Lipids in Health and Disease

REVIEW

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Protein, fiber, and exercise: a narrative review of their roles in weight management and cardiometabolic health

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Abstract

More than 40% of adults in the United States have obesity, which is an independent risk factor for cardiometabolic dysfunction and several chronic diseases, including atherosclerotic cardiovascular disease and type 2 diabetes mellitus. Interventions for obesity include lifestyle modification, pharmacotherapy, and metabolic surgery. Lifestyle interventions have minimal side effects and are the most economical, yet long-term adherence is poor. Challenges for long-term adherence are related, in part, to metabolic adaptations that occur during weight loss that affect appetite and energy expenditure. However, a lifestyle intervention that involves higher intakes of protein and fiber and increased participation in exercise may help to blunt the increases in hunger and cravings that occur with weight loss while increasing energy expenditure, thus assisting with both weight loss and weight loss maintenance. These changes also promote improved cardiometabolic health, independent of weight loss. This narrative review summarizes the evidence for the roles of increasing protein, fiber, and exercise for weight management and improving the cardiometabolic risk factor profile.

Keywords Cardiometabolic risk, Exercise, Fat-free mass, Fiber, Lipoprotein lipids, Physical activity, Protein, Weight loss, Weight maintenance

Introduction

Based on current data, over 40% of adults in the United States (U.S.) have obesity [1], which contributes to increased cardiometabolic risks, such as elevated blood pressure, blood glucose, and lipoprotein lipid levels. The cardiometabolic dysfunction that can occur with obesity increases the risks for several chronic diseases, including atherosclerotic cardiovascular disease and type 2 diabetes mellitus (T2D) [2]. In 2016, the estimated total medical cost related to obesity in the U.S. was $126 billion [3], and cardiovascular diseases and T2D are major drivers of this cost [4]. Interventions for obesity include lifestyle modification, pharmacotherapy, and metabolic surgery [5]. Of these options, lifestyle interventions may be economical and practical, yet long-term adherence can be challenging [6]. Caloric restriction for body weight reduction often results in changes in appetite and energy expenditure that contribute to difficulty with long-term adherence [6]. Developing nutrition interventions that mitigate the potential effects of reduced calorie intake on hunger and cravings while encouraging increased exercise may improve weight loss and maintenance of lost

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body weight and fat mass, which will improve cardiometabolic health.

Although very-low-carbohydrate and ketogenic diets have been promoted for weight loss and favorable effects on cardiometabolic risk factors, long-term adherence with such restrictive diets can be difficult [7]. Alternatively, there is evidence that adequate intakes of protein and fiber and participation in exercise increase feelings of satiety, energy expenditure, and maintenance of fat-free mass [8–11]. However, intakes of protein and fiber are often below optimal levels, particularly for individuals attempting to lose weight or maintain weight loss [12, 13]. Additionally, in 2020, 46% of U.S. adults did not meet the recommended amounts of either moderate-intensity aerobic exercise or muscle strengthening activities each week [14]. It is feasible that a lifestyle intervention that ensures adequate intakes of protein and fiber and exercise may promote weight loss and weight maintenance. A simple message that emphasizes this approach is "30-30-30," which represents consuming ≥ 30 g protein/meal, ≥ 30 g of dietary fiber/day, and engaging in ≥ 30 min of exercise/day. While these goals may need to be adjusted somewhat for individuals at the extremes of height and/or weight, they represent a simple and achievable set of objectives for a large portion of the population. The "30-30-30" approach would be best suited as a self-directed plan for those with overweight or Stage 1 obesity but could be part of a medically supervised weight loss plan for those with Stage 2 or higher obesity. This narrative review summarizes the evidence on the effects of protein, fiber, and exercise on weight loss, prevention of weight regain, and optimization of the cardiometabolic risk factor profile.

Protein

Protein recommendations and consumption

While some individuals, such as athletes and active adults, consume protein above recommendations based on the U.S. Recommended Dietary Allowance (RDA) [15], growing evidence suggests that intake may be lower than is optimal for some subgroups, especially older adults and women [16]. The RDA for protein is the minimum amount necessary to maintain nitrogen balance in ~98% of healthy individuals [17]. The current RDA (0.8 g protein/kg/day) was developed in 1943 and was based exclusively on nitrogen balance in an effort to determine the minimum amount of protein intake required to prevent malnutrition for the troops during World War II [12]. Conversely, the Acceptable Macronutrient Distribution Range (AMDR) is "a range of intakes for a particular energy source that is associated with reduced risk of chronic diseases while providing adequate intakes of essential nutrients" [18]. The AMDR for protein is 10–35% of total daily energy (TDE). The AMDR is more practical than the RDA because it is expressed as a range, thus consuming 10% TDE from protein will approximately meet the RDA for protein, while consuming up to 35% TDE from protein may provide additional physiological benefit [19]. Furthermore, the AMDR is more representative of real-world intakes since it is expressed as a percentage of TDE intake. If the intake of protein increases, then intakes of carbohydrate and fat will change proportionally.

Further evidence suggests that nitrogen balance may not be an accurate representation of the protein intake needed for development and maintenance of optimal fat-free mass, muscle strength, and muscle function over the lifespan, as well as to promote cardiovascular health and weight management [18, 19]. Protein intake plays a crucial role in maintaining skeletal muscle mass during the aging process [20]. Muscle mass peaks at around age 30, then decreases by 3–8% each decade until approximately age 60 years, after which the rate of loss increases, although adequate physical activity, especially resistance training, can partially counteract this loss [21]. Fanelli et al. [22] examined data from the 2005–2016 National Health and Nutrition Examination Survey (NHANES) and reported that 34% of adults aged ≥ 31 years in the U.S. did not meet the RDA of 0.8 g protein/kg/day. Results from an additional NHANES analysis indicated that protein intake was below the RDA in many older adults, including 34.6% and 41.7% of men aged 61–70 years and >70 years of age, respectively, and 48.4% and 50.3% in women aged 61–70 and > 70 years of age, respectively [16]. The results of these analyses become even more concerning when considering that the RDA may not represent an adequate intake level of protein to promote general health, as well as maintenance of fat-free mass, weight management, and cardiometabolic health [19].

