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ORIGINAL ARTICLE

Clinical Trials and Investigations

Isocaloric replacement of ultraprocessed foods was associated with greater weight loss in the POUNDS Lost trial

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Abstract

Objective: Higher intake of ultraprocessed foods (UPFs) is associated with obesity. We examined whether replacing UPFs (NOVA 4) with minimally processed foods and culinary ingredients (NOVA 1 + 2) was associated with differential weight change in this secondary prospective analysis of the Preventing Overweight Using Novel Dietary Strategies (POUNDS) Lost trial.

Methods: We estimated percent energy intake (%kcal) from the four NOVA groups using 24-h dietary recalls in a subset of 356 participants. Multivariable-adjusted substitution models examined whether replacing %kcal from UPFs with NOVA 1 + 2 was associated with greater weight, body fat percentage, trunk fat, and waist circumference reduction at 6 months; changes in parameters were compared among NOVA 1 + 2 tertiles (T).

Results: Participants were on average 52.3 years of age, 85% White, 55% female, and 58.2% nonsmoking, with a mean BMI of 32.7 kg/m^2. Replacing 10%kcal of UPFs with NOVA 1 + 2 was associated with greater 6-month weight (ß = 0.51, 95% CI: −0.93 to −0.09, $p = 0.02$), body fat percentage (ß = 2.7, 95% CI: −5.10 to −0.43, $p = 0.02$), and trunk fat reduction (ß = 3.9, 95% CI: −7.01 to −0.70, $p = 0.02$), but not waist circumference reduction. Participants in T3 (−8.33 kg) versus T1 (−5.32 kg) of NOVA 1 + 2 had greater weight loss ($p < 0.001$).

Conclusions: Isocaloric substitution of UPFs with NOVA 1 + 2 was associated with marginally greater weight loss under energy restriction. These modest findings support more research exploring the mechanisms linking UPFs with body weight regulation beyond energy intake.

INTRODUCTION

Dietary patterns are a critical modifiable risk factor in the development of obesity. Despite the existing efforts, obesity prevalence continues to grow at an alarming rate, with nearly half of US adults projected to develop obesity by 2030 [1]. Although obesity risk is multifactorial, one emerging risk factor that parallels trends in obesity is the increased availability of ultraprocessed foods (UPFs) in the global food system [2]. These are often defined as "ready-to-eat" or "ready-to-heat" items formulated from substances derived from foods but containing little to no whole foods [3, 4]. Over the past two decades, consumption of UPFs (i.e., percent energy intake [%kcal]) increased among both US adults and children, from 53.5% to 57% and from 61.4% to 67%, respectively [5–7]. As UPFs constitute the majority of daily total energy intake, further investigation on how UPFs affect obesity and obesity-related chronic diseases is warranted [6, 8, 9].

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There are many biobehavioral mechanisms through which UPFs are postulated to contribute to obesity. Many UPFs have lower nutritional value and higher energy density, which may displace minimally processed foods that are often healthier and with lower energy density, potentially contributing to changes in appetite control [10], faster eating rate [11], delayed satiety signaling [12], activation of dopaminergic hedonic neurocircuitry [13], changes in gut microbiome composition [14], and altered insulin profiles [12]. In addition to biological pathways, large portion packaging [15], heavy marketing [16], lower cost [17], and vast availability of UPFs in the food environment [2] may influence food choices, hence energy intake and weight gain.

Although the mechanisms are not entirely clear, existing evidence derived from large-scale prospective cohort and cross-sectional studies has consistently indicated that higher total UPF intake is associated with greater risks of excess energy intake, weight gain, obesity, and obesity-related diseases such as type 2 diabetes and cancer [18–20]. In a randomized crossover trial comparing two diets matched for presented calories, energy density, and macronutrients with participants instructed to consume as much or as little as desired, Hall et al. demonstrated that ad libitum consumption of a diet high in UPFs for 2 weeks led to both a greater energy intake of 500 kcal/day and weight gain of 0.9 kg, compared to the minimally processed diet, among normal-weight adults and adults with overweight [10]. This landmark study established initial causal evidence that UPF intake affected energy balance and led to short-term weight gain. However, as epidemiological studies have all been in free-living populations who were not intentionally adhering to restricted energy patterns, less is known about obesity trajectory in relation to UPF intake among individuals prescribed an energy-restricted diet. In light of the current gaps, we examined whether replacing energy intake from UPFs with minimally processed foods and culinary ingredients (NOVA 1 + 2) was differentially associated with weight loss efforts among individuals with overweight or obesity following an energy-restricted diet in a secondary analysis of prospective data from the Preventing Overweight Using Novel Dietary Strategies (POUNDS Lost) study [21].

