Weight Loss and Reduced Hunger over Four Weeks of Trilogiii Use: A Prospective, Single-Arm Study of a Multi-Target Nutritional Satiety System in 395 Participants, with Separate Extension Cohorts Through Week 12

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Abstract

Background. The success of glucagon-like peptide-1 (GLP-1) receptor agonists has highlighted sustained satiety as central to weight loss. Trilogiii is a four-product nutritional system designed to support satiety through mechanosensory, hormonal and metabolic (nutrient-repletion) routes, within a framework of complete essential nutrition, gut-microbiome support, and thermogenesis paired with induction of endogenous antioxidant defenses.

Methods. A prospective, single-arm, open-label, nonrandomized study was conducted between July and December 2025. Of 497 people who received the products, 422 submitted results, and 27 returned packets were excluded. Participants were supplied the four products and instructed to use them daily alongside a flexible protocol of water intake and small whole-food meals. Weight and waist/hip circumference were self-reported through paper study packets and/or a private online study group (hosted on Facebook), which all participants were required to join and which was used to standardize reporting and product use; results in the group were posted as cumulative totals. Volunteers could continue for 4- or 8-week extensions. The co-primary outcomes were 4-week change in self-reported weight and in the frequency of hunger, cravings and food noise. Hunger, cravings and food noise were rated on a four-point frequency scale at the start and end of the initial period and at the start and end of each participant's extension, and were also rated weekly as a self-estimated improvement multiple relative to the start of the study, with the final week of each period analyzed.

Results. A total of 395 participants reported 4-week results (257 eligible packet participants and 138 group-only reporters); packet participants' mean starting body mass index (BMI) was 32.9 kg/m². Mean weight loss was 12.66 lb (95% CI 12.15–13.18; median 11.80); packet participants lost 6.03% of body weight (95% CI 5.82–6.24%), and 180 of 257 (70.0%; 95% CI 64.2–75.3%) lost at least 5%. In separate, self-selected extension cohorts, mean within-period loss was 8.09 lb over weeks 5–8 (n = 91) and 6.37 lb over weeks 9–12 (n = 57). Cumulative totals posted in the study group by reporters in the weight-loss phase averaged 20.85 lb at 8 weeks (n = 101) and 28.25 lb at 12 weeks (n = 65). Among 57 study-group reporters with cumulative totals at all three time points, mean loss was 29.09 lb by week 12. Among packet participants with paired ratings, 62.3% reported less frequent hunger, 60.8% less food noise (frequency of thoughts about food) and 75.1% less frequent

cravings after four weeks, and only 1.7–4.5% reported each as more frequent (sign test, $P < 0.001$ for each). On the separate self-estimated multiple, the median rating after four weeks was 2 ("twice as good") for each measure (means 2.26–2.34), and 81.6–85.4% reported improvement. Reported adverse effects were mainly gastrointestinal and transitional symptoms (such as headache and fatigue) that declined over the four weeks; no cardiovascular symptoms were reported by eligible packet participants without a pre-existing cardiovascular condition. No participant reported a serious adverse event or needing emergency care; events were self-reported and not independently adjudicated.

Conclusions. In this uncontrolled, self-reported study, Trilogiii with a flexible dietary protocol was associated with substantial short-term weight loss and marked reductions in hunger, cravings and food noise. The design cannot separate product effects from those of the protocol, group support or expectancy, and the formulation's proposed mechanisms were not measured; a controlled trial is required to confirm these effects and establish the products' specific contribution.

Key findings

- **Weight loss:** among 395 participants who reported four-week results (257 eligible packet participants and 138 group-only reporters), mean loss was 12.66 lb; among the 257 packet participants, mean loss was 6.03% of starting weight, and 180 (70.0%) lost at least 5%.
- **Satiety:** comparing each packet participant's ratings before and after four weeks, 62.3% reported less frequent hunger, 60.8% less frequent food noise (frequency of thoughts about food) and 75.1% less frequent cravings; only 1.7–4.5% reported each as more frequent ($P < 0.001$). The share reporting each "regularly" or "constantly" fell from about half to under 10%. On a separate measure, participants' own written improvement multiples after four weeks had a median of 2 ("twice as good") for each, and 81.6–85.4% reported improvement.
- **Extension cohorts:** separately analyzed, self-selected extension cohorts reported mean within-period losses of 8.09 lb in weeks 5–8 and 6.37 lb in weeks 9–12, and 83–91% of packet participants answering rated their hunger, cravings and food noise as improved relative to the start of the study.
- **Cumulative loss:** among study-group reporters in the weight-loss phase, mean total loss since starting was 20.85 lb at 8 weeks and 28.25 lb at 12 weeks, and 52 of 65 (80.0%) 12-week reporters had lost 20 lb or more. The 57 with a total at every time point lost a mean 14.83, 23.21 and 29.09 lb by weeks 4, 8 and 12, and every one of them lost weight in each 4-week interval.
- **Consistency across reporting channels:** the 146 packet returners who also posted in the study group reported about 12.53 lb of loss at 4 weeks, a similar aggregate mean to the 12.41 lb across all 257 eligible packet records (an unpaired comparison of differently constituted groups).
- **Adherence:** product adherence was 89–93% in every period.
- **Tolerability:** reported side effects were mainly gastrointestinal and transitional and declined over four weeks; no one reported needing emergency care, and cardiovascular reports came from only two eligible packet participants, both with a pre-existing cardiovascular condition. Nine participants stopped early after reporting gastrointestinal symptoms and were excluded as non-adherent.
- **Prior GLP-1 RA use:** participants who had previously used a GLP-1 receptor agonist ($n = 17$) lost 6.00% of starting weight, similar to the packet cohort as a whole (6.03%).
- **Interpretation:** these findings describe the combined products and dietary protocol in participants who reported results; a controlled study is needed to determine the products' separate contribution.

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1. Introduction

The clinical success of glucagon-like peptide-1 (GLP-1) receptor agonists has reframed weight management around a single principle: durable weight loss follows when hunger is reliably suppressed. These agents act primarily by amplifying satiety signaling, and the pivotal trials report mean losses of about 15–21% of body weight over 68–72 weeks [1,2]. Their limitations — cost, injection, gastrointestinal intolerance and loss of lean mass [1], and regain of about two-thirds of the weight lost within a year of stopping treatment [3] — have prompted interest in whether nutritional systems can address the same satiety pathways through complementary, lower-intensity means.

Satiety is not a single signal but the integrated output of mechanical, endocrine and metabolic inputs converging on the hypothalamus and brainstem. Trilogiii was formulated to act on three of these inputs simultaneously: mechanosensory fullness from a viscous fiber; enteroendocrine hormone release from a fermented protein complex, with proposed dipeptidyl peptidase-4 (DPP-4) inhibition (shown in vitro for its peptide classes and for botanicals in the Calorie Burner / Cell Protector [CC] capsule); and repletion of essential micronutrients whose inadequacy is proposed to sustain nutrient-seeking hunger. These satiety targets sit within a broader three-part design comprising complete essential nutrition, pre- and probiotic support for the gut microbiome, and thermogenic stimulation paired with activation of the nuclear factor erythroid 2–related factor 2 (Nrf2) endogenous antioxidant pathway.

Trilogiii is named for this three-fold architecture. Three approaches — complete essential nutrition, biotic support, and thermogenesis with cellular protection — are designed together to engage three routes to satiety (mechanosensory, hormonal and metabolic) which act over three timescales: minutes, hours, and days to weeks. The protein complex at the center of the system is designed to extend the hormonal route across three digestion phases in the hours after a meal. Table 1 summarizes how these elements relate; the sections that follow describe each in turn.

Table 1. The three-fold design of Trilogiii

Approach or component (Section 2)	Satiety route supported (Section 3)	Proposed principal timescale	Delivered by
Complete essential nutrition (FS, EN)	Metabolic — essential-nutrient repletion	Days to weeks	42 essential nutrients; BIACTIN as carrier
Biotic support (FS, BP)	Hormonal — SCFA-driven GLP-1/PYY release; metabolic — support for micronutrient absorption	Several hours after ingestion; may develop with repeated use	Fermentation cultures, nine-species blend, four fiber-containing prebiotic ingredients
Thermogenesis with cellular protection (CC)	Hormonal — DPP-4 inhibition (shown in vitro) proposed to prolong active GLP-1	Postprandial hour	Berberine, quercetin; Nrf2 activators
Konjac glucomannan (BP)	Mechanosensory — gastric distension and fullness	Minutes	Viscous fiber
BIACTIN protein complex (FS, BP)	Hormonal, across three digestion phases	0–1 h, 1–3 h, 3 h onward	Whey, peptides, casein

Products: FS, Foundation + Stimulation nutrient-dense shake; EN, Essential Nutrients Booster capsule; CC, Calorie Burner / Cell Protector capsule; BP, Bioactive Protein Booster; BIACTIN, the fermented protein complex in FS and BP (Appendix B.1.2). The four products are described in Section 2.1. Physiological terms (not ingredients): SCFA, short-chain fatty acid, produced when gut bacteria ferment fiber; GLP-1, glucagon-like peptide-1, and PYY, peptide YY, gut hormones that signal satiety; DPP-4, dipeptidyl peptidase-4, the enzyme that inactivates GLP-1.

This paper describes the formulation rationale, the mechanistic basis for each satiety target, and the results of a single-arm, open-label study in which 395 participants who were supplied the full system reported results after four weeks, with smaller self-selected cohorts continuing for a further four or eight weeks.

2. Product and Formulation Rationale

Sections 2 and 3 summarize the formulation rationale; the full rationale and supporting evidence are given in Appendix B. Unless otherwise stated, the mechanisms described are drawn from published studies of individual ingredients or ingredient classes — in vitro, in animals or in humans — and were not measured for the finished Trilogiii products or in this study's participants; where the text says an ingredient acts in a particular way, it refers to that published evidence, not to an effect observed here.

2.1 Four products, three approaches

Trilogiii comprises four products. Two — the Foundation + Stimulation nutrient-dense shake (FS) and the Essential Nutrients Booster capsule (EN) — deliver the essential-nutrient platform, with EN supplementing the same platform in additional forms and amounts; FS also supplies most of the BIACTIN protein (30 of 43 g a day), the nine-species probiotic blend and 4 g of inulin. The Calorie Burner / Cell Protector capsule (CC) is formulated for thermogenesis with cellular protection, DPP-4 inhibition, nicotinamide adenine dinucleotide (NAD^+) support and anti-inflammatory activity. The Bioactive Protein Booster (BP) delivers additional BIACTIN protein (13 g a day) together with 3 g each of konjac glucomannan, high-amylose resistant starch and ground flaxseed, plus medium-chain triglyceride (MCT) oil powder. Together they constitute three approaches (Table 2).

Table 2. Products and approaches

Approach	Products	Principal components
Complete essential nutrition	FS, EN (with BP)	13 vitamins, choline, 14 minerals, 12 amino acids (9 indispensable, 3 conditionally indispensable), 2 essential fatty acids; BIACTIN fermented protein complex
Biotics for gut health, hormone release and absorption	FS, BP	Fermentation cultures; nine-species probiotic blend; inulin, glucomannan (konjac), flaxseed, resistant starch; medium-chain triglyceride oil powder
Thermogenesis with cellular protection	CC	Thermogenic botanicals; Nrf2 activators; ingredients with in vitro DPP-4 inhibitory activity; NAD^+ support

Daily regimen. Three CC capsules (2,390 mg) once daily; four EN capsules once daily; two scoops of FS shake mix (62.6 g chocolate or 59 g vanilla) and two scoops of BP (28 g), which could be mixed as a single shake or divided into two half-shakes. Timing of the shake relative to meals was left to the participant: it could be taken with a small meal, separately from meals, or as a full meal replacement.

2.2 Approach 1 — Complete essential nutrition (FS + EN)

"Complete" here means that every essential nutrient in the framework described in Appendix B.1.1 is supplied; the products are designed to be used alongside the protocol's small meals of lean protein and low-carbohydrate vegetables, which supply the remainder of daily protein, energy and fatty acids and of the minerals provided below the Daily Value (Table B1). The products alone are therefore not intended to meet each requirement in full. FS and EN, together with the protein and flaxseed in BP, supply 13 vitamins, choline, 14 minerals, the 9 indispensable and 3 conditionally indispensable amino acids, and both essential fatty acids — 42 nutrients in the framework used here, 43 with water — several of them in more than one chemical form; FS and EN together provide 100–200% of the Daily Value for every vitamin (Appendix B.1.1, Tables B1 and B2). Completeness is the point of the design, which proposes that when essential-nutrient requirements go unmet, hunger can persist even when calories are sufficient. The best human evidence concerns protein — lowering dietary protein from 15% to 10% of energy increased total energy intake by 12% in a controlled feeding study [4] — and multivitamin supplementation during energy restriction has reduced appetite in women [5] (Section 3.3). Completeness matters most during restriction itself, when eating less makes nutrient adequacy harder — popular diet plans can fall well short of micronutrient requirements [6] — and when lean mass is at risk (Appendix B.1.1).

The protein is delivered as BIACTIN: 43 g a day from 23 g cultured (fermented) milk protein, 16 g whey protein isolate and 4 g hydrolyzed collagen peptides, approximately 47:53 casein:whey excluding collagen. The combination is designed so that fast-digesting whey and peptides, and more slowly digested casein, overlap to provide satiety signals across early, intermediate and sustained phases (Appendix B.1.3); protein digestion products are a potent dietary stimulus for cholecystokinin (CCK), GLP-1 and PYY release, and whey has produced greater responses than casein in acute feeding studies [7–9]. Fermentation changes how milk protein is delivered: in human intubation studies, fermented milk left the stomach more slowly while overall protein absorption remained high [10,11]. BIACTIN is also designed as a delivery matrix for the nutrients supplied with it: dairy increased zinc absorption from high-phytate meals in two human isotope studies [12,13], fermentation by particular organisms can increase some B vitamins [14] (not measured for BIACTIN), milk-derived peptides can carry minerals in cell and animal models [15,16], and glucagon-like peptide-2 (GLP-2), the intestinotrophic hormone released with GLP-1 after meals, increases absorptive capacity [17–19] (Appendix B.1.2–B.1.4). Absorption of individual nutrients from Trilogiii itself was not measured; the integrated hypothesis is set out in Section 6.5.

2.3 Approach 2 — Biotics for gut health, hormone release and absorption (FS + BP)

FS supplies the BIACTIN fermentation cultures (*Lactobacillus delbrueckii* subsp. *bulgaricus* and *Streptococcus thermophilus*, 15×10^9 colony-forming units [CFU] each, per the manufacturer's specification [20]; viable counts in the finished product were not independently assayed), a nine-species probiotic blend (1×10^9 CFU) and 4 g of inulin; BP adds 3 g each of konjac glucomannan, high-amylose resistant starch and ground flaxseed — 13 g of fiber-containing prebiotic ingredients a day in total — together with MCT oil powder (5.5 g a day across FS and BP). The design follows an intended synbiotic approach [21], combining live cultures with fermentable substrates, with probiotic levels chosen to act with the prebiotic substrates rather than as standalone doses; whether the combination meets the evidentiary criteria of the International Scientific Association for Probiotics and Prebiotics (ISAPP) for a complementary synbiotic remains to be established. In published studies, microbial fermentation of such substrates produces short-chain fatty acids that stimulate GLP-1 and PYY release [22], lower luminal pH and increase mineral absorption — inulin-type fructans increased stable-isotope-measured calcium absorption in adolescents [23] and calcium and magnesium absorption in postmenopausal women [24]. The substrates are also intended to support intestinal barrier function. In animal models, metabolic endotoxemia (raised circulating bacterial lipopolysaccharide) initiates weight gain and insulin resistance [25], and a weakened gut barrier is one proposed route by which it arises. Fermentable prebiotics have increased GLP-1 and PYY and reduced hunger in a randomized trial [26] and increased self-reported satiety in healthy adults across trials [27], and specific probiotic strains have improved micronutrient status [28] (Appendix B.2).

2.4 Approach 3 — Responsible thermogenesis: metabolic stimulation with cellular protection (CC)

Energy expenditure falls during caloric restriction [29]. CC combines thermogenic agents acting on complementary pathways — capsaicin, 6-gingerol and 6-paradol (transient receptor potential vanilloid 1 [TRPV1] and brown adipose tissue), forskolin (cyclic AMP [cAMP]), berberine (AMP-activated protein kinase [AMPK]), L-carnitine and conjugated linoleic acid [30–38] — in a deliberately low-stimulant formula: less than 5 mg of *p*-synephrine and less than 0.5 mg of yohimbine a day, well below the doses used in clinical studies [39–43] (European regulators consider the data on yohimbe inadequate to establish its safety in food [44]), and 2 mg of caffeine per serving (Appendix B.3.1). Because thermogenic activation can involve increased mitochondrial reactive oxygen species (ROS) signaling, and excess fatty-acid supply has increased mitochondrial hydrogen peroxide emission in experimental studies [45,46], and because high-dose exogenous antioxidants can blunt the body's adaptive responses [47], CC pairs thermogenic agents with activators of the Nrf2 pathway (carnosic acid, silymarin, withaferin A, pterostilbene, quercetin and epigallocatechin gallate [EGCG]), which induces the body's own antioxidant enzymes, together with holy basil, which has preclinical antioxidant and cytoprotective evidence [48–55]; a low-dose phytochemical combination designed on the same principle, in an uncontrolled before-and-after study, increased red-cell superoxide dismutase by 30% and catalase by 54% and reduced lipid peroxidation by 40% in healthy adults [56], and its components synergistically induce the cytoprotective enzyme heme oxygenase-1 in cell studies [57] (Appendix B.3.2). Several CC ingredients have published in vitro DPP-4 inhibitory activity and support NAD^+/sirtuin pathways in preclinical models [58–61] (Appendix B.3.3). Combining components that act through different mechanisms, each below the level at which its own side effects have been reported, is the design intent; whether CC's specific ingredients and doses produce more than additive effects has not been measured, and holding each component below its own reported side-effect level does not by itself establish the safety of the combination.

2.5 Separation from caffeinated beverages

Participants were instructed to take no coffee, tea or other caffeinated beverages within one hour of any Trilogiii product. Tea and coffee polyphenols reduce non-heme iron absorption, by up to 94% for black tea [62], and delaying tea by one hour after an iron-containing meal substantially attenuates this effect [63]; polyphenols also reduce zinc absorption when phytate is present [64], caffeine transiently increases urinary calcium and magnesium losses [65], coffee consumption is associated with lower circulating concentrations of some B vitamins [66], and tea and coffee contain factors that inactivate thiamine in vitro [67]. The separation also limits co-exposure of caffeine with CC; because a product combining caffeine with *p*-synephrine raised post-exercise diastolic blood pressure [68], CC was formulated with negligible caffeine (2 mg per serving; Appendix B.3.4).

3. Mechanistic Rationale: Three Satiety Targets

Energy restriction remains the foundation of weight loss, but adherence is its limiting factor: hunger rises as intake falls, and hunger and appetite-regulating hormones remain altered for at least a year after diet-induced weight loss, which is thought to contribute to weight regain [69]. Trilogiii is designed to support satiety through three physiological routes that operate on different timescales; the full evidence for each is given in Appendix B.4.

3.1 Mechanosensory satiety — konjac glucomannan

Stretch of the stomach wall produces fullness well before nutrients are absorbed [70]. Konjac glucomannan, a highly viscous soluble fiber, absorbs many times its weight in water, increases gastric content viscosity and delays gastric emptying [71]; viscous fibers are the fibers most consistently associated with reduced appetite and intake [72], and, on a favorable opinion from the European Food Safety Authority (EFSA), the European Union authorizes a claim that 3 g a day, taken as three 1 g doses with water before meals, contributes to weight loss during energy restriction [73]; BP supplies the same daily amount, though not in the three pre-meal doses the claim specifies. Glucomannan's effect on body weight as a standalone agent is modest [74–76], which is why it is combined with the two further targets.

3.2 Hormonal satiety — fermented protein and botanical extracts with in vitro DPP-4 inhibitory activity

Nutrient arrival in the gut releases CCK, GLP-1 and PYY, each of which reduces food intake in animals and humans [77–79]; protein is a potent dietary stimulus, and whey has produced greater responses than casein in acute feeding studies [7,8]. GLP-1 is inactivated within minutes by DPP-4, and milk-derived peptides and several botanicals inhibit DPP-4 in vitro [60,61,80,81]. In Trilogiii this target is addressed by BIACTIN (including milk-derived peptide classes with published in vitro DPP-4 inhibitory activity), the SCFA-generating fibers in FS and BP, and botanical constituents of CC with the same in vitro activity, including berberine; finished-product DPP-4 activity and circulating hormones were not measured in this study.

3.3 Metabolic satiety — essential nutrient repletion

The Protein Leverage Hypothesis proposes that people keep eating until protein needs are met [82], and controlled human feeding has shown partial protein leverage: a lower-protein diet increased total energy intake by 12% [4]. A parallel mechanism is proposed for vitamins and minerals, for which nutrient-specific appetites are documented in animals [83]. In humans, adults with obesity frequently have inadequate micronutrient intakes despite excess energy intake [84]; in a randomized, double-blind trial during energy restriction, multivitamin and mineral supplementation reduced hunger and desire to eat in women [5]; and in a subgroup of women with very low calcium

intake, calcium plus vitamin D supplementation was accompanied by greater fat loss and lower spontaneous fat intake [85]. Protein leverage has the more direct human evidence; which specific micronutrient inadequacies drive hunger is a testable component of the model. In Trilogiii this target is addressed by the complete essential-nutrient platform of FS and EN, with absorption intended to be supported by Approach 2 (not measured; Section 6.5).

3.4 Integrated rationale

These three targets operate on different timescales and through different afferent routes: mechanosensory fullness arrives within minutes of ingestion; the protein-driven gut-hormone response builds over the postprandial hour and may be extended by DPP-4 inhibition, with SCFA-driven release following over several hours; and micronutrient repletion is proposed to act over days to weeks and may improve the metabolic background against which hunger is perceived. The three digestion phases of BIACTIN (Appendix B.1.3) sit within the hormonal timescale rather than forming a separate route: the rapidly absorbed whey and peptides, the continuing digestion of whey and partly processed milk proteins, and the more slowly digested casein are intended to extend the protein-driven hormonal signal across the hours after a meal. In the formulation rationale, satiety support is intended to make a caloric deficit sustainable; thermogenic support with Nrf2 protection is intended to offset part of the fall in energy expenditure that restriction provokes while limiting oxidative cost; and gut support is intended to improve absorption of the micronutrients central to Section 3.3 and to support the gut-hormone response central to Section 3.2. The hypothesis underlying the formulation is that this integrated approach produces greater and more sustained reductions in hunger and energy intake than any single component; the present single-arm study had no single-component comparison and did not test it.

4. Methods

4.1 Design

This was a prospective, single-arm, open-label, nonrandomized intervention study conducted under real-world conditions: participants were supplied a defined product regimen and directed to follow a protocol, and outcomes were compared with each participant's self-reported starting values. All participants received the four Trilogiii products (FS in two flavors, EN, CC and BP). A single-arm design was chosen for practical reasons: the intervention comprises five distinct product presentations, and producing matched placebos for each, at the scale and cost required, was not feasible. The absence of a control group is the study's principal limitation (Section 7).

The primary outcomes were change in self-reported body weight and change in the frequency of hunger, cravings and food noise over the initial 4 weeks; all other outcomes were secondary or exploratory. The study design, data-collection instruments, outcome measures and planned analyses were specified before enrollment; the packet was designed to capture the data required for them, including before-and-after satiety ratings, daily fasting and meal records, named diets, adherence factors and weekly reports of side effects. The specific statistical test applied to within-person satiety change (the exact sign test) was selected after data collection, and the published-comparator context in Appendix A is descriptive and was assembled during reporting. Also defined after data collection were the comparison of group-reported with packet figures, the analysis of cumulative totals posted in the study group, the loss thresholds (10–30 lb) and rates of loss used to summarize it, the exclusion of one group-reported value that could not be traced (Section 5.1), the matched comparison of the written satiety multiples with the frequency ratings, and the sensitivity analysis capping written multiples at 3 (Section 5.8). The initial-period written satiety multiples (the final, week-4 entries), a secondary measure specified before enrollment and recorded by participants during the study, were transcribed into the dataset after the initial analysis of the frequency ratings. The study was not registered in a public trial registry.

4.2 Ethics and consent

The protocol was not reviewed by an independent ethics committee. Packet participants gave written consent, on the study-packet cover sheet, for their data to be collected and used. Group-only reporters did not return a signed cover sheet. Every participant received the packet, including its consent and safety paperwork, and the private Facebook study group stated that it was a formal part of the study and that results posted there would be used as study data; posting results in the group is therefore treated as consent to that use. Cover sheets bearing names and signatures were separated from data sheets by an independent law firm before the data reached the study team; only the law firm saw names linked to packet data, and no attempt was made to identify participants during analysis.

Participant safety relied on informed self-screening with physician consultation, a requirement stated at several points. Before paying the study participation fee, participants agreed to a statement, also printed on the product labels and on each product description sheet, to consult a physician before use if pregnant, nursing, taking any medication, or having or suspecting any medical condition. The packet cover sheet required a signed acknowledgment that the participant had been given the product sheets for review and doctor consultation and was responsible for examining the ingredients, potential allergens and possible contraindications with any health conditions, medications and other supplements, including consulting their primary care physician about participating in the protocol and taking the products. A section of the packet explained that Trilogiii is a dietary supplement not intended to diagnose, treat, cure or prevent any disease; that the study team could not assess any individual's medical history or medications; and that anyone taking any medication or with any medical issue should research the ingredients and consult their physician first. It noted in particular that several botanical ingredients in CC may affect blood clotting, blood pressure, immune function or inflammation, making physician consultation important for anyone with a related condition or medication, and that participants who decided against CC could still use FS, EN and BP. The packet's medication section again instructed participants to consult their physician about current medications and any medication changes. Physician consultation was self-attested and was not verified by the study team. Results shared in the private study group were not permitted to be reproduced outside the group with identifying information.

4.3 Sponsorship and costs

The study was sponsored and facilitated by an independent third party, Nelo Life, which has since ceased operations. Trilogiii was never offered for retail sale by the sponsor; the only way to obtain the products through the sponsor was by enrolling in the study, for which the participation fee covered the products supplied. No officer, investor or employee of Triii Therapeutics held a role with the sponsor or vice versa. Triii supplied products at cost and bore protocol-support, legal, insurance, data-handling and publication costs. Participants paid a study participation fee (US$150 for the initial 4 weeks; US$400 for both 4-week extensions together, or US$200 for a single 4-week extension) that covered product, printing, distribution and study aids. Neither Triii nor the sponsor derived net income from the study. The fee was intended to promote adherence and complete reporting; its implications for selection are discussed in Section 7.

4.4 Participants and recruitment

Participants were recruited openly by Triii and the sponsor, and through health-related Facebook groups administered by Triii's founder. The study was intended for adults. Enrollment was open to members of the public not currently using a GLP-1 receptor agonist (GLP-1 RA); prior users were required to have fully tapered off the medication at least one month before starting the study. As a condition of participation, all participants were required to review the full list of Trilogiii ingredients and, if they had or suspected any medical condition or were taking any medication, to consult their physician before starting (Section 4.2). Participants reported demographic information, health and

weight-loss goals, medical history, current medications and supplements, and prior GLP-1 RA use and response; participants reporting prior use were asked whether they had been a non-responder to GLP-1 RA therapy. The packet did not specify a threshold; non-response has been defined in the clinical literature, for example, as failure to achieve at least 5% weight loss after 52 weeks of treatment [86]. The prior drug, dose and duration were not recorded, and self-reported response was not verified. Three minors (aged 13–16), each with both parents enrolled in the study, also used the products after full ingredient disclosure to their parents and a requirement to consult their physician. Their parents were told they could send in the children's paperwork out of interest, but the children were not study participants. Their packets, including extension-period packets completed by a parent, were excluded from all analyses, so every analyzed packet is from an adult; the age of group-only reporters could not be independently verified. Because the study had no independent ethics review, the minors' use of the products was not subject to external oversight; excluding their data does not address that concern, which is noted among the study's limitations (Section 7).

4.5 Intervention and protocol

Daily product use was as described in Section 2.1. In addition, participants were asked to: drink a glass of water on waking (preferably with lemon juice and a pinch of salt) and a daily total, in US fluid ounces, of approximately half their body weight in pounds (for example, about 90 fl oz for a person weighing 180 lb, including the water used to mix the FS shakes), completed 3 hours before bed; either eat two meals smaller than they would normally consume or replace one meal altogether, choosing whole, unprocessed foods and prioritizing lean protein and low-carbohydrate vegetables and avoiding grains and starches for the first two weeks, after which lower-glycemic fruits and other carbohydrates could be added, although participants were strongly encouraged to continue with lean protein and low-carbohydrate vegetables until they reached their target weight; avoid eating within 3 hours of bedtime; consume no coffee, tea or other caffeinated beverages within one hour of any Trilogiii product; and, as recommendations rather than requirements, take 30 minutes of daily movement and aim for 7–9 hours of sleep. No calorie counting was required.