Higher protein intake and weight management

Higher protein intake appears helpful for weight management. In a meta-analysis of 24 short-term (mean duration 12 weeks) randomized controlled trials (RCTs), Wycherley et al. [23] reported that energy-restricted, high-protein (mean 1.25 g/kg/day), low-fat diets resulted in greater reductions in body weight [weighted mean difference (WMD): -0.79 kg; 95% confidence interval (CI): -1.50, -0.08 kg] and fat mass (WMD: -0.87 kg; 95% CI: -1.26, -0.48 kg) and greater relative increases in fat-free mass (WMD: 0.43 kg; 95% CI: 0.09, 0.78 kg) and resting energy expenditure (WMD: 142 kcal/day; 95% CI: 16.0, 269 kcal/day), compared to standard-protein (0.72 g/kg/day), low-fat diets in participants with overweight or obesity. Kim et al. [24] observed similar effects of higher protein diets (≥ 25% TDE), compared to lower protein diets (< 25% TDE), on body weight and body composition in a meta-analysis of 20 RCTs (mean duration 25 weeks) that involved adults ≥ 50 years of age with overweight or obesity and various health conditions, including T2D. Furthermore, the authors of a more recent meta-analysis of 37 RCTs (mean duration 32 weeks) reported that higher protein diets (ranging from 18 to 59% TDE) resulted in greater reductions in body weight [mean difference (MD): -1.6 kg; 95% CI: -1.2, -2.0 kg], compared to various isocaloric control diets with lower protein intakes [25]. The magnitudes of differences in weight loss and the preservation of fat-free mass during weight loss described in these meta-analyses were modest, yet potentially clinically relevant, especially because approximately 25–35% of weight lost is typically fat-free mass [26]. However, the impacts of higher protein diets in the long-term must also be considered.

The results of two meta-analyses in which the impacts of long-term (≥ 12 months) higher protein diets on weight loss and maintenance were examined are somewhat conflicting. A meta-analysis of 15 RCTs (duration ≥ 12 months) by Schwingshackl et al. [27] reported no difference for body weight, waist circumference, and fat mass with higher protein (≥ 25% TDE), lower fat (≤ 30% TDE) diets, compared to lower protein (≤ 20% TDE), lower fat (≤ 30% TDE) diets. Conversely, the results of a meta-analysis of 32 RCTs (duration ≥ 12 months) by Clifton et al. [28] showed small but significant reductions in body weight [standardized MD (SMD): -0.14; 95% CI: -0.23, -0.05] and fat mass (SMD: -0.22; 95% CI: -0.32, -0.12) with higher protein (generally > 25% TDE) vs. lower protein (generally 15–20% TDE) diets. Translating these SMDs into mass units showed that the higher protein diets yielded greater reductions of 0.39 kg for body mass and 0.44 kg for fat mass. The main difference between these meta-analyses was that Schwingshackl et al. [27] required that both the higher and lower protein interventions were low in fat (≤ 30% TDE), while Clifton et al. [28] did not include that requirement. Clifton et al. also included studies that utilized low-carbohydrate interventions, which resulted in TDE from fat ranging from 5% to 61%. As a result, the meta-analysis by Clifton et al. [28] included more than twice as many studies as the meta-analysis by Schwingshackl et al. [27]. In summary, it appears that higher protein diets are slightly more favorable for weight management in the long-term, but the effect is small.

The results of other RCTs not included in the meta-analyses described previously provide further evidence to support favorable effects of higher protein intake on weight loss and weight management. In the Diet, Obesity, and Genes (DiOGenes) study, 938 adults with overweight or obesity from eight European countries followed an 8-week, low-calorie (800-1,000 kcal/day) diet during a weight-loss phase [29]. The participants who lost ≥ 8% of their body weight from baseline ($n = 773$) continued with the 6-month weight-maintenance phase of the study and were randomized in a factorial design to one of five *ad libitum* diets that were either lower or higher in protein (13% vs. 25% TDE, respectively) and glycemic index (differing by 15 units). During the weight maintenance phase, the participants in the lower protein diet groups gained a mean 0.93 kg (95% CI: 0.31, 1.55 kg) more than the participants in the higher protein diet groups ($P = 0.003$) [29].

The PREVention of diabetes through lifestyle intervention and population studies In Europe and around the World (PREVIEW) trial had a study design similar to the DiOGenes study but included a larger sample ($N = 2{,}326$) and had a longer duration (3 years) (30). Participants were adults with prediabetes who lost ≥ 8% of body weight from baseline during the initial 8-week weight-loss phase and were subsequently randomized to a higher-protein diet (25% TDE protein, 45% TDE carbohydrate, 30% TDE fat) with low glycemic index (< 50) or a moderate-protein diet (15% TDE protein, 55% TDE carbohydrate, 30% TDE fat) with moderate glycemic index (> 56) and either high- or moderate-intensity physical activity. Neither the incidence of T2D, the primary outcome, nor changes in body weight differed between the study groups. However, results from a post hoc analysis indicated that participants who consumed ≥ 0.8 g/kg/day protein regained 1.5% less weight, compared to participants who consumed < 0.8 g/kg/day protein during the weight-maintenance phase ($P = 0.005$). The results of these two large, multinational, long-term trials suggest that dietary interventions that include higher protein may provide modest benefits for weight maintenance following weight loss.

There has been concern about the sustainability and safety of long-term consumption of a high-protein diet. A high-protein diet is often defined as ≥ 1.5 g/kg/day or ≥ 20% TDE. It should be noted that consuming ≥ 30 g of protein per meal would not necessarily produce a high-protein diet. For an 80 kg person, energy needs for weight maintenance with 30 min of exercise per day would be approximately 2400 kcal/day. If 100 g/day of protein were consumed (400 kcal), this would be ~ 17% TDE and ~ 1.25 g/kg/day. The percentage would be higher if a reduced energy intake were being consumed to promote weight loss (22% TDE for 1800 kcal/day).

Potential mechanisms for improved weight management with higher protein intake

There is evidence that protein produces a stronger satiety effect, compared to carbohydrate and fat, when evaluated by subjective ratings from visual analog scales (VAS) as well as levels of hormones that are associated with appetite [e.g., cholecystokinin (CCK), glucagon-like peptide-1 (GLP-1), and peptide YY (PYY)] [30, 31]. The results of a meta-analysis of 49 acute studies showed that meals containing a larger amount of protein decreased subjective hunger (-7 mm VAS; $P < 0.001$), desire to eat (-5 mm VAS; $P = 0.045$), and prospective food consumption (-5 mm VAS; $P = 0.001$) and increased fullness (10 mm VAS; $P < 0.001$), compared to isocaloric control meals [30]. Also, there was a decrease in the level of ghrelin (a hormone associated with hunger) and increases in the levels of CCK and GLP-1 (hormones associated with satiety) with the acute intake of higher protein meals. Subgroup analysis results indicated that there were significant increases in CCK and GLP-1 following meals containing the median level of protein or higher (≥ 35 g) but not after meals with below-median protein content [31]. The results of this meta-analysis support the view that there may be a protein threshold in which a meal must contain enough protein to elicit a satiety response, which is often estimated to be in the range of ~ 25–30 g [31].