Study Importance

What is already known?

- The association between overall higher intake of ultra-processed foods (UPFs) and risk of obesity has been established by population studies.
- Initial causal evidence demonstrated that UPF intake affects energy balance and short-term weight gain in an ad libitum environment.

What does this study add?

- Isocaloric substitution of UPFs with minimally processed foods and culinary ingredients is associated with greater reduction in body weight and adiposity among individuals prescribed an energy-restricted diet.

How might these results change the direction of research or the focus of clinical practice?

- There may be attributes of UPFs that affect body weight and adiposity regulation beyond energy intake.
- More mechanistic studies to investigate the pathways through which UPFs contribute to obesity beyond energy intake are needed.

METHODS

Study population and measures

The POUNDS Lost trial (ClinicalTrials.gov NCT0072995) was a 2-year randomized control clinical trial that used a 2 × 2 factorial design to investigate the effects of four energy-reduced diet prescriptions of varying macronutrient distributions on weight loss. Detailed information about the study design has been previously published [21]. Briefly, 811 participants between 30 and 70 years of age with body mass index (BMI) between 25 and 40 kg/m^2 at baseline were randomized into one of four diet arms: low fat (20% of energy), average protein (15%); low fat (20%), high protein (25%); high fat (40%), average protein (15%); and high fat (40%), high protein (25%). The 2 × 2 factorial design allowed for dose–response testing of carbohydrates (35%, 45%, 55%, or 65% of energy). The caloric prescription of a 750-kcal deficit per day was based on each participant's measured resting energy expenditure and activity level. Dietary intake was assessed in a random sample of 50% of the participants via 5-day food records at baseline and via three nonconsecutive 24-h dietary recalls at 6 months [21]. For this study, we included a subset of participants ($n = 356$) who had at least 2 days of food record data at baseline, at least 1 day of 24-h dietary recall at 6 months, and four weight and adiposity outcome measures (body weight, waist circumference [WC], total percentage body fat, trunk fat) at baseline and 6 months.

The POUNDS Lost trial was approved by human subjects committees at Harvard School of Public Health and Brigham and Women's Hospital and at Pennington Biomedical Research Center.

Exposure definition

NOVA is a framework of partitioning foods into categories based on the extent and purpose of industrial processing [3, 22]. Before being classified into four NOVA groups to estimate %kcal in each group—unprocessed or minimally processed foods (NOVA 1), processed culinary ingredients (NOVA 2), processed foods (NOVA 3), and ultraprocessed foods (NOVA 4)—participants' dietary data were linked with Food and Nutrient Database for Dietary Studies to estimate energy value of each food using standard reference codes or ingredient codes. To obtain more accurate estimates, mixed dishes were

disaggregated and classified according to the highest industrial processing level of constituent ingredient codes. Foods classified under NOVA 1 or NOVA 2 were combined because NOVA 2 foods are usually extracted directly from foods in NOVA 1, and previous research showed little difference between these two groups in relation to health outcomes. NOVA 1 + 2 %kcal, the exposure variable, was calculated by dividing kilocalories in NOVA 1 + 2 over total energy intake.

Outcome definition

Participants were weighed in the morning with a calibrated hospital scale on 2 nonconsecutive days to calculate the average body weight at baseline and at 6 months. Body composition was measured by dual-energy X-ray absorptiometry (DXA) on a Hologic QDR 4500A bone densitometer after an overnight fast to obtain total percentage body fat and trunk fat. WC was measured with an inelastic tape measure, 4 cm above the iliac crest, at the same time points. Six-month changes in weight, total percentage body fat, trunk fat, and WC were calculated as the differences between month 6 and baseline.