4.6 Duration and packet anonymization

The study, including the extension periods, was conducted between July 15, 2025, and December 31, 2025. Most participants began within the first few days; to accommodate vacations and other commitments, participants could begin and end their reporting periods at any point within this window. Study packets were accepted until January 15, 2026, and none arrived after that date. The formal study period was 4 weeks. Near its end, all participants, irrespective of results or adherence, were invited to volunteer for a further 4 or 8 weeks. Extension participants received a new packet with the same reporting requirements. Extension periods could be reported on a two-period extension packet, a single-period packet, or an additional initial-period packet, and eight initial-period packets also contained weeks 5–8 results; each completed 4-week period was treated as one period report regardless of format. Some participants also returned weeks 13–16 results, and some posted 16-week totals in the study group; these were outside the study protocol and were not analyzed. To protect confidentiality, returned packets were anonymized by a law firm before the study team received them: the firm removed the signed cover sheets and supplied the names of participants who had returned packets as a separate typed spreadsheet, so that the study team received no mapping between participants' identities and their packets. The team therefore knew who had returned packets, but not which packet belonged to whom. Because of this procedure, separately submitted extension packets could not be matched to initial-period records, so packet results are reported independently for each period. Periods recorded on the same physical packet — the eight initial-period packets that also contained weeks 5–8 results, and two-period extension packets, whose week-8 weight served as the weeks 9–12 starting weight — were also analyzed as separate period reports and were not used to construct longitudinal packet trajectories; cumulative loss is available from the running totals posted in the study group (Section 5.5).

4.7 Data collection

Membership in the private study group was a protocol requirement for every participant (Section 4.8). Participants could report their results through a 59-page paper study packet, through posts in the study group, or both. Packets captured daily product use, meal type and timing, fasting, water, exercise and sleep, weekly weight, waist and hip measurements, and self-rated health domains. Perceived change was captured in two complementary formats, both specified before enrollment: frequency ratings of hunger, cravings and food noise at the start and end of the initial period and of each participant's extension, and self-estimated improvement multiples for hunger, cravings, food noise and health domains (below). Weight and circumference were self-measured and self-reported. Participants were required to weigh themselves on the same scale for every weighing, at the same time of day and under the same conditions (for example, before the morning meal and water, or after a morning bowel movement), so that each participant's change was measured consistently; scales were not calibrated or standardized across participants. Waist and hip were measured with a flexible seamstress tape measure supplied with the packet, accompanied by written and illustrated instructions on where and how to measure. Because accurate self-measurement is difficult without a second person to read the tape, some participants left circumference blank; circumference means are therefore calculated over those reporting each measure, and the number reporting is given for each. Study-group reporting captured weight and inches lost only, posted as cumulative totals since the start of the study.

Perceived improvement was recorded as a self-estimated multiple relative to the start of the study. The packet instructions read, in part: "If you perceived any improvements in the following (since starting the Study, not week-to-week), please enter an estimated multiple improvement number for each statement. For example, if you feel your mood has positively doubled since starting the study, please enter the number 2 … If you have no perceived improvement, please enter the number 1 … If you experienced a setback, please enter a fraction multiple … Please don't enter an exaggerated unrealistic multiple … For most people this multiple will generally range from 1/3 … to 3 … If you're simply unsure in any category, please just leave that category blank." The measure is therefore explicitly subjective: it captures the participant's own estimate of change rather than any external observation, and the worked example of a doubled rating (2) and the instruction that typical responses fall between one-third and three provide anchors that are likely to have shaped the distribution of answers. The same instruction was repeated each week, and participants recorded their multiples weekly, each relative to the start of the study; the final week's entry in each period was tabulated. The primary satiety outcome was the frequency of hunger, cravings and food noise, rated on a four-point scale (rarely / occasionally / regularly / constantly) at the start and end of the initial 4-week period and of each participant's extension (for the 8-week extension, one pair spanning weeks 5–12).

Adverse effects were collected through open-ended prompts rather than a symptom checklist, so as not to suggest particular symptoms to participants. At the end of each week, the packet asked participants to "share any other observations with us, including any issues or side effects," and instructed those taking medication for blood pressure or diabetes to check their levels regularly, consult their physician, and record their results and any medication changes. At the end of the study, three further open-ended sections asked for other general health improvements or setbacks, final observations or suggestions, and other thoughts or suggestions. Each section provided ample space for free-text responses. During analysis, the data analyst coded these responses into 18 predefined categories in four groups: gastrointestinal (gas or bloating, constipation, loose stools, diarrhea, nausea, other gastrointestinal); transitional symptoms anticipated with carbohydrate reduction and weight loss — a descriptive label that does not attribute cause (fatigue, brain fog, skin rash, headache, dizziness, poor sleep, irritability, anxiety, hot flashes, other); cardiovascular; and respiratory. Because open-ended collection typically captures fewer symptoms than structured questioning, reported frequencies should be regarded as minimum estimates.

4.8 Study group: purpose and operation

Alongside the paper packet, the study used a private, closed online study group, hosted on Facebook, as a protocol-support and data-reporting platform rather than as a public social-media channel. Membership was limited to enrolled participants, the study team, group moderators, and various observers and associated parties. Joining the group was a protocol requirement for every participant, and the packet data sheets asked participants to confirm that they were members for the duration of the study; only the choice of reporting channel was optional (Section 4.7).

The group had four functions. First, it standardized reporting: the study team and moderators answered questions and posted clarifications on how to weigh, measure and record, so that participants reported the same quantities in the same way. Second, it standardized product use: questions about the products and the protocol directions were answered in one place, providing every participant with a common source of instructions and clarifications. Third, it was designed to support adherence to product use, the protocol and reporting; because every participant had access to the group, its effect on adherence could not be measured separately. Fourth, it provided a second reporting channel: participants who preferred not to keep the daily records required by the packet could instead post their cumulative weight and inches lost, and the totals posted by all members could be compared with the packet records (Section 5.5). Private online groups, Facebook most often, have been used to deliver and support weight-management programs [87–89], and a recent systematic review associated informational support and higher engagement with better adherence to weight-loss goals, while noting that social comparison and negative group dynamics can work against it [89].

The two reporting channels were kept separate in analysis. A participant who returned a packet was counted once, under their packet data, and their group posts were not used in any combined cohort; group-only reporters are those who posted results and did not return a packet (Section 4.10). Every combined figure therefore comes from two non-overlapping sets of people, and no participant is counted twice. The only analyses that use group posts from packet returners are analyses of the study group's own records — the comparison of reporting channels and the cumulative totals in Section 5.5 and Table 4 — which are reported separately and are not combined with packet data. Posted totals in the group are attributed to named members, so each figure in those analyses can be traced to an individual post; the group records, including every posted total, are retained and are available for independent verification by qualified reviewers under a confidentiality agreement (Declarations).

4.9 Adherence and eligibility

Participants recorded their daily product use, meals, water intake, exercise and sleep in the study packet; adherence scores were derived from these entries during analysis. Product adherence was the proportion of daily product servings taken, with partial-use days scored proportionally (for example, half the products = 0.5). Dietary adherence was the product of two daily scores: the meal requirement (two smaller-than-usual meals or one meal replaced, either of which counted as full adherence for the day) and adherence to lean protein and low-carbohydrate vegetables; multiplying the two makes this a deliberately strict measure. The lean-protein, low-carbohydrate score was assessed against the stricter first-two-week standard throughout, so from week 3, when other carbohydrates were permitted, lower dietary adherence was expected and indicates the extent to which participants relaxed the initial diet rather than a departure from the protocol. Lifestyle adherence was a weighted score of meeting the daily water target (50%), 30 minutes of exercise (25%), water on waking (10%), 7–9 hours of sleep (10%) and no eating within 3 hours of bedtime (5%); exercise and sleep were recommendations rather than requirements and together account for approximately 12% of overall protocol adherence. Weekly scores were averaged to give a score for each period, and overall protocol adherence was the mean of product, dietary and lifestyle adherence. Because the protocol was designed to be flexible, skipped and partial days were recorded rather than treated as violations, subject to the eligibility thresholds below; the aim was to assess

Trilogiii's performance under the deviations of daily life rather than under a strictly regimented protocol that few people sustain. Packets with product adherence below 50%, or adherence to the first-two-week meal requirement below 50%, were classified as non-adherent and excluded; packets were also classified as non-adherent for concurrent GLP-1 RA use, extended periods without protocol adherence (such as vacations), product cessation or gaps of two weeks or more, missing key pages or progress metrics, or completion by someone other than the participant. Packets submitted for anyone under 18 years of age were excluded from all analyses. Participants who took part from the outset for general health or to maintain a prior weight loss, rather than to lose weight, were excluded from all analyses; anyone could submit results, but participants were told that only those taking part to lose weight would be analyzed and summarized. Results from participants taking part for general health or weight maintenance will be examined separately in future work. Group-only reporters were screened through direct communication with the lead researcher before being counted as reporters, and those who stated they were taking part out of curiosity, for general health or to maintain a prior weight loss were not counted; their age and adherence could not be verified. For the analysis of cumulative totals, every study-group poster was screened the same way: totals were excluded for anyone who posted or messaged that they were taking part for general health or maintenance, and totals posted after a participant reported reaching their goal were classed as maintenance. Packet exclusion decisions could not be applied to study-group posts, because packets could not be matched to names (Section 4.6). The maintenance exclusion was applied at the level of observations, not participants. Packet periods that began during active weight loss were retained through their scheduled endpoint even if the participant reached their goal during that period; subsequent maintenance periods were excluded. Consequently, some retained packet periods included both active-weight-loss and maintenance days. In the study-group analyses, posts made after maintenance began were excluded, while earlier weight-loss-phase posts were retained.

4.10 Analysis

Body mass index (BMI) was calculated from self-reported height and weight. Data were compiled in Microsoft Excel, and statistics were computed in Python (SciPy). No formal sample-size calculation was performed; enrollment was open to all eligible adults during the study period. Results are reported as means, medians and percentages by period. For packet participants, weight change in every period was calculated as the period's starting weight minus its final weight; for group-only reporters, it was the loss they reported for weeks 1–4 and, for each extension period, the difference between their own successive cumulative totals; group-only reporters who lacked a preceding total, or who had reached their goal and moved to maintenance, were not included in extension-period figures. The final weight was taken from the end-of-study assessment page where the period was the last in the participant's packet and that weight was recorded, and otherwise from the last weekly weight of the period; for two participants whose end-of-study entry differed slightly from their scheduled week-12 weight, the confirmed week-12 weight was used. The starting weight was the entry weight for weeks 1–4; for the extensions it was the starting weight recorded on the extension packet or, for participants continuing from weeks 5–8 into weeks 9–12, their week-8 weight. Weights were checked against the original paper forms for every period. Initial-period entries required no correction; in the extension periods, five week-8 entries that differed from the paper forms were corrected to the paper values. Participants who both returned a packet and reported in the study group were counted once, under the packet data; group-only reporters are those who reported in the study group and did not return a packet. Every combined cohort therefore consists of unique individuals, and where packet and group-only groups are combined, means are weighted by n (for circumference, by the number reporting each measure). For all eligible participants in each period, standard deviations, 95% confidence intervals (t-distribution), interquartile ranges, skewness and Shapiro–Wilk normality statistics were computed from individual-level weight-loss values, and 95% confidence intervals for proportions by the Wilson score method. For packet participants in every period, mean percentage loss is the mean of each participant's own percentage change (each participant weighted equally), and its 95% confidence interval was calculated from those individual percentage changes, not derived from the pound-loss interval. Personal goal attainment, a planned

analysis, was assessed among packet participants who stated a numeric one-month weight-loss goal; the goal was counted as met when the recorded 4-week loss was equal to or greater than the stated goal. For hunger, cravings and food noise, each participant's before and after frequency ratings were compared: a move to a less frequent category was classified as improved, the same category as unchanged, and a more frequent category as worse; the mean change is expressed in scale categories. Consistency between reporting channels was assessed by comparing means from the study group with means calculated from packet weights: the 4-week totals and waist and hip for the initial period, and each group reporter's change between successive totals for the extension periods. Cumulative weight loss was summarized from the totals posted in the group at 4, 8 and 12 weeks, for all reporters in the weight-loss phase at each time point and for the subset who reported at all three; each total was assigned to the 4-, 8- or 12-week time point stated in the post, counted from the participant's own start, so intervals are nominal 4-week periods; totals posted after a participant had reached their goal were classed as maintenance and excluded, consistent with the exclusion of packet maintenance periods (Section 4.9). Cumulative loss was also summarized as the proportion reaching 10, 15, 20, 25 and 30 lb and, for participants with a total at all three time points, as the mean weekly rate of loss over each nominal 4-week interval. Confidence intervals were calculated with the t-distribution for means and the Wilson method for the proportion reporting a cumulative loss of 20 lb or more; for the interval losses of participants with a total at all three time points, the t-interval was calculated from each participant's own loss over the interval (the difference between successive totals), not by combining the endpoint intervals. The within-person change in hunger, food noise and cravings in each period was tested with an exact two-sided sign test (binomial test of improved versus worse, excluding unchanged participants), which makes no assumption about the spacing of the frequency categories. The written satiety multiples for weeks 1–4, recorded by participants during the study and transcribed after the initial analysis, were summarized in the same way as the other multiples. As with the weights, the transcribed multiples were checked against the original paper forms. In participants with both measures, they were cross-tabulated against the frequency ratings (improved, unchanged, worse), and percentage agreement and Cohen's kappa were calculated for improved versus not improved; this comparison was defined after data collection, as was a sensitivity analysis capping written multiples at 3. Weight loss was also summarized descriptively by sex, age band, self-reported diabetes, prior GLP-1 RA use, and concurrent fasting regimen and named diet (defined in Section 5.6); where participant-level values were unavailable for weeks 1–4, complementary-group means were derived by subtraction from the overall mean. No other hypothesis tests comparing groups, periods or time points were performed; the study was otherwise descriptive, and the confidence intervals and normality tests reported characterize the precision and distribution of the weight-loss data rather than test any comparison.

5. Results

5.1 Participant flow

The sponsor received 519 study participation fees, which covered product, printing, distribution and study-aid costs (Section 4.3); 22 were refunded, leaving 497 packet recipients. Reporters were defined as recipients who returned a completed packet or reported initial-period results in the study group; 422 recipients (84.9%) did so, and eligibility was then assessed against the criteria in Section 4.9 (group-only reporters had already been screened through direct communication, and those who stated they were taking part out of curiosity, for general health or to maintain a prior weight loss were not counted among them). Of the 75 who did neither in the initial period, 58 stated in direct communication with the lead researcher that they had paid the participation fee out of curiosity, did not need to lose weight, and would not be participating; the remaining 17 gave no reason, although 5 of them, all group-only, later posted an 8-week total in the study group, which is included only in the cumulative analysis (Section 5.5). Of the 422 reporters, 284 (57.1% of recipients) returned packets and 138 reported in the group only; 146 of those returning packets also reported in the group, identified from the law firm's list of packet returners' names (Section 4.6), and are counted once,

under their packet data, so the 422 are unique individuals. Of the 284 packets, 17 were excluded as non-adherent, 7 as not intended for weight loss and 3 because they were submitted for minors who were not study participants (Section 4.4), leaving 257 eligible packet participants; with the 138 non-overlapping group-only reporters, whose weight-loss intent was confirmed through direct communication but whose age and adherence could not be verified, 395 unique participants reported initial-period results.

Extension results were received in 84 packets from 73 individuals, supplemented by 8 initial-period packets that also contained weeks 5–8 results, and were counted as period reports (Section 4.6). For weeks 5–8, 78 period reports were received (7 maintenance, 1 non-adherent, 3 under 18; 67 eligible) and 24 non-overlapping participants reported via the group only (91 unique participants). One further group-only value (7.5 lb) was excluded because it could not be traced to a post in the study group when the group records were re-verified; it lay close to the period median (7.65 lb with it included), and excluding it changed the weeks 5–8 mean by less than 0.01 lb. For weeks 9–12, 62 period reports were received (8 maintenance, 4 non-adherent, 3 under 18; 47 eligible) and 10 non-overlapping participants reported via the group only (57 unique participants). Twelve reports covering weeks 13–16 were also received and were not analyzed. Extension cohorts were smaller because participants had initially committed to 4 weeks only, because of the additional cost and reporting burden, and, for some, because they had reached their weight-loss goal (Figure 1).

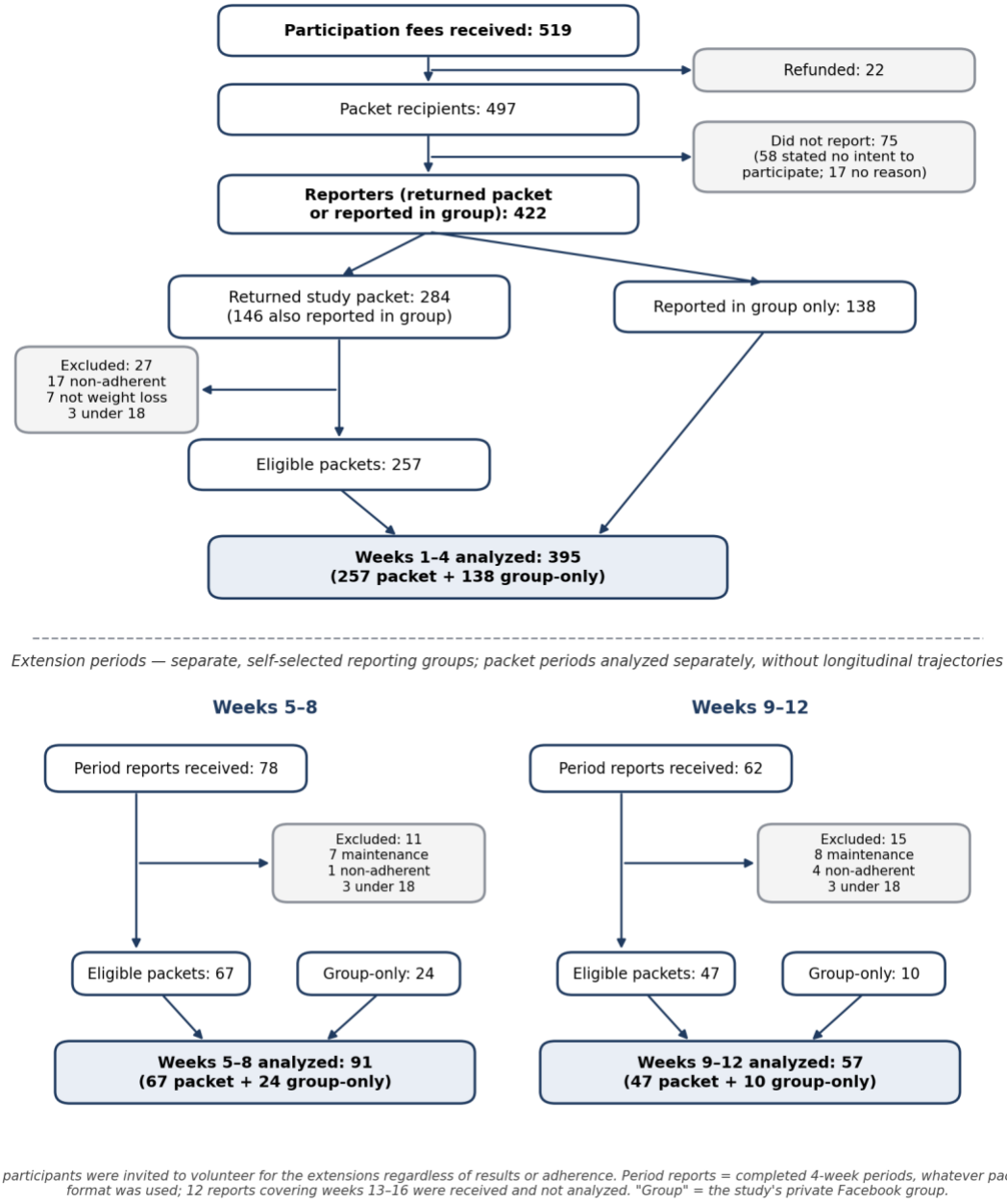


Figure 1. Participant flow.

5.2 Demographics

Starting weight and BMI (mean ± SD) were 204.95 ± 53.12 lb (range 114.9–502.0) and 32.90 ± 7.03 kg/m² (range 21.01–64.45) for packet participants in the initial period (n = 257) — on average in the obesity range — and, measured at the start of each extension period, 201.35 ± 53.98 lb and 31.97 ± 7.13 kg/m² in weeks 5–8 (n = 67) and 189.85 ± 41.99 lb and 30.19 ± 6.10 kg/m² in weeks 9–12 (n = 47; week-8 weight for continuing participants and the starting weight recorded on the extension packet for three participants who reported weeks 9–12 only). In the initial period, 151 of 257 packet participants (58.8%) had obesity — 71 (27.6%) class I (BMI 30 to <35), 43 (16.7%) class II (35 to <40) and 37 (14.4%) class III (≥40) — 89 (34.6%) had overweight (25 to <30) and 17 (6.6%) had a

BMI below 25; none was below 18.5. The corresponding counts were 39 with obesity (58.2%; 22, 9 and 8 in classes I–III), 21 with overweight and 7 below 25 in weeks 5–8, and 23 with obesity (48.9%; 15, 4 and 4), 14 with overweight and 10 below 25 in weeks 9–12. BMI categories use unrounded values. Initial period (n = 257): 184 female (71.6%), 70 male (27.2%), 3 not reported (1.2%); age 22–85 years (5 not reported); race: white 215 (83.7%), other 16 (6.2%), not reported 26 (10.1%). Weeks 5–8 (n = 67): 49 female (73.1%), 18 male (26.9%); age 22–83 years. Weeks 9–12 (n = 47): 35 female (74.5%), 12 male (25.5%); age 45–80 years; white 43 (91.5%), other 1 (2.1%), not reported 3 (6.4%). Group-only reporters in the initial period (n = 138) were 108 female (78.3%) and 30 male (21.7%); combined packet and group-only participants (n = 395) were 292 female (73.9%), 100 male (25.3%) and 3 not reported (0.8%). Combined participants were 73.7% female in weeks 9–12.

5.3 Weight and circumference change

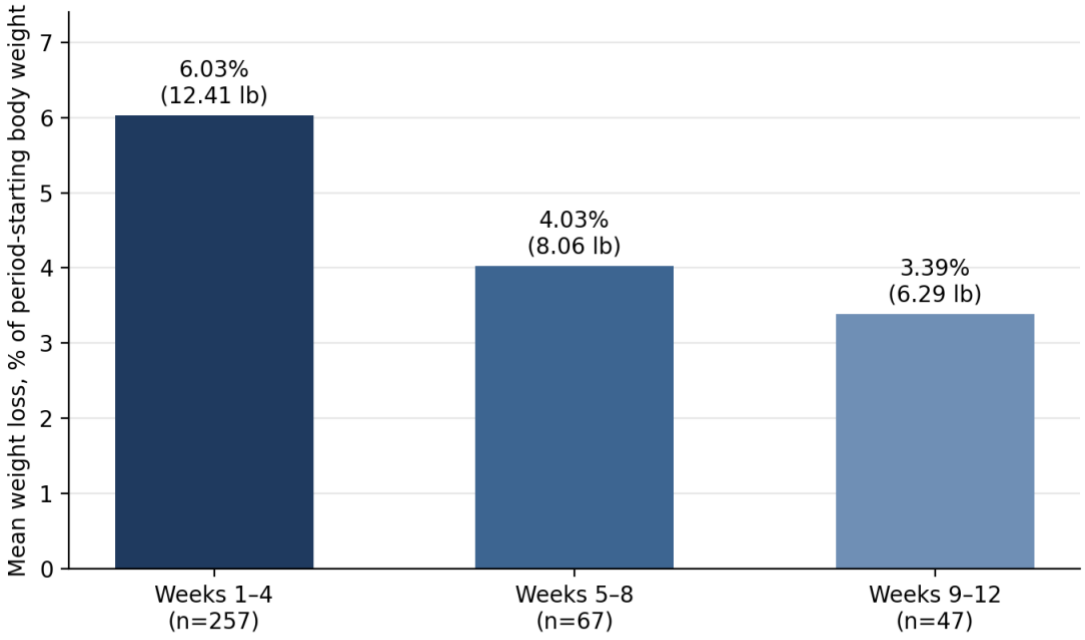
Table 3. Weight and circumference change by period and reporting channel

Period	Group	n	Mean lb lost (SD)	95% CI of mean	Median lb lost (IQR)	Waist lost, in (n)	Hip lost, in (n)
Weeks 1–4	Packet	257	12.41	—	11.40	2.80 (238)	2.54 (228)
	Group-only (non-overlapping)	138	13.13	—	—	2.88 (84)	2.27 (80)
	All eligible	395	12.66 (5.22)	12.15–13.18	11.80 (9.0–15.0)	2.82 (322)	2.47 (308)
Weeks 5–8	Packet	67	8.06	—	7.60	1.49 (64)	1.60 (63)
	Group-only (non-overlapping)	24	8.18	—	—	1.76 (22)	1.63 (22)
	All eligible	91	8.09 (3.47)	7.37–8.81	7.70 (6.0–9.0)	1.56 (86)	1.61 (85)
Weeks 9–12	Packet	47	6.29	—	6.20	1.17 (46)	0.92 (46)
	Group-only (non-overlapping)	10	6.75	—	—	1.04 (6)	1.40 (5)
	All eligible	57	6.37 (2.70)	5.65–7.09	6.20 (4.5–8.0)	1.16 (52)	0.97 (51)

SD, standard deviation; CI, confidence interval (t-distribution); IQR, interquartile range. “All eligible” rows combine packet and group-only participants, each individual counted once; age, product use and adherence were documented in the packets but were unavailable for group-only reporters, so combined means cover two differently documented groups. SD, CI and IQR are given for all eligible participants in each period. Circumference means are calculated over participants reporting each measure (n in parentheses); combined circumference means are weighted by those n. Weeks 5–8 group-only circumference values are as originally tabulated; whether the one untraceable group-only weight value excluded from the weight analysis (Section 5.1) had associated circumference entries could not be determined, so these means may include one additional reporter. This uncertainty also applies to the combined weeks 5–8 circumference means, which incorporate the group-only values.

Weight and circumference results for each period are shown in Table 3. Packet participants lost a mean 6.03% of period-starting body weight in weeks 1–4 (95% CI 5.82–6.24%; BMI −1.98), 4.03% in weeks 5–8 (3.73–4.34%; BMI −1.28) and 3.39% in weeks 9–12 (3.02–3.76%; BMI −1.00). The proportion losing ≥5% of period-starting weight was 70.0% (180/257; 95% CI 64.2–75.3%, Wilson), 20.9% (14/67; 95% CI 12.9–32.1%) and 10.6% (5/47; 95% CI 4.6–22.6%), respectively. Of the 237 packet participants who stated a numeric one-month weight-loss goal (mean 10.56 lb), 159 (67.1%; 95% CI 60.9–72.8%, Wilson) met or exceeded their own goal; the 20 without a usable stated goal are not included in this proportion. Because packet periods were analyzed separately rather than as linked trajectories, these figures describe loss within each period for the participants in that period

and should not be summed (Figure 2); cumulative loss, from the totals posted in the study group, is reported in Section 5.5.

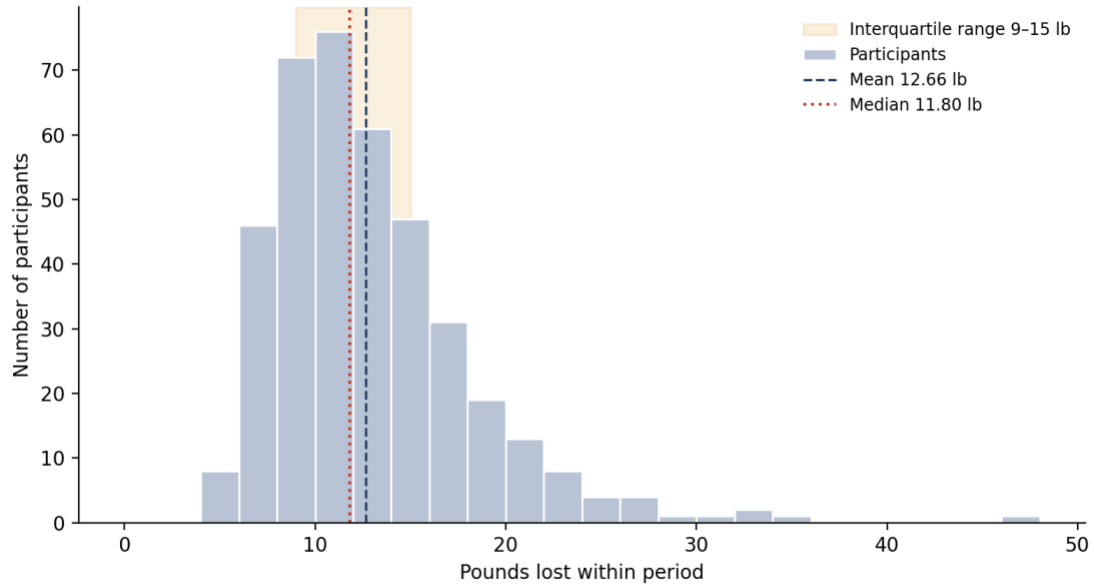


Each period comprises a separate, progressively smaller and self-selected cohort. Values are loss within that period by that period's participants, measured from the period start; they are not cumulative and must not be summed. Weights self-reported.