The available evidence suggests that meals and diets containing higher protein content elicit higher energy expenditure than those containing less protein [32, 33]. Guarneiri et al. [34] conducted a systematic review and meta-analysis of 52 RCTs that investigated the impact of acute meals and longer-term diets containing different amounts of protein on energy expenditure. In acute studies, consuming higher vs. lower protein meals yielded greater diet-induced thermogenesis (DIT) (SMD: 0.45; 95% CI: 0.26, 0.65; $P < 0.001$) and total daily energy expenditure (TDEE) (SMD: 0.52; 95% CI: 0.30, 0.73; $P < 0.001$). In longer-term studies (4 days to 1 year), consuming higher vs. lower protein diets yielded greater TDEE (SMD: 0.29; 95% CI: 0.10, 0.48; $P = 0.003$) and resting energy expenditure (SMD: 0.18; 95% CI: 0.01, 0.35; $P = 0.039$) but no differences in DIT (SMD: 0.10; 95% CI: -0.08, 0.28; $P = 0.27$). The pooled SMD for TDEE in longer-term studies was estimated to represent an increase of ~72 kcal/day or ~3% of TDEE [34]. These small increases in energy expenditure may be clinically meaningful because excess consumption of 10–20 kcal/day may contribute to the average yearly weight gain of 0.5–1 kg among adults in the U.S. [35, 36].

Emerging evidence suggests that sources of protein may impact energy balance and cardiometabolic risk differently. The results of an RCT found that, compared to soy protein, micellar casein and pea protein isolates consumed for 3 days reduced post-prandial appetite scores and increased satiety signals, whereas whey protein did not. However, the source of protein had no effect on subsequent energy intake, either immediately after or 4 h after the protein preload [37]. It has been hypothesized that protein sources with higher levels of branched chain amino acids may elicit stronger satiety responses, but additional research is needed due to conflicting evidence [37, 38]. Furthermore, the results of a meta-analysis that examined the effects of various protein sources on DIT and resting energy expenditure found no differences between the different protein sources, which included both animal and plant proteins, on these energy expenditure parameters [34]. Regarding cardiometabolic risk, results from meta-analyses of observational studies have shown that higher intakes of total and animal protein are associated with increased risk for incident T2D [39, 40]; however, higher intakes of some protein-rich foods, such as fish, eggs, dairy products, and soy protein, have neutral or inverse relationships to incident T2D [39]. Results of meta-analyses of RCTs demonstrate that, compared with animal-based protein, plant-based protein significantly reduces total cholesterol, low-density lipoprotein cholesterol (LDL-C), and apolipoprotein B (apoB) levels [41, 42], but does not differ in the effect on body weight or body mass index [41]. The currently available evidence does not consistently support that there are differences between protein sources on energy balance but additional research is warranted.

The protein leverage hypothesis was first introduced by Simpson and Raubenheimer in 2005 to explain how protein intake is regulated more strongly than intakes of carbohydrates and fats, which may result in an overconsumption of nonprotein energy until protein needs are met [43]. Simpson and Raubenheimer subsequently suggested that the protein leverage hypothesis may play a causal role in the development of obesity [44]. Briefly, the protein leverage hypothesis suggests an interaction in which protein intake is regulated independently and preferentially to carbohydrates and fats. When the proportion of protein intake decreases, the drive to consume adequate protein increases overall food and energy intake, which results in changes in body composition and potentially weight gain [45] (Fig. 1). There have been studies in both animal and humans that support the protein leverage hypothesis in the development of obesity, which is outlined in detail in a review by Simpson and Raubenheimer [44].

Fiber

Dietary fiber is a non-digestible form of carbohydrate that is found in a variety of foods, such as fruits, vegetables, whole grains, legumes/pulses, nuts, and seeds [46]. The 2020–2025 Dietary Guidelines for Americans recommend an intake of 14 g of fiber/1,000 kcals consumed (e.g., 28 g of fiber for a 2,000 kcal diet), yet > 90% of adults in the U.S. do not meet this recommendation [47]. The average intake of dietary fiber in 2017–2018 was 8.1 g/1,000 kcals [48]. Types of fiber are categorized based on source, solubility, viscosity, and fermentability [49]. Soluble fibers (e.g., pectin and gums) can be mixed into water, while insoluble fibers (e.g., cellulose, lignin, and resistant starch) do not dissolve in water.