Covariates of interest

Sociodemographic and health behavioral variables including age, race, sex, and smoking status ("never smoker," "ever smoker") were collected at baseline. Total energy intake at 6 months was estimated using values reported in 24-h dietary recalls. Adherence to prescribed energy deficit at 6 months was calculated as the total energy consumed minus prescribed. Although lower diet quality has been postulated to be part of the causal pathway linking UPFs with weight gain, prior prospective cohorts have found significant associations between UPFs and obesity even after controlling for diet quality or

TABLE 1 Descriptive characteristics of a subgroup of POUNDS Lost[a] participants ($n = 356$) with sociodemographic data at baseline (BL), anthropometric measures at both BL and 6 months, and energy intake (kcal and %kcal) by NOVA[b] classification at both BL and 6 months.

	BL (% or mean ± SD)	6 months (mean ± SD)	Δ in BL to 6 months
Age, y	52.3 ± 8.8	-	-
Sex		-	-
Female	54.8%	-	-
Race/ethnicity		-	-
White	84.6%	-	-
Non-White	15.4%	-	-
Education		-	-
College graduate or beyond	71.1%	-	-
Smoking status		-	-
Never smoked	58.2%	-	-
BMI	32.7 ± 3.8	30.2 ± 4.0	−2.5 ± 1.9
Δ Physical activity score[c]	-	-	0.3 ± 1.1
%kcal NOVA 1 + 2[d]	30.1 ± 14.5	37.4 ± 15.5	7.3 ± 18.7
kcal NOVA 1 + 2	594.0 ± 321.3	583.4 ± 284.2	−11.6 ± 363.1
%kcal NOVA 3[d]	16.7 ± 11.3	15.1 ± 10.9	−1.6 ± 14.8
kcal NOVA 3	392.3 ± 277.2	295.4 ± 218.6	−97.3 ± 325.7
%kcal NOVA 4[d]	53.3 ± 16.8	47.5 ± 14.2	−5.8 ± 20.0
kcal NOVA 4	1106.1 ± 557.8	783.0 ± 413.4	−323.2 ± 563.6
Weight, kg	94.2 ± 16.0	87.1 ± 16.0	-
Δ Weight, kg	-	-	−7.0 ± 5.7
Waist circumference, cm	104.8 ± 13.2	97.5 ± 13.2	-
Δ Waist circumference, cm	-	-	−7.3 ± 6.3
Total body fat, %	36.9 ± 6.9	34.0 ± 7.7	-
Δ Body fat, %	-	-	−3.0 ± 2.8
Δ Trunk fat, %	-	-	−3.8 ± 3.8

[a]Preventing Overweight Using Novel Dietary Strategies (POUNDS Lost: NCT00072995) weight loss trial ($N = 811$) explored the effects of four energy-restricted diets of varying macronutrient composition on weight loss among individuals with BMI > 25 kg/m^2.
[b]NOVA, not an abbreviation, a system for categorizing foods by the nature, extent, and purpose of processing. NOVA 1: Unprocessed or minimally processed foods; NOVA 2: Processed culinary ingredients; NOVA 3: Processed foods; NOVA 4: Ultraprocessed foods.
[c]Physical activity self-reported via validated 16-item Baecke physical activity questionnaire at baseline and 6 months.
[d]Mean %kcal are mean between day 1 and 2 of each time point.

patterns [23]. Moreover, POUNDS Lost participants were counseled by registered dietitians and had relatively high diet quality, so diet quality was not considered as a covariate [24].

Statistical analysis

Multivariable-adjusted linear regression models that hold calories from NOVA 3 foods constant were used to investigate if isocaloric substitution of UPFs with NOVA 1 + 2 foods was associated with greater changes in body weight, total percentage body fat, trunk fat, and WC at 6 months. The base substitution model adjusted for participants' age, race, sex, and diet arm allocation, which were considered as confounders a priori, holding energy intake from processed foods at 6 months constant [25]. Following the base model, two additional substitution models were developed to control for potential confounding. Additional covariates were retained if they contribute at least a 2% increase in the total variance explained by the model, including self-reported baseline smoking status (never smoker, ever smoker), baseline weight, total energy intake at 6 months, and adherence to prescribed energy deficit. Additionally, multivariable-adjusted regression models were used to compare if 6-month changes in weight and adiposity parameters varied by tertiles (T3 vs. T1) of NOVA 1 + 2 food intake. All analyses were performed with Stata SE 16.0.