Figure 2. Trilogiii weight loss within each 4-week period, packet participants.

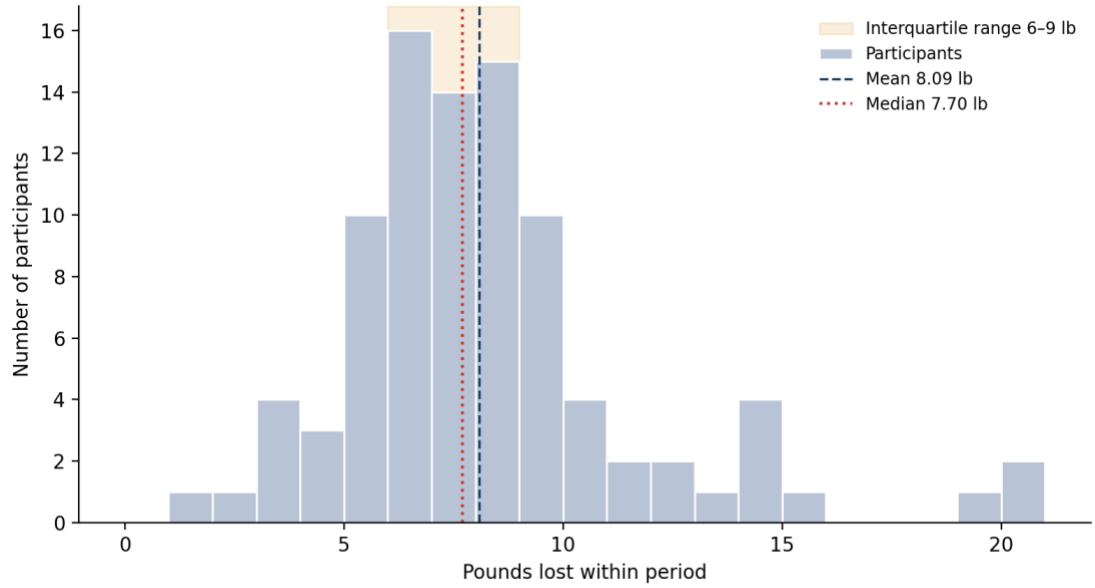
5.4 Distribution of individual weight loss

Figures 3–5 show the distribution of individual weight loss in each period as a histogram, with the median, mean and interquartile range marked. The distribution was right-skewed in every period (skewness 1.84, 1.39 and 0.76; Shapiro–Wilk $P < 0.001$, $P < 0.001$ and $P = 0.050$), with a majority of participants clustered below the mean and a tail of larger losses extending to 48.0, 20.2 and 14.2 lb respectively; the skew was mild in weeks 9–12, where the mean and median were similar (6.37 and 6.20 lb). In each period the mean exceeded the median because of the right-skewed distribution; both measures are reported to describe the outcomes. No eligible participant in any period reported a gain or zero change; among all eligible participants (Table 3), the smallest losses were 4.5, 1.5 and 1.8 lb. The two lowest 4-week totals in Table 4 (3.4 and 4.0 lb) were posted in the study group by participants who also returned packets and are not part of Table 3 (Section 5.5). Two features of the design make such a floor plausible: eligibility required at least 50% product and meal adherence for packet participants, so the analyzed group excludes those least likely to have followed the program, and the protocol's caloric restriction — reduced portions of whole foods with grains and starches removed for the first two weeks — would be expected to produce some loss in nearly all adherent participants. Because reporting was voluntary, however, under-reporting by participants who did not lose weight cannot be excluded as a contributing factor.



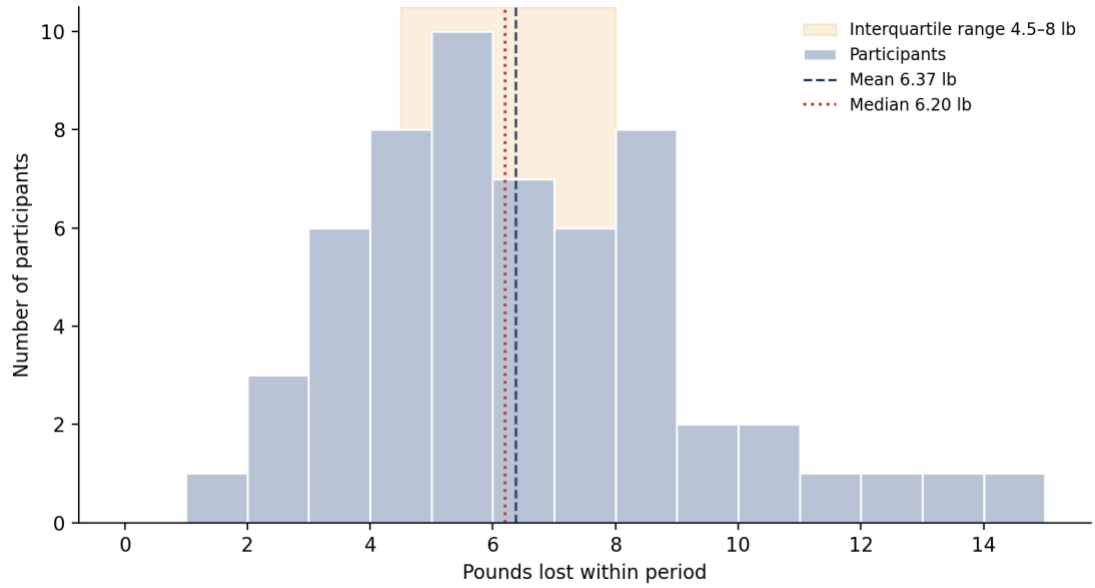
Skewness 1.84; Shapiro–Wilk P < 0.001. Right-skewed distribution; median and IQR are the more representative summaries.
Self-reported; all 395 eligible participants.

Figure 3. Distribution of weight loss, weeks 1–4 (all eligible participants, n = 395), with mean, median and interquartile range.



Skewness 1.39; Shapiro–Wilk P < 0.001. Right-skewed distribution; median and IQR are the more representative summaries.
Self-reported; all 91 eligible participants.

Figure 4. Distribution of weight loss, weeks 5–8 (all eligible participants, n = 91), with mean, median and interquartile range.



Skewness 0.76; Shapiro–Wilk P = 0.050. Mildly right-skewed distribution; mean and median are similar.
Self-reported; all 57 eligible participants.

Figure 5. Distribution of weight loss, weeks 9–12 (all eligible participants, n = 57), with mean, median and interquartile range.

5.5 Study-group reports: consistency and cumulative weight loss

Participants who reported in the private study group posted their total (cumulative) weight lost since starting, most at 4, 8 and 12 weeks. Because a 4-week total is also the loss for the initial period, the group totals can be compared directly with the packet records for weeks 1–4. Four-week totals were posted by 284 study-group reporters: 138 group-only reporters and 146 who also returned packets. All were screened for weight-loss intent (Section 4.9). Because packets could not be matched to names, packet exclusion decisions, such as for non-adherence, could not be applied to study-group posts, so the 146 may include some participants whose packets were excluded; like group-only reporters, their posted totals were not checked against adherence records. The 146 packet returners who also posted reported a mean 4-week total of about 12.53 lb (derived by subtraction from the group and group-only means), compared with 12.41 lb calculated from the recorded weights of all 257 eligible packet participants — an unpaired comparison of differently constituted groups; the 138 group-only reporters posted 13.13 lb, and all 284 a mean 12.82 lb. Group waist and hip means were 2.73 and 2.26 in (n = 220 and 211), compared with 2.80 and 2.54 in from packets (n = 238 and 228); these differences are small relative to the precision of self-measurement with a flexible tape.

For the extension periods, each group reporter's change was calculated as the difference between their own successive totals, excluding totals posted after the participant had reached their goal and moved to maintenance: 7.49 lb in weeks 5–8 (n = 96) and 5.88 lb in weeks 9–12 (n = 57, the same participants summarized in Table 4, not the weeks 9–12 cohort of Table 3), compared with 8.06 and 6.29 lb calculated from packet weights. The group figures were therefore slightly higher than the packet figures in the initial period, where they included the 138 group-only reporters, and slightly lower in both extension periods, so the self-reported group totals were not systematically higher than the figures calculated from packet weights. The extension comparison is less direct than the initial-period comparison: the group changes are differences between two posted totals, and because a reporter's extension packet may have been excluded or not returned, the group figures include some participants who are not in the Table 3 extension cohorts. Because the two channels share participants (146 packet returners also posted in the initial period), these similar aggregate means

reflect consistency of reporting rather than independent verification; the combined eligible cohorts themselves contain no duplicate individuals.

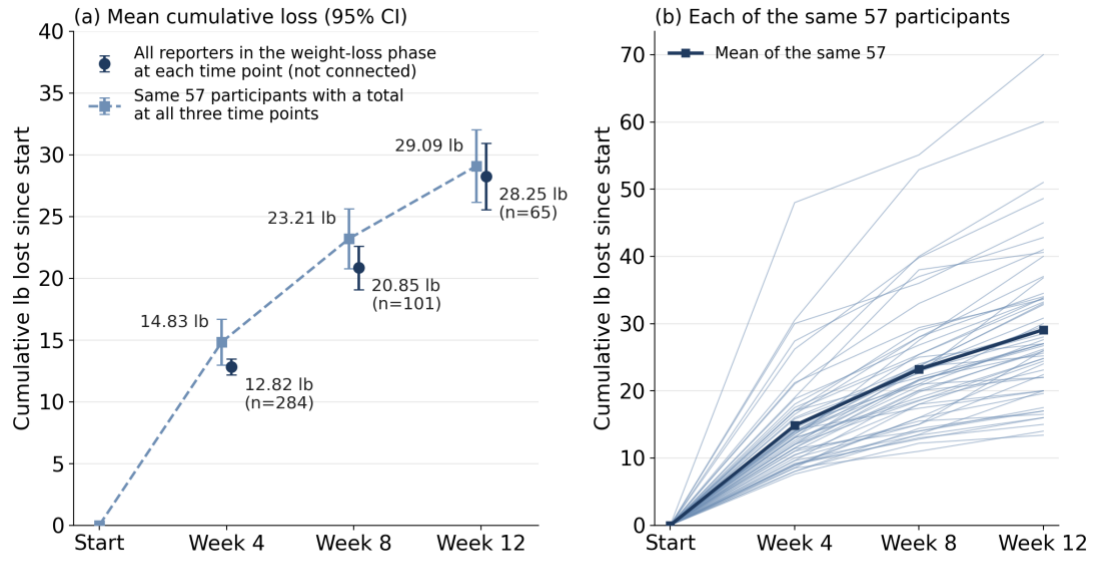
The similar aggregate means in the initial period support using the group totals for the one measure the packets could not provide. Packet periods were analyzed separately and were not used to construct longitudinal trajectories (Section 4.6); each group total, by contrast, covers all the weight lost since the participant started. Table 4 and Figure 6a summarize the totals posted at each time point by all reporters still in the weight-loss phase, whether or not they posted at other time points, and by the 57 who posted at all three, and Figure 6b shows each of the 57 individually. Consistent with the exclusion of packet maintenance periods (Section 4.9), totals posted after a participant had reached their goal (five posts from five participants) were excluded because the study measured outcomes during the weight-loss phase, and totals posted after week 12 were excluded as outside the study protocol. Only posts made after maintenance began were excluded; the earlier weight-loss-phase totals of these five participants were retained.

Table 4. Cumulative weight loss reported in the study group by reporters in the weight-loss phase

Measure	Week 4	Week 8	Week 12
All reporters in the weight-loss phase at each time point			
Number reporting	284	101	65
Mean lb lost (95% CI)	12.82 (12.17–13.47)	20.85 (19.09–22.61)	28.25 (25.55–30.94)
Median lb lost (IQR)	12.00 (9.00–15.00)	19.50 (14.40–23.70)	27.00 (20.00–33.20)
Range, lb	3.4–48.0	7.7–55.1	12.0–70.0
Lost 10 lb or more, n (%)	198 (69.7%)	97 (96.0%)	65 (100.0%)
Lost 15 lb or more, n (%)	77 (27.1%)	74 (73.3%)	62 (95.4%)
Lost 20 lb or more, n (%; 95% CI)	29 (10.2%; 7.2–14.3%)	48 (47.5%; 38.1–57.2%)	52 (80.0%; 68.7–87.9%)
Lost 25 lb or more, n (%)	9 (3.2%)	24 (23.8%)	39 (60.0%)
Lost 30 lb or more, n (%)	5 (1.8%)	12 (11.9%)	23 (35.4%)
Same 57 participants with a total at all three time points			
Mean lb lost (95% CI)	14.83 (12.99–16.67)	23.21 (20.77–25.64)	29.09 (26.14–32.03)
Median lb lost (IQR)	13.20 (10.50–17.00)	21.60 (17.40–25.40)	27.00 (22.00–33.80)

Values are cumulative pounds lost since starting, as posted in the study group; CI, confidence interval (t-distribution for means, Wilson for proportions); IQR, interquartile range. Totals posted after a participant had reached their goal (maintenance) are excluded; three participants who posted at all three time points are therefore not among the 57, because their 12-week totals were maintenance posts. Starting weights were not posted, so percentages of body weight cannot be calculated; group reporting did not include adherence records. All reporters, including the same-57 series, were screened for weight-loss intent and maintenance (Section 4.9); packet eligibility could not be established for posters who also returned packets, because packets could not be matched to names. Of 289 people who posted at least one total, 284 posted at 4 weeks and 5 group-only posters posted only an 8-week total (Section 5.1); 102 posted at 8 weeks (101 after one maintenance total was excluded, of whom 96 also had a 4-week total); 69 posted at 12 weeks (65 after four maintenance totals were excluded, all with a 4-week total and 57 with an 8-week total); 60 posted at all three time points, 57 after exclusions. The loss thresholds are exploratory; the 20 lb threshold, reported with a confidence interval, is the principal one. The two lowest 4-week totals (3.4 and 4.0 lb) were posted by participants who also returned packets; posted totals from packet returners were not used in Tables 3 and 5–11, which used eligible anonymized packet records (and, in Table 3, the posts of group-only reporters).

Among reporters in the weight-loss phase, mean cumulative loss was 12.82 lb at 4 weeks, 20.85 lb at 8 weeks and 28.25 lb at 12 weeks (medians 12.00, 19.50 and 27.00 lb). Every included 12-week total was at least 12.0 lb; 95.4% were 15 lb or more, 80.0% were 20 lb or more and 35.4% were 30 lb or more (Table 4). Because different participants reported at different time points, the 57 with a (non-maintenance) total at all three were also examined: their mean cumulative loss rose from 14.83 lb at 4 weeks to 23.21 lb at 8 weeks and 29.09 lb at 12 weeks, a within-person loss of 8.37 lb (95% CI 7.35–9.40) in weeks 5–8 and 5.88 lb (5.03–6.73) in weeks 9–12, and every one of the 57 lost weight in each interval (Figure 6b). Their mean rate of loss, averaged over each nominal 4-week interval, slowed from 3.71 lb a week in weeks 1–4 to 2.09 lb in weeks 5–8 and 1.47 lb in weeks 9–12, the gradual deceleration expected as body weight, and with it energy expenditure, falls; the faster early rate likely includes a contribution from glycogen-associated water lost during the low-carbohydrate weeks (Section 6.2), and by weeks 9–12 the rate lay within the 1–2 lb a week recommended in clinical guidelines [90]. Participants who continued reporting had lost somewhat more in the first four weeks (13.66 lb among the 96 posting both a 4- and an 8-week total, and 14.56 lb among the 65 posting a 12-week total, against 12.82 lb among all 4-week reporters), so the later cumulative means partly reflect who continued; the same-participant figures show that the continued loss is not an artifact of changing composition, but they describe a self-selected group of continuing reporters.



Cumulative totals posted in the study's Facebook group; error bars are 95% confidence intervals. Posts made after a participant reached their goal (maintenance) are excluded. Weights self-reported; starting weights were not posted, so percent of body weight is not available.

Figure 6. Cumulative weight loss reported in the study group at 4, 8 and 12 weeks: (a) mean for all reporters in the weight-loss phase at each time point (unconnected, because the reporters differ between time points) and for the same 57 participants with a total at all three time points (95% confidence intervals); (b) each of the same 57 participants, with their mean; lines run from the start (0) through each participant's posted totals at weeks 4, 8 and 12 and do not represent weekly measurements.

5.6 Subgroups (packet participants)

Weight loss by sex, age, diabetes and prior GLP-1 RA use is shown in Table 5 and, for sex, age and diabetes, in Figures 7–9, and by concurrent fasting regimen and named diet in Table 6; these results are discussed in Section 6.3.

Table 5. Weight loss by subgroup (packet participants): mean lb lost (n); mean % of body weight

Subgroup	Weeks 1–4	Weeks 5–8	Weeks 9–12
Male	15.84 (70); 6.44%	10.80 (18); 4.36%	6.93 (12); 3.15%
Female	11.01 (184); 5.88%	7.05 (49); 3.91%	6.07 (35); 3.47%
Age 18–34	12.70 (7)	6.90 (1); 2.66%	—
Age 35–49	12.54 (31)	8.08 (5); 3.81%	4.97 (3); 2.59%
Age 50–64	12.91 (120)	7.47 (41); 3.88%	6.16 (29); 3.31%
Age 65+	11.56 (94)	9.33 (20); 4.47%	6.81 (15); 3.71%
Diabetes (type 1 or 2)	14.01 (32); 5.98%	9.07 (7); 3.86%	5.30 (5); 2.92%
No reported diabetes	12.19 (225); 6.04%	7.94 (60); 4.05%	6.41 (42); 3.45%
Prior GLP-1 RA use	14.26 (17); 6.00%	6.40 (3); 3.03%	5.15 (2); 2.32%
Prior GLP-1 RA use, self-identified non-responder	13.26 (5); 5.89%	—	—
No reported prior GLP-1 RA use	12.28 (240)	8.14 (64); 4.08%	6.34 (45); 3.44%
All packet participants	12.41 (257); 6.03%	8.06 (67); 4.03%	6.29 (47); 3.39%

Percentages are the mean of each participant's loss relative to period-starting weight; where only pounds are shown for weeks 1–4, percent was not calculated for that subgroup. Sex not reported: 3 (weeks 1–4). Age not reported: 5 (weeks 1–4). Diabetes was self-reported (initial period: 30 type 2, 2 type 1; all extension-period reports were type 2). Prior GLP-1 RA users had discontinued the medication at least one month before starting (Section 4.4); the non-responder subset is included in the prior-use row, and no self-identified non-responders took part in the extension periods. In weeks 1–4, the "no reported prior GLP-1 RA use" mean is derived by subtraction from the overall packet mean; extension-period values are calculated from participant-level data. Extension cohorts are separate, self-selected groups. Subgroups with n < 10 are shown for completeness and described only; the non-responder subgroup (n = 5) is discussed descriptively in Section 6.3. Figures 7–9 present the sex, age and diabetes data graphically; in the figures, bars with n ≤ 5 are hatched.

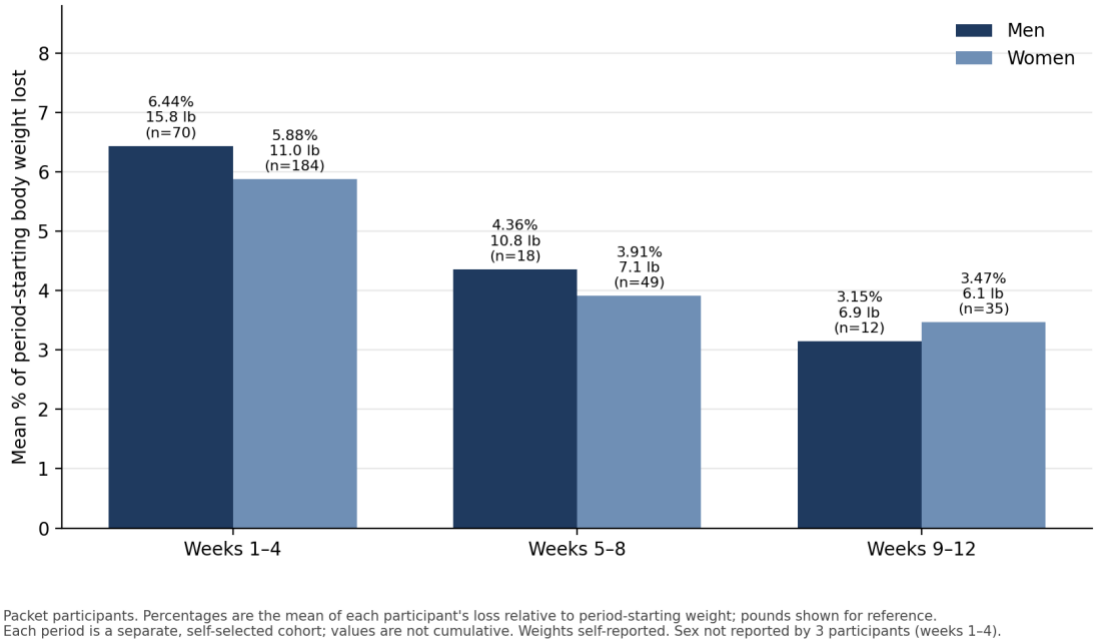
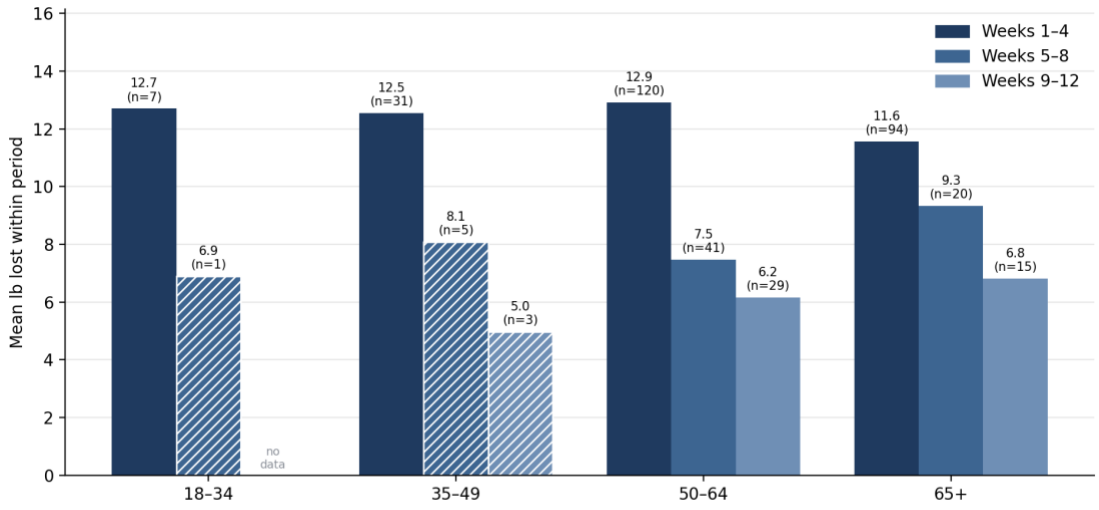
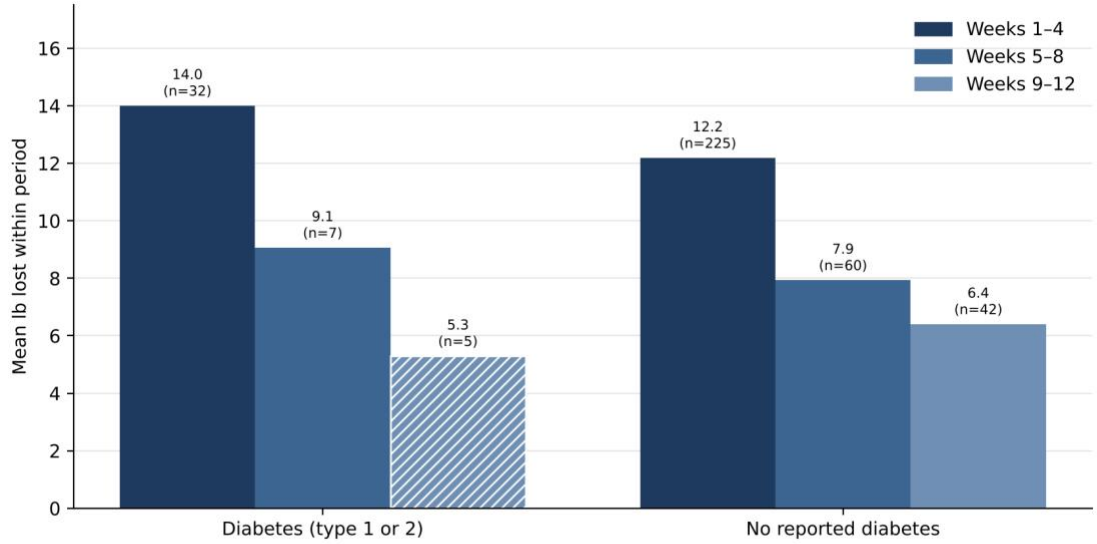


Figure 7. Mean percentage of body weight lost by sex, by period.



Packet participants. Hatched bars: n ≤ 5. Age not reported by 5 participants (weeks 1–4).
Each period is a separate, self-selected cohort; values are not cumulative. Weights self-reported.

Figure 8. Mean weight loss (lb) by age group, by period.



Packet participants. Diabetes self-reported (initial period: 30 type 2, 2 type 1; extensions: type 2). Hatched bars: n ≤ 5.
No standardized glycemic data were collected; medication changes were not systematically analyzed.
Each period is a separate cohort; values are not cumulative.

Figure 9. Mean weight loss (lb), participants with vs without diabetes, by period.

Concurrent fasting regimens and diets. The Trilogiii protocol itself restricts intake daily, through two smaller-than-usual meals or one replaced meal (Section 4.5). Participants also recorded whether they combined it with a named fasting regimen (one meal a day [OMAD] or another intermittent-fasting pattern) and/or a named diet (low-carbohydrate, carnivore, Mediterranean or paleo). Fasting groups are defined by practice rather than intention: a participant is counted in a fasting group for a period if they marked the regimen and recorded at least one fasting day in that period. Daily fasting adherence was also tracked. Named diets were recorded at the start of each period; adherence to them was not tracked. In weeks 1–4, participants could select one named fasting regimen and one named diet, so fasting and diet groups overlap; on the extension forms, a few participants marked more than one of each. Each group is compared with packet participants not in that group (Table 6).

Alternate-day fasting was also offered, but too few participants practiced it to report it as a group. In weeks 1–4, mean loss was similar whether or not participants practiced OMAD or other intermittent fasting (12.30 vs 12.46 lb), and participants without a named diet lost slightly more than those with one (12.78 vs 11.70 lb); every regimen subgroup lost between 4.9% and 6.4% of body weight; mean fasting adherence was 80.8% for OMAD and 82.2% for other intermittent fasting. In the extensions, participants in a fasting group lost slightly less in weeks 5–8 than those who were not (7.37 vs 8.27 lb) and more in weeks 9–12 (7.11 vs 6.10 lb), and those following a named diet — all low-carbohydrate — showed the same pattern (7.86 vs 8.13 lb; 7.56 vs 5.75 lb); these groups are small, and no consistent difference is evident.