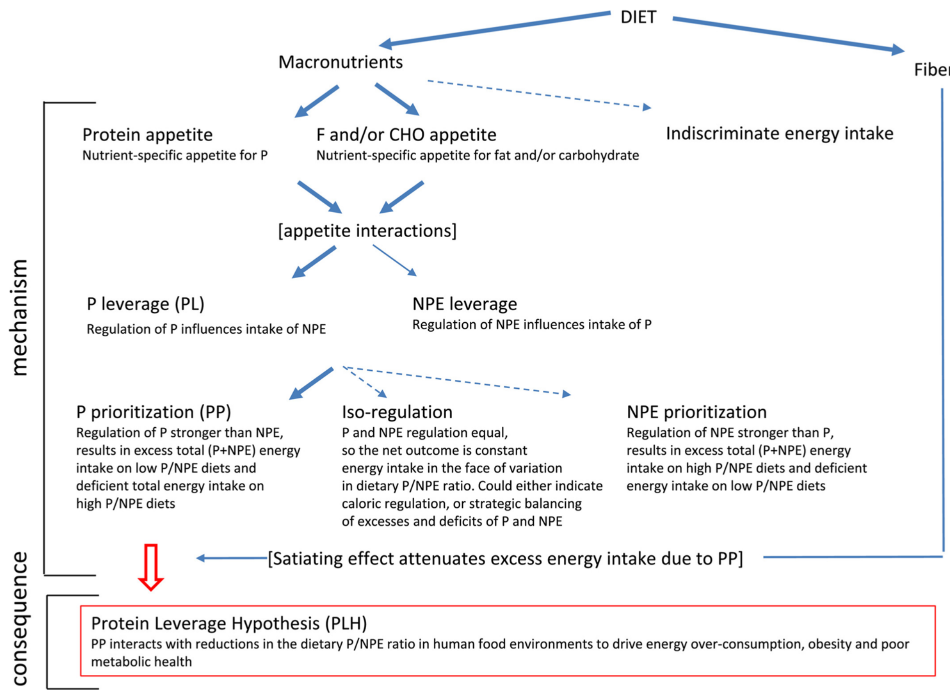

Fig. 1 The components of the protein leverage hypothesis. Solid arrows indicate links that apply to humans and dashed arrows indicate links that do not. The thin solid arrow to nonprotein energy leverage indicates it exists to a considerably lesser extent than protein leverage, specifically for diets with high protein to nonprotein energy ratios [44]. Abbreviations: CHO, carbohydrates; F, fats; NPE, nonprotein energy; P, protein; PL, protein leverage; PLH, protein leverage hypothesis; PP, protein prioritization. Adapted from Raubenheimer and Simpson [44] with permission from John Wiley and Sons, the publisher of Obesity, on behalf of The Obesity Society

The viscosity of fiber refers to its ability to thicken when mixed with fluids [50]. Insoluble fibers are generally less viscous than soluble fibers, and higher intakes are associated with improved regularity and volume of bowel movements [46, 50]. Viscous, soluble fibers slow digestion of starches and sugars, and reduce postprandial glucose and insulin responses [50]. Viscous fibers also trap cholesterol and bile acids in the intestine, thus reducing their absorption/reabsorption, which lowers plasma levels of total cholesterol and LDL-C [46, 50]. Both viscous and non-viscous fibers reduce energy density (calories per 100 g of food consumed) and increase postprandial satiety [51, 52].

The fermentability of fiber refers to the susceptibility to fermentation by the microbiota in the intestine, a process that liberates short-chain fatty acids [53]. Short-chain fatty acids can be absorbed into the circulation and have a variety of metabolic effects [54], including influencing body weight and appetite. Cornejo-Pareja et al. [55] review several mechanisms that have been proposed to explain the relationships between the gut microbiota and obesity. One of the proposed mechanisms is that short chain fatty acids produced from the fermentation of fiber bind to G protein-coupled receptors 41 and 43, which results in increased secretion of GLP-1 and PYY, thereby reducing appetite and improving glucose homeostasis [55]. Higher consumption of fermentable fibers has been associated with improved insulin sensitivity and reduced inflammation, both of which are influenced by short-chain fatty acids produced from the fermentation of fiber by the intestinal microbiota [53, 55]. It is important to consume a variety of types and sources of dietary fibers because different dietary fibers vary in their impacts on physiological functions [49].

Fiber intake and weight management

Jovanovski et al. [56] conducted a meta-analysis of 62 RCTs ($N = 3{,}877$) that investigated the impact of viscous dietary fiber supplements vs. control supplements (fiber-free, non-viscous fiber, or placebo) on body weight and composition in the context of *ad libitum* diets (not involving intentional energy restriction). The authors reported that a median dose of 8 g/day of viscous fiber for a median duration of 8 weeks resulted in greater reductions in body weight (MD: -0.33 kg; 95% CI: -0.51, -0.14 kg) and waist circumference (MD: -0.63 cm; 95% CI: -1.11, -0.16 cm), compared to the control conditions. There were no differences for changes in percent body fat. Huwiler et al. [57] conducted a meta-analysis of 22 RCTs ($N = 1{,}428$) that examined the effects of long-term (≥ 12 weeks) soluble fiber supplementation on body weight in participants with overweight and obesity and reported that soluble fiber supplements resulted in greater reductions in body weight, body mass index, and waist circumference, but not percent body fat, compared to supplements without soluble fiber. Kim et al. [58] conducted a meta-analysis comparing the effects of hypocaloric or eucaloric diets with and without dietary pulses (a rich source of dietary fiber) on body weight, body fat, and waist circumference, and Lee et al. [59] conducted a meta-analysis to examine the effects of foods fortified with soluble or insoluble fiber on body composition, compared to the unfortified version of the test food or placebo. The results of both meta-analyses demonstrated greater reductions in body weight, but no differences in waist circumference or percent body fat with the fiber compared to the control conditions [58, 59].

Higher consumption of dietary fiber may improve weight management by increasing energy excretion and appetite regulation. For example, higher fiber intake reduces the metabolizable energy content of foods by increasing energy excretion in the feces [60]. Regarding appetite regulation, the increased time and effort required for chewing fiber-containing foods may enhance satiety signals [9]. Similarly, viscous and insoluble fibers increase gastric distention, which stimulates vagal afferents to the regions of the brain that enhance perceptions of fullness and satiation [51]. The slower rate of passage of food through the stomach and small intestine with the consumption of viscous soluble dietary fiber enhances macronutrient interaction with the intestinal wall, increasing the secretion of gastrointestinal hormones associated with increased satiety (e.g., CCK, GLP-1, and PYY) [9]. Additionally, there is some evidence that the production of short-chain fatty acids from the fermentation of fiber in the colon also contributes to greater secretion of anorectic hormones and increased energy expenditure [61–63].

Exercise

Daily physical activity is recommended for promoting overall health and preventing chronic diseases, as well as facilitating weight loss and maintaining a healthy body weight [64, 65]. Physical activity is defined as bodily movement produced by skeletal muscle contraction that results in increased energy expenditure [65, 66], and includes occupational, household, and leisure time activities, and sports and conditioning [64, 66]. Supervised and unsupervised exercise is a type of physical activity, and includes activities that are planned, structured, and repetitive with a goal of improving and/or maintaining physical fitness. All forms of exercise are considered physical activity but not all physical activity is considered exercise [65]. The American College of Sports Medicine (ACSM) [64] and the 2018 Physical Activity Guidelines for Americans [65] recommend 150–300 min/week of moderate-intensity physical activity to reduce the risk of chronic disease and prevent weight gain in adults. Muscle-strengthening and resistance training activities of moderate or greater intensity on two or more days/week are also encouraged in the 2018 Physical Activity Guidelines for Americans [65]. However, for facilitation of weight loss and maintenance of lost weight, the ACSM acknowledges a larger amount of physical activity, as supervised or unsupervised exercise, is needed beyond the amount needed for general health [64].

