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Efficacy of Olibra: A 12-Week Randomized Controlled Trial and a Review of Earlier Studies

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Abstract

Background:

Intervention strategies that harness the body's appetite and satiety regulating signals provide a means of countering excessive energy intake.

Methods:

Eighty-two subjects were enrolled (18–60 years, body mass index: 25–40 kg/m^2) in a randomized, placebo-controlled, double-blind, parallel trial. During a 12-week period, the effects of Olibra™ fat emulsion (2.1 g twice daily) on food intake, appetite, satiety, weight, and body composition were compared with those of a twice daily administered placebo (1.95 g milk fat). On days -7, 0, and 28, Olibra or the placebo added to 200 g of yogurt was served at breakfast and lunch. Food intake, appetite, and satiety were assessed after lunch and dinner. Body weight was measured on days -7, 0, 14, 28, 56, and 84. Body fat, waist circumference, and waist-hip ratio were determined on days 0 and 84. The Eating Inventory was administered at screening and on day 28. Data relating to 71 subjects were analyzed using analysis of covariance.

Results:

At 12 weeks, body weight was reduced in the test group (2.17 ± 0.46 kg standard error of the mean, $p < .0001$) and the control group (1.68 ± 0.42 kg, $p < .0001$). Waist circumference decreased by 2.93 ± 0.85 cm in the test group ($p = .001$) and by 1.78 ± 0.74 cm in the control group ($p = .02$). Differential weight and waist circumference reductions were not significant. Hunger scores (Eating Inventory) decreased more in the test group ($p = .0082$). Differential group effects were not significant for body fat, waist-hip ratio, food intake, appetite, and satiety.

Conclusions:

At this dose, Olibra did not exert a consistent effect on food intake, appetite regulation, body weight, or body composition.

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Abbreviations: (ANCOVA) analysis of covariance, (β-hCG) β-human chorionic gonadotropin, (BMI) body mass index, (EI) Eating Inventory, (GI) gastrointestinal, (kcal) kilocalorie, (PBRC) Pennington Biomedical Research Center, (PROP) 6-n-propylthiouracil, (SD) standard deviation, (SEM) standard error of the mean, (US) United States, (USDA) United States Department of Agriculture, (VAS) visual analog scale

Keywords: appetite, emulsion, energy intake, fats, satiety, weight loss

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Introduction

The overweight and obese population both in the United States (US) and globally has increased over several decades. For example, in the US, 68% of adults are overweight or obese.[1] The consequent rise in associated diseases such as type 2 diabetes, cardiovascular diseases, and some cancers[2,3] is a major public health concern. It is estimated that health care costs attributable to overweight and obesity will double every decade, reaching 860.7 to 956.9 billion US dollars and accounting for 16–18% of total US health care costs by 2030.[4]

Body weight is influenced by the interaction of biological, environmental, and physiological factors. A number of hormonal, neuronal, and metabolic responses that orchestrate this process are located in the gut.[5–7] Thus, the gastrointestinal (GI) tract plays a pivotal role in regulating food intake. The ileal brake is a negative feedback mechanism that is activated by the entry of nutrients into the ileum.[8] The inhibitory effects of the activation of the ileal brake are a result of the interaction of neural and humoral signals[9] exerting their influence on the proximal parts of the intestine. Exposure of the ileum to fats and fatty acids delays gastric emptying,[10,11] prolongs GI transit time,[12] and influences satiety.[13–15] The physicochemical properties of fat affect its ability to regulate GI motor function, gut hormone release, and satiety. These effects are more pronounced with long chain fatty acids (≥12 carbons) than with shorter chain fatty acids (≤10 carbons).[16,17] There is also growing evidence that free fatty acids are stronger mediators of the GI effects of fat than triacylglycerides.[18] The role played by the degree of saturation in modulating the effects of fat on the GI tract has not been resolved fully.[19,20]

Delaying lipid digestion is an important factor in stimula-ting the ileal brake. By manipulating oil emulsions using galactolipids, lipolysis can be delayed through the inhibition of lipase activity.[21] Olibra™ (Lipid Technologies Provider AB, Karishamn, Sweden) is a fat emulsion composed of fractionated palm and oat oil in the proportion of 95:5. The palm oil is emulsified by hydrophilic galactolipids derived from oat oil.[22] Olibra has been demonstrated in some studies to increase satiety and reduce food intake.[23–25] Other studies, however, have not replicated these effects on food intake[26,27] although a positive effect on maintenance of weight loss[28] and fat loss[28,29] have been demonstrated. Randomized, clinical weight-loss trials have not been reported. Studies that employed methods of delivering the emulsion directly into the GI tract have demonstrated a delay in GI transit.[22,30] However, when ingested orally