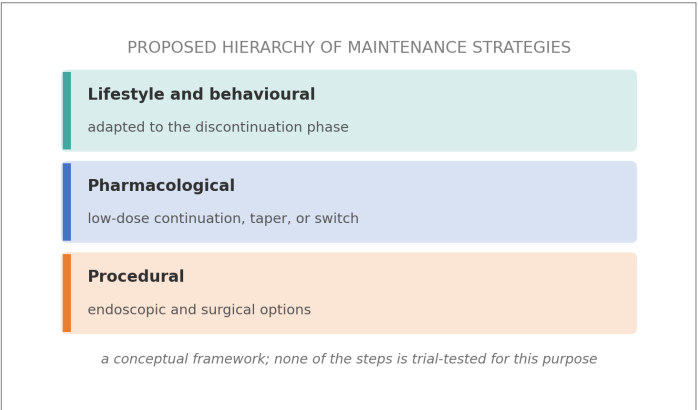


Figure 5: Proposed hierarchy of maintenance strategies [7]

What has been tested: The same review states that no randomised controlled trials have evaluated specific tapering, transition or maintenance regimens following withdrawal, and that pharmacological strategies to mitigate regain remain largely exploratory (Figure 6) [7]. The theoretical case for gradual dose reduction rather than abrupt cessation is that it may ease physiological rebound by allowing slower re-emergence of appetite and gastrointestinal motility [7,13].

Table 2: Proposed maintenance strategies and the evidence behind each

Table 3: What is and is not established about care after discontinuation

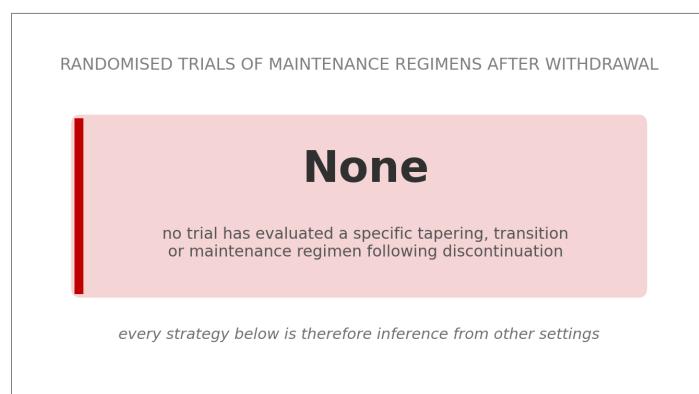


Figure 6: Randomised evidence for maintenance regimens after withdrawal [7]

The tapering cohort: A study presented at a congress described a digital weight-management programme in which participants received the lowest effective dose, with increases considered on reaching a plateau. Among 353 who wished to discontinue after reaching target weight, the dose was reduced to zero over nine weeks alongside coaching on diet and activity. Of those 353, 240 tapered to zero (Figure 3). Data from 85 followed for 26 weeks after reaching zero indicated that weight remained stable, with a mean further loss of 1.5 per cent (Figure 4) [7,14].

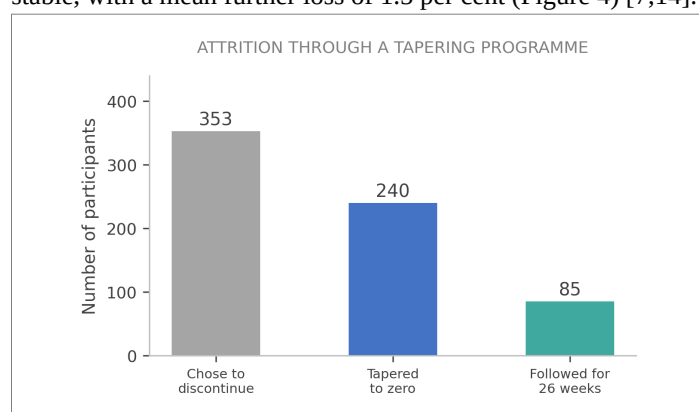


Figure 3: Attrition through a tapering programme [7,14]

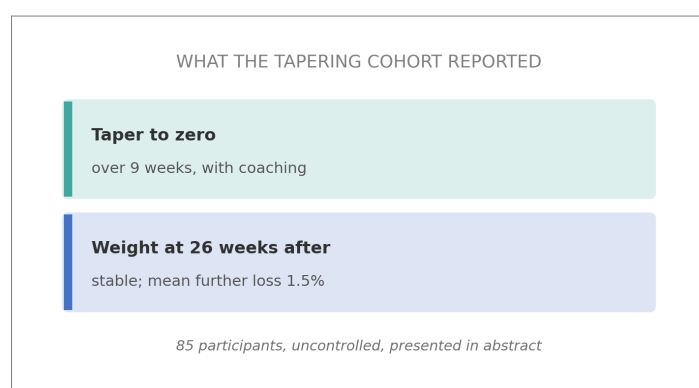


Figure 4: What the tapering cohort reported [7,14]

The degree of weight loss retained matters clinically because improvement in comorbidity is graded rather than all-or-nothing [30]. A pathway that preserved half the loss would be worth having even if it did not preserve all of it, and framing discontinuation as a binary success or failure obscures that [22,30].

Stage	Number	Share of those starting
Wished to discontinue at target	353	—
Tapered to zero	240	68.0%
Followed 26 weeks after zero	85	24.1%

Table 1: Attrition through the tapering programme, as reported [7,14]

The pharmacological rationale for tapering: These agents do not produce a physiological withdrawal syndrome, so abrupt cessation is not in itself hazardous [13,17]. The reasons offered for a step-down are practical rather than pharmacological: a more gradual return of appetite, opportunity to adjust glucose- and blood-pressure-lowering treatment as their requirement changes, and a less abrupt behavioural transition [13,17,18]. The physiology that drives regain, including persistent hormonal adaptation and reduced energy expenditure, is well described and is not specific to these agents [19,20,21].