Exercise and weight management

There appears to be a dose-response effect of exercise for weight loss and weight maintenance (Fig. 2) [64, 67]. In studies that ranged from 12 weeks to 2 years in duration, moderate-intensity aerobic activity < 150 min/week was associated with minimal weight loss, whereas 150–225 min/week resulted in 2–3 kg weight loss, and 225–420 min/week resulted in 5–7.5 kg weight loss. Based on the available evidence, the amount of moderate-intensity

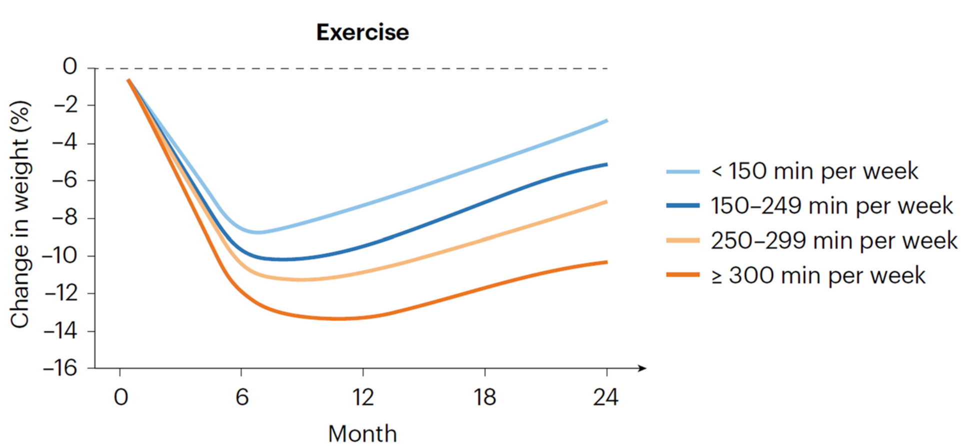

Fig. 2 Percent change in weight from baseline with varying amounts of weekly exercise. Adapted from Rosenbaum et al. [67] with permission from Springer Nature, the publisher of *Nature Metabolism*

aerobic activity needed to support weight maintenance after weight loss is 200–300 min/week [64, 67].

In addition to contributing to an energy deficit during weight-loss efforts [60, 65], exercise can blunt the reduction in resting energy expenditure and TDEE that may occur with weight loss [67, 68]. This may be due to an increase, or at least maintenance of, fat-free mass that can occur with increased exercise, even in the presence of weight loss [64, 68]. Preventing a reduction in resting energy expenditure and TDEE may increase the likelihood of continued weight loss success and reduce weight regain. A secondary analysis of the DiOGenes study discussed previously showed that a higher level of physical activity during the weight-loss phase was associated with less weight regain or additional weight loss during the weight maintenance phase of the study [69]. Additionally, a higher amount of physical activity during the weight maintenance phase of the study was associated with lower body weight and fat mass [69]. The Look Action for Health in Diabetes (Look AHEAD) trial was a large RCT ($N = 5145$) that examined whether weight loss achieved with an intensive lifestyle intervention, which entailed reduced caloric intake and increased physical activity, would reduce cardiovascular morbidity and mortality in participants with overweight or obesity and T2D, compared to usual care (i.e., diabetes support and education). The intensive lifestyle intervention was designed to promote a mean weight loss ≥ 7% of initial weight. At the end of the first year of the study, participants in the intensive lifestyle intervention group ($n = 2570$) lost a mean 8.6% of initial body weight, compared to 0.7% in the usual care group ($n = 2575$) [70]. Participants in the intensive lifestyle intervention group maintained a mean weight loss of 4.7% at year 4 compared with 1.1% in the usual care group [71]. Wadden et al. [72] examined the factors associated with continued weight loss or weight maintenance at year 4 in the Look AHEAD participants. Of the 887 individuals who lost ≥ 10% of their initial body weight at the end of year 1, 374 (42.2%) maintained that weight loss at year 4. The participants who maintained ≥ 10% weight loss at year 4 reported a significantly higher weekly calorie expenditure from physical activity (mean 1998 kcal/week), compared to participants who maintained 0-9.9% weight loss (mean 1127–1406 kcal/week) or those who gained weight (949 kcal/week) [72].

Exercise may also influence weight loss through its effects on energy intake and appetite. The potential relationship between physical activity and energy intake was first examined by Mayer et al. (74) in a study of jute mill workers. The results of their study demonstrated a J-shaped curve for the relationship between physical activity and energy intake. There was a linear relationship between energy expenditure and energy intake in workers with high levels of physical activity; however, workers with low levels of activity also had increased energy intake [73]. These results have been replicated in other studies [74, 75]. Researchers have hypothesized that physical inactivity (or a sedentary lifestyle] causes dysregulation of appetite, which results in an inability of the body to identify when it is being overfed, thus leading to overconsumption and weight gain [75]. Higher levels of physical activity also appear to impact appetite by enhancing the secretion and sensitivity to hormones that influence hunger and satiety, such as ghrelin, CCK, GLP-1, and PYY [10, 75]. Additionally, high-intensity exercise produces a greater suppression of ghrelin levels, compared to moderate-intensity exercise [76]. The potential mechanisms that explain the effects of physical activity on appetite and energy intake are not fully understood. However, it is clear that the effects of increasing physical activity on weight loss and weight maintenance go beyond energy expenditure.

Combining exercise with a weight-loss dietary intervention typically produces more weight loss than exercise alone. One RCT examined the effects of a reduced-calorie, low-fat diet ($n = 118$), a supervised aerobic exercise program ($n = 117$), a diet + exercise program ($n = 117$), or control (delayed intervention; $n = 87$) on weight loss [78]. The results demonstrated that participants in the diet + exercise group lost 10.8% of their initial body weight, compared to 8.5% in the diet only group, 2.4% in the exercise only group, and 0.8% in the control group [77]. The results of other studies have shown similar findings [64, 68]. However, if the dietary intervention included a severe caloric restriction (e.g., 1000 kcal/day deficit), the addition of physical activity did not enhance weight loss, whereas the addition of physical activity to dietary interventions with a more moderate caloric restriction (e.g., 500–700 kcal/day deficit) resulted in significantly more weight loss than the dietary interventions alone [64].