RESULTS

Descriptive characteristics of the study participants ($n = 356$) are shown in Table 1. Participants were, on average, 52.3 (SD 8.8) years old, 85% White, and 55% female; 58.2% were nonsmokers; and 71% had college or higher degrees with an average BMI of 32.7 kg/m^2 at baseline. Participants' %kcal intake from NOVA 1 + 2 increased from 30.1% at baseline to 37.4% at 6 months (+7.3%, $p < 0.0001$), whereas %kcal intake from UPFs was reduced from 53.3% at baseline to 47.5% at 6 months (−5.8%, $p < 0.0001$), with a smaller decrease of %kcal intake from NOVA 3 at 6 months (−1.6%, $p = 0.05$). Between baseline and month 6, participants lost a mean of 7.0 kg of weight and 7.3 cm of WC. In the subgroup with complete DXA data ($n = 309$), participants lost a mean of 3.0% of total percentage body fat and 3.8% of trunk fat. Descriptive characteristics of the subgroup with complete DXA data and the group missing body composition measures at 6 months are shown in Table S1. Only age, sex, race, and changes in body weight and WC differed between the group with complete DXA ($n = 309$) and the group missing DXA ($n = 47$). No differences in education level, smoking status, weight, or adiposity measures at baseline or 6-month changes of total energy intake or energy intake (%kcal) by NOVA classification were observed.

We examined whether replacing UPFs with NOVA 1 + 2 foods was differentially associated with changes in body weight loss, total percentage body fat, trunk fat, and WC between baseline and

TABLE 2 Multivariable-adjusted substitution analyses of the association between replacing %kcal from UPFs with NOVA group 1 + 2 foods on weight loss, waist circumference reduction, and total percentage fat body reduction at 6 months among participants in the POUNDS Lost study.

	Minimally processed food and culinary ingredients (NOVA 1 + 2) 10%kcal		
	β coefficient	95% CI	*p* value
Weight loss, kg, $n = 356$			
Base model	−0.36	[−0.79, 0.07]	0.10
Model 1	−0.52	[−0.96, −0.09]	0.02*
Model 2	−0.51	[−0.93, −0.09]	0.02*
Total percentage body fat reduction, $n = 309$			
Base model	−1.77	[−4.13, 0.58]	0.14
Model 1	−2.69	[−5.03, −0.34]	0.03*
Model 2	−2.76	[−5.10, −0.43]	0.02*
Trunk fat percentage reduction, $n = 309$			
Base model	−2.55	[−5.72, 0.61]	0.11
Model 1	−3.74	[−6.90, −0.57]	0.02*
Model 2	−3.85	[−7.01, −0.70]	0.02*
Waist circumference reduction, $n = 356$			
Base model	−0.32	[−0.08, 0.17]	0.21
Model 1	−0.47	[−0.97, 0.02]	0.06
Model 2	−0.46	[−0.95, 0.03]	0.07

Note: Base model: Adjusted for age, race, sex, diet, and 6-month NOVA 3 kcal. Model 1: Adjusted for variables in base model + total kcal, adherence to prescribed energy deficit, and smoking status (ever smoker compared with nonsmoker). Model 2: Adjusted for variables in Model 1 + baseline body weight.
*$p < 0.05$.