Table 6. Weight loss by concurrent named fasting regimen and named diet (packet participants)

Period	Group	n	Mean lb lost (median)	% body weight	Fasting adherence, mean (median)
Weeks 1–4	*Named fasting regimen*				
	One meal a day (OMAD)	36	11.57 (11.05)	5.8%	80.8% (85.7%)
	Other intermittent fasting	44	12.90 (10.95)	6.4%	82.2% (91.1%)
	OMAD or other intermittent fasting	80	12.30	—	—
	Neither OMAD nor other intermittent fasting	177	12.46	—	—
	Named diet				
	Low-carbohydrate	51	11.74 (10.40)	5.7%	—
	Carnivore	18	12.39 (12.10)	5.6%	—
	Mediterranean	14	11.56 (11.10)	5.8%	—
	Paleo	5	9.20 (8.40)	4.9%	—
	Any named diet	88	11.70	—	—
	No named diet	169	12.78	—	—
Weeks 5–8	*Named fasting regimen*				
	One meal a day (OMAD)	10	6.92 (7.30)	3.8%	76.0% (85.7%)
	Other intermittent fasting	8	7.86 (7.95)	3.8%	73.0% (70.2%)
	Either fasting group	16	7.37	3.8%	—
	Not in a fasting group	51	8.27	4.1%	—
	Named diet				
	Low-carbohydrate	18	7.86 (7.75)	3.8%	—
	Carnivore	2	8.15 (8.15)	4.2%	—
	Any named diet	18	7.86	3.8%	—
	No named diet	49	8.13	4.1%	—
Weeks 9–12	*Named fasting regimen*				
	One meal a day (OMAD)	4	5.75 (5.60)	3.5%	66.3% (62.5%)
	Other intermittent fasting	5	8.20 (9.40)	4.0%	86.5% (100.0%)
	Either fasting group	9	7.11	3.8%	—
	Not in a fasting group	38	6.10	3.3%	—
	Named diet				
	Low-carbohydrate	14	7.56 (7.30)	3.8%	—

Period	Group	n	Mean lb lost (median)	% body weight	Fasting adherence, mean (median)
	Carnivore	1	9.40 (9.40)	5.6%	—
	Any named diet	14	7.56	3.8%	—
	No named diet	33	5.75	3.2%	—

In weeks 1–4, each participant could select one named fasting regimen and one named diet, so the combined rows ("OMAD or other intermittent fasting", "Any named diet") include each participant once, and the "Neither" and "No named diet" rows are derived by subtraction from the overall packet mean, so medians and percentages are not shown for these weeks 1–4 summary rows. Extension-period values are calculated from participant-level data, and each participant is counted once in the "Either fasting group" and "Any named diet" rows, which are compared with packet participants not in those groups; two participants in weeks 5–8 qualified for both fasting groups, and all extension participants who marked carnivore (two in weeks 5–8, one in weeks 9–12) also marked low-carbohydrate. Fasting groups include participants who marked the regimen and recorded at least one fasting day in the period; fasting adherence is the proportion of the seven days in each reported week on which fasting was recorded, pooled across all reported weeks in the group (mean) and across participants' individual averages (median). In weeks 1–4, the combined rows compare OMAD or other intermittent fasting with neither; the three participants who recorded alternate-day fasting (too few to report as a group) fall in the "Neither" row. Adherence to named diets was not tracked. Fasting and diet categories overlap. Subgroups with n < 10 are shown for completeness and described only.

5.7 Hunger, cravings and food noise

Table 7. Reported frequency before and after the initial 4-week period (packet participants answering each item)

Measure	Time point	n	Rarely	Occasionally	Regularly	Constantly
Thoughts of food (food noise)	Before	256	3.5%	43.4%	46.5%	6.6%
	After 4 wk	246	25.2%	65.9%	8.9%	0.0%
Hunger	Before	255	3.9%	46.7%	45.9%	3.5%
	After 4 wk	246	34.1%	60.2%	5.7%	0.0%
Cravings	Before	253	10.3%	41.9%	39.5%	8.3%
	After 4 wk	241	64.7%	32.4%	2.9%	0.0%

The proportion reporting hunger "regularly" or "constantly" fell from 49.4% to 5.7%; food noise from 53.1% to 8.9%; and cravings from 47.8% to 2.9%. The proportion reporting cravings "rarely" rose from 10.3% to 64.7% (Table 7, Figure 10).

Comparing each participant's own before and after ratings confirms the shift at the individual level (Table 8). In the initial period, 62.3% of participants reported less frequent hunger, 60.8% less frequent food noise and 75.1% less frequent cravings, a mean improvement of 0.77, 0.73 and 1.07 scale categories respectively. Only 2.9%, 4.5% and 1.7% reported a more frequent category, so improvement outnumbered worsening by 152 to 7, 149 to 11 and 178 to 4 (sign test, $P < 0.001$ for each); the remainder reported the same category, including 7, 4 and 21 participants who were already at "rarely" and remained there. The 22 measure-specific cases of worsening came from 20 participants. Their mean overall protocol adherence was similar to that of participants who improved

for hunger (83.6% vs 83.8%) and food noise (82.4% vs 83.2%), and lower for cravings (73.6% vs 83.7%, n = 4); these comparisons are descriptive.

In the extension periods, most participants reported the same frequency at the start and end of the period. These participants had already completed the initial period, and in the extension ending at week 12 (a comparison spanning weeks 5–12 for all 42 with usable pairs), 18 of the 42 began at "rarely" for hunger, leaving little room for further change; 13 of the 18 remained there. More frequent hunger and food noise were each reported by 6 of these 42 participants; within the extension periods, the numbers improving and worsening did not differ significantly for any measure (Table 8). The extension comparisons measure change within the extension only; they do not show whether a benefit gained in the initial period was maintained, which the improvement ratings in Section 5.8 address only indirectly.

Table 8. Within-person change in reported frequency of hunger, food noise and cravings (packet participants with both ratings)

Period	Measure	Paired n	Improved	Unchanged	Worse	Mean change (categories)	P (sign test)
Weeks 1–4	Hunger	244	152 (62.3%)	85 (34.8%)	7 (2.9%)	−0.77	< 0.001
	Food noise	245	149 (60.8%)	85 (34.7%)	11 (4.5%)	−0.73	< 0.001
	Cravings	237	178 (75.1%)	55 (23.2%)	4 (1.7%)	−1.07	< 0.001
4-week extension (weeks 5–8)	Hunger	11	2 (18.2%)	8 (72.7%)	1 (9.1%)	—	1.00
	Food noise	11	2 (18.2%)	9 (81.8%)	0 (0.0%)	—	0.50
	Cravings	10	4 (40.0%)	5 (50.0%)	1 (10.0%)	—	0.38
Extension ending at week 12	Hunger	42	6 (14.3%)	30 (71.4%)	6 (14.3%)	—	1.00
	Food noise	42	11 (26.2%)	25 (59.5%)	6 (14.3%)	—	0.33
	Cravings	42	8 (19.0%)	31 (73.8%)	3 (7.1%)	—	0.23

Improved = a less frequent category at the end of the period than at its start; worse = a more frequent category. Scale: 1 = rarely, 2 = occasionally, 3 = regularly, 4 = constantly; a negative mean change indicates lower frequency. Weeks 1–4 compare ratings before and after the initial period. Extension comparisons run from the extension baseline to the participant's final extension assessment: the 4-week extension row includes participants who completed weeks 5–8 only (10–11 usable pairs of 23, depending on the item); the three participants who reported weeks 9–12 only are not included in either extension row; the row for the extension ending at week 12 includes participants completing the 8-week extension, whose comparison spans weeks 5–12, and is therefore not confined to weeks 9–12 or identical to the weeks 9–12 weight-loss cohort in Table 3. P values are from an exact two-sided sign test of improved versus worse; in weeks 1–4 all three were below 10^{-30}. Unchanged includes participants already at "rarely" at both assessments (weeks 1–4: hunger 7, food noise 4, cravings 21; extension ending at week 12: hunger 13).

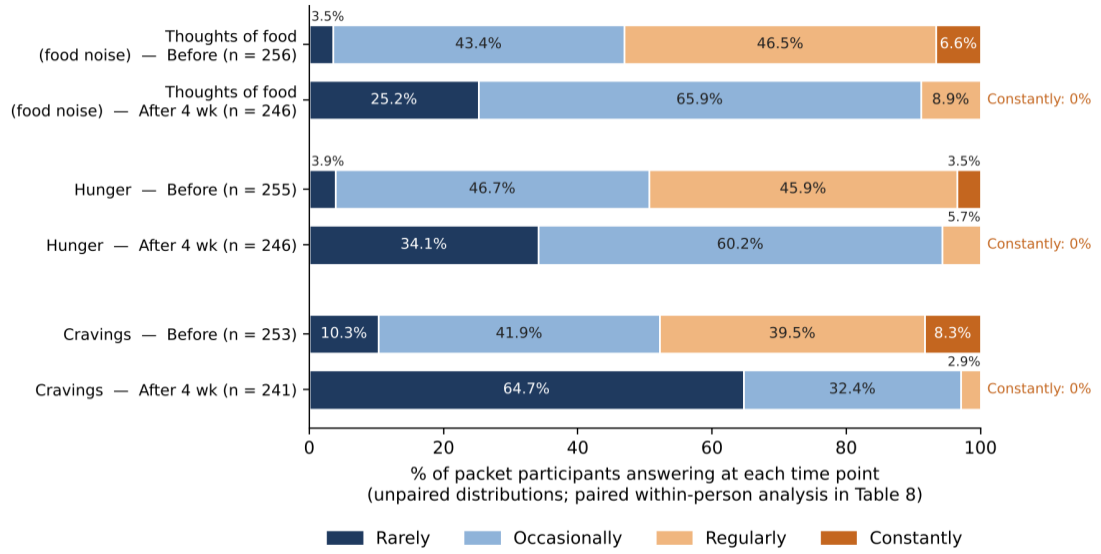


Figure 10. Reported frequency of food noise, hunger and cravings before vs after 4 weeks (all packet participants answering at each time point; the paired within-person analysis is in Table 8).

5.8 Perceived improvement

Perceived improvement was recorded as a self-estimated multiple relative to the start of the study (Section 4.7). Item response was incomplete: participants were instructed to leave a multiple blank if they could not quantify it, and some left individual items or the whole section blank on that basis; in addition, some extension packets were returned with the final assessment page missing. Percentages and medians are therefore calculated among those answering each item (n = 230–241 of 257 in the initial period, 57–62 of 67 in weeks 5–8 and 42–44 of 47 in weeks 9–12; Table 9).

Participants rated hunger, cravings and food noise as multiples, alongside seven well-being domains. This secondary measure was planned before enrollment to corroborate the paired frequency ratings, the primary satiety outcome (Section 5.7, Table 8). In the initial period, the median was 2 for each satiety item, with means of 2.28 for hunger (n = 233), 2.34 for cravings (n = 233) and 2.26 for food noise (n = 234). Improvement (a multiple above 1) was reported by 85.4% for hunger (199 of 233), 84.1% for cravings (196 of 233) and 81.6% for food noise (191 of 234), and three or four participants per measure reported a setback. Participants entered these multiples in their packets during the study; they were transcribed after the initial analysis (Section 4.1). Written satiety multiples ranged from 0.5 to 8 across the three periods, and 5.2–7.3% of initial-period responses exceeded 3, the upper end of the range suggested in the instructions; capping responses at 3 would lower the initial-period means to 2.15–2.22 but leave the medians and the proportions reporting improvement unchanged, so the few high responses have little effect on the results.

In a matched comparison of the 219–226 participants with both measures for each item, 87–89% of those whose frequency rating improved also wrote a multiple above 1, and few rated one measure improved and the other worse (3–6 per item). Most participants whose frequency rating did not improve also wrote a multiple above 1 (73–80%), so agreement between the two measures at the individual level (63.4% for hunger, 72.6% for cravings and 63.7% for food noise) was only slightly better than chance (Cohen's kappa 0.10, 0.17 and 0.16, on improved versus not improved): the measures agree in direction for the group but do not identify the same individuals closely. Most of the disagreement came from participants who chose the same frequency category at both assessments but wrote a multiple above 1 (63 for hunger, 40 for cravings and 58 for food noise); most of these were above "rarely" at baseline (56, 25 and 54 respectively), so the gap does not mainly

reflect a lack of room to improve on the frequency scale (Section 6.4). A matched comparison was not made for the extension periods, because the frequency ratings there measure change from the start of the extension, whereas the written multiples measure change from the start of the study, and no frequency rating was recorded at the end of week 8 for participants who continued to week 12.

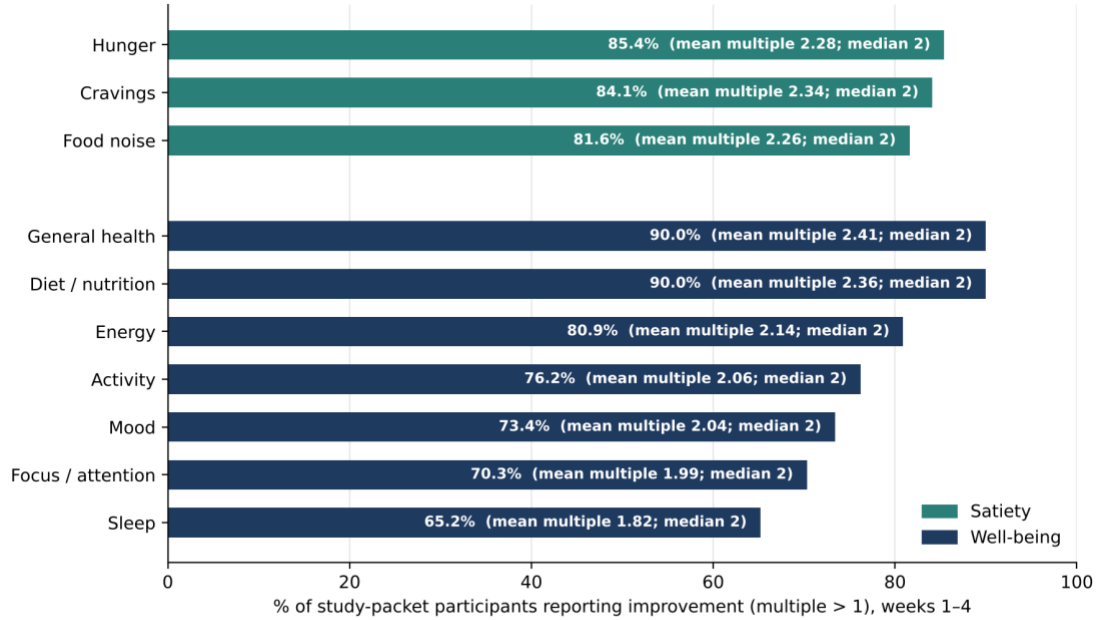
In the initial period, the median multiple was 2 in every well-being domain — that is, the typical participant reported feeling "twice as good" — with means ranging from 1.82 (sleep) to 2.41 (general health), and the proportion reporting any improvement (multiple > 1) ranged from 65.2% (sleep) to 90.0% (general health and diet). Extension-period cohorts reported higher means and, for general health and diet, a median of 3. In the extensions, participants also rated hunger, cravings and food noise as multiples relative to the start of the study: 83–91% reported improvement, and no more than one participant in either period reported a setback on any satiety item. These cohorts were smaller and self-selected, and their ratings covered a longer time since the start of the study; because they could not be linked to initial-period records, the higher values may reflect the characteristics of participants who chose to continue and should not be read as a within-person increase. A multiple scale is bounded at zero but unbounded above, so the median is the more representative summary. The median of 2 for every initial-period item, including hunger, cravings and food noise, is also consistent with the instruction's worked example of a doubled rating (2) and its suggested range of one-third to three, which likely anchored responses toward whole-number multiples; where the mean falls below the median, ratings below the median outweighed those above it (Table 9, Figure 11).

Table 9. Self-rated improvement multiples and proportion reporting improvement (packet participants answering each item)

Domain	Wk 1–4 n	Wk 1–4 mean (median)	Wk 1–4 % improved	Wk 5–8 n	Wk 5–8 mean (median)	Wk 5–8 % improved	Wk 9–12 n	Wk 9–12 mean (median)	Wk 9–12 % improved
Satiety									
Food noise	234	2.26 (2)	81.6%	58	2.42 (2)	87.9%	42	2.27 (2)	83.3%
Hunger	233	2.28 (2)	85.4%	58	2.45 (2.25)	91.4%	42	2.37 (2)	88.1%
Cravings	233	2.34 (2)	84.1%	58	2.50 (2.5)	89.7%	42	2.31 (2)	88.1%
Well-being									
General health	241	2.41 (2)	90.0%	62	2.54 (3)	90.3%	44	2.44 (3)	88.6%
Diet / nutrition	241	2.36 (2)	90.0%	62	2.52 (3)	88.7%	43	2.47 (3)	88.4%
Sleep	230	1.82 (2)	65.2%	61	2.05 (2)	68.9%	44	2.03 (2)	72.7%
Mood	237	2.04 (2)	73.4%	57	2.24 (2)	84.2%	43	2.21 (2)	83.7%
Energy	235	2.14 (2)	80.9%	57	2.27 (2)	80.7%	43	2.26 (2)	76.7%
Activity	235	2.06 (2)	76.2%	57	2.21 (2)	80.7%	43	2.24 (2)	74.4%
Focus / attention	236	1.99 (2)	70.3%	57	2.17 (2)	73.7%	43	2.10 (2)	69.8%

Multiple: 1 = no change, 2 = twice as good, 0.5 = half as good. n is the number of packet participants answering the item (of 257, 67 and 47 eligible in each period). "% improved" is the proportion of those answering who entered a multiple greater than 1. Weeks 1–4 satiety multiples, entered by participants during the study, were transcribed from the packets after the initial analysis; entries that were blank, check marks or non-numerical were excluded. Weeks 1–4 satiety change on the separate frequency scale is reported in Table 8. The self-rated satiety multiples were unchanged or worse for a minority of participants (food noise, hunger and cravings, in table order): weeks 1–4, 40 unchanged and 3 worse (n = 234), 31 and 3 (n = 233), 33 and 4 (n = 233); weeks 5–8, 7 and 0, 5 and 0, 6 and 0 (n = 58); weeks 9–12, 6 and 1, 4 and 1, 4 and 1 (n = 42). All multiples are relative to the start of the study; participants recorded them weekly, and the final week's entry in each period is shown. Ranges

of written satiety multiples (lowest–highest; food noise, hunger and cravings): weeks 1–4, 0.5–7, 0.5–7 and 0.5–8; weeks 5–8, 1–8, 1–6 and 1–8; weeks 9–12, 0.75–5, 0.75–5 and 0.5–5.



Self-estimated improvement multiple written by each participant, relative to study start (1 = no change, 2 = twice as good). Median was 2 for every item. Percentages are of participants answering each item (n = 230–241). Satiety change on the separate frequency scale is shown in Table 8 and Figure 10.

Figure 11. Self-rated improvement multiples for satiety and well-being after the initial 4-week period.

5.9 Adherence

Because the protocol was designed to be flexible, adherence is reported not as a pass/fail measure but to characterize how closely participants followed it; the weight and satiety results should therefore be read as the performance of the program under real-world deviation. Mean adherence by period is shown in Table 10; weeks 1–2 are also shown separately because the dietary requirement was strictest in that interval.

Table 10. Mean adherence by period (eligible packet participants)

Period	n	Product	Dietary	Lifestyle	Overall protocol
Weeks 1–2	257	92.8%	86.4%	79.9%	86.3%
Weeks 1–4	257	90.6%	79.2%	78.8%	82.9%
Weeks 5–8	67	92.1%	66.5%	77.5%	78.7%
Weeks 9–12	47	88.9%	64.1%	80.6%	77.9%

Scores are derived from daily self-recorded entries (Section 4.9). Four participant-weeks with no adherence entries (three in weeks 5–8, one in weeks 9–12) were treated as missing rather than as zero adherence. Overall protocol adherence is the mean of product, dietary and lifestyle adherence, calculated from unrounded values. Dietary adherence is scored against the stricter weeks 1–2 standard in every period. Extension cohorts are separate, self-selected groups.

Product adherence remained high and stable, between 88.9% and 92.8% in every period. Lifestyle adherence was similarly steady at 77.5–80.6%. Dietary adherence declined as expected once the initial restriction ended: from 86.4% in weeks 1–2 to 79.2% across weeks 1–4, and to 66.5% and 64.1% in weeks 5–8 and 9–12, when lower-glycemic fruits and other carbohydrates were permitted

but participants were scored against the stricter initial standard. Within-period weight loss continued in the extension cohorts despite this relaxation of the diet (Table 3), consistent with the program's intended flexibility, although the packet cohorts differ and were not linked; continued within-person loss is shown only by the study-group totals (Section 5.5), which lack adherence records.

5.10 Tolerability and reported adverse effects

Adverse effects were self-reported by participants in response to open-ended weekly and end-of-study prompts and coded into predefined categories during analysis (Section 4.7); they were not independently monitored, graded for severity or followed up clinically, and the findings below describe what participants reported rather than a structured safety assessment. Because symptoms were not specifically solicited, the absence of a reported symptom does not establish that it did not occur. No serious adverse events were reported, and no participant reported needing emergency care, hospitalization or urgent treatment, either in the packets or in the study group. Reports were grouped as gastrointestinal (bloating, gas, altered bowel habit and related symptoms), transitional (the descriptive category defined in Section 4.7, covering symptoms such as headache, fatigue and irritability that commonly accompany abrupt reduction of sugar and refined carbohydrate), cardiovascular, or respiratory, and counted once per symptom per participant per week for the incidence totals; Table 11 shows the number of participants reporting at least one symptom in each category. Where a participant's packet documented a history of a matching condition, the report is also shown as associated with a prior condition; this identifies overlap with recorded history, not cause.

Table 11. Participants reporting symptoms, by week (packet participants)

Week	Respondents	Gastrointestinal	GI, with matching prior condition	Transitional symptoms	Cardiovascular	Respiratory
1	257	48 (18.7%)	19	61 (23.7%)	1	1
2	257	37 (14.4%)	13	37 (14.4%)	1	0
3	257	39 (15.2%)	13	19 (7.4%)	1	0
4	257	31 (12.1%)	15	12 (4.7%)	1	0
5	67	4 (6.0%)	0	0	0	0
6	67	5 (7.5%)	0	0	0	0
7	66	4 (6.1%)	0	0	0	0
8	67	4 (6.0%)	0	0	0	0
9	47	4 (8.5%)	0	0	0	0
10	47	4 (8.5%)	1	0	0	0
11	47	3 (6.4%)	1	0	0	0
12	47	3 (6.4%)	1	0	0	0

Values are numbers of participants reporting at least one symptom in the category that week (percentage of that week's respondents). Respondents are participants who returned that week's record; a week with recorded weights but blank adherence or symptom fields counts as returned, and a blank symptom entry is not taken as confirmation that no symptom occurred. Table 11 describes eligible packet participants only (257 in weeks 1–4; 67 and 47 in the extension periods), not everyone who received the products. Of the 17 initial-period packets excluded as non-adherent, nine came from participants who stopped after reporting gastrointestinal symptoms early in the initial period; symptoms in the other excluded packets were not tabulated. Because participants who stopped early are not represented in the weekly percentages, the decline over weeks 1–4 may partly reflect who continued. A participant may appear in more than one week and more than one category. Counted as symptoms (incidences), weeks 1–4 recorded 186 gastrointestinal, 168 transitional, 5 cardiovascular

and 1 respiratory reports; the single respiratory report occurred in week 1. All five cardiovascular reports were in participants with a documented pre-existing cardiovascular condition; the atrial fibrillation reports (weeks 1, 2 and 4) and the higher-blood-pressure report (week 2) came from one participant, and the low-blood-pressure report (week 3) from a second. Extension participants' prior conditions were taken from their own extension records. Zero indicates no report in that category and does not establish absence of symptoms.

Two patterns stand out. First, reports were concentrated early and declined over the four weeks. Gastrointestinal reports fell from 18.7% to 12.1% of respondents, and transitional symptoms fell more steeply, in step with the dietary protocol: from 23.7% in week 1 to 14.4% in week 2, while grains and starches were excluded, then to 7.4% in week 3, when other carbohydrates could be reintroduced, and 4.7% in week 4. This is consistent with carbohydrate withdrawal as one contributor, alongside general adaptation to the program. In the extension periods no transitional, cardiovascular or respiratory symptoms were reported, and gastrointestinal symptoms were reported by 3–5 participants a week (6.0–8.5%). Second, a substantial share of gastrointestinal reports came from participants with a documented history of a matching gastrointestinal condition — 19 of the 48 participants reporting gastrointestinal symptoms in week 1, and 13–15 of 31–39 in weeks 2–4. Gastrointestinal symptoms were also the most common reason for stopping early among the 17 initial-period packets excluded as non-adherent (nine of the 17; Table 11 note); their outcomes are not included in this analysis.

The age profile of the cohort is relevant to interpreting these reports. Of packet participants with a recorded age, 214 of 252 (84.9%) were aged 50 or older and 94 (37.3%) were 65 or older, an older population than in the pivotal pharmacological weight-loss trials, whose participants averaged about 45–46 years [1,2]. Gastrointestinal complaints become more common with age: constipation affects about one in five older adults [91], and in a nationwide audit of liraglutide treatment for type 2 diabetes the proportion reporting gastrointestinal side effects rose with each decade of age from 30 onward, from 9.7% to 20.0% [92]. In a large US cohort starting GLP-1 RA therapy, adults aged 65 or older were more likely to discontinue, and moderate or severe gastrointestinal adverse events were associated with discontinuation [93]; a systematic review of antiobesity medication studies in adults aged 65 and older likewise reported frequent gastrointestinal adverse events and discontinuation [94]. These studies concern pharmacological treatment and are cited only to indicate that gastrointestinal complaints are more common with age and that older adults have been more susceptible to them during pharmacological weight-loss treatment; they do not establish how age affects tolerance of this regimen, and are not used to compare rates. Within this cohort, the proportion of packet participants reporting at least one gastrointestinal symptom during weeks 1–4 was similar across age bands: 10 of 38 (26.3%) aged under 50, 28 of 120 (23.3%) aged 50–64 and 26 of 94 (27.7%) aged 65 or older. These figures describe analyzed participants only. All nine participants who stopped early after reporting gastrointestinal symptoms (Table 11 note) were over 65; adding them to the analyzed participants, 35 of 103 aged 65 or older (34.0%) reported gastrointestinal symptoms, compared with 38 of 158 (24.1%) aged under 65, and gastrointestinal discontinuation occurred only in the oldest group. These age comparisons are descriptive: the bands are small, no hypothesis test was applied, and a blank symptom field could reflect either no symptom or an unanswered section. Against that background, gastrointestinal symptoms were reported by a minority of participants (12.1–18.7% a week in weeks 1–4), declined over the initial period, and included no serious events; because collection methods differ and there was no comparison group, these figures cannot be compared directly with rates from other studies.

Cardiovascular reports were rare and confined to participants with a documented pre-existing cardiovascular condition. Five were recorded in weeks 1–4: atrial fibrillation in weeks 1, 2 and 4 (the week-4 report described as a recurrence), higher blood pressure in week 2, and low blood pressure in week 3. The atrial fibrillation reports and the higher-blood-pressure report came from the same participant, whose documented medical history included atrial fibrillation and high blood pressure, so the five reports came from two participants (0.8% of 257). None were reported in the extension periods. The low-blood-pressure report came from a participant taking antihypertensive medication

who had lost 3.5% of body weight over the preceding three weeks. Weight loss lowers blood pressure by about 1 mm Hg per kilogram (2.2 lb) lost, and the diastolic reduction is larger in people taking antihypertensive drugs [95]; a fall in blood pressure during rapid weight loss is a recognized effect of weight loss in treated hypertension and is one plausible explanation, although causation cannot be assessed here. The packet instructed participants taking blood-pressure medication to check their levels regularly and to consult their physician about any change in medication (Section 4.7). Thermogenic and sympathomimetic agents can raise heart rate and blood pressure irrespective of cardiovascular history — a product combining *p*-synephrine (21 mg) with caffeine (304 mg) raised diastolic blood pressure [68], and the French food safety agency has advised against combining them (as summarized in [40]). Capsaicinoids can also increase heart rate at higher doses (see below). The formulation was deliberately designed to limit stimulant exposure (Appendix B.3.1). No cardiovascular symptom was reported in any week by analyzed packet participants without a recorded pre-existing cardiovascular condition; this study did not determine whether that reporting pattern resulted from the formulation's stimulant profile. Blood pressure and heart rhythm were not systematically measured as study outcomes or independently verified, symptoms were collected through open-ended reports over a short period, and there was no comparator group, so neither causation nor the incidence of unreported or asymptomatic changes can be determined. The packet advised that several CC botanicals may affect blood pressure and that participants with a related condition should consult their physician before use and could omit CC while continuing the other products (Section 4.2); whether these participants did so is not known. National Institutes of Health guidance likewise advises that people with heart disease or high blood pressure consult a healthcare provider before using any weight-loss supplement [96], so these were the participants for whom that consultation mattered most. The reports cannot be attributed to the products, but they indicate that people with a pre-existing cardiovascular condition should use CC only with their physician's approval, and that future studies should monitor blood pressure and heart rhythm in this group.