Strategy	Evidence level	What supports it
Behavioural support in this phase	Proposal	Adapted from general obesity care [7]
Gradual dose reduction	Observational, abstract	353-patient cohort [7,14]
Low-dose continuation	Proposal	Step-down analogy from other diseases [7,12]
Switch to older agents	Observational	Two-year maintenance reported [15]
Procedural options	Proposal	Established for other indications [7]

Question	Status
Does weight return after stopping?	Established by randomised withdrawal [4,5,6]
Does tapering reduce regain?	Not tested in any trial [7]
Does low-dose continuation work?	Not tested in any trial [7]
Does switching agents work?	One observational report [15]
Who is a candidate for stopping?	Not defined in any study [7,8]

What is known about maintenance generally: Weight-loss maintenance was a research field long before these agents existed. Extended-care programmes, in which contact continues after an initial intensive phase, improve maintenance relative to no continued contact [25,26], and long-term follow-up of intensive lifestyle intervention describes the trajectory over years [23,24]. That literature is the closest available analogue and is the basis for the behavioural component of the proposed pathways [22,29].

Exercise as a maintenance component: A randomised placebo-controlled trial examined weight-loss maintenance with exercise, a GLP-1 receptor agonist, or both, followed by a year without treatment, and reported outcomes after treatment ended [34]. This is among the few randomised designs that follows participants beyond the treatment period, and its post-treatment analysis addresses the question this review is concerned with more directly than the withdrawal trials do [6,34].

Discussion

The framing in the title of this review deserves examination rather than assumption. A cliff edge implies an elective step taken at a chosen moment, and most discontinuation is not that. Cost, insurance change and supply constraint account for a large share of stopping, and none of them arrives with notice [7,11]. A maintenance pathway designed around a planned taper at an agreed target therefore addresses the minority of stops.

That has a concrete implication for service design. If most people who stop do so abruptly and for external reasons, then the useful preparation happens while treatment is still working, not at the point of stopping. A conversation early in treatment about what will happen if supply or funding is lost is more likely to reach the people who will need it than a tapering protocol available only to those who reach target.

On the tapering evidence itself, the honest summary is that it is thin and encouraging. Of 353 people who wished to stop, 240 completed the taper and 85 had 26-week follow-up, among whom weight was stable [7,14]. That final group represents about a quarter of those who started, and there is no control arm, no randomisation and the material is congress-presented. It is compatible with tapering working. It is equally compatible with the 85 being those for whom things were going well.

The most important sentence in this literature is a negative one. No randomised trial has evaluated a specific tapering, transition or maintenance regimen following withdrawal [7]. Everything else described here, the hierarchical framework, the low-dose maintenance phase, the analogy with step-down in hypertension, is reasoning from other settings. That reasoning may well be correct; it has simply not been tested, and services building pathways should know they are building on proposal rather than evidence.

Switching to older, cheaper anti-obesity agents is the strategy with the clearest practical logic, precisely because it addresses the commonest reason for stopping. A two-year maintenance result has been reported [15]. That is one observational study and does not establish the approach, but it points at the right problem, which is that a pathway requiring continued access to an expensive medicine cannot serve the people who stopped because they could not afford one.

A further consideration concerns what a maintenance pathway is being asked to achieve. If the goal is to hold the full weight loss, the evidence suggests that requires continued pharmacotherapy at some dose, and the pathway question becomes one of funding rather than of clinical design [5,6]. If the goal is to slow regain and preserve part of the benefit, the behavioural and switching approaches become more plausible, but no study reviewed here states which goal it is testing [7,15].

2. Jastreboff AM, Aronne LJ, Ahmad NN, Wharton S, Connery L, Alves B, et al. "Tirzepatide once weekly for the treatment of obesity". *N Engl J Med* 387(2022):205-216.

Study limitations

The limitations belong to the underlying literature and are unusually severe. No randomised evidence exists for any maintenance regimen after discontinuation, so the central question of this review is unanswered by design rather than by omission [7]. The principal tapering data are congress-presented, uncontrolled, and report 85 people of the 353 who entered, so attrition exceeds the follow-up sample [7,14]. The switching report is observational and the comparison group is not described in the material reviewed [15]. Discontinuation rates vary between 50 and 65 per cent across sources using different definitions of stopping [7,9,10]. Reasons for stopping are self-reported and are likely to be incompletely captured, particularly where cost and shame interact [11,16]. The proposed frameworks are expert constructions and have not been prospectively evaluated as pathways [7,12]. And the withdrawal trials that establish the problem enrolled participants who had tolerated and responded to treatment, so they describe regain in a selected group [4,5,6].

Conclusion

Weight returns after these agents are stopped, and roughly two thirds of what was lost comes back within a year. What should be offered to the person stopping is not established: no randomised trial has evaluated any tapering, transition or maintenance regimen, and the most encouraging observational report follows 85 of the 353 people who entered it. Proposed pathways combining low-dose continuation, behavioural review and dietetic oversight are reasonable inference from step-down practice in other chronic conditions, and should be described as inference. The design point that follows from the data on why people stop is that most discontinuation is not elective, so preparation belongs early in treatment rather than at the point of stopping, and a pathway that depends on continued access to an expensive drug will miss the people who stopped because of its price.

Acknowledgements

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Conflict of Interest

The authors declare no competing interests.

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Ethics Statement

This article reviews previously published studies only. No new patient data were collected and no participants were recruited, so ethical approval was not required.

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