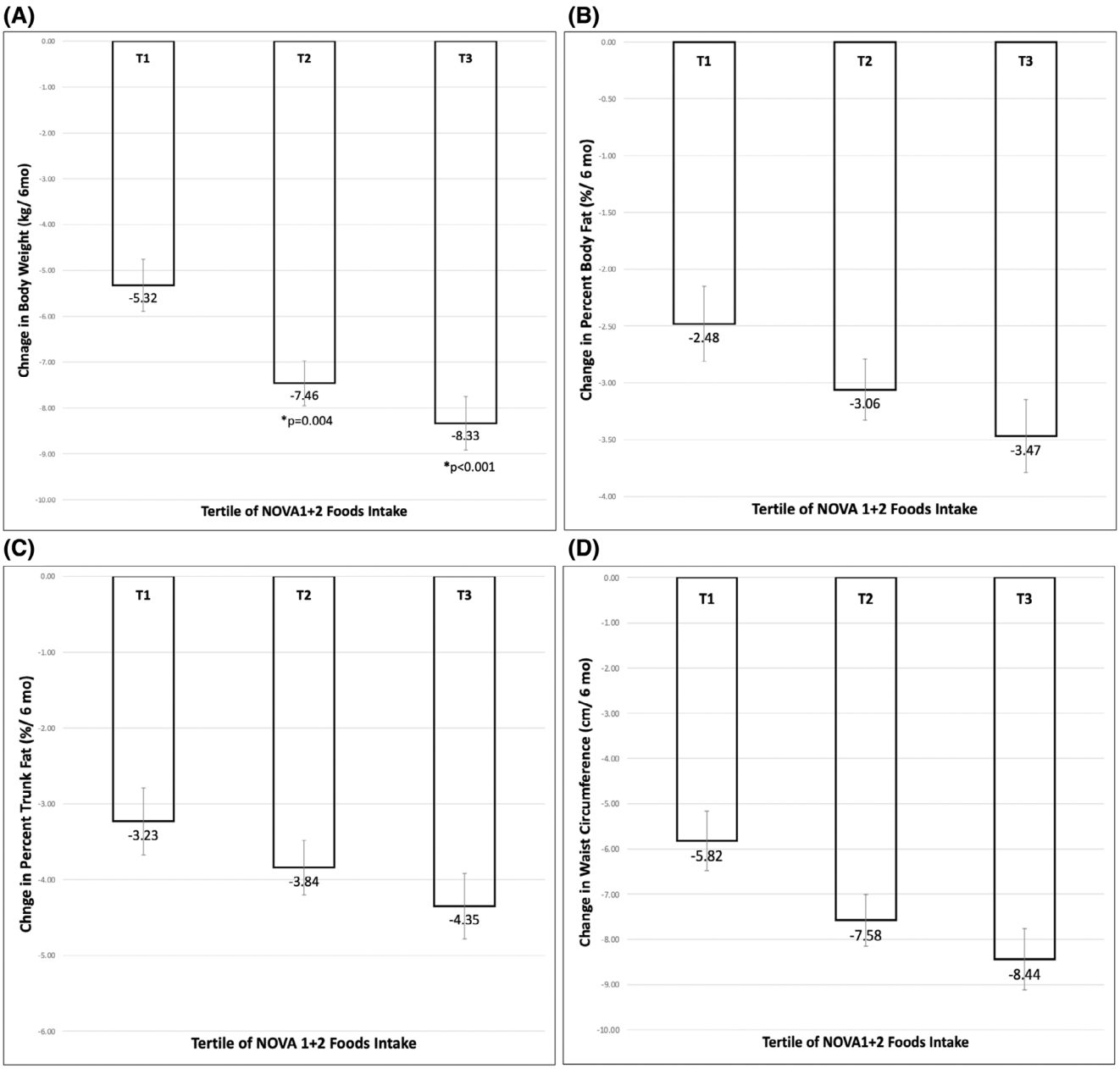

FIGURE 1 Mean differences in (A) body weight, (B) percentage body fat, (C) percentage trunk fat, and (D) waist circumference from baseline to 6 months by tertiles (T) of NOVA 1 + 2 food intake at 6 months among POUNDS Lost participants with overweight and obesity. Data are presented as adjusted means with SE. Mean changes are adjusted for age, race, sex, diet, 6-month NOVA 4 %kcal, total kcal, adherence to prescribed energy deficit, smoking status (ever smoker compared with nonsmoker), and baseline body weight. NOVA 1 + 2 food intake at 6 months was categorized into the following tertiles: T1 (reference group) ($n = 118$, mean %kcal: 20.7%, SD: 7.2%), T2 ($n = 119$, mean %kcal: 36.9%, SD: 4.1%), and T3 ($n = 119$, mean %kcal: 54.7%, SD: 8.3%). %kcal, percent energy intake.

month 6 (Table 2). In the base models adjusted for age, sex, race, and diet arm, while holding calories from NOVA 3 constant, no differential changes in weight and adiposity measures were observed. But when further adjusted for participants' total energy intake, adherence to prescribed energy deficit, and smoking status in Model 1, replacing 10%kcal of UPFs with NOVA 1 + 2 foods was associated with 0.52-kg greater weight loss ($p = 0.02$), 2.7% greater total percentage body fat reduction ($p = 0.03$), 3.7% greater trunk fat (%) reduction ($p = 0.02$), and 0.47-cm greater WC reduction ($p = 0.06$). The direction and magnitude of these associations were essentially unaltered following additional adjustment for baseline body weight in Model 2, resulting in statistically significant greater weight loss ($\beta = -0.51$, 95% CI: −0.93 to −0.09, $p = 0.02$), greater total percentage body fat reduction ($\beta = -2.76$, 95% CI: −5.10 to −0.43, $p = 0.02$), greater trunk fat (%) reduction ($\beta = -3.85$, 95% CI: −7.01 to −0.70, $p = 0.02$), and marginal but not statistically significant greater WC reduction ($\beta = -0.46$, 95% CI: −0.96 to −0.30, $p = 0.07$).