Each of the reported symptoms has several possible explanations, and without clinical follow-up the cause in any individual cannot be assigned: several ingredients and the dietary change itself could produce similar effects. Three well-documented processes, and one hypothesis, are relevant. First, gut adjustment: fermentable fibers — inulin, resistant starch, glucomannan and flaxseed — and live cultures alter colonic fermentation within days, transiently increasing gas production until the microbial community adapts; gastrointestinal symptoms are the most commonly reported effects of inulin-type fructans; they are generally mild at moderate doses [97], and such responses are typically transient [98]. Berberine, a component of CC, is also associated with mild to moderate gastrointestinal effects — nausea, constipation and diarrhea in several randomized trials, and flatulence in one [99]. Magnesium is supplied at 445 mg a day, all from supplemental sources, which exceeds the 350 mg upper intake level for supplemental magnesium [100]; intakes above that level can loosen stools and may have contributed to some reports. Second, carbohydrate reduction: in a randomized trial of a ketogenic low-carbohydrate diet — a stricter carbohydrate restriction than this protocol's — constipation (68% vs 35%), headache (60% vs 40%), muscle cramps (35% vs 7%), diarrhea (23% vs 7%), general weakness (25% vs 8%) and rash (13% vs 0%) were more common than on a low-fat diet; three participants (5%) withdrew because of adverse effects — two for raised low-density lipoprotein (LDL) cholesterol and one for symptoms — and the authors described these effects as typically occurring at initiation and short-lived [101]. A descriptive analysis of online consumer reports describes a similar transient cluster of flu-like symptoms, headache, fatigue, nausea and dizziness during the first week of very-low-carbohydrate diets [102]. A likely contributor is sodium and fluid loss: carbohydrate restriction increases renal sodium and water excretion through ketone-associated natriuresis, glycogen depletion and lower insulin concentrations [103], and this fluid and electrolyte loss may contribute to the dizziness and fatigue described in the first week [102]. The protocol's daily water target, its glass of water on waking with a pinch of salt, and its emphasis on vegetables and complete micronutrient supply were intended to limit these effects. Third, thermogenic stimulation: capsaicinoids such as the capsaicin in CC, and related TRPV1 agonists, are recognized to cause warmth, sweating, abdominal pain and, at higher doses, increased heart rate. In a 28-day randomized trial of a sustained-release capsaicinoid formulation, four

participants in the higher-dose group reported abdominal pain in the first three days and two had diarrhea that settled within a week, with no change in heart rate or blood pressure [104]; that product differs from CC, so the trial indicates the kinds of effects capsaicinoids can produce rather than CC's own tolerability. Warmth, flushing or sweating — coded with hot flashes among the transitional symptoms — could also plausibly reflect the thermogenic components of CC, whose stimulant ingredients (*p*-synephrine, yohimbine and caffeine) are included at deliberately low levels (Appendix B.3.1). Fourth, weight loss itself: lipophilic persistent organic pollutants accumulate in adipose tissue and are released into the circulation as fat mass falls, with measurable rises in circulating levels during weight loss [105,106], and some dietary fibers, notably rice bran fiber, bind these compounds strongly in vitro [107]; whether this mobilization contributes to transient symptoms has not been established, and it is offered here as a hypothesis only. The pattern of reported effects — predominantly gastrointestinal and transitional, and concentrated early — is consistent with these processes, though consistency with a known process does not establish the cause.

6. Discussion

6.1 Principal findings

In this single-arm study, four weeks of Trilogiii use with a flexible dietary protocol was associated with a mean loss of 12.66 lb among the 395 participants who reported results (6.03% of body weight among packet participants), and 180 of 257 eligible packet participants (70.0%) lost at least 5% of their starting weight. The changes in reported hunger, cravings and food noise were large and consistent across all three items: among packet participants, the proportion reporting each "regularly" or "constantly" fell from roughly half of participants to under 10%. Smaller within-period losses were reported by the successive, separate, self-selected extension cohorts, and cumulative totals posted in the study group by reporters in the weight-loss phase reached a mean 20.85 lb at 8 weeks and 28.25 lb at 12 weeks (29.09 lb among the 57 participants with a total at every time point). The three satiety targets described in Section 3 were not tested individually, but the pattern of results — rapid early loss accompanied by marked reductions in subjective hunger — is consistent with, though not a test of, the hypothesis that combined satiety support made caloric restriction tolerable for most participants.

The study tested Trilogiii as it is intended to be used: with support. Throughout the study, the private study group clarified product use, protocol directions and reporting and was designed to support adherence (Section 4.8), and ongoing use of Trilogiii is planned to include comparable support, through a personal AI coaching system and the option to join similar support groups. The study conditions therefore approximate intended real-world use, although the contribution of this support cannot be separated from that of the products (Section 7).

6.2 Context

The size of the initial-period loss is notable. Packet participants lost 6.03% of body weight in four weeks, and 70.0% lost at least 5% — the degree of loss clinical guidelines set as an initial goal to be reached within six months [108]. In the pivotal GLP-1 receptor agonist trials, whose doses are titrated gradually, mean loss at week 4 was roughly 2–3% [1,2]; in the randomized DIRECT diet trial it was roughly 1.4–1.9% [109], and intensive lifestyle intervention produced 8.6% over a full year [110]. Trilogiii participants following the named diets with DIRECT percentage comparators (low-carbohydrate and Mediterranean) lost 5.7–5.8% in four weeks (Table A3; Figure A2) — a magnitude that warrants a controlled test. Trials of diet composition and meal timing also indicate that the energy deficit achieved, however it is scheduled or composed, is the main driver of weight loss across dietary regimens [109,111–114] — the element that Trilogiii's satiety support is designed to make sustainable. Part of any rapid early loss, particularly during the two low-carbohydrate weeks, reflects

glycogen and associated water rather than fat [103]. Reported changes extended beyond scale weight: waist circumference decreased by a mean 2.82 in among 322 respondents. Body composition was not measured, so the contributions of fat, lean tissue and water to the weight lost could not be quantified. The comparator trials were randomized, clinic-measured and longer, in different populations, whereas the present study was uncontrolled, self-reported and short, and its extension cohorts were self-selected; the comparison therefore situates the magnitude of the observed change rather than showing that Trilogiii caused it or would sustain it. Cumulative totals posted in the study group by reporters in the weight-loss phase reached a mean 28.25 lb at 12 weeks among continuing reporters, who had lost more than average in the first four weeks (Section 5.5), against approximately 13–19 lb in the GLP-1 receptor agonist trials and 9–13 lb in DIRECT over the same period (Table A1), although the Trilogiii totals are self-reported. Detailed comparisons, including the extension periods and the published regimen studies, are given in Appendix A with their qualifications.

6.3 Subgroups

Sex. Men lost more absolute weight than women in every period: 15.84 vs 11.01 lb in weeks 1–4, 10.80 vs 7.05 lb in weeks 5–8, and 6.93 vs 6.07 lb in weeks 9–12. This pattern is expected: men typically enter weight-loss interventions at higher body weight with greater lean mass and resting energy expenditure, and a systematic review of weight-loss trials found that men tend to lose more absolute weight than women [115]. Relative to starting weight, the difference was much smaller — 6.44% vs 5.88% in weeks 1–4 and 4.36% vs 3.91% in weeks 5–8 — and in weeks 9–12 women lost a slightly larger share than men (3.47% vs 3.15%; Figure 7). Women and men therefore lost a similar share of body weight in each period, and most of the gap in pounds is consistent with men's higher starting weight. The larger male advantage in weeks 1–4 is consistent with men having a larger early water and glycogen component during the first two low-carbohydrate weeks, but with 18 and 12 men in the extension periods the later comparisons are descriptive only.

Age. Initial-period weight loss was broadly uniform across adult age bands: 12.70 lb (18–34), 12.54 lb (35–49), 12.91 lb (50–64) and 11.56 lb (65+). The slightly lower value in participants aged 65 and over is consistent with age-related declines in resting metabolic rate and lean mass, but the difference is small. The two largest groups (50–64 and 65+, together 84.9% of those with a recorded age) responded comparably, and participants aged 65 and over in the separate extension cohorts lost more than younger participants in the same periods (9.33 lb and 4.47% in weeks 5–8, n = 20; 6.81 lb and 3.71% in weeks 9–12, n = 15). This matters because older adults are often under-represented in weight-management research.

Diabetes. Thirty-two initial-period packet participants reported diabetes (30 type 2, 2 type 1). Their mean weight loss was 14.01 lb (5.98% of body weight), compared with 12.19 lb (6.04%) among participants without reported diabetes; in the smaller extension cohorts the figures were 9.07 lb (n = 7) vs 7.94 lb in weeks 5–8 and 5.30 lb (n = 5) vs 6.41 lb in weeks 9–12. Relative to starting weight, the two groups therefore lost a similar share of body weight in the initial period, and the larger loss in pounds may reflect the higher baseline weight typical of people with type 2 diabetes; in the extensions, participants with diabetes lost a similar or slightly smaller share (3.86% vs 4.05% and 2.92% vs 3.45%). As context only, this differs from the pattern in GLP-1 receptor agonist trials, in which participants with type 2 diabetes lose considerably less than those without, although the designs are not comparable: 9.6% vs 14.9% for semaglutide (STEP 2 vs STEP 1) [1,116] and 12.8–14.7% vs 15.0–20.9% for tirzepatide (SURMOUNT-2 vs SURMOUNT-1, treatment-regimen estimand) [2,117]. However, the subgroup is small, no standardized glycemic endpoints (glycated hemoglobin [HbA1c], fasting glucose) were obtained or analyzed, and diabetes-medication changes, although recorded by some participants, were not systematically ascertained or analyzed. Participants with diabetes who undertake caloric restriction while on insulin or sulfonylureas are at risk of hypoglycemia, and the absence of reported events should not be taken as evidence of safety in

this group. These observations warrant a dedicated study in people with type 2 diabetes with glycemic endpoints and medication monitoring.

Prior GLP-1 receptor agonist use. Seventeen initial-period packet participants reported prior use of a GLP-1 RA, all of whom had stopped the medication at least one month before starting (Section 4.4). They lost a mean of 14.26 lb (6.00% of body weight) in four weeks, compared with 12.28 lb among participants without reported prior use (Table 5); relative to starting weight, their mean percentage loss was similar to that of the packet cohort as a whole (6.03%), so the larger loss in pounds is consistent with a higher starting weight. Five of the 17 identified themselves as GLP-1 RA non-responders (no threshold was specified; in the literature non-response is defined, for example, as failure to reach at least 5% weight loss after 52 weeks of treatment [86]) — a group that made up roughly 9–15% of participants in the pivotal semaglutide and tirzepatide trials [1,2] — and they lost a mean of 13.26 lb (5.89%) in four weeks; three of the five individually exceeded 5% (5.35%, 7.36% and 7.89%), and the other two lost less than 5%. These observations are exploratory. Weight regain after stopping a GLP-1 RA is well documented: one year after semaglutide was withdrawn in the STEP 1 extension, participants had regained two-thirds of their prior loss [3], and in SURMOUNT-4, over the 52 weeks following randomization at week 36, participants switched from tirzepatide to placebo had a mean 14.0% increase from their week-36 weight, whereas those continuing treatment had a further mean 5.5% reduction [118]. This provides relevant clinical context, but exact discontinuation timing and appetite were not recorded here, so these participants' results cannot be interpreted specifically as outcomes during post-treatment rebound. Whether satiety routes other than GLP-1 — the mechanosensory and metabolic routes, and hormones such as CCK and PYY (Section 3) — contribute in people who did not respond to GLP-1 RA therapy warrants investigation. Few prior users continued into the extensions (3 in weeks 5–8, losing 3.03%, and 2 in weeks 9–12, losing 2.32%), and none of the non-responders did. The subgroups are small (n = 17 and 5); non-response was self-identified and was not verified from medical records; and the exact timing, dose and duration of prior GLP-1 RA use were not recorded. People who have stopped GLP-1 RA therapy, including non-responders, are a growing population, and these results warrant a dedicated study in this group.

Concurrent fasting and diets. Weight loss on the Trilogiii protocol was similar with or without an added named fasting regimen or named diet (Table 6). Because the protocol already builds in daily caloric restriction through smaller or replaced meals, participants without a named regimen were not eating freely; in weeks 1–4, adding OMAD, other intermittent fasting or a named diet on top of this restriction was not associated with greater mean loss, and the smaller extension subgroups showed no consistent difference. This is consistent with the program functioning as a self-contained protocol, and with trial evidence that the timing pattern of caloric restriction adds little beyond the restriction itself [111–113].

As exploratory context, the four-week losses in the regimen subgroups shown in Figure A2 (5.7–6.4% of body weight) were larger than those reported over 4 to 12 weeks in published studies of the same regimens. Those are separate, differently designed studies and the Trilogiii subgroups were self-selected and in some cases small, so the comparison describes the magnitude of the observed losses, not an effect of Trilogiii on the other regimens (Appendix A, Table A3, Figures A2–A3).

6.4 Implications for the three-target model

The satiety data are the study's most consistent result: nearly all packet participants answered the frequency questions before and after the initial period, and the direction of change matched the mechanistic hypothesis. During four weeks of deliberately reduced intake, most participants reported less frequent hunger, not more — the opposite of the rise often reported during energy restriction [69]. The change was confirmed within individuals: comparing each participant's own ratings, 61–75% reported less frequent hunger, food noise or cravings after four weeks and only 1.7–4.5% reported each as more frequent ($P < 0.001$ for each; Table 8), and extension participants continued to rate their hunger, cravings and food noise as improved relative to the start of the study

(Section 5.8). Participants' written improvement multiples, a separate secondary measure, pointed the same way, with a median of 2 for each measure and 81.6–85.4% reporting improvement (Section 5.8). The written measure shows a higher share improving than the frequency scale (82–85% vs 61–75%). A plausible reason is sensitivity: the frequency scale has only four steps, so a participant whose hunger fell, for example, from the upper to the lower end of "occasionally" would choose the same category at both assessments and be counted as unchanged, whereas the written multiple can register such a change. The matched comparison is consistent with this: most participants who wrote a multiple above 1 while choosing the same frequency category were above "rarely" at baseline (56 of 63 for hunger, 25 of 40 for cravings and 54 of 58 for food noise); the rest were already at "rarely," with no room to improve on that scale (Section 5.8). The written multiple is, however, a judgment of change relative to the start of the study rather than a comparison of two separate ratings. Weekly recording kept that judgment current, but each entry still depended on the participant's sense of how they felt at the start and may have been anchored by earlier entries and by the instruction's example of 2. The two measures also agreed only slightly better than chance at the individual level, so greater sensitivity cannot be fully separated from a general tendency to report improvement. Both measures were specified before enrollment and recorded by participants during the study. The frequency ratings, recorded as separate ratings at the start and end of the period, are the primary satiety outcome; the written multiple is a corroborating secondary measure. Both point in the same direction for the group, so the reduction in hunger, cravings and food noise is consistent across two response formats; because both are self-reported, that consistency does not show what caused the change. The study also cannot attribute the effect to any one target or distinguish the products' contribution from that of the low-carbohydrate first two weeks, which may itself reduce hunger. The combined protein-and-fiber approach on which FS and BP are built has randomized support: in a 12-week double-blind trial of 206 adults following an energy-restricted diet, a shake providing 17 g protein and 6 g fiber (including inulin and flaxseed) taken before breakfast and lunch produced greater weight loss than an isocaloric shake low in protein and fiber (1 g protein and 3 g fiber; 7.3 vs 4.0 lb [3.3 vs 1.8 kg] among the 133 who completed per protocol) [119]. That trial does not identify which ingredient was responsible and does not predict Trilogiii's result, but it shows that a protein-and-fiber shake used this way can add to the effect of energy restriction; FS and BP together supply 43 g of protein and 13 g of fiber-containing prebiotic ingredients a day (Table B2). Participants could take the shake with a meal, apart from meals or as a meal replacement; this study did not evaluate whether timing relative to meals affected reported satiety. Hourly satiety profiling, measurement of circulating active GLP-1, and a placebo-controlled design are the obvious next steps.

Two features of the within-person data deserve comment. First, food noise and hunger had lower proportions improving than cravings (60.8% and 62.3% vs 75.1%), but the difference reflects participants reporting the same frequency rather than deterioration. The protocol itself also directs attention to food: participants planned and recorded small whole-food meals daily and avoided grains and starches for two weeks, and the "thoughts of food" item does not distinguish this deliberate attention from intrusive thoughts of food. Second, within the extension periods most participants reported the same frequency at the start and end, and in the extension ending at week 12 a minority (6 of 42 for each of these two measures) reported more frequent hunger or food noise. These participants began the extension after the initial period, many already at low frequency, so the extension comparisons test for further change rather than maintenance; whether the initial reduction is sustained over longer use should be tested in a study that follows the same individuals from baseline. Participants' weekly improvement multiples were recorded in the packets but, apart from the final week of each period, not tabulated; their week-by-week course is a planned future analysis.

6.5 Nutrient delivery: an integrated hypothesis

Trilogiii was formulated to couple a broad supply of essential nutrients (Appendix B.1.1) with complementary mechanisms that may influence how those nutrients are delivered and used. Each mechanism has published support, ranging from human isotope and feeding studies to cell and

animal models. Fermentation of the BIACTIN milk-protein fraction alters protein digestion and peptide release, and human intubation and feeding studies show that it changes the time course of protein delivery while overall protein absorption remains high [10,11,120]; the casein:whey ratio shapes the timing of essential amino acid release [121]; dairy eaten with a high-phytate meal increased zinc absorption in two human isotope studies [12,13]; and selected milk-derived peptide preparations have increased iron uptake by intestinal cells and calcium absorption in rats [15,16].

Meal-related gut hormones provide a second set of links between protein ingestion and nutrient handling, each with a distinct role. GLP-2 is the clearest link to nutrient handling: it influences intestinal lipid absorption, with human infusion studies reporting increased postprandial lipid appearance, and animal studies support effects on intestinal nutrient transport, including amino acid uptake [18,19] (Appendix B.1.2). CCK coordinates the pancreatic enzyme secretion and gallbladder contraction on which protein and fat digestion depend [122]. GLP-1 chiefly regulates the pace of nutrient entry by slowing gastric emptying [123]; its contribution is to the timing of delivery rather than the amount absorbed. Milk proteins and their digestion products stimulate these hormones in experimental models: an α-lactalbumin hydrolysate raised GLP-2 secretion in suckling rats [124], intact casein and milk fermented with *L. helveticus* (cultures different from BIACTIN's) stimulated GLP-1 secretion from enteroendocrine cells [125], and peptides found in the human jejunum after casein or whey ingestion stimulated CCK and GLP-1 secretion [126].

The biotic component adds a third, independent pathway. In human isotope studies, inulin-type fructans increased fractional calcium absorption in adolescents [23], and in a double-blind crossover trial in 15 postmenopausal women, six weeks of 10 g/day of an oligofructose-enriched inulin increased stable-isotope-measured absorption of both calcium and magnesium relative to placebo [24] — evidence that fermentable substrates can increase the extent, and not only the timing, of mineral absorption. In addition, the probiotic strain *L. plantarum* 299v increased non-heme iron absorption (from 17.4% to 22.4% and from 20.9% to 24.5% in two studies in women [127], with a moderate pooled effect across eight studies of that strain [128]). These effects are specific to the substrates, strains and doses tested; Trilogiii supplies 4 g a day of inulin within a different fiber mixture, and *L. plantarum* without a specified strain designation, so whether its components produce comparable effects remains to be determined (Appendix B.2).

We therefore hypothesize that these components — the combined and fermented milk proteins, peptide–mineral interactions, protein-stimulated GLP-2 and CCK release, and the intended synbiotic intestinal environment — act together to improve the delivery and bioavailability of selected essential nutrients, particularly those for which human absorption evidence exists: amino acids (delivery timing), calcium and magnesium (fermentable substrates), and zinc (dairy consumed with high-phytate foods). Evidence for iron is more limited: it comes from one specific probiotic strain and from cell models, and adding dairy to a high-phytate diet did not improve iron absorption in women [12]. The hypothesis also connects to satiety through the metabolic target (Section 3.3): the more completely the supplied micronutrients are absorbed, the stronger that route to reduced hunger would be expected to be, in people for whom inadequate nutrient availability contributes to hunger. The cited studies establish the individual pathways; their interaction within the finished regimen, and any resulting change in nutrient absorption, were not tested in the present study, and no gut hormones were measured in participants. The hypothesis is directly testable, beginning with simulated-digestion bioaccessibility testing of the finished products (Section 8) and followed by stable-isotope absorption studies of selected minerals with postprandial measurement of GLP-1, GLP-2 and CCK.

7. Limitations

This study has important limitations that constrain interpretation. It was uncontrolled, so the contribution of the products cannot be separated from that of the dietary protocol, water intake,

movement recommendation, group support and the expectancy effects of an open-label design. Support through the study group was part of the intervention as delivered (Section 4.8), and because totals in the group were posted under participants' names and seen by other members, social desirability may have encouraged favorable reporting or discouraged posting by those who lost less.

All outcomes were self-measured and self-reported, without clinic verification; self-reported weight tends to be underestimated, and home scales were not calibrated or standardized across participants, although each participant was required to use the same scale at the same time of day and under the same conditions. Hunger, cravings, food noise and perceived improvement were rated on study-specific instruments that have not been formally validated. Body composition was not measured, so the fat, lean-tissue and water components of the loss, including the glycogen-associated water lost early in carbohydrate restriction, cannot be separated, and baseline dietary intake and nutrient status were not assessed.

Participants paid to take part (Section 4.3) and were recruited in part through communities associated with the founder, which selects for motivated individuals and likely inflates results relative to a general population. Packet extension cohorts were self-selected, progressively smaller, and, because separately submitted packets could not be matched, were not linked to individual baseline data, so packet period results must not be summed. Cumulative loss is available only from totals posted in the study group, which were self-reported, recorded in pounds without starting weights, not accompanied by adherence records, and, at 8 and 12 weeks, came from continuing reporters who had lost more than average in the first four weeks (13.66 and 14.56 lb vs 12.82 lb; Section 5.5). Similar means across reporting channels reflect reporting consistency rather than independent validation, because the same people could not be compared individually. The study-group analyses could include posts from individuals whose anonymized packets were excluded, because packet eligibility could not be linked to named posters; these analyses applied the weight-loss-intent and maintenance screening described in Section 4.9, not the packet adherence criteria. Reported means describe participants who returned results (age and adherence were documented only for packet participants; group-only reporters' weight-loss intent was confirmed through direct communication): 75 of 497 packet recipients did not report, and 27 returned packets were excluded (Section 5.1); outcomes of excluded packets are not reported, so the results should not be read as the expected outcome for everyone who began the program (in a sensitivity scenario defined after data collection, assigning zero weight change to the 17 non-adherent packet participants and the 17 non-reporters who gave no reason [5 of whom subsequently posted an 8-week loss, although their 4-week changes were unavailable], mean four-week loss would remain approximately 11.7 lb across 429 individuals; zero change is an assumption, since some could have gained weight, and the scenario does not remove other sources of reporting or selection bias), and the absence of any reported weight gain among analyzed participants is sensitive to this selection.

Adverse effects were self-reported through open-ended prompts, which tend to under-capture symptoms, and were not independently monitored, graded or followed up, so the study cannot establish safety. Physician consultation was required but self-attested, and three minors used the products outside the study's intended adult population without independent oversight. The absence of independent ethics review (Declarations) means the protocol was not scrutinized by anyone outside the study team, and consent from participants who reported only in the group (138 in the initial period) was given by posting results rather than by signature.

Apart from the sign tests of within-person satiety change and the Shapiro–Wilk normality tests, no hypothesis tests were performed, so no P values are reported for differences between subgroups or periods; the planned analyses were specified before enrollment, and the follow-on analyses they led to, including the choice of sign test (Section 4.1), were defined after data collection; because the study was not registered, the pre-specification cannot be independently verified; moreover, a significant within-person change in an uncontrolled study does not establish that the products caused it. Confidence intervals are reported for weight loss in pounds (by period and cumulatively), mean percentage weight loss in each period, the proportion losing at least 5%, the proportion

meeting their own stated goal and the proportion reporting a cumulative loss of 20 lb or more; circumference changes and subgroup means are presented without measures of variability, so their precision is unknown. Perceived-improvement multiples are subjective and unbounded above, and are judgments of change relative to the start of the study, recorded weekly, rather than separate before-and-after ratings, and so depend on participants' sense of how they felt at the start; because participants were permitted to leave items blank, the proportions reporting improvement are calculated among respondents and could be biased in either direction by who chose to answer. Neither circulating gut hormones nor oxidative-stress markers were measured, so the mechanisms proposed in Sections 2 and 3 and Appendix B remain untested in this population.

The study population was predominantly female, white and aged 50 or over, limiting generalizability. Finally, the study was designed, conducted and reported by parties with a commercial interest in the products (Declarations), which readers should weigh in interpreting every judgment made in this paper.

8. Conclusion

This study set out to examine whether a nutritional system designed around three routes to satiety — mechanosensory, hormonal and metabolic (nutrient repletion) — could make caloric restriction tolerable enough to produce meaningful weight loss without pharmacological appetite suppression. Among 395 participants who reported results (257 eligible packet participants and 138 group-only reporters), four weeks of Trilogiii use with a flexible whole-food protocol was associated with a mean loss of 12.66 lb; packet participants lost 6.03% of body weight, and 180 of 257 (70.0%) lost at least 5%, the degree of loss that clinical guidelines set as an initial goal to be reached within six months. Weight loss continued among those who remained in the weight-loss phase: cumulative totals posted in the study group by weight-loss-phase reporters reached a mean 28.25 lb at 12 weeks, and the 57 participants with a total at every time point lost a mean 14.83, 23.21 and 29.09 lb by weeks 4, 8 and 12.

The satiety findings are the study's most distinctive result. Among packet participants, about half reported being hungry, craving food or thinking about food "regularly" or "constantly" before the study; after four weeks, fewer than one in ten did, and comparing each participant's own ratings, fewer than 5% reported any one of them as more frequent. The changes were consistent across all three items and aligned with the system's satiety hypothesis. The ratings were self-reported, however, and the products' contribution cannot be separated from that of the protocol.

Several further observations are worth noting. In the initial period, mean weight loss was similar among participants who did and did not add OMAD, other intermittent fasting or a named diet, and the protocol accommodated the range of eating patterns participants already used. Weight loss was similar across adult age groups, and participants aged 65 and over — often under-represented in weight-management research — lost nearly as much as younger adults in the initial period (11.56 vs 12.54–12.91 lb) and, in the small self-selected extension cohorts, more than younger participants. Participants with diabetes lost a similar share of body weight to those without, but the subgroup was small and lacked standardized glycemic outcomes, and this warrants a dedicated study. Reported adverse effects were mainly early gastrointestinal symptoms, of the kinds commonly reported with increased fiber intake and dietary change, and transitional symptoms such as headache, fatigue and irritability, which fell from about one participant in four in week 1 to one in twenty by week 4. No participant reported needing emergency care or hospitalization. The few cardiovascular reports came from two packet participants, both with a pre-existing cardiovascular condition — the group the packet had directed to consult their physician before using CC — and no analyzed packet participant without a recorded cardiovascular condition reported a cardiovascular symptom, although the study did not determine whether this reflected the formulation's stimulant profile; for people with a

cardiovascular condition, CC should be used only with physician approval. Adverse effects were, however, self-reported and not independently monitored or graded.

These results do not establish efficacy or safety. The study was uncontrolled, self-reported, short, and conducted in a self-selected and predominantly female, white, older population; its packet extension cohorts were not linked to baseline, and cumulative loss rests on self-reported group totals; and the contribution of the products cannot be separated from that of the dietary protocol, the group support or expectancy. The satiety results support a controlled test of the three-target model; the absorption, thermogenic and cytoprotective rationale, which this study did not examine, would need its own testing. Assays of the finished products' nutrient content, and standardized simulated-digestion testing characterizing BIACTIN's peptide profile and the bioaccessibility of its minerals, vitamins and fatty acids, would provide product-specific evidence for the nutrient-delivery rationale at modest cost; a controlled stable-isotope comparison of selected minerals would then test the absorption hypothesis directly (Section 6.5). The research priorities follow in stages. The first is a randomized, placebo-controlled trial of the combined program with independent ethics and safety oversight, clinic-measured weight and body composition, structured adverse-event monitoring and satiety ratings. Focused studies could then examine circulating gut hormones and hourly satiety profiles, energy expenditure and oxidative-stress markers, and outcomes in a dedicated type 2 diabetes cohort. Together they would test whether a complete, low-stimulant nutritional system can deliver a meaningful share of the satiety benefit that has made GLP-1 receptor agonists the current standard of obesity pharmacotherapy. That is the question this study raises, and the one it argues is worth answering.