The totality of the evidence supports the view that participation in exercise during weight loss promotes improvements in body composition. Bellicha et al. [68] reviewed 12 systematic reviews and meta-analyses that included 149 controlled trials (both randomized and nonrandomized) that examined the effects of exercise training on body weight and composition in adults with overweight or obesity. The authors reported that exercise training (i.e., aerobic activity alone, muscle-strengthening alone, or the combination) resulted in significantly greater weight loss (MDs ranging from -1.5 to -3.5 kg), total fat loss (MDs ranging from -1.3 to -2.6 kg), and visceral fat loss (MDs ranging from -0.3 to -0.6 kg), compared to control conditions [68]. Although resistance training, with or without an energy-restricted diet, does not produce significant weight loss, it does promote the maintenance or gain of fat-free mass during active weight loss [64, 68]. Bellicha et al. [68] reported that the results of one meta-analysis of six RCTs indicated that resistance training reduced the loss of fat-free mass when added to a weight-loss dietary intervention, compared to dietary intervention alone [78].

Impact of protein, fiber, and physical activity on other markers of cardiometabolic health

In addition to promoting weight loss and weight loss maintenance, higher intakes of protein and fiber and increased participation in exercise may improve other markers of cardiometabolic health. In the Optimal Macronutrient Intake Trial to Prevent Heart Disease (OmniHeart) study, a randomized, 3-period, crossover, controlled-feeding trial (all food was provided), 164 adults with prehypertension or stage 1 hypertension consumed three diets for 6 weeks each that emphasized either carbohydrate (58/15/27% TDE from carbohydrate/protein/fat, respectively), protein from both animal and plant sources (48/25/27%), or unsaturated fatty acids (48/15/37%) [79]. The results indicated that, compared to habitual intake at baseline, systolic blood pressure, LDL-C, non-high-density lipoprotein cholesterol (non-HDL-C), and triglyceride levels were significantly reduced during all three dietary interventions. However, the reductions in each of these parameters were significantly greater with the higher protein diet, compared to the higher carbohydrate diet.

In a randomized, double-blind, controlled-feeding crossover trial, Maki et al. [80] examined the effects of replacing refined starches and added sugars with egg protein + unsaturated fatty acids (UFAs) on cardiometabolic health markers in participants with overweight or obesity and triglycerides $\geq$ 1.69 mmol/L ($N = 25$). The carbohydrate, protein, and fat contents were 42%, 23%, and 35% TDE, respectively, for the egg protein + UFAs condition and 58%, 15%, and 27% TDE, respectively, for the refined carbohydrate condition. The participants consumed each diet for 3 weeks with a 2-week washout between treatments. Compared to the habitual diet at baseline, both diet interventions significantly improved LDL-C, non-HDL-C, and apoB levels. However, the egg protein + UFAs diet significantly reduced triglyceride and very-low-density lipoprotein cholesterol levels, increased LDL particle size, and improved markers of insulin sensitivity and pancreatic β-cell function, compared to the refined carbohydrate condition [80]. The results of the OmniHeart and egg protein + UFAs studies provide evidence that a higher protein diet achieved with the substitution of protein for carbohydrates, especially added sugars and refined starches, improves the cardiometabolic risk factor profile.

The results of several meta-analyses of RCTs have demonstrated that interventions involving various types and doses of dietary fiber improve cardiometabolic risk factors. The results from a meta-analysis that examined the effect of soluble fiber (both viscous and non-viscous forms), compared to control interventions, demonstrated greater reductions in total cholesterol, LDL-C, non-HDL-C, apoB, and triglyceride levels [81]. The reductions in total cholesterol and LDL-C were greater for soluble fiber sources that were fermentable viscous, only viscous, or only fermentable fiber, compared to sources of fiber that were nonfermentable non-viscous. Based on the evidence that supports the beneficial effect of fiber on lipoprotein lipid levels, particularly LDL-C, the U.S. Food and Drug Administration has approved health claims for two soluble viscous soluble fibers, β-glucan and psyllium [82].

Intake of dietary fiber also improves markers of glycemia, especially in individuals with greater glucose dysregulation. Results from two meta-analyses that studied the effect of consuming any form of dietary fiber or viscous fiber supplements, compared to control interventions, in participants with T2D indicated greater reductions in glycated hemoglobin (HbA1c), fasting blood glucose, and the homeostatic model assessment for insulin resistance (HOMA-IR) with the fiber interventions [83, 84]. Similarly, a meta-analysis completed by Reynolds et al. [85] to examine the cardiometabolic effects of carbohydrate and fiber content in diets of participants with type 1 or T2D indicated that diets higher in both fiber and carbohydrate resulted in greater reductions in HbA1c (MD: -0.50%; 95% CI: -0.99, -0.02%), fasting insulin (MD: -6.88 pmol/L; 95% CI: -12.7, -1.04 pmol/L), total cholesterol (MD: -0.16 mmol/L; 95% CI: -0.27, -0.05 mmol/L), and LDL-C (MD: -0.16 mmol/L; 95% CI: -0.31, -0.01 mmol/L), compared to diets lower in fiber and carbohydrate. The results of the meta-analysis by Huwiler et al. [57] discussed previously indicated that supplements with soluble fiber reduced HOMA-IR and fasting insulin, compared to supplements without soluble fiber, but there were no differences in HbA1c or fasting blood glucose. The lack of difference in HbA1c and fasting blood glucose in the Huwiler et al. [57] meta-analysis is likely because the population involved participants mostly without T2D, while the other meta-analyses included individuals with T2D.

Adequate amounts of exercise improve many cardiometabolic risk factors independent of weight loss. The results of RCTs that examined the effects of exercise training on cardiometabolic risk factors demonstrated that at least 150 min/week of moderate-intensity aerobic exercise significantly improved triglyceride and high-density lipoprotein cholesterol levels [86, 87], systolic and diastolic blood pressure [88], glycemic control in participants with prediabetes and/or T2D [89, 90], and insulin sensitivity in adults with overweight or obesity with or without T2D [91]. Reduced LDL-C levels generally occurred with a higher amount of moderate-intensity aerobic activity (200–300 min/week) with concurrent weight loss [87]. Resistance training has also been shown to favorably effect lipoprotein lipid levels [86], systolic and diastolic blood pressure, and glycemic control [92]. The combination of aerobic and resistance training exercise appears to produce favorable effects on multiple cardiometabolic risk factors while promoting improved body composition, and was encouraged by the writing committee for the 2023 American Heart Association Scientific Statement on Resistance Exercise Training in Individuals with and without Cardiovascular Disease [92]