We also examined whether 6-month changes in weight and adiposity parameters varied among different tertiles (T3 vs. T1) of

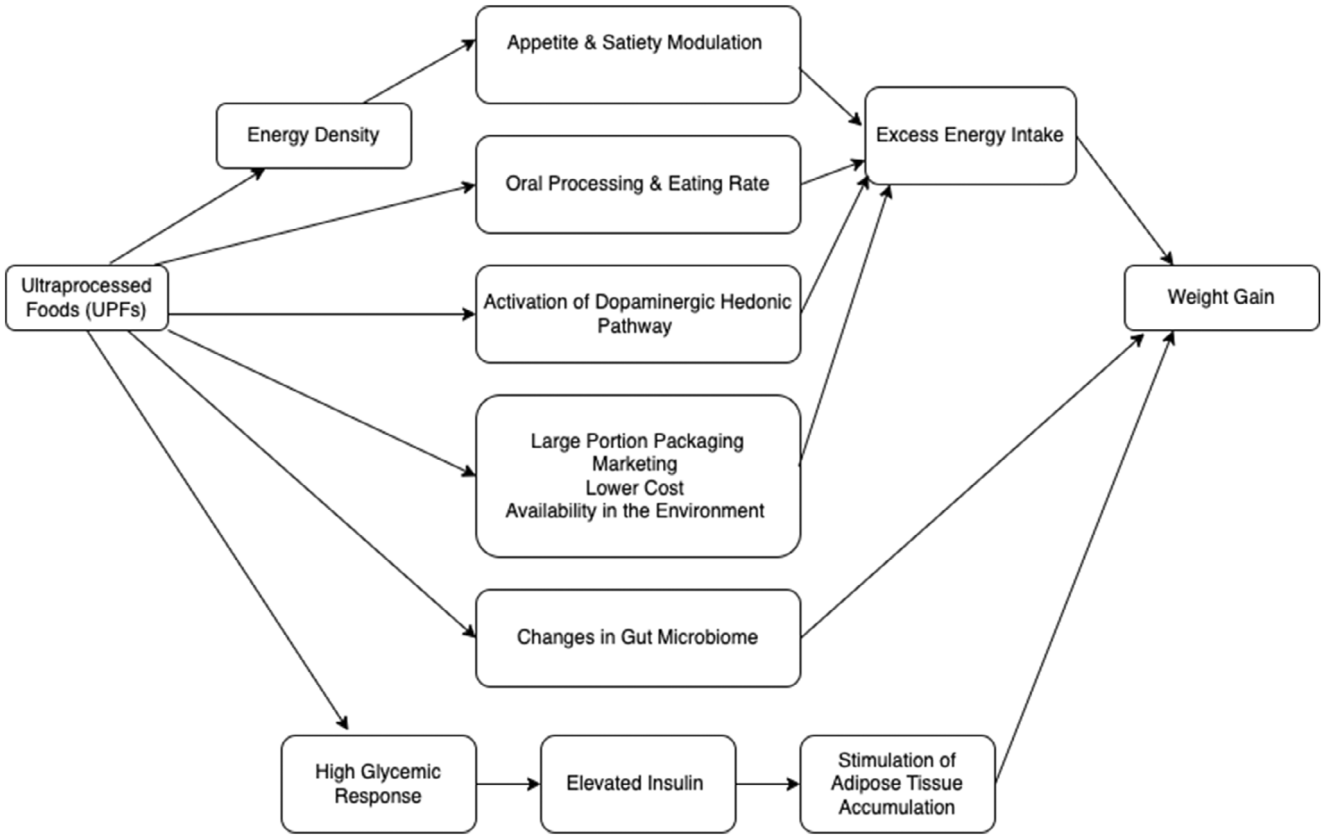

FIGURE 2 Postulated biobehavioral mechanisms through which UPFs affect weight change. High-energy-density UPFs may disrupt appetite and satiety regulated by the gut–brain axis via neural and hormonal signaling [10, 12], leading to overconsumption. The hyperpalatable UPFs [31] may activate the dopaminergic hedonic neurocircuitry [13], which can reinforce the value of UPFs, enhancing consumption and potentially inducing additive-like eating behaviors [32]. Large portion packaging [15], heavy marketing and advertising [16], lower cost due to the use of inexpensive ingredients [17], and vast availability of UPFs in the food environment are also important factors for food choices [2], thus impacting energy consumption. Besides overconsumption, the absence or restructured food matrix of UPFs may prompt changes in gut microbiota composition, which alter nutrient absorption and metabolism, resulting in lipid accumulation and subsequently development of obesity [32–34]. Additionally, UPFs with high glycemic response are suggested to induce elevated insulin response [12], which may promote adipose tissue storage and excess weight gain.

NOVA 1 + 2 food intake (Figure 1). Across tertiles, mean %kcal intake from NOVA 1 + 2 foods was 20.5%, 36.9%, and 54.7%, respectively. In alignment with findings from the isocaloric substitution models, participants in T3 had greater reduction in body weight compared to those in T1 (−8.33 kg vs. −5.32 kg, $p < 0.001$), after controlling for UPF intake, age, race, sex, diet arm, total energy intake, adherence to prescribed energy deficit, smoking status, and baseline body weight. No statistically significant differences between tertiles were found in 6-month changes in total percentage body fat (T3 vs. T1: −3.83% vs. −2.11%, $p = 0.052$), trunk fat (T3 vs. T1: −4.76% vs. −2.81%, $p = 0.101$), or WC (T3 vs. T1: −8.88 cm vs. −5.39 cm, $p = 0.060$).

DISCUSSION