Abbreviations

ACE, angiotensin-converting enzyme; AMPK, AMP-activated protein kinase; ARE, antioxidant response element; ATP, adenosine triphosphate; BAT, brown adipose tissue; BMI, body mass index; BP, Bioactive Protein Booster; cAMP, cyclic adenosine monophosphate; CC, Calorie Burner / Cell Protector capsule; CCK, cholecystokinin; CD38, cluster of differentiation 38 (NAD^+ glycohydrolase); CFU, colony-forming units; CI, confidence interval; CPP, casein phosphopeptide; DFE, dietary folate equivalents; DHA, docosahexaenoic acid; DIAAS, digestible indispensable amino acid score; DMT-1, divalent metal transporter 1; DPP-4, dipeptidyl peptidase-4; EFSA, European Food Safety Authority; EGCG, epigallocatechin gallate; EN, Essential Nutrients Booster capsule; FS, Foundation + Stimulation shake; GI, gastrointestinal; GIP, glucose-dependent insulinotropic polypeptide; GLP-1, glucagon-like peptide-1; GLP-1 RA, GLP-1 receptor agonist; GLP-2, glucagon-like peptide-2; HbA1c, glycated hemoglobin; IQR, interquartile range; ISAPP, International Scientific Association for Probiotics and Prebiotics; IU, international units; Keap1, Kelch-like ECH-associated protein 1; LDL, low-density lipoprotein; MCT, medium-chain triglyceride; MTF-1, metal-regulatory transcription factor 1; MTHFR, methylenetetrahydrofolate reductase; NAD^+, nicotinamide adenine dinucleotide; NF-κB, nuclear factor kappa B; NHANES, National Health and Nutrition Examination Survey; Nrf2, nuclear factor erythroid 2–related factor 2; OMAD, one meal a day; PARP, poly(ADP-ribose) polymerase; PYY, peptide YY; RCT, randomized controlled trial; ROS, reactive oxygen species; SCFA, short-chain fatty acid; SD, standard deviation; SIRT1, sirtuin 1; SOD, superoxide dismutase; TBARS, thiobarbituric acid reactive substances; TRPV1, transient receptor potential vanilloid 1; UCP1, uncoupling protein 1.

Declarations

Funding. The study was sponsored and facilitated by Nelo Life, an independent third party that recovered direct costs through participant fees and has since ceased operations; the products were not otherwise sold by the sponsor. Triii Therapeutics supplied products at cost and bore protocol-

support, legal, insurance, data-handling and publication costs. Neither Triii Therapeutics nor Nelo Life derived net income from the study.

Conflict of interest. PRM is the founder and formulator of Triii Therapeutics, which developed Trilogiii and holds a commercial interest in it. PRM is a co-author of a cited study of a related antioxidant formulation [56] and a named inventor on a cited patent [129] underlying the cellular-protection design principle. AJM is an independent contractor engaged by Triii for data analysis; he is also enrolled in the Trilogiii customer rewards program and has received a small referral commission for referring one personal acquaintance. He declares no other competing interests.

Trial registration. The study was not registered in a public trial registry.

Publication. This is an author-prepared study report published on the Triii Therapeutics research website; it has not undergone journal peer review.

Ethics. The protocol was not reviewed by an independent ethics committee. Packet participants provided written consent for collection and use of their data; group-only reporters consented by posting results in the study group, which stated that shared results would be used as study data. All participants received the full ingredient list and were required to review it and, by the acknowledgment in the packet, to consult their physician beforehand if they had or suspected any medical condition or were taking any medication (Section 4.2). For packet data, identifying information was separated from the data by an independent law firm before analysis; group-only results were taken from posts in the private Facebook study group, visible only to its members.

Data availability. Individual-level data are held by Triii Therapeutics and are not publicly available. The study-group records, including every posted total, are retained and are available for independent verification by qualified reviewers under a confidentiality agreement; requests may be made to the corresponding author.

Author contributions. PRM conceived and designed the study, formulated the products and wrote the manuscript; AJM managed data capture and performed the analysis. Both authors approved the final version.

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Appendix A. Exploratory context: published comparators

A.1 Published trials used for context

For context, the pivotal GLP-1 receptor agonist trials report mean weight loss of 14.9% for semaglutide 2.4 mg at 68 weeks (STEP 1) [1] and 15.0–20.9% for tirzepatide 5–15 mg at 72 weeks (SURMOUNT-1) [2]. Because these agents are started at low doses and escalated over several months, the duration depending on the drug and the assigned maintenance dose, early loss is gradual: the published STEP 1 trajectory shows roughly 2% at week 4, 3–4% at week 8 and 5–6% at week 12, and the SURMOUNT-1 trajectory roughly 2–3%, 5–6% and 7–9% at the same time points. These trajectory values, and the DIRECT values below, were read visually from the mean weight-change-over-time figure in each trial's primary report at weeks 4, 8 and 12; they are approximate, are marked ≈, and are given as ranges where the curve could not be read more precisely. Intensive lifestyle intervention alone produced a mean 8.6% at one year in Look AHEAD [110] and 4.7% at four years [130]. In the present study, packet participants lost 6.03% of body weight in the initial 4 weeks, 4.03% of period-starting weight in weeks 5–8 (n = 67) and 3.39% in weeks 9–12 (n = 47), and totals posted in the study group by reporters in the weight-loss phase reached a mean 20.85 lb at 8 weeks (n = 101) and 28.25 lb at 12 weeks (n = 65) (Section 5.5). These figures come from designs,

populations and measurement methods that differ substantially from this study's and are not directly comparable.

Published dietary interventions provide further context. In head-to-head trials of macronutrient composition, mean loss at 12 months was 12–13 lb (5.3–6.0 kg; roughly 6% of body weight) regardless of low-fat or low-carbohydrate assignment (DIETFITS) [114], and about 6–10 lb (2.9–4.7 kg) at 2 years for Mediterranean, low-fat and low-carbohydrate diets [109,131]. Commercial programs such as Weight Watchers and Jenny Craig achieved at least 2.6% and 4.9% greater loss, respectively, than control at 12 months in a systematic review [132]. Intermittent-fasting regimens, which some participants added to the protocol at their own discretion, produce weight loss comparable to conventional caloric restriction rather than superior to it: alternate-day fasting and daily restriction yielded about 6.0% and 5.3% greater loss, respectively, than a no-intervention control at 12 months in a head-to-head trial, with higher dropout in the fasting arm [111]; adding time-restricted eating to caloric restriction did not significantly improve 12-month loss (−17.6 vs −13.9 lb; −8.0 vs −6.3 kg) [112]; and 16:8 time-restricted eating without a caloric target produced less than 2.2 lb (1 kg) of loss over 12 weeks [113]. A particularly useful comparator is the DIRECT trial, which compared low-carbohydrate, Mediterranean and low-fat diets within a single randomized study of 322 adults and measured weight monthly [109]. Approximate readings from its published curve give cumulative losses of 1.9%, 5.2% and 6.5% of body weight at 4, 8 and 12 weeks on the low-carbohydrate diet, 1.4%, 4.1% and 4.5–4.6% on the Mediterranean diet, and 1.8%, 4.2% and 4.6% on the low-fat diet; the reported 24-month losses were 10.4, 9.7 and 6.4 lb (4.7, 4.4 and 2.9 kg) on the low-carbohydrate, Mediterranean and low-fat diets respectively (roughly 5%, 5% and 3% of starting weight). DIRECT participants were 86% male, averaged 52 years, started at approximately 201 lb, and received dietitian-led group sessions, workplace cafeteria labeling, monthly weighing and motivational calls — a structured, professionally supported program.

Per-period comparisons for the weeks 5–8 and 9–12 extension cohorts, in pounds and as percent of body weight (including the GLP-1 trial trajectories), are presented in Section A.2 (Tables A1 and A2), and cumulative comparisons in Table A1 and Figure A4; the qualifications that follow apply with additional force to them, because those Trilogiii cohorts are smaller and self-selected.

These comparisons must be read with the following qualifications. The drug trials were randomized, placebo-controlled and clinic-measured in participants with obesity, or overweight with a weight-related condition, followed for more than a year; DIRECT was randomized and clinic-measured in a predominantly male workforce with intensive support; the present study was uncontrolled, self-reported, 4 to 12 weeks in duration, and included participants across the weight spectrum (mean starting BMI 32.90 kg/m² among packet participants in the initial period). Its extension cohorts were progressively smaller and self-selected — participants who may have responded well and chose to pay for and continue reporting — and were not linked to their own baseline data, so the packet period losses must not be summed; the cumulative 8- and 12-week figures come instead from totals posted in the study group, which are self-reported, in pounds only, and from self-selected continuing reporters (Section 5.5). The comparison is offered only to situate the magnitude of the observed changes; it is not evidence of equivalence, and the question of whether Trilogiii produces weight loss beyond that attributable to the accompanying dietary protocol, group support and expectancy can only be answered by a controlled trial.

For the named regimens, the four-week losses in the Trilogiii subgroups compare with published studies as follows: 6.4% with other intermittent fasting (mean fasting adherence 82.2%) against 2.6% relative to historical controls over 12 weeks for 16:8 time-restricted eating [133]; 5.7% and 5.8% on low-carbohydrate and Mediterranean diets against approximately 1.9% and 1.4% at 4 weeks in the DIRECT trial [109]; and 5.8% with one meal a day, a pattern for which we found no published weight-loss trial. The controlled OMAD studies identified were conducted at weight-maintenance intake: an 8-week crossover study [134], and an 11-day randomized crossover in 11 lean adults in which reported body-mass changes were −3.1 lb (−1.4 kg) during the one-meal condition and −1.1 lb (−0.5 kg) during the three-meal condition [135]. These are separate studies that differ in population,

intervention, measurement and selection, and the Trilogiii subgroups were self-selected and in some cases small; the comparison therefore shows how large the observed losses were, not that Trilogiii caused them or enhanced the other regimens — a question that a trial randomizing participants on the same regimen to Trilogiii or a control could answer.

A.2 Comparative tables and figures

The tables and figures below set Trilogiii's losses in each 4-week period, and cumulatively, beside the incremental losses in the DIRECT diet trial and the GLP-1 receptor agonist trials. They are presented as exploratory context only, not as tested comparisons, because Trilogiii's extension cohorts (n = 91 and 57 overall; 67 and 47 for percent-of-body-weight) are self-selected subsets that were not linked to their own baseline data, whereas the comparators follow the same participants over time. Table A1 also compares cumulative loss at 8 and 12 weeks, using the totals posted in the study group; this compares the same measure, total loss since starting, although the Trilogiii totals are self-reported. The qualifications in Section A.1 apply throughout.

Table A1. Exploratory context: weight loss within each 4-week period and cumulatively — Trilogiii vs published trials (comparators: same participants over time)

Period	Trilogiii	STEP 1 semaglutide	SURMOUNT-1 tirzepatide	DIRECT low-carb	DIRECT low-fat	DIRECT Mediterranean
Weeks 1–4	12.66 lb (n = 395)	≈4.6 lb	≈5.8 lb	≈3.7 lb	≈3.5 lb	≈2.9 lb
Weeks 5–8	8.09 lb (n = 91)	≈4.1 lb	≈6.9 lb	≈6.9 lb	≈4.9 lb	≈5.3 lb
Weeks 9–12	6.37 lb (n = 57)	≈4.6 lb	≈5.8 lb	≈2.6 lb	≈0.9 lb	≈0.8–1.1 lb
Cumulative, week 8	20.85 lb (study group, n = 101)	≈8.7 lb	≈12.7 lb	≈10.6 lb	≈8.4 lb	≈8.2 lb
Cumulative, week 12	28.25 lb (study group, n = 65)	≈13.3 lb	≈18.5 lb	≈13.2 lb	≈9.3 lb	≈9.0–9.3 lb
Same 57, week 8	23.21 lb (study group)	—	—	—	—	—
Same 57, week 12	29.09 lb (study group)	—	—	—	—	—

Trilogiii period rows are mean loss within each period by all eligible participants in that period's cohort (packet and group-only combined); cohorts differ and these values are not cumulative. Trilogiii cumulative values are mean totals posted in the study group by all weight-loss-phase reporters at each time point and, for the 57 with a total at all three time points, by the same participants (Table 4); comparator cumulative values are the sums of the incremental values above. The weeks 9–12 row (n = 57) and the "Same 57" rows are differently defined groups. DIRECT values are incremental losses by the same participants, read from the published monthly curve in kilograms [109], so they may differ slightly from values implied by the percentage readings in Table A2. STEP 1 and SURMOUNT-1 values are approximate incremental percentages from the published trajectories (for SURMOUNT-1, central estimates of the range spanning the three dose arms) converted to pounds using each trial's mean baseline weight (≈232 lb and ≈231 lb) [1,2]; the drug-trial participants were substantially heavier than DIRECT's (≈201 lb), which inflates their pound values relative to their percentages.

Table A2 presents the comparison for all three 4-week blocks on a percent-of-body-weight basis. For the GLP-1 trials, incremental losses are derived from the approximate cumulative trajectories of STEP 1 (≈2%, 3–4% and 5–6% at weeks 4, 8 and 12) and SURMOUNT-1 (≈2–3%, 5–6% and 7–9%, ranges spanning the three tirzepatide dose arms), and for DIRECT from the percentages in Section A.1; both are figure readings, not reported values. Trilogiii's within-period losses are larger than the comparators' incremental losses in each block, but the Trilogiii cohorts shrink and self-select from one block to the next, whereas the comparators follow the same participants, so the later blocks are not like-for-like.

Table A2. Exploratory context: within-period weight loss by 4-week block, percent of body weight (comparator values approximate) — separate studies

Period	Trilogiii packet cohort (n)	STEP 1 semaglutide (incremental, approx.)	SURMOUNT-1 tirzepatide (incremental, approx.)	DIRECT low-carb	DIRECT low-fat	DIRECT Mediterranean
Weeks 1–4	6.03% (257)	≈2.0%	≈2–3%	≈1.9%	≈1.8%	≈1.4%
Weeks 5–8	4.03% (67)	≈1.8%	≈3%	≈3.4%	≈2.4%	≈2.7%
Weeks 9–12	3.39% (47)	≈2.1%	≈2–3%	≈1.4%	≈0.4%	≈0.4–0.5%

All values are percent of period-starting weight. Trilogiii values come from separate cohorts. Comparator values are incremental losses by the same participants, approximated from published curves [1,2,109] and converted, for every block, from percentage points of original baseline weight to percent of the weight at the start of the block (block loss, % = 100 × [cumulative loss at block end − cumulative loss at block start] ÷ [100 − cumulative loss at block start], with cumulative losses in percentage points, calculated from the underlying cumulative estimates and then rounded); because the curves were read by eye, all comparator values are approximate. STEP 1 values are shown to one decimal from the point readings (2.0%, 3.75% and 5.75% cumulative) that underlie the ranges given in Section A.1; SURMOUNT-1 values are shown to the nearest whole percent, as ranges where the reading is uncertain. The conversion changes the displayed values only for STEP 1 (weeks 9–12, 2.0 to 2.1%) and DIRECT low-carbohydrate (weeks 5–8, 3.3 to 3.4%; weeks 9–12, 1.3 to 1.4%).

Table A3 summarizes the principal published studies used for context in the concurrent fasting and diet comparisons (Sections 6.2, 6.3 and A.1).

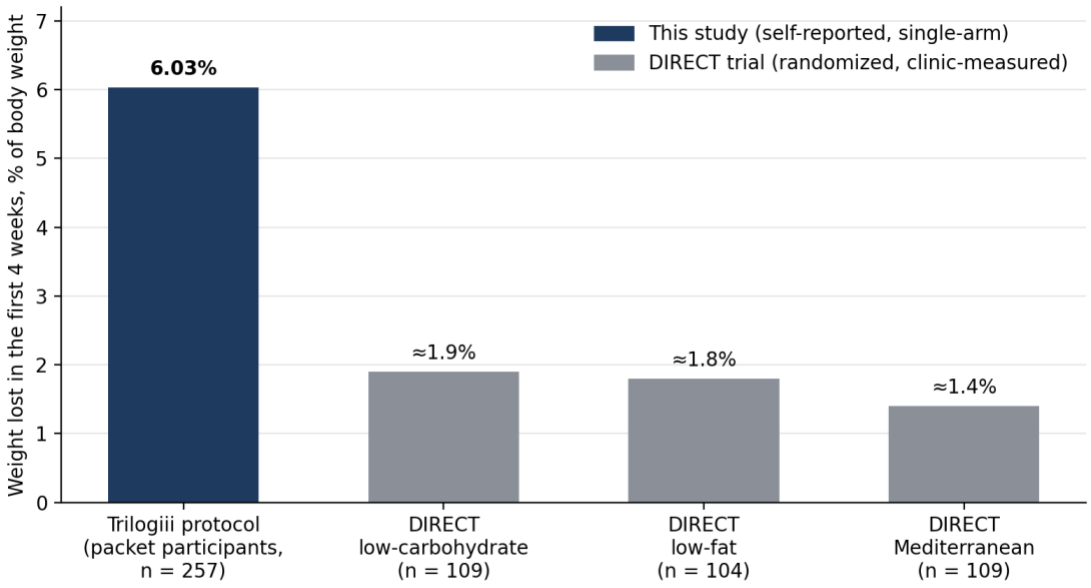
Table A3. Exploratory context: weight loss in Trilogiii regimen subgroups (weeks 1–4) and in published studies of the same regimen — separate studies

Regimen	Trilogiii subgroup, weeks 1–4	Published study	Population	Duration	Reported loss
Other intermittent fasting	12.90 lb; 6.4% (n = 44; fasting adherence 82.2%)	Gabel et al. [133], 16:8 time-restricted eating	Adults with obesity (n = 23)	12 weeks	2.6% vs historical controls
		Lowe et al. [113], TREAT	Adults with overweight or obesity (n = 116)	12 weeks	2.1 lb (0.94 kg); not different from control
One meal a day	11.57 lb; 5.8% (n = 36; fasting adherence 80.8%)	Stote et al. [134]	Normal-weight adults at weight-maintenance intake (n = 15)	8 weeks	Weight held within 4.4 lb (2 kg) of baseline; fat mass reduced
Low-carbohydrate	11.74 lb; 5.7% (n = 51)	Shai et al. [109], DIRECT	Adults, 86% male (n = 322)	4 weeks (curve reading)	≈1.9%
Mediterranean	11.56 lb; 5.8% (n = 14)	Shai et al. [109], DIRECT	Adults, 86% male (n = 322)	4 weeks (curve reading)	≈1.4%

Regimen	Trilogiii subgroup, weeks 1–4	Published study	Population	Duration	Reported loss
Paleo	9.20 lb; 4.9% (n = 5)	Österdahl et al. [136]	Healthy volunteers (n = 14)	3 weeks	5.1 lb (2.3 kg)
		Genoni et al. [137]	Healthy women (paleo arm n = 22)	4 weeks	7.1 lb (3.20 kg), 4.3%
Carnivore	12.39 lb; 5.6% (n = 18)	Lennerz et al. [138]	Self-reported online survey (n = 2,029)	Median 14 months	Median BMI 27.2 to 24.3 kg/m²
Diet chosen by participant	—	Jospe et al. [139]	Adults with overweight or obesity (n = 250)	12 months	8.8 lb (4.0 kg), ≈4.1% (5:2 fasting); 6.2 lb (2.8 kg), ≈3.0% (Mediterranean); 4.0 lb (1.8 kg), ≈1.8% (paleo)

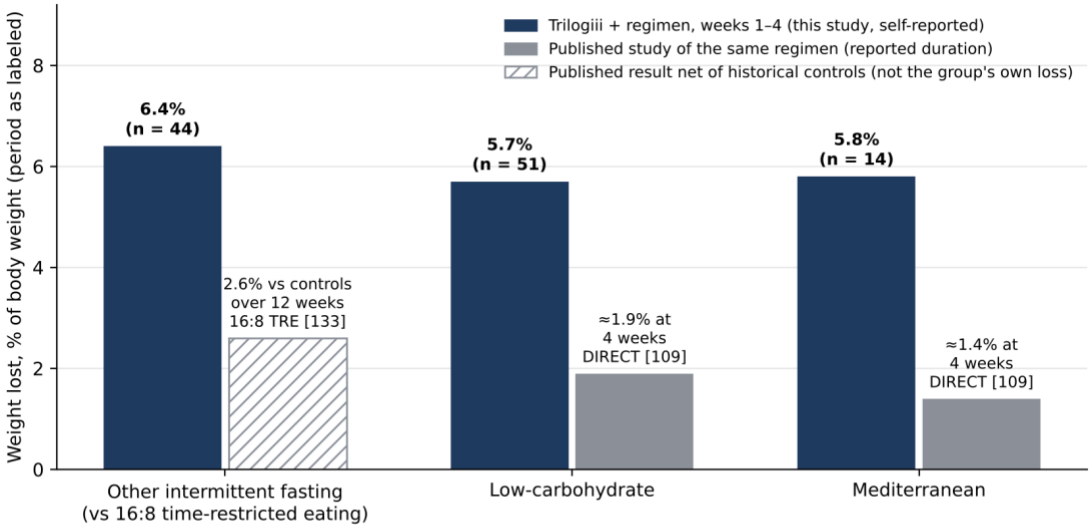
Trilogiii values are self-reported losses among packet participants practicing or following each regimen in weeks 1–4. Published values are as reported, derived from reported kilogram losses and baseline weight (Jospe et al.), or, where noted, approximate readings from published curves. Losses reported in kilograms are shown in pounds (1 kg = 2.2046 lb), with the published kilogram value in parentheses. Studies differ in population, intervention, duration, measurement and selection; values are not directly comparable and do not constitute a head-to-head comparison.

Figures A1–A3 present the same exploratory context graphically for the first four weeks. The within-period extension results are shown in Tables A1 and A2 but not charted, because each comes from a different group, and a line through them would imply a trajectory no participant followed. Figure A4 instead charts cumulative totals posted in the study group (Section 5.5), which include a same-participant series, against the DIRECT diet trial. Pounds are used as a shared reporting unit. The study-group reporters' starting weights were not posted and are unknown; about half of the 4-week reporters (146 of 284) also returned packets, and eligible packet participants averaged 205 lb, similar to DIRECT's approximately 201 lb. DIRECT values are approximate readings from a published graph. The Trilogiii totals are self-reported by continuing participants, whereas DIRECT weights were clinic-measured in a randomized trial with a different population and intervention. The GLP-1 receptor agonist trials are not charted, because their participants were substantially heavier (approximately 231–232 lb), so the same loss in pounds represents a smaller share of their body weight; they are compared in Tables A1 and A2.



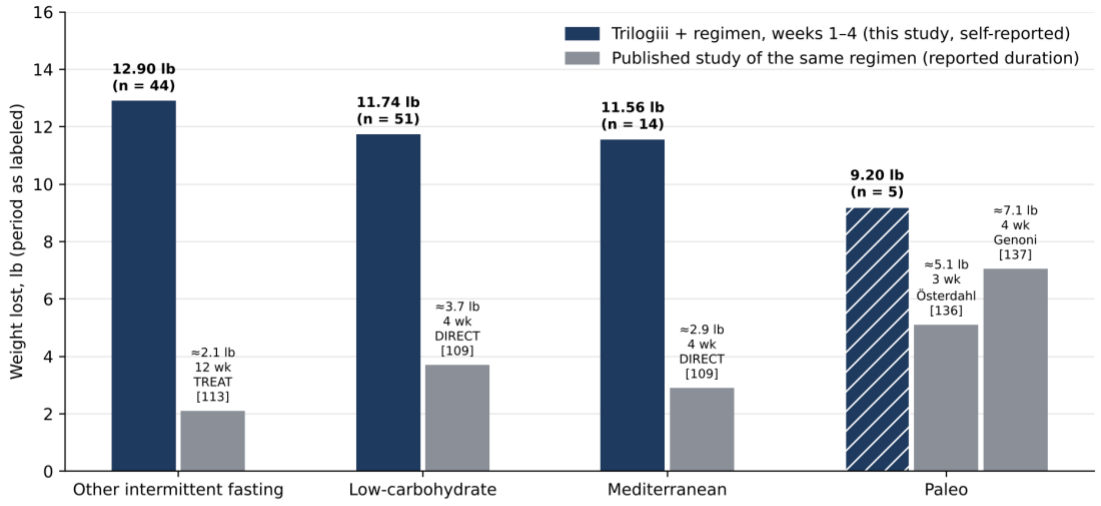
Exploratory context, not a head-to-head comparison. Trilogiii: eligible packet participants, weeks 1–4, self-reported.
DIRECT (Shai et al., 2008): approximate 4-week readings from the published weight curve; participants 86% male, mean age 52, dietitian-supported. Populations, measurement and selection differ.

Figure A1. Exploratory context: weight lost in the first 4 weeks on the Trilogiii protocol (eligible packet participants) and on three diets in the DIRECT trial — separate studies, not a head-to-head comparison.



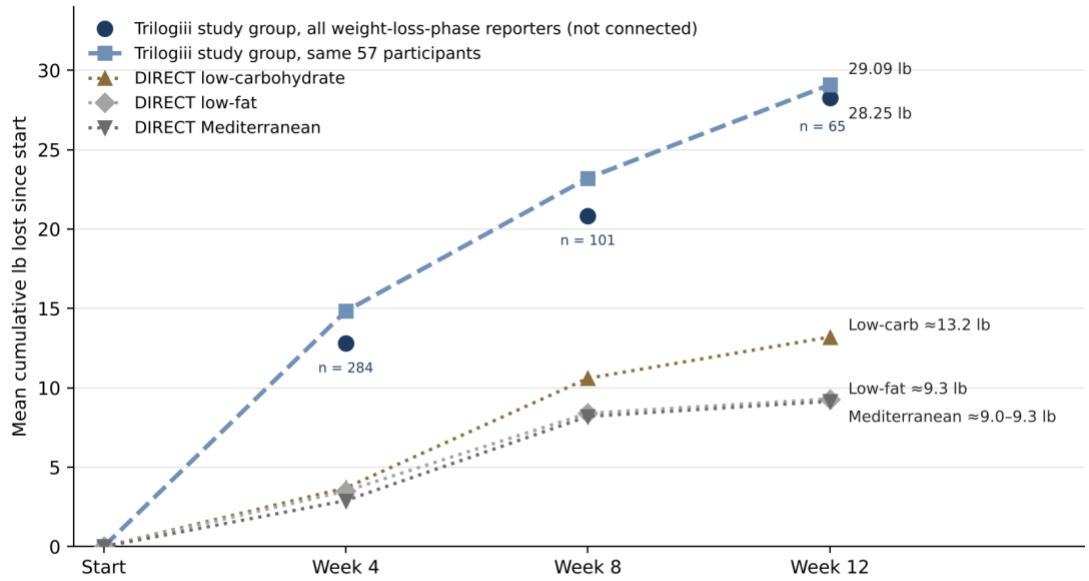
Trilogiii: packet participants practicing or following each regimen in weeks 1–4; self-reported, single-arm; mean fasting adherence 82.2% for other intermittent fasting. Comparators shown for their reported duration, not converted: 16:8 time-restricted eating, 2.6% relative to historical controls over 12 weeks in adults with obesity (Gabel et al., 2018); DIRECT (Shai et al., 2008), approximate 4-week readings from the published curve. Separate studies with different populations and measurement; not a head-to-head comparison.

Figure A2. Exploratory context: weight lost in weeks 1–4 by participants combining Trilogiii with a named regimen, and weight lost over the reported duration of published studies of the same regimen (4 or 12 weeks, as labeled), % of body weight; the hatched bar is a result net of historical controls rather than the group's own loss — separate studies, not a head-to-head comparison.



Trilogiii: packet participants practicing or following each regimen in weeks 1–4; self-reported, single-arm. Comparators shown for their reported duration, in lb with published kg in parentheses: TREAT, 2.1 lb (0.94 kg) over 12 weeks (Lowe 2020); DIRECT, approximate 4-week readings from the published curve (Shai 2008); paleo diets in healthy volunteers, 5.1 lb (2.3 kg) over 3 weeks (Österdahl 2008) and 7.1 lb (3.20 kg) over 4 weeks (Genoni 2016). The 16:8 time-restricted eating result (Gabel 2018) was reported only relative to historical controls and is shown in Figure A2. The hatched paleo bar has n = 5. Pounds lost depend on starting weight, and several comparator populations were lighter than this study's; percent comparisons (Figure A2) are the fairer measure. Separate studies; not a head-to-head comparison.

Figure A3. Exploratory context: as Figure A2, in pounds lost over each study's reported duration (3, 4 or 12 weeks, as labeled), which also allows both paleo studies to be shown (Österdahl et al. reported kilograms only); the 16:8 time-restricted eating result, reported only relative to historical controls, appears in Figure A2 only; the hatched paleo bar marks a group of only five participants; pounds depend on starting weight, so Figure A2 is the fairer measure — separate studies, not a head-to-head comparison.



Separate studies, not a head-to-head comparison. Trilogiii: cumulative totals self-reported in the study group (Table 4); the all-reporters points are unconnected because later time points reflect participants who continued reporting. DIRECT: randomized trial, clinic-measured weights, approximate readings from the published monthly curve [109]; starting weight ≈201 lb.

Figure A4. Exploratory context: mean cumulative weight lost over 12 weeks by Trilogiii study-group reporters (all reporters in the weight-loss phase at each time point, n = 284, 101 and 65, shown unconnected, and the same 57 participants at every time point) and on three diets in the DIRECT trial — separate studies, not a head-to-head comparison.