Table 1 Example daily menu for a high-protein (25% TDE), high-fiber diet containing approximately 2,000 kcal

Meal/Snack Description	Energy (kcal)	Protein (g)	Fiber (g)
Breakfast: Chocolate and peanut butter smoothie			
Milk (ultra-filtered, high-protein, 2%, 8 oz.)	120	13	0
Greek yogurt (plain, non-fat, 0.25 cup)	33	6	0
Banana (medium)	105	1	3
Peanut butter powder (2 tbsp)	60	7	2
Cocoa powder (unsweetened, 2 tbsp)	25	2	2
Oats (dry, 0.5 cup)	150	5	4
Black coffee or tea	0	0	0
Meal Total	***493***	***34***	***11***
Lunch: Chili made with lean ground beef and beans served with sweet potato fries			
Chili made with lean ground beef and beans (10 oz.)[a]	400	20	6
Cheddar cheese (1.5 oz.)	74	11	0
Sweet potato fries (3 oz.)	120	1	3
Water (8 oz.)	0	0	0
Meal Total	***594***	***32***	***9***
Snack: Greek yogurt parfait			
Greek yogurt (plain, nonfat, 0.75 cup)	100	17	0
Raspberries (0.5 cup)	32	1	4
Peach (medium)	59	1	2
Mixed nuts (0.25 cup)	172	6	2
Water (8 oz.)	0	0	0
Snack Total	***363***	***25***	***8***
Dinner: Grilled salmon served with broccoli, brown rice, and blueberries			
Salmon (4 oz.)[b]	236	23	0
Broccoli (1 cup)	31	3	2.5
Brown rice (0.25 cup)	178	4	1.5
Blueberries (1 cup)	84	1	3.5
Water (8 oz.)	0	0	0
Meal Total	***529***	***31***	***7.5***
Daily Total	**1,979**	**122[c]**	**35.5**

[a] Substitute veggie crumbles and extra beans for ground beef as a vegetarian option.

[b] Substitute firm tofu for salmon as a vegetarian option.

[c] 25% TDE.

and the European Association for the Study of Obesity Physical Activity Working Group [91].

Long-term adherence to higher protein and higher fiber diets and increased participation in exercise

When evaluating the potential favorable effects on weight loss and weight maintenance of diets with higher amounts of protein and fiber and increasing exercise, it is important to consider the feasibility of long-term adherence with consuming ≥ 30 g protein/meal, ≥ 30 g fiber/day, and participating in ≥ 30 min of exercise/day. A sample daily menu for a high-protein, high-fiber diet is provided in Table 1. This menu is rich in fruits, vegetables, and proteins from both plant and animal sources.

Difficulty in adhering to a higher protein intake has been observed in RCTs. In three large weight-loss studies, the higher-protein diets were designed to contain ≥ 10% more protein than the lower-protein diets, yet the actual difference in protein intake between the groups after 6 months to 3 years was 2–5% [29, 93, 94]. There were no differences between groups for changes in body weight in each of these studies, which may have been due to the lack of difference in protein intake between groups. This is illustrated by the experience from the Preventing Overweight Using Novel Dietary Strategies (POUNDS LOST) study in which adults with overweight were randomized to one of four hypocaloric diets and 10% TDE from carbohydrate was replaced with 10% protein in two of the diets. The target intake of protein in the average-protein diets was 15% TDE from protein, and the target intake of protein in the high-protein diets was 25% TDE from protein [94]. All the participants ($N = 811$) received intensive behavioral counseling and instructions to engage in 90 min/week of moderate-intensity exercise and consume ≥ 20 g fiber/day. After 2 years, weight loss was similar in participants assigned to diets containing 15% and 25% TDE from protein (3.0 and 3.6 kg, respectively; $P = 0.22$). Notably, participants in the average- and higher-protein diets self-reported that they consumed 18% and 22% TDE from protein at 6 months and 20% and 22% at 2 years, respectively. Self-reported physical activity was similar across diet groups.

In a sub-study of the POUNDS LOST trial, dietary intake data was collected in approximately half of the participants ($n = 345$) at baseline and 6 months [95]. In a regression analysis, fiber intake was the most influential predictor of weight loss (β = -0.37; $P < 0.0001$) and was strongly associated with adherence to the macronutrient prescriptions ($P < 0.0001$). Increasing intake of dietary fiber by an average of 3.7 g/day was associated with a 1.4 kg greater weight loss over 6 months. In a separate sub-study of the POUNDS LOST trial, physical activity was objectively measured using pedometers at baseline ($n = 535$), 6 months ($n = 559$), and 24 months ($n = 367$)

Table 2 Potential benefits of increased levels of protein, dietary fiber, and exercise during weight loss interventions

Category	Protein	Fiber	Exercise
Energy balance	↑ Satiety	↑ Satiety	↑ Satiety
	↑ DIT, REE, TDEE	↓ Energy density	↑ TDEE
		↑ Energy excretion	
Cardiometabolic effects	↓ LDL-C, non-HDL-C	↑ Insulin sensitivity	↑ Insulin sensitivity
	↓ TGs	↓ PP glucose, insulin	↓ TGs
	↓ FFM loss	↓ LDL-C	↑ HDL-C
		↑ BM regularity	↓ FFM loss
			↓ SBP, DBP

Abbreviations: BM = bowel movement; DBP = diastolic blood pressure; DIT = diet-induced thermogenesis; FFM = fat-free mass; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; PP = post-prandial; REE = resting energy expenditure; SBP = systolic blood pressure; TDEE = total daily energy expenditure; TGs = triglycerides

[96]. Increased physical activity was significantly associated with decreases in body weight, waist circumference, and measures of body composition over 24 months ($P < 0.0001$ for all). Increasing daily steps by 1000 was associated with greater reduction in body weight from baseline to 6 months and 24 months ($P < 0.0001$). Participants with the greatest increase in physical activity maintained their weight loss from 6 months to 24 months, while individuals with smaller increases regained weight [96]. The results of the POUNDS LOST study indicate that weight loss was enhanced with higher fiber intake and increased amounts of physical activity.