In the POUNDS Lost trial, participants in general reduced UPF intake and lost weight and body adiposity. Isocaloric substitution of UPFs with minimally processed foods and culinary ingredients was associated with significantly greater weight loss, total percentage body fat reduction, and trunk fat reduction. The detectable differences achieved from shifting an equivalent proportion of energy intake from UPFs to minimally processed foods, while not yet clinically meaningful, remain compelling and added to the effects on weight and adiposity parameters—particularly when altering %kcal from UPFs to minimally processed foods was not an intervention target. Given that UPFs still constituted 47.5% of daily total energy intake at 6 months, greater and more clinically meaningful differences in weight reduction might be achieved with greater isocaloric substitution of UPFs with NOVA 1 + 2 foods. Furthermore, these findings have important implications from prior research on UPFs because they showed that under intentional energy restriction, people with higher proportion of UPFs in their diet lost weight, but not as effectively as people with higher proportion of less-processed foods, suggesting that there may be other attributes of food processing through which UPFs affect regulation of body weight and adiposity beyond excess energy consumption.

Findings from prospective cohorts have demonstrated similar associations between UPF consumption and measures of weight gain after controlling for energy intake. In the Brazilian Longitudinal Study for Adult Health (ELSA-Brasil) with a mean 3.8-year follow-up, a 15% increment increase of energy consumption from UPFs was associated with a 27% increased risk of weight gain greater than 1.68 kg per year [26]. Similarly, in the French NutriNet-Sante cohort 2009–2019, every 10% increase in UPFs by weight in the diet was associated with a 0.21-unit increase in BMI [27]. Furthermore, a dose–response relationship between higher consumption of UPFs and greater 5-year weight gain (0.12 kg per 250-g increment/5 years) was found within a multinational European cohort [28]. For adiposity measures, Li et al. and Canhada et al. observed significant associations between higher UPF intake and greater WC gain and risk of central obesity [26, 29]. A similar trend was observed in the current study, albeit nonsignificant for WC reduction but significant for trunk fat reduction measured by DXA. The borderline significant findings for WC reduction may be due to its increased measurement variability and reduced accuracy in individuals with BMI of 35 or higher, which constituted a third of the study population in POUNDS Lost [30].