Appendix B. Formulation and mechanistic rationale

This appendix gives the full formulation rationale summarized in Sections 2 and 3; the qualification in Section 2 — that mechanisms are drawn from published studies of ingredients, not measured in the finished products or in this study's participants — applies throughout.

B.1 Approach 1 — Complete essential nutrition (FS + EN)

B.1.1 The 42 (43) essential nutrients

An essential nutrient is one the body cannot synthesize in sufficient quantity and must obtain from the diet. The Institute of Medicine's Dietary Reference Intakes define requirements for 13 vitamins, choline and some 15 minerals, together with the 9 indispensable amino acids and the two essential fatty acids, linoleic and α-linolenic acid [100,140]. FS and EN, together with the protein and flaxseed in BP, provide all 13 vitamins, choline (recognized as essential in 1998), 14 minerals, the 9 indispensable amino acids (histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, valine), 3 of the conditionally indispensable amino acids (arginine, cysteine, tyrosine), whose synthesis can become insufficient under some physiological conditions [100], and both essential fatty acids — 42 nutrients in the framework used here, which counts the three conditionally indispensable amino acids alongside the strictly essential nutrients. Water, itself an essential nutrient [141], is considered separately and brings the total to 43. Chromium is included on the basis of the US Food and Nutrition Board's 2001 Adequate Intake [100]; its essentiality has since been questioned, and the European Food Safety Authority concluded in 2014 that no requirement or adequate intake could be set [142]. Chloride is supplied by sea salt in FS and by potassium chloride and pink salt in EN.

FS and EN deliberately supply several nutrients in different chemical forms to broaden bioavailability and delivery timing. Vitamin B_{12} is provided as cyanocobalamin in FS and methylcobalamin in EN; vitamin K as phylloquinone (K_1) in FS and menaquinone-7 in EN, the latter having a much longer plasma half-life, more stable serum levels and greater carboxylation of osteocalcin [143]; chromium as chromium chloride in FS and an amino acid chelate in EN; and iron, copper, manganese, selenium and molybdenum as bisglycinate or glycinate chelates in EN (zinc in EN is supplied as zinc citrate). Chelated minerals were chosen because they may be less affected by dietary inhibitors such as phytate; their absorption mechanisms differ by mineral and preparation, and absorption of the intact chelate has not been established generally. Human evidence is strongest for iron, where ferrous bisglycinate was absorbed about 3.5 times as well as ferrous sulfate from a high-phytate whole-maize meal (6.0% vs 1.7%) [144], although its interpretation has been disputed [145], and for zinc, where a bisglycinate chelate was better absorbed than zinc gluconate in a human crossover study [146] (Trilogiii's zinc is supplied as citrate, so this evidence does not apply to it directly); comparable human data for the other chelated minerals are limited. Omega-3 is supplied as α-linolenic acid from flaxseed in BP and as both flaxseed omega-3 and preformed DHA in EN. FS supplies magnesium as magnesium malate, selenium as L-selenomethionine and molybdenum as a glycinate chelate. Daily amounts and forms of every declared vitamin and mineral, and of the protein, fiber and other components, are given in Tables B1 and B2.

Choice of forms. Nutrient forms were selected against several criteria rather than for maximal single-nutrient bioavailability alone: stability in the finished format, interactions among co-formulated nutrients, the time course of absorption and retention, and delivery alongside BIACTIN. Vitamin B_{12} illustrates stability and interaction: reducing agents such as ascorbic acid degrade methylcobalamin fastest and cyanocobalamin slowest, and cyanocobalamin is also less light-sensitive than methylcobalamin [147]. The stable cyanocobalamin is therefore used in the FS shake, which is mixed in water with ascorbic acid, and methylcobalamin in the EN capsule, which remains dry until swallowed. Folate is supplied as folic acid. Common variants of the *MTHFR* gene, such as C677T, do not prevent people from using folic acid [148]; for people homozygous for C677T, riboflavin — the

cofactor of the MTHFR enzyme — lowered plasma homocysteine by about 22% at 1.6 mg/day in a randomized trial [149]. The regimen supplies 1.9–2.0 mg of riboflavin a day (146–154% of the Daily Value, depending on FS flavor), together with vitamin B_{12} (150%), the cofactor for remethylation of homocysteine to methionine; vitamin B_6 (150%), the cofactor for its conversion to cysteine; and choline, which provides the betaine used in a second remethylation route (Table B1). Vitamin K and selenium illustrate retention: menaquinone-7 has a much longer plasma half-life than phylloquinone [143], and selenomethionine is incorporated into body proteins in place of methionine, forming a storage pool with an average whole-body half-life of about 252 days compared with 102 days for selenite [150]. EN supplies a second form, selenium glycinate. Magnesium illustrates format: magnesium oxide supplies the most elemental magnesium per capsule, while the more soluble malate is used in the shake. Calcium is supplied from four sources — calcium lactate, the calcium naturally present in cultured milk protein and whey protein, and calcium carbonate — and potassium as four salts (citrate, phosphate, iodide and chloride), spreading each across forms that differ in solubility and gastrointestinal handling. Finally, because milk proteins and their phosphopeptides bind calcium, zinc and iron and keep them soluble (Appendix B.1.4), the formulation assumes that minerals delivered with BIACTIN need not all be supplied in chelated form; neither this assumption nor whether these combinations improve absorption relative to single forms has been tested.

Table B1. Daily amounts of vitamins and minerals from the Trilogiii regimen (FS + EN + BP)

Nutrient	FS	EN	BP	Daily total	% Daily Value	Form
Vitamin A	450	900	—	1,350 mcg	150%	Retinyl palmitate (FS, EN)
Vitamin C	45	90	—	135 mg	150%	Ascorbic acid (FS, EN)
Vitamin D	20	20	—	40 mcg	200%	Cholecalciferol (FS, EN)
Vitamin E	7.5	15	—	22.5 mg	150%	Tocopheryl acetate (FS); d-α-tocopheryl acetate (EN)
Vitamin K	60	60	—	120 mcg	100%	Phylloquinone, K_1 (FS); menaquinone-7 (EN)
Thiamin (B_1)	0.6	1.2	—	1.8 mg	150%	Not stated
Riboflavin (B_2)	0.7	1.3	—	2 mg	154%	Not stated
Niacin (B_3)	8	8	—	16 mg	100%	Not stated (FS); niacinamide (EN)
Vitamin B_6	0.85	1.7	—	2.55 mg	150%	Pyridoxine HCl (FS, EN)
Folate	340	200	—	540 mcg DFE	135%	Folic acid (FS, EN)
Vitamin B_{12}	1.2	2.4	—	3.6 mcg	150%	Cyanocobalamin (FS); methylcobalamin (EN)
Biotin	15	15	—	30 mcg	100%	Not stated
Pantothenic acid	2.5	2.5	—	5 mg	100%	Calcium pantothenate (FS, EN)
Calcium	1,200	130	312	1,642 mg	126%	Calcium lactate and milk proteins (FS); carbonate (EN); milk proteins (BP)
Iron	1	8	—	9 mg	50%	Not stated (FS); bisglycinate chelate (EN)
Phosphorus	330	200	186	716 mg	57%	Not stated (FS, BP); chelate (EN)
Iodine	70	75	—	145 mcg	97%	Potassium iodide (FS, EN)
Magnesium	245	200	—	445 mg	106%	Malate (FS); oxide (EN)
Zinc	4.3	6	—	10.3 mg	94%	Citrate (FS, EN)
Selenium	20	27.5	—	47.5 mcg	86%	L-selenomethionine (FS); glycinate (EN)

Nutrient	FS	EN	BP	Daily total	% Daily Value	Form
Copper	—	0.45	—	0.45 mg	50%	Bisglycinate chelate (EN)
Manganese	0.8	1.2	—	2 mg	87%	Sulfate (FS); bisglycinate chelate (EN)
Chromium	20	17.5	—	37.5 mcg	107%	Chloride (FS); amino acid chelate (EN)
Molybdenum	10	22.5	—	32.5 mcg	72%	Glycinate chelate (FS, EN)
Sodium	250	85	45	380 mg	17%	Sea salt (FS); pink salt (EN)
Potassium	2,500	470	48	3,018 mg	64%	Citrate, phosphate, iodide (FS); chloride (EN)
Choline	190	In blend	—	≥190 mg	≥35%	Choline bitartrate (FS, EN)
Chloride	130	In blend	—	≥130 mg	≥6%	Sea salt (FS); potassium chloride, pink salt (EN)

Amounts per daily serving as declared on the product Supplement Facts panels (label formulation, not measured content of the finished products). FS values are for the chocolate flavor; the vanilla flavor is identical except riboflavin, 0.6 mg (daily total 1.9 mg, 146%). % Daily Value uses the US Food and Drug Administration adult Daily Values. “In blend”: present in the EN Essential Blend (1,290 mg; choline bitartrate, pink Himalayan salt, flaxseed extract with omega-3, DHA powder, 12 amino acids, lutein, lycopene), whose individual amounts are not declared. The nine indispensable and three conditionally indispensable amino acids are supplied by the 43 g of daily protein (Table B2) and as free amino acids in the EN blend; the essential fatty acids are supplied as α-linolenic acid (740 mg omega-3) and linoleic acid (200 mg omega-6) from flaxseed in BP, with additional flaxseed omega-3 and preformed DHA in the EN blend.

The regimen supplies 1,642 mg of calcium, 445 mg of magnesium and 3,018 mg of potassium a day before nutrients from other foods are counted. These are label amounts, not amounts absorbed: mineral absorption depends on chemical form and on the other nutrients taken at the same time, and forms and combinations were chosen with these interactions in mind (*Choice of forms*, above). Upper intake levels, however, apply to the amounts ingested from the specified sources, not to the amounts absorbed. The magnesium exceeds the 350 mg upper intake level for supplemental magnesium, which is set to avoid gastrointestinal intolerance rather than toxicity [100]; with calcium from other foods added, total calcium intake in adults over 50 could exceed the 2,000 mg upper intake level [151], because the regimen’s 1,642 mg leaves about 360 mg for all other sources; and potassium intake is relevant for people with reduced kidney function or taking medications that affect potassium balance, who were directed to consult their physician before use (Section 4.2). Mineral intake from other foods was not measured, and no laboratory monitoring was performed.

Table B2. Daily protein, fiber, fat and other components (FS + BP + CC)

Component	FS	BP	CC	Daily total
Energy	170 kcal	90 kcal	—	260 kcal
Protein	30 g	13 g	—	43 g
BIACTIN protein blend (cultured milk protein concentrate, whey protein isolate, hydrolyzed bovine collagen)	37 g	15 g	—	52 g
of which collagen peptides	3 g	1 g	—	4 g
Inulin (organic)	4 g	—	—	4 g
Konjac glucomannan	—	3 g	—	3 g
High-amylose resistant starch	—	3 g	—	3 g
Flaxseed (finely milled)	—	3 g	—	3 g

Component	FS	BP	CC	Daily total
Medium-chain triglyceride oil powder	1.5 g	4 g	—	5.5 g
Probiotic blend (nine species)	250 mg; 1×10^9 CFU	—	—	1×10^9 CFU
CC proprietary blend (Appendix B.3)	—	—	2,390 mg	2,390 mg

Label formulation per daily serving (FS chocolate; vanilla: 160 kcal). Blend weights include the non-protein fraction of each ingredient; protein content is given in the Protein row. The CC blend contains berberine HCl, ginger root extract (5% gingerols), L-carnitine, conjugated linoleic acid, *Coleus forskohlii* root extract, green tea leaf extract (50% EGCG), holy basil leaf extract, grains of paradise seed extract, carnosic acid (rosemary extract), milk thistle fruit extract (80% silymarin), pterostilbene, quercetin dihydrate, synephrine (bitter orange fruit), ashwagandha root extract, cayenne pepper extract and yohimbe extract; individual amounts are proprietary, apart from the *p*-synephrine and yohimbine limits stated in Appendix B.3.1. The BIACTIN fermentation cultures are part of the protein manufacturing process and are not declared as a probiotic on the label. Other FS ingredients are natural flavors, stevia leaf extract and sea salt, with cocoa powder in the chocolate flavor; FS is sweetened with stevia leaf extract rather than sugar (2 g total sugars per serving), consistent with the protocol's avoidance of sugar and refined carbohydrate, and BP is unflavored and unsweetened.

The rationale for completeness rather than selective supplementation follows from the nutrient-specific appetite evidence in Section B.4.3. For protein, controlled human feeding shows protein leverage: lowering dietary protein from 15% to 10% of energy increased total energy intake by 12% as participants ate more in a partial attempt to maintain protein intake [4]. For micronutrients, nutrient-specific appetites are well documented in animals [83], and in humans multivitamin supplementation reduced appetite in women during energy restriction [5] and, in a subgroup of women habitually consuming very little calcium, calcium plus vitamin D supplementation was accompanied by greater fat loss and lower spontaneous fat intake [85]. The model therefore proposes that when essential-nutrient requirements go unmet, hunger persists even when calories are sufficient, and that meeting all of them removes a driver of hunger that calories alone do not.

Nutrient adequacy during energy restriction. The case for complete supply is strongest during energy restriction. Even counting fortified foods and supplements, a large share of Americans have usual intakes below the Estimated Average Requirement — about 70% for vitamin D, 60% for vitamin E, 45% for magnesium, 38% for calcium and 34% for vitamin A [152] — and eating less makes adequacy harder: in an analysis of four popular diet plans, none met the Reference Daily Intake for all 27 micronutrients assessed, providing on average 43.5% sufficiency, with biotin, vitamins D and E, chromium, iodine and molybdenum consistently low [6], all of which Trilogiii supplies (Table B1). Appetite suppression with GLP-1 receptor agonists raises the same concern: a 2025 joint advisory from four professional societies lists prevention of micronutrient deficiencies, and adequate protein intake with strength training to preserve lean mass, among the nutritional priorities of GLP-1 therapy [153]. Protein is the best-established dietary lever for lean mass during restriction: in a meta-analysis of 24 randomized trials, higher-protein energy-restricted diets preserved 0.9 lb (0.43 kg) more fat-free mass and produced 1.9 lb (0.87 kg) more fat loss than standard-protein diets [154]. Trilogiii was designed to supply the full essential-nutrient platform and 43 g of protein a day during restriction for these reasons; body composition was not measured in the present study, so its effect on lean mass has not been tested.

B.1.2 BIACTIN — fermented protein as proposed carrier and secretagogue

BIACTIN combines a cultured (fermented) milk protein concentrate, whey protein isolate and hydrolyzed bovine collagen. The fermentation uses proprietary strains of *Lactobacillus delbrueckii* subsp. *bulgaricus* and *Streptococcus thermophilus*. Fermentation of milk proteins by lactic acid bacteria releases bioactive peptides encrypted within casein and whey — sequences that are inert in

the intact protein but active once liberated [155,156]. Three consequences are relevant. First, hydrolysis can accelerate amino acid appearance, depending on the parent protein and preparation; fermentation changes the time course over which milk protein is delivered while overall absorption remains high (Section B.1.4), and fermented dairy presents minerals such as calcium in a low-pH matrix in which they are more soluble. Second, protein digestion products are a potent dietary stimulus for enteroendocrine hormone release: protein hydrolysates and specific peptides act on I-cells and L-cells to release CCK, GLP-1 and PYY, and whey produces greater GLP-1 and CCK release and satiety than casein [7–9]. Fermentation may add to this: in an enteroendocrine cell study, milk fermented with two *Lactobacillus helveticus* strains stimulated GLP-1 secretion 3.4- to 3.8-fold, within the range of enzymatic casein hydrolysates (2.5- to 4.7-fold) and well above whey or whey hydrolysates, while intact casein produced the largest response (5.8-fold) [125]. Those cultures differ from the *L. delbrueckii* subsp. *bulgaricus* and *S. thermophilus* used to ferment BIACTIN, so the study supports the mechanism rather than BIACTIN's own response; the strong effect of intact casein is relevant because BIACTIN's casein remains largely intact (Section B.1.3). In addition, peptides identified in the human jejunum after casein or whey ingestion stimulated CCK and GLP-1 secretion in the same cell type [126]. Third, milk-derived peptides released by fermentation or hydrolysis include DPP-4 inhibitory sequences [80,81], which could extend the action of the incretins released in response to protein. These effects have been shown for milk-protein hydrolysates and peptides in the cited studies; they have not been measured for BIACTIN itself.

Why milk protein. Milk proteins were chosen over plant proteins on three grounds: protein quality, fermentation performance and nutrient delivery. On the digestible indispensable amino acid score (DIAAS), milk protein concentrate (141), whey protein concentrate (133) and whey protein isolate (125) score well above soy protein isolate (98), pea protein concentrate (73) and wheat (54), scored against the reference pattern for older children, adolescents and adults [157]. Milk proteins also contain more essential amino acids than most plant protein isolates (whey 43% and milk 39% of protein, compared with 21–22% for oat, lupin and wheat), and plant proteins are typically lower in lysine and methionine [158]; dairy protein also lacks the mineral-binding phytates and tannins found in many plant proteins. For fermentation, the acid-induced gelation of casein is the basis of cultured dairy products and of the cultured milk protein process. For delivery, casein micelles can carry hydrophobic nutrients: in a human trial in 94 volunteers, vitamin D_3 delivered in fat-free yogurt fortified with reassembled casein micelles was as bioavailable as vitamin D_3 dissolved in milk fat [159]. Fermentation reduces lactose for people with lactose intolerance (Appendix B.1.4); the products contain milk and are not suitable for people with milk allergy.

BIACTIN was also designed to support release of glucagon-like peptide-2 (GLP-2), which is co-secreted with GLP-1 from intestinal L-cells in response to protein and fermentable fiber. GLP-2 is not a satiety hormone — physiological infusion has no effect on appetite or energy intake in humans [160] — but it is the principal intestinotrophic hormone, increasing mucosal surface area, epithelial barrier integrity and nutrient absorptive capacity [17]. In healthy men, GLP-2 infusion raised postprandial triglyceride and free fatty acid concentrations, consistent with enhanced intestinal lipid absorption [18]; in mice, GLP-2 receptor signaling is required for normal intestinal amino acid uptake [19]; an α-lactalbumin hydrolysate stimulated GLP-2 secretion in suckling rats [124]; and, in healthy adults, a protein-enriched meal produced greater GLP-2 secretion than carbohydrate- or fat-enriched meals [161]. GLP-2's inclusion in the BIACTIN rationale is therefore as a support for nutrient absorption (Section 6.5) rather than for satiety.

B.1.3 The BIACTIN protein complex: designed for three-stage satiety by digestion kinetics

A full daily serving of FS and BP delivers 43 g of protein from three sources: 23 g cultured milk protein (18.4 g casein, 4.6 g whey), 16 g whey protein isolate and 4 g hydrolyzed collagen peptides, giving an overall profile of 47.9% whey, 42.8% casein and 9.3% collagen peptides. Excluding collagen, the milk protein is approximately 47:53 casein:whey; the cultured milk protein alone is 80:20. The fermented fraction has a degree of hydrolysis of approximately 1–3% (manufacturer's

specification [20]), meaning the casein and whey remain predominantly intact with a small population of liberated bioactive peptides. The complex was designed so that the digestion kinetics of its components overlap to produce satiety signals across three timeframes. The hour ranges below are proposed from studies of the component proteins; they have not been measured for the finished blend, and because digestion depends on the food matrix, the blend's actual kinetics may differ.

Dietary proteins differ markedly in how quickly they deliver amino acids to the circulation. Whey is soluble at gastric pH, empties rapidly and produces a sharp rise in plasma amino acids peaking at roughly 80–100 minutes, whereas casein clots in the acidic stomach and releases amino acids gradually over six to seven hours — the "fast" and "slow" protein model established by Boirie et al. [162]. Hydrolysis can accelerate amino acid appearance further, depending on the parent protein and preparation. The proportion of the two proteins matters: in a laboratory model combining simulated gastric and intestinal digestion with ex vivo intestinal tissue, mixtures containing 50% or more casein (50:50 and 80:20 casein:whey) formed persistent gastric coagula that slowed gastric emptying and leucine digestion and absorption, whereas whey-rich mixtures emptied faster and delivered leucine sooner and in greater amounts [121]. The casein:whey ratio therefore shapes the timing of essential amino acid delivery, which is the basis for combining the two in BIACTIN; the cultured milk protein itself was not tested in that model.

Rapid phase (0–1 h). Whey protein isolate, the native whey of the fermented fraction, the collagen peptides and the small hydrolyzed milk-peptide fraction are absorbed quickly. Whey produces a greater early rise in GLP-1 and CCK and greater subjective satiety than casein, and lower energy intake at a meal 90 minutes later [7], and gelatin, a collagen-derived protein, reduced subsequent energy intake compared with casein or soy in an acute feeding study [163]; its application to the hydrolyzed collagen peptides in BIACTIN is an extrapolation. Whey is also strongly insulinotropic [164], and the early insulin response may contribute to short-term satiety.

Intermediate phase (1–3 h). Continuing digestion of whey and of the partially processed milk proteins is expected to sustain enteroendocrine stimulation — GLP-1, PYY and CCK — and to suppress the hunger hormone ghrelin, which protein lowers more effectively than carbohydrate [165]. Protein-induced thermogenesis is also associated with satiety [166].

Sustained phase (3 h onward). The 18.4 g casein fraction is expected to digest more gradually than the whey and peptide fractions, which would maintain plasma amino acids and enteroendocrine signaling after the whey has been cleared, and, with adequate total protein, is intended to support lean mass retention during energy restriction [154]. The most direct evidence for combining the two comes from a study of 18 healthy adults in which 12 ingested isotope-labeled whey and casein together in a mixed meal: amino acid appearance from the two proteins was similar over the first two hours, but by 220–260 minutes appearance from whey had slowed while appearance from casein was sustained, and casein's contribution to muscle protein retention was better maintained [167]. The fermentation leaves this casein largely unhydrolyzed (degree of hydrolysis 1–3%) and is held at pH 4.5–5.5 [20], at or near the isoelectric point of casein. Fermentation-induced acidification is expected to alter casein mineralization and gastric coagulation, but the specified pH range does not by itself establish the finished ingredient's micellar structure or digestion rate, which have not been characterized (Section B.1.4). The design hypothesis is that this casein digests faster than native micellar casein yet more slowly than whey, placing the sustained phase of BIACTIN between the profile of whey and the seven-hour profile of intact casein.

The literature on whether "slow" casein yields measurably longer satiety than "fast" whey is mixed: several acute studies find whey more satiating than casein over 3–4 hours, and a review concluded that whey is more satiating in the short term and casein in the longer term [168]. Human feeding studies show that co-ingested whey and casein provide different time courses of amino acid appearance [167], while fermentation and dairy-matrix structure can modify the postprandial appearance of individual amino acids [120,169,170]. These findings provide a mechanistic rationale for combining whey, casein and cultured milk protein in the formulation. The rationale for BIACTIN

is therefore not that casein outperforms whey, but that combining both — with peptide fractions added — is intended to avoid the trough that follows a single fast protein, so that satiety signaling may be continuous rather than interrupted. The satiety findings in Section 5 reflect the combined system and cannot attribute effects to individual phases; hourly satiety profiling would be required to test the three-stage model directly.

B.1.4 Fermented protein: nutrient protection, delivery and bioavailability

Lactic-acid fermentation of milk protein may confer several advantages over unfermented protein that are directly relevant to a nutrient-delivery formulation.

Mineral solubility and absorption. Fermentation lowers pH through lactic acid production, which converts colloidal calcium phosphate in milk to soluble ionic calcium and improves the solubility of magnesium, zinc and iron; in an in vitro digestion study of iron-fortified dairy products, fermentation and acidification increased iron and zinc dialyzability, whereas calcium dialyzability changed little [171]; dialyzability is a laboratory measure, not demonstrated human absorption. Fermentation also releases casein phosphopeptides (CPPs) — phosphoserine-rich fragments of casein that bind calcium, zinc and iron, keep them soluble in the alkaline environment of the small intestine where they would otherwise precipitate, and enhance their passive absorption in animal and in vitro models [172,173], although human trials of isolated CPPs have given inconsistent results. The most direct human evidence comes from a stable-isotope study in women eating a phytate-rich plant-based diet: adding milk raised zinc absorption by about 50%, and adding yogurt by about 68%, but neither improved iron absorption [12] — so the in vitro gains in iron dialyzability described above did not translate into greater iron uptake in that human study. A second isotope study in young women found that zinc absorption from high-phytate rice was higher when the rice was eaten with milk than with water (20.7% vs 12.8%) [13]; like the first, it reflects the dairy matrix rather than an effect of fermentation specifically. In a human intestinal-intubation study, calcium disappeared from the lumen earlier after fermented milk than after milk (67% vs 44% by the duodenum), although overall calcium absorption was not shown to be greater [10]. Laboratory and animal work indicates that milk-derived peptides can also act as mineral carriers, and that the effect depends on which peptides are present: selected peptide fractions isolated from simulated digests of milk increased iron uptake by human intestinal (Caco-2) cells, whereas other fractions did not [15], although in a follow-up study the fractions more than doubled iron dialyzability from water but generally did not increase it when added to meals, and did not alter expression of divalent metal transporter 1 (DMT-1) in Caco-2 cells [174]; and a calcium chelate prepared from whey peptides generated by *Lactobacillus helveticus* fermentation released calcium gradually during simulated digestion and, in rats fed a low-calcium diet, improved calcium absorption and bone measures relative to inorganic calcium phosphate [16]. These findings concern milk and yogurt consumed with meals and specific peptide preparations. They provide a rationale for investigating mineral delivery from the cultured milk protein complex; absorption of individual minerals from the EN and FS products was not measured in the present study.

B-vitamin synthesis. Lactic acid bacteria synthesize several B vitamins during fermentation — folate, riboflavin and, for some species, vitamin B_{12} — so that fermented milk can contain more of these vitamins than the starting milk [14]; whether BIACTIN's fermentation does so was not measured.

Altered protein digestion kinetics and lactose reduction. Independently of proteolysis, acidification during fermentation changes casein mineralization and aggregation; subsequent gastric breakdown depends on processing and the food matrix [175]. In human feeding studies, fermentation and the dairy matrix modified both the size and the timing of amino acid appearance: in older adults, yogurt produced higher peak essential amino acid concentrations than milk [169]; in young men, seven free amino acids reached higher postprandial concentrations after yogurt than after chemically acidified milk [170]; and, although studies differ on whether peaks occur earlier or later, in a pooled analysis of younger and older men, the serum kinetics of lysine, phenylalanine, tyrosine and threonine were delayed by 22–45 minutes after yogurt compared with milk [120]. Intestinal intubation studies in

healthy adults show the same pattern at the level of the gut: in six volunteers, fermented milk emptied from the stomach more slowly than milk (half-time 60 vs 35 minutes), yet about 90% of the protein from either drink had been absorbed by the terminal ileum [10]; and in 16 volunteers given ^{15}N-labeled milk or yogurt, delivery of yogurt protein from the stomach was again slower, while absorption in the upper jejunum did not differ significantly [11]. Fermentation therefore alters the digestion of milk proteins and the peptides released during digestion, changing the time course of protein delivery, while overall absorption remains high from both fermented and unfermented milk. BIACTIN's fermentation is held at pH 4.5–5.5; acidification in this range alters casein mineralization, but the finished ingredient's micellar structure and digestion kinetics have not been characterized, so where it falls relative to milk and yogurt is a design hypothesis rather than a measured property. Bacterial β-galactosidase reduces lactose content, improving tolerance in lactose-sensitive individuals; improved lactose digestion from live yogurt cultures is an authorized EU health claim, based on a favorable EFSA opinion [155,176].

Release of bioactive peptides. Beyond the DPP-4-inhibitory peptides described above, milk-protein digestion and fermentation can liberate peptides with antioxidant and ACE-inhibitory activity in vitro that are inert within the intact protein [155,156]. The antioxidant peptides are proposed to protect labile nutrients — polyunsaturated fatty acids, vitamins A and E — from oxidative degradation within the product matrix and the gut lumen; the antioxidant activity of such peptides has been shown in vitro, but protection of these nutrients has not been tested.

Microbiome and inflammation. A 17-week randomized study found that a diet high in fermented foods increased gut microbial diversity and reduced markers of systemic inflammation, effects not seen with a high-fiber diet alone [177]. Regular fermented-dairy consumption is also associated with lower cardiometabolic risk in cohort studies [155].

Taken together, the cultured milk protein is intended to act as a delivery matrix, and the proposed mechanisms have related experimental support; together with GLP-2 (Section B.1.2) and the biotic component (Section B.2), these elements form the integrated nutrient-delivery hypothesis set out in Section 6.5. BIACTIN's contribution to satiety operates in parallel, through the staged digestion kinetics described in Section B.1.3 and the enteroendocrine response to protein digestion products (Section B.1.2). Whether these mechanisms increase absorption of individual nutrients from Trilogiii itself has not been measured.