Difficulty with long-term adherence to weight loss interventions is commonly observed, independent of macronutrient composition and exercise prescriptions. In a meta-analysis of 80 RCTs ($N = 26{,}455$) that investigated weight loss interventions ≥ 1 year, the attrition rate was 29% [97]. Wang et al. [98] conducted an umbrella review of 21 systematic reviews to identify the most important factors that improve adherence to weight-loss programs and found 47 factors that were modulators of adherence. The main findings were that adherence to dietary interventions is greatest when they are personalized based on the characteristics of the target population and when behavioral interventions that involve self-monitoring, financial incentives, and supervision are incorporated. Multicomponent interventions that use more than two behavioral strategies (e.g., nutrition and physical activity with self-monitoring) were more effective than single interventions. Wang et al. [98] identified limited evidence for factors that were related to adherence to physical activity interventions, although results from previous reviews suggest that supervised exercise interventions improve adherence [99, 100].

Evidence for the benefits of combining protein, fiber, and exercise

The results of clinical trials that examined weight-loss interventions using protein, fiber, and exercise separately or with protein and fiber combined indicated favorable physiological effects that would promote weight loss, weight loss maintenance, and reduce cardiometabolic risk factors (Table 2). However, few studies have combined all three of these interventions to assess effects on weight loss or weight loss maintenance. In one RCT, researchers examined the effects of a worksite group weight-loss program that included a high-protein (25% TDE), high-fiber (40 g/day) dietary intervention ($n = 94$) on body weight and cardiometabolic risk factors, compared to control worksites in which employees could enroll in a wait-listed weight-loss program ($n = 39$) [101]. Participants in the weight-loss dietary intervention group were instructed to maintain their physical activity level at the beginning of the study but were encouraged to increase their physical activity later in the study. After 6 months, participants in the higher protein + higher fiber group lost a mean 8.0 kg, whereas the participants at the control worksites gained 0.9 kg ($P < 0.0001$). The participants in the weight-loss intervention group also had significantly improved systolic and diastolic blood pressures and fasting non-HDL-C and glucose levels, compared to the participants in the control group. While the results of this study indicate that the combination of protein and fiber provides favorable effects on body weight and other cardiometabolic risk factors, future research that includes specific daily or weekly goals for protein, fiber, and physical activity (and/or exercise) are needed to further assess whether the combination of the three will produce significant weight loss and enhance long-term weight loss maintenance. Additionally, although adequate intakes of protein and fiber combined with sufficient exercise may attenuate the metabolic adaptations that promote hunger and reduce satiety [102], some individuals may find it helpful to use antiobesity medications that have been shown to suppress hunger and promote satiety, such as GLP-1 receptor agonists [103, 104], as an adjunct to the "30-30-30" approach.

The currently available evidence indicates that the mean weight loss achieved with non-intensive lifestyle interventions is modest and generally in the range of 2–4% of body weight and weight loss achieved with intensive lifestyle interventions is ~7% of body weight [103]. Because of the potential for an additive effect on weight loss when combining protein, fiber, and exercise, the implementation of a "30-30-30" lifestyle intervention might be expected to roughly double the average weight loss achieved with non-intensive lifestyle interventions and equal the weight loss achieved with other intensive lifestyle interventions, although this remains to be demonstrated in randomized, controlled trials.

Conclusion

Higher intakes of protein and fiber and consistent participation in exercise support weight loss, weight loss maintenance, and overall cardiometabolic health. The benefits appear to be partially due to improvements in satiety, energy expenditure, and maintenance of fat-free mass. Therefore, it is reasonable to expect that the "30-30-30" lifestyle intervention of ≥ 30 g protein/meal, ≥ 30 g fiber/day, and participating in ≥ 30 min of exercise/day will promote improvements in body weight, cardiometabolic risk factors, and, ultimately, overall health.

Abbrevations

ACSM	American College of Sports Medicine
AMDR	Acceptable Macronutrient Distribution Range
ApoB	Apolipoprotein B
CCK	Cholecystokinin
CI	Confidence interval
DiOGenes	Diet, Obesity, and Genes
DIT	Diet-induced thermogenesis
GLP-1	Glucagon-like peptide-1
HbA1c	Glycated hemoglobin
HOMA-IR	Homeostatic model assessment for insulin resistance
LDL-C	Low-density lipoprotein cholesterol
Look AHEAD	Look Action for Health in Diabetes
MD	Mean difference
NHANES	National Health and Nutrition Examination Survey
Non-HDL-C	Non-high-density lipoprotein cholesterol
OmniHeart	Optimal Macronutrient Intake Trial to Prevent Heart Disease
PREVIEW	PREVention of diabetes through lifestyle intervention and population studies In Europe and around the World
PYY	Peptide YY
RCT	Randomized controlled trial
RDA	Recommended Dietary Allowance
SMD	Standardized mean difference
T2D	Type 2 diabetes
TDE	Total daily energy
TDEE	Total daily energy expenditure
UFAs	Unsaturated fatty acids
VAS	Visual analog scales
WMD	Weighted mean difference

Acknowledgements
Not applicable.

Author contributions
Conceptualization: L.L.G., C.F.K., and K.C.M.; Writing– original draft: L.L.G., C.F.K., and K.C.M.; Writing– review and editing: L.L.G., C.F.K., and K.C.M. All authors read and approved the final manuscript.

Funding
Not applicable.

Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
L.L.G. is an employee of Midwest Biomedical Research, which has received research funding and consulting fees from food and pharmaceutical companies; no other disclosures. C.F.K. is an employee of Midwest Biomedical Research, which has received research funding and consulting fees from food and pharmaceutical companies; no other disclosures. K.C.M. is an employee of Midwest Biomedical Research and Indiana University and has received research grant support from Cargill, General Mills, Global Organization for EPA and DHA, Greenyn Biotechnology, Hass Avocado Board, Helaina, Indiana University Foundation, Matinas BioPharma, MD Lifespan, Medifast, National Cattlemen's Beef Association/Beef Checkoff, National Dairy Council, Naturmega, NewAmsterdam Pharma, Novo Nordisk, PepsiCo, Pharmavite, and Ro; and received consulting fees from and/or served on advisory boards of 89Bio, Acasti Pharma, Beren Therapeutics, Bragg Live Products, Campbell's, Eli Lilly and Company, Esperion, Helaina, Lonza Group, Matinas BioPharma, MD Lifespan, National Cattlemen's Beef Association, National Dairy Council, NewAmsterdam Pharma, NorthSea Therapeutics, Novo Nordisk, Seed, Inc., and Soy Nutrition Institute Global.

Received: 6 June 2025 / Accepted: 30 June 2025
Published online: 12 July 2025

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