Taken together, this secondary analysis of the POUNDS Lost study is largely consistent with prior research findings and adds important insight into the mechanisms behind the consistently observed associations between UPF intake and obesity. Although imperfectly understood, many plausible biobehavioral mechanisms linking UPFs and weight gain have been postulated (Figure 2). Most focus on pathways related to excess energy intake, due to attributes of UPFs that impact appetite modulation [10], satiety signaling [12], oral processing speed [11], and activation of the dopaminergic hedonic pathway due to hyperpalatability [13, 32]. Distinct from biological pathways, other research studies suggest that behavioral traits of UPFs may also lead to excess energy intake, including large portion packaging [15], heavy marketing and advertising [16], lower cost with cheaper ingredients [17], and vast availability in the food environment [2]. Nonetheless, our findings suggest that energy-independent mechanisms may also contribute to weight gain and risk of obesity. The present study was conducted among individuals with a prescribed energy-restricted diet and with dietary counseling by registered dietitians, with analyses further adjusted for adherence to energy restriction targets, suggesting that energy overconsumption was not the primary driver of differential weight loss. One mechanism that could potentially explain our findings is related to UPF-induced changes to the gut microbiome. It is postulated that the absence or restructured food matrix of UPFs may prompt shifts in gut microbiota composition, which alter nutrient absorption kinetics and fuel partitioning, resulting in lipid accumulation and subsequently development of obesity [32–34]. Additionally, UPFs with high glycemic response are suggested to induce elevated insulin response [12], which may promote adipose tissue storage and excess weight gain.

Our study has some limitations. Consistent with prior research [20, 35], our study investigated overall UPF intake rather than food group–specific associations. However, given three large prospective cohorts revealed inverse associations between intake of UPF subgroups, including ultraprocessed cereals, commercial dark and whole-grain breads, fruit-based products, and yogurt and dairy-based desserts, and risk of type 2 diabetes [19], it would be beneficial to disentangle UPF subgroups and the health effects they elicit. Furthermore, participants with missing DXA data at 6 months lost significantly less body weight and WC compared to participants with complete DXA, suggesting some overestimation of effect size. Additionally, there is measurement error associated with dietary recall. However, because the recalls were unlikely to be differential based on UPF intake, it is unlikely to introduce substantial bias or affect the study validity. Lastly, given that our study population was in a homogenous population, the generalizability of our finding to populations of different characteristics should be done with caution.

Our study also has several strengths. To our knowledge, the present study is the first to examine the association between isocaloric substitution of UPFs with minimally processed foods and differential weight change within an energy-restricted dietary intervention. Our findings align with existing cohorts and extend current evidence on the role of other mechanisms of UPFs beyond excess energy intake in body weight and adiposity regulation. In addition, multiple food records and 24-h diet recalls were used to access dietary intake instead of Food Frequency Questionnaires, allowing for more accurate capture and categorization of UPF intake and estimation of total energy intake [36]. For anthropometric measures, body weight and WC were consistently measured in the morning before breakfast on 2 days at baseline and at 6 months with calibrated hospital equipment to ensure accuracy. Additionally, by examining replacement of food intake as %kcal, we further minimized the potential impact of energy over- or underestimation.

CONCLUSION

We found that isocaloric substitution of UPFs with minimally processed foods and culinary ingredients is associated with greater body weight loss, percentage body fat reduction, and trunk fat reduction in a weight loss trial with a prescribed energy-restricted diet. These findings support that there may be other attributes of UPFs that affect body weight and adiposity regulation in addition to energy intake. As the field is moving toward evaluating food processing as an independent risk factor, future studies are needed to determine specific pathways through which overall UPF and certain groups of UPF intakes may affect the obesity trajectory beyond energy intake.O

AUTHOR CONTRIBUTIONS

George A. Bray, Catherine M. Champagne, and Frank M. Sacks conceived and carried out the experiments. Carolina D. de Araujo and Filippa Juul created the analytical dataset. Qisi Yao and Carolina D. de Araujo analyzed the data and wrote the initial draft of the manuscript. Maya K. Vadiveloo conceived and supervised the analyses and had primary responsibility for the final content. All authors were involved in manuscript preparation and had final approval of the submitted and published versions.

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In accordance with the recommendations of the International Committee of Medical Journal Editors (ICMJE), we provide the following information regarding data sharing for this secondary analysis. We attest that our use of the shared data from the POUNDS Lost study (NCT00072995) was in accordance with the terms agreed to upon our receipt. Our analyses differed from previous analyses by using multivariable-adjusted substitution models to determine if the replacement of UPFs with less-processed foods was differentially associated with body weight and adiposity measures, which has not been investigated in prior research.

FUNDING INFORMATION

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CONFLICT OF INTEREST STATEMENT

The authors declared no conflict of interest.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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