B.2 Approach 2 — Biotics for gut health, hormone release and absorption (FS + BP)

The gut microbiota is now recognized as an active participant in energy balance. Germ-free mice colonized with microbiota from donors with obesity gain more fat than those receiving microbiota from lean donors [178], and this transfers across species: microbiota from human twins with obesity induces greater adiposity in recipient mice than microbiota from their lean co-twins [179]. Trilogiii includes probiotics — live microorganisms which, when administered in adequate amounts, confer a health benefit on the host [180] — and prebiotics, substrates selectively utilized by host microorganisms conferring a health benefit [181], to support a microbial community favorable to weight management and, critically, to the absorption of the nutrients delivered in Approach 1.

Trilogiii FS provides live bacteria from two sources. The BIACTIN fermentation contributes *L. delbrueckii* subsp. *bulgaricus* and *S. thermophilus* at 15×10^9 CFU each per serving according to the manufacturer's specification [20] (viable counts in the finished product were not independently assayed); these fermentation cultures deliver documented benefits, when present as live cultures in yogurt, including improved lactose digestion in people with lactose maldigestion [176], and contribute bioactive peptides during fermentation, and can survive transit through the human gastrointestinal tract [182]. A separate nine-species probiotic blend (*Lacticaseibacillus rhamnosus*, *Lactiplantibacillus plantarum*, *Lacticaseibacillus casei*, *Bifidobacterium lactis*, *B. bifidum*, *B. longum*, *Lactobacillus helveticus*, *Ligilactobacillus salivarius*, *Lactobacillus acidophilus*),

standardized to contain 2% β-glucan as a prebiotic carrier, contributes 1×10^9 CFU per serving (*L. plantarum* 4×10^8; *L. rhamnosus*, *L. casei*, *B. lactis* and *L. acidophilus* 1×10^8 each; *B. bifidum*, *B. longum*, *L. helveticus* and *L. salivarius* 5×10^7 each) and was selected specifically to support gut barrier integrity and nutrient absorption. Strain designations were not specified by the supplier. Several of these species have human evidence in weight management from specific strains; because probiotic effects are strain-specific, these findings support biological plausibility rather than establish an effect of the strains used here: *L. rhamnosus* CGMCC1.3724 at 3.2×10^8 CFU/day combined with dietary restriction produced greater weight and fat loss than placebo in women over 24 weeks, although not in the whole sample [183], and the same strain improved satiety efficiency and reduced hunger and food craving in women during a weight-reducing program [184]; *B. animalis* subsp. *lactis* 420 reduced body fat mass over six months in per-protocol analysis when combined with polydextrose fiber, but not significantly on its own in the pairwise per-protocol comparison (a factorial analysis attributed a significant effect to B420), and between-group differences in body fat mass were not significant in the primary intention-to-treat analysis [185]; and in a meta-analysis of randomized trials in adults with overweight or obesity, probiotic supplementation produced modest reductions in body weight, body mass index and fat percentage [186].

Trilogiii's biotic component therefore follows an intended synbiotic approach, combining live cultures with fermentable substrates, with the intended complementary functions of supporting the resident microbiota and nutrient handling. The ISAPP consensus defines a synbiotic as a mixture of live microorganisms and substrates selectively utilized by host microorganisms that confers a health benefit; for the complementary type, in which the substrates support the resident microbiota broadly rather than being selected for the co-administered strains, each component must meet the respective probiotic and prebiotic criteria and the combination must show a benefit [21]. Whether this formulation meets those criteria remains to be established; the design intent is a synbiotic rather than a high-dose probiotic. This choice reflects the view that probiotic effects depend on strain and may depend on the availability of fermentable substrate, not only on CFU count. In the two trials cited above, the effective *L. rhamnosus* dose was 3.2×10^8 CFU/day formulated with oligofructose and inulin [183], whereas *B. lactis* 420 at 10^{10} CFU/day produced no significant change in fat mass on its own but did so, in per-protocol analysis, when combined with polydextrose fiber [185]. The per-species levels in Trilogiii — including 1×10^8 CFU of *L. rhamnosus*, below the dose used in [183] — were accordingly chosen to act in combination with the prebiotic substrates supplied in FS and BP rather than as standalone doses; the contribution of the probiotic fraction on its own was not tested in this study. The prebiotic fraction supplies the substrate from which SCFAs are generated, and in published studies SCFAs stimulate GLP-1 and PYY release [22]; the resident microbiota, supplemented by the live cultures, supplies the fermentative capacity. Providing both is intended to allow a moderate probiotic dose to contribute alongside the substrate; whether this outperforms a larger dose without substrate has not been tested.

FS and BP together supply four prebiotic substrates with complementary fermentation profiles: 4 g of inulin in FS and 3 g each of resistant starch, flaxseed and glucomannan in BP (Table B2). Inulin-type fructans raise colonic short-chain fatty acid (SCFA) production, and SCFAs stimulate PYY and GLP-1 release [22]; oligofructose reduced energy intake and body weight in adults with overweight over 12 weeks [187]. In a randomized, placebo-controlled trial, 16 g/day of a fermentable prebiotic increased postprandial GLP-1 and PYY and reduced hunger within two weeks [26], and a systematic review of 26 randomized trials found that prebiotic supplementation increased self-reported satiety in healthy adults, although effects on energy intake and body weight were inconsistent [27]. These effects appear dose-dependent — in a crossover trial, 16 g/day of oligofructose increased morning PYY relative to 10 g/day and placebo and reduced energy intake over time, although the energy-intake difference from placebo was not significant [188] — so Trilogiii's 4 g of inulin is intended to act together with its three other fiber-containing prebiotic ingredients rather than alone. High-amylose resistant starch improved insulin sensitivity over four weeks [189] and reduced energy intake acutely [190] in humans; human gut-hormone findings are mixed: increases in GLP-1 and

PYY have been shown mainly in rodents [190], although 40 g/day of high-amylose resistant starch for 12 weeks increased postprandial GLP-1 in adults with type 2 diabetes [191], a far larger amount than the 3 g of resistant-starch ingredient supplied here. Flaxseed fiber (mucilage) extract increased satiety and reduced energy intake at the next meal in acute human trials [192]; BP supplies whole milled flaxseed, which also provides α-linolenic acid. Konjac glucomannan (Section B.4.1) also serves as a fermentable substrate. Medium-chain triglycerides are rapidly oxidized to ketones, increase postprandial energy expenditure relative to long-chain fats, and have reduced subsequent food intake in short-term studies [193–195], generally at larger doses than the 5.5 g of MCT oil powder supplied here; elevated ketones may additionally suppress ghrelin and hunger [196].

Three mechanisms link these substrates to the rest of the system. First, microbial fermentation produces acetate, propionate and butyrate, which activate free fatty acid receptors 2 and 3 on enteroendocrine L-cells and stimulate GLP-1 and PYY release; targeted delivery of propionate to the colon in humans acutely increased PYY and GLP-1, reduced energy intake, and over 24 weeks reduced weight gain and abdominal adiposity [22]. This provides a direct link to the hormonal satiety target in Section B.4.2. (CCK is released from duodenal I-cells in response to protein and fat rather than SCFA, and would be expected to respond to the protein in BIACTIN.) Second, SCFAs lower luminal pH and enhance mineral solubility and epithelial transport: inulin-type fructan supplementation increased fractional calcium absorption (by 8.5 percentage points at 8 weeks and 5.9 at one year) and bone mineral content and density in adolescents over one year [23], and prebiotic fiber has improved mineral absorption, with effects more prominent in animal models than in human studies [197]; in postmenopausal women, oligofructose-enriched inulin increased stable-isotope-measured calcium and magnesium absorption [24], and the probiotic strain *Lactiplantibacillus plantarum* 299v increased non-heme iron absorption [127,128]. The effect extends across prebiotic classes: galacto-oligosaccharides at 5 g/day increased calcium absorption in girls aged 10–13 in a double-blind crossover trial, alongside an increase in fecal bifidobacteria [198]. For probiotics, a systematic review of 14 clinical trials reported that specific strains improved the status of vitamin B_{12}, calcium, folate, iron and zinc in healthy people, although results varied by strain, dose and duration [28]. Third, in animal models, metabolic endotoxemia (raised circulating bacterial lipopolysaccharide) drives low-grade inflammation and insulin resistance [25]; the biotic component is intended to support intestinal barrier integrity, one proposed route for limiting it. At the clinical level, meta-analyses indicate that probiotic supplementation produces modest but significant reductions in body weight, BMI and body-fat percentage or fat mass in adults with overweight, with effects varying by strain and duration and no consistent dose–response [186,199]. The gut component is not positioned as a standalone weight-loss agent but as a foundation intended to support the other approaches.

B.3 Approach 3 — Responsible thermogenesis: metabolic stimulation with cellular protection (CC)

B.3.1 Thermogenic agents

Weight loss depends on both sides of the energy balance equation, and energy expenditure falls during caloric restriction as the body adapts [29]. Dietary thermogenic agents may partially offset this by increasing sympathetic drive and uncoupling-protein activity in brown and beige adipose tissue, raising resting energy expenditure and fat oxidation [30]. The CC formula combines agents acting on complementary pathways. Capsaicin from cayenne is a TRPV1 agonist that increases sympathetic outflow and diet-induced thermogenesis [31]; 6-gingerol from ginger also acts on TRPV1, and ginger increased the thermic effect of food and reduced hunger in men with overweight [32]. Grains of paradise extract (6-paradol) activates brown adipose tissue and increased whole-body energy expenditure in men with detectable BAT [33]. Forskolin activates adenylyl cyclase, raising cAMP and lipolysis, and reduced body fat percentage in a 12-week placebo-controlled trial in men with overweight [34]. Berberine activates AMP-activated protein kinase in experimental models [200] and improves insulin sensitivity and lipid profile in human trials [35,36]; L-carnitine supports

fatty-acid transport into mitochondria and produced modest weight reduction in meta-analysis [37]; and conjugated linoleic acid produces small reductions in fat mass [38].

p-Synephrine is supplied as a standardized, patented *Citrus aurantium* extract (Advantra Z®, Nutratech Inc.) at a level providing less than 5 mg of *p*-synephrine per daily dose (manufacturer's formulation records; data on file). This is well below the doses, typically 10–53 mg a day, used in most clinical studies of the extract, including those reviewed by researchers who have served as consultants to its manufacturer [39], and well below the doses used in the trials pooled in an independent 18-article meta-analysis, which found a rise in blood pressure with prolonged use and no significant weight loss [40]. As with yohimbe (below), the inclusion level reflects the formula's low-stimulant design rather than reliance on synephrine for thermogenic effect; the branded extract carries its own published safety data at doses well above that used here [39]. Yohimbe bark extract, specified by the manufacturer at 2% yohimbine alkaloids, is included at a low level providing less than 0.5 mg of yohimbine per daily dose — less than 4% of the 15–30 mg/day of yohimbine used therapeutically [41,42] and of the 20 mg/day used in the one body-composition trial [43]. At this yohimbine content no pharmacological contribution is expected, and the extract is not relied upon for the formula's thermogenic effect; its low inclusion level is a deliberate design choice. Trilogiii is formulated for and sold only in the United States, where yohimbe is permitted in dietary supplements; EFSA was unable to establish its safety as a food ingredient [44], and it is restricted in several other jurisdictions.

The CC formula as a whole was designed around synergy rather than single-agent dosing: its thermogenic agents act through complementary pathways (TRPV1-mediated sympathetic activation, cAMP and AMPK), and its cellular-protection agents activate Nrf2 through partially distinct mechanisms (Section B.3.2), on the same principle by which low-dose combinations of Nrf2 activators produce more than additive induction [57]. This design approach — combining low doses of several components so that the combination achieves its effect "without the undesirable side-effects associated with the individual components" — was described by one of the authors in a patented composition [129] that also underlies references [56,57], and is applied here, using components that act through different mechanisms, to both the thermogenic and the cytoprotective components of CC. The synergy described here is the design intent: the combination work in [57] supports the principle, but whether CC's specific ingredients and doses produce more than additive thermogenic or Nrf2 activity has not yet been measured, and the principle applies to the components included at active levels rather than to the low-level yohimbe and *p*-synephrine inclusions described above.

Green tea extract (50% EGCG) is included for its Nrf2-activating catechins rather than for caffeine-mediated thermogenesis: total caffeine in the CC formula is 2 mg per serving. (Evidence on green tea's thermogenic effect is mixed: one respiratory-chamber study found a catechin–caffeine extract more thermogenic than the same amount of caffeine alone [201], whereas in a meta-analysis caffeine alone raised energy expenditure about as much as catechin–caffeine mixtures, although only the mixtures significantly increased fat oxidation [202].)

B.3.2 Cellular protection: induction of the endogenous antioxidant system

Thermogenic activation can involve increased mitochondrial reactive oxygen species (ROS) signaling. Increased mitochondrial respiration can increase ROS formation, and thermogenically activated brown adipose tissue shifts toward a pro-oxidant redox state [203]; in mice, acute activation of brown-fat thermogenesis is accompanied by a marked rise in mitochondrial ROS, which function as part of thermogenic signaling [45]. In healthy lean men, a single high-fat meal raised skeletal-muscle mitochondrial hydrogen peroxide emission more than twofold and shifted cellular redox state toward oxidation within 4 hours, and the changes persisted over a 5-day high-fat diet [46]. Long-term moderate caloric restriction, by contrast, lowers markers of oxidative damage [204]; the rationale for CC's cellular-protection component therefore concerns the additional oxidative load of stimulated energy expenditure and fat oxidation, not weight loss itself. Endogenous antioxidant

capacity declines with age as Nrf2 signaling becomes less responsive [205], and Nrf2 is further downregulated in insulin-resistant tissue in animal models [206]. High-dose supplementation with exogenous antioxidants has been disappointing: direct antioxidants are consumed as they neutralize radicals unless regenerated by other antioxidants, and large trials of high-dose vitamin E and β-carotene have shown no benefit and, in some cases, harm [207]. Scavenging can also blunt the body's adaptive responses: in healthy men, high-dose vitamins C and E abolished the exercise-induced increase in insulin sensitivity and the induction of superoxide dismutase and glutathione peroxidase [47]; in a randomized trial of 54 adults they blunted training-induced increases in muscle mitochondrial proteins [208]; and in mice, depleting mitochondrial reactive oxygen species impaired brown-fat thermogenesis itself [45]. The Trilogiii regimen's vitamin C (135 mg) and vitamin E (22.5 mg) are nutritional amounts, far below the 1,000 mg of vitamin C and the 235 mg or 400 IU of vitamin E used in those trials. The alternative is to induce the body's own catalytic antioxidant enzymes — superoxide dismutase, catalase and glutathione peroxidase, which remove reactive oxygen species catalytically rather than being consumed — and cytoprotective enzymes such as heme oxygenase-1. This is the body's own adaptive route: in mice, Nrf2 is required for the exercise-induced increase in antioxidant enzymes and mitochondrial biogenesis [209], and in humans, a sulforaphane-containing broccoli-sprout preparation, a dietary Nrf2 activator, dose-dependently increased expression of genes encoding phase II enzymes, including heme oxygenase-1 and NAD(P)H quinone oxidoreductase-1, in nasal lavage cells [210].

Nelson, Bose, Grunwald, Myhill (an author of the present study) and McCord reported that a combination of phytochemicals at low doses, in an uncontrolled before-and-after study, increased erythrocyte SOD by 30% and catalase by 54% over 120 days, and reduced plasma lipid peroxidation (TBARS) by 40% within 30 days, in healthy adults [56], and subsequent work in cultured cells showed that the components act synergistically to induce heme oxygenase-1, an Nrf2 target gene [57]. A later randomized, placebo-controlled trial of the same formulation in 38 trained runners found no overall improvement in resting TBARS, SOD or glutathione peroxidase relative to placebo, although an exploratory subgroup aged 35 or older showed a greater increase in SOD [211]; trained athletes' already elevated antioxidant capacity may limit measurable change. The CC formula is designed around this same synergistic-induction principle. Under basal conditions Nrf2 is held in the cytoplasm by Keap1 and continuously degraded; electrophilic or oxidative stimuli modify Keap1 cysteine residues, freeing Nrf2 to translocate to the nucleus and induce cytoprotective genes including heme oxygenase-1, NAD(P)H quinone oxidoreductase-1, glutathione-synthesis enzymes and superoxide dismutase [48]. Carnosic acid from rosemary is a Keap1-reactive electrophile that activates Nrf2 in experimental models [49]; silymarin from milk thistle [55], withaferin A from ashwagandha [50], pterostilbene [51], quercetin [52] and EGCG [53] each activate the Keap1–Nrf2–ARE pathway in cell or animal studies, through partially distinct mechanisms; holy basil, a source of eugenol and ursolic acid, has shown antioxidant and cytoprotective effects in animal studies [54]; and several of these botanicals are also direct inhibitors of NF-κB, the transcription factor that drives the low-grade inflammation associated with adiposity. Importantly, Nrf2 is not only a defensive factor but a participant in energy metabolism: β_3-adrenergic induction of UCP1 and oxygen consumption in mice with diet-induced obesity is partly Nrf2-dependent [203], and pharmacological Nrf2 induction has been reported to ameliorate obesity-associated insulin resistance and hepatic steatosis in mouse models [212]. The preclinical literature contains conflicting findings, with both Nrf2 activation and global Nrf2 knockout reported to protect against diet-induced obesity [213,214]. The rationale for Trilogiii is not that Nrf2 activation drives weight loss per se, but that it is intended to allow thermogenic stimulation to be delivered while supporting redox balance. Oxidative-stress markers were not measured in the present study; their measurement is a priority for future work.

B.3.3 NAD⁺ support and DPP-4 inhibition

NAD^+ declines with age and metabolic stress, limiting sirtuin and PARP activity essential for mitochondrial function and DNA repair [215]. Quercetin and related flavonoids inhibit CD38, the principal NAD^+-consuming enzyme, in preclinical models [58], and pterostilbene has been reported

to activate SIRT1 in preclinical studies [59]; the formula is therefore positioned as supporting NAD^+ availability rather than as a demonstrated NAD^+ elevator in humans. Several CC ingredients also have published in vitro DPP-4 inhibitory activity, notably berberine [60] and dietary flavonoids of the class that includes quercetin [61]; in the formulation rationale they complement the milk-derived peptide classes represented in BIACTIN and could prolong active GLP-1, although this has not been measured in humans taking Trilogiii. Circulating active GLP-1 was not measured in the present study.

B.3.4 Caffeine and polyphenol restriction

The one-hour separation from caffeinated beverages (Section 2.5) is based primarily on non-heme iron absorption. Coffee, black tea, herb teas and cocoa are potent inhibitors of non-heme iron absorption, reducing uptake from a meal by up to 94% in a dose-dependent manner (79–94% for black tea); the effect is attributable to their polyphenols and tannins, which bind iron in the gut lumen [62]. A controlled stable-isotope trial showed that simply delaying tea by one hour after an iron-containing meal substantially attenuates this inhibition, which is the basis for the one-hour interval used here [63]. Polyphenols also bind zinc and other divalent minerals; in adults, a higher-polyphenol meal reduced fractional zinc absorption by about 20% when phytate was also present [64]. Caffeine itself produces a small, transient increase in urinary calcium and magnesium excretion in the hours after ingestion [65]; its net effect on calcium balance is very small and can be offset by 1–2 tablespoons of milk [216]. Habitual coffee consumption is also associated with lower circulating folate, riboflavin and vitamin B_6 in a population study, possibly through increased urinary excretion (vitamin B_{12} was not significantly affected) [66], and tea and coffee contain antithiamine factors that inactivate vitamin B_1 in vitro [67]. Higher caffeine intake has also been associated with slightly lower serum 25-hydroxyvitamin D in cross-sectional data (adjusted odds ratio for deficiency 1.48 at the highest vs lowest caffeine intake in NHANES), though the mechanism is unclear (the authors cite in vitro reduction of vitamin D receptor expression) [217]. The one-hour interval is supported most directly by this evidence concerning tea and non-heme iron absorption; whether it also improves the absorption or retention of zinc, calcium, magnesium or B vitamins in this regimen has not been tested. The restriction targets coffee and tea, the largest habitual dietary sources of these polyphenols; the formula's own polyphenol-containing ingredients — cocoa in the chocolate FS, and green tea extract and quercetin in CC — are present in smaller, fixed amounts, and whether they affect mineral absorption from the regimen was not assessed.

The second reason concerns the CC formula. Several of its components — capsaicin and 6-paradol, and the low-level *p*-synephrine and yohimbine — act through the sympathetic nervous system, and caffeine is itself a sympathomimetic that potentiates these effects: a product combining *p*-synephrine (21 mg) with caffeine (304 mg) raised diastolic blood pressure [68], and the French food safety agency has advised against combining them (as summarized in [40]); caffeine itself contributes substantially to the thermogenic effect of green tea [202]. The CC formula was deliberately designed with negligible caffeine (2 mg per serving) so that its thermogenic dose is defined by the botanicals alone. A cup of coffee adds 80–100 mg of caffeine; the one-hour separation discourages taking the two together, although caffeine taken later remains active for several hours, so the separation limits rather than eliminates combined exposure.

B.4 Three satiety targets

Section 3 summarizes the three satiety targets and how they are intended to work together (Section 3.4); this section gives the supporting evidence for each.

B.4.1 Mechanosensory satiety — konjac glucomannan

The earliest satiety signal after a meal is mechanical: stretch of the stomach wall activates vagal mechanoreceptors that project to the nucleus of the solitary tract and onward to hypothalamic satiety centers, producing the sensation of fullness well before nutrients are absorbed [70]. Konjac

glucomannan, a highly viscous soluble fiber, exploits this pathway. It absorbs many times its weight in water, expands in the stomach, increases gastric content viscosity, delays gastric emptying and slows nutrient absorption, prolonging the mechanical and post-absorptive signals of fullness [71]. A systematic review of fiber intervention trials found that viscous fibers are more consistently associated with reduced appetite and energy intake than non-viscous fibers [72], and on a favorable opinion from the European Food Safety Authority, the European Union authorizes a health claim that 3 g a day of glucomannan, taken in three 1 g doses with water before meals, contributes to weight loss in the context of an energy-restricted diet [73]. The weight-loss trial literature is mixed: Sood et al. pooled 14 RCTs (n = 531) and found a small but significant reduction in body weight (−1.7 lb; −0.79 kg) together with reductions in lipids [74], and a 2020 meta-analysis of six RCTs reported a small but significant weight reduction [75], whereas Onakpoya et al. found no significant effect overall (mean difference −0.5 lb; −0.22 kg; 8 trials) [76]. Taken together, glucomannan often increases subjective fullness and reduces intake; its effect on body weight as a standalone agent is modest, which is precisely why it is combined with the two additional targets below. Preliminary support for pairing it with protein comes from an acute crossover study in five healthy volunteers, in which desire to eat fell significantly at 90 minutes after 1 g of glucomannan and 500 mg of white bean extract taken with 8 g of whey, but not after the same combination with casein, and the rise in GLP-1 correlated with the fall in desire to eat [218]; the study was very small, had no protein-only or glucomannan-only condition, and does not establish synergy or effects on weight. In Trilogiii, BP supplies 3 g of glucomannan per day — the daily amount specified in the EFSA claim — but as part of a shake whose timing relative to meals was left to the participant, rather than in three 1 g doses taken before meals (Section 6.4).

B.4.2 Hormonal satiety — fermented protein and botanical extracts with in vitro DPP-4 inhibitory activity

Nutrient arrival in the gut triggers enteroendocrine cells to release a cascade of peptides that signal satiety to the brain and slow gastric emptying. Cholecystokinin (CCK) from duodenal I-cells was the first gut hormone shown to reduce meal size [77]; GLP-1 infusion increased satiety and fullness and reduced ad libitum energy intake by 12% in healthy men [78]; and peptide YY (PYY_{3-36}) infusion reduces ad libitum intake by roughly one-third [79]. Glucose-dependent insulinotropic polypeptide (GIP) is co-released with GLP-1 and potentiates insulin secretion; its independent role in appetite remains under investigation. Protein is a potent dietary stimulus for these hormones, and whey has produced greater responses than casein in acute feeding studies [7,8]. The limiting factor is that GLP-1 and GIP are inactivated within minutes by DPP-4. Bioactive peptides released from dietary proteins by enzymatic hydrolysis or microbial fermentation inhibit DPP-4 in vitro, with milk- and whey-derived peptides the best characterized [80,81]. In Trilogiii this target is addressed by BIACTIN (FS, BP), the SCFA-generating fibers in FS and BP, and milk-derived peptide classes and botanical constituents with published in vitro DPP-4 inhibitory activity (Sections B.1.2 and B.3.3); DPP-4 inhibition has not been measured for BIACTIN or CC themselves. The DPP-4 inhibitory evidence for food-derived peptides and botanicals is predominantly in vitro, and confirming a measurable effect on circulating active GLP-1 in humans is a priority for future study.

B.4.3 Metabolic satiety — essential nutrient repletion

Appetite is regulated not only by energy balance but by nutrient-specific signaling: the body monitors protein intake and is proposed to respond similarly to key micronutrients, sustaining hunger when those needs are unmet, even if caloric intake is adequate or excessive. This is the logic behind the Protein Leverage Hypothesis [82], which proposes that humans keep eating until absolute protein targets are reached, so diets diluted with nutrient-poor, energy-dense foods drive overconsumption. The effect has been demonstrated in controlled human feeding: when dietary protein was lowered from 15% to 10% of energy over four days of ad libitum eating, total energy intake rose by 12% — partial protein leverage, since the extra eating did not fully restore protein intake — and hunger rose more in the hours after a low-protein breakfast than after a high-protein

one [4]. A parallel mechanism has been proposed for vitamins and minerals: in animals, feeding behavior is driven not only by caloric need but by nutrient-specific appetites that guide animals toward foods correcting specific deficiencies [83].

Importantly, the body does not "know" its micronutrient status through a single hunger sensor; rather, it monitors and regulates several key minerals directly while expressing inadequacy in others through downstream metabolic effects. Dedicated sensing exists for a handful of minerals: the calcium-sensing receptor on parathyroid cells detects extracellular calcium and adjusts parathyroid hormone secretion [219]; hepatic hepcidin production is tuned to iron status and controls intestinal iron absorption via ferroportin [220]; intracellular zinc is sensed by the transcription factor MTF-1, which regulates zinc transporter expression [221]; and sodium is the one micronutrient with a well-mapped appetite circuit, in which distinct angiotensin-responsive neurons of the subfornical organ drive salt intake, separately from those driving thirst, and are suppressed by other inhibitory circuits [222,223]. For most vitamins, however, a specific deficiency-to-appetite signaling pathway has not been established; status is maintained homeostatically at the point of use, and inadequacy is felt indirectly. Because B vitamins, iron, magnesium and zinc participate in cellular energy metabolism, including mitochondrial ATP production, marginal deficiency impairs cellular energy metabolism and is associated with fatigue and low energy even in otherwise healthy individuals [224], while zinc deficiency blunts taste acuity [225] — states that may be experienced as hunger or as a lack of satisfaction after eating.

This is consistent with the well-documented "hidden hunger" phenomenon, in which many adults with obesity have inadequate intakes of iron, calcium, magnesium, zinc, copper, folate and vitamins A and B_{12} despite excessive energy intake [84], and with the finding that people consume roughly 500 more kcal/day and gain weight when eating ultra-processed diets than when eating unprocessed diets matched for presented macronutrients [226], although that study did not identify the cause of the higher intake. The most direct human evidence comes from a randomized, double-blind, placebo-controlled trial at Laval University: forty-five adults with obesity who did not use supplements undertook 15 weeks of energy restriction with either placebo or a multivitamin and mineral supplement; weight loss did not differ, but fasting and postprandial appetite ratings — desire to eat, hunger and prospective food consumption — were significantly reduced in supplemented women ($P < 0.05$) and remained so after adjusting for weight change, suggesting that adequate vitamin and mineral intake may influence satiety [5]. A nutrient-specific effect has also been proposed for calcium: in a 15-week randomized, double-blind trial of calcium plus vitamin D during energy restriction in 63 women, supplementation did not significantly increase fat loss overall, but in the subgroup of 13 women with very low habitual calcium intake (≤600 mg/day), those receiving calcium and vitamin D lost significantly more body weight and fat mass than those on placebo and reduced their spontaneous fat intake, which the authors proposed reflects a calcium-specific appetite control [85]. In the cross-sectional arm of the same Laval study [5], female supplement consumers had lower disinhibition and hunger scores on the Three-Factor Eating Questionnaire. A separate 26-week RCT in 96 Chinese women with obesity found that multivitamin/mineral supplementation reduced body weight and fat mass and improved lipid profiles relative to placebo [227]. In Trilogiii this target is addressed by the complete essential-nutrient platform of FS and EN, with absorption intended to be supported by Approach 2 (not measured; Section 6.5). Of the two nutrient routes to hunger, protein leverage has the more direct human evidence; the micronutrient route is supported by animal, cross-sectional and randomized human data, and which specific nutrient inadequacies drive hunger is a testable component of the model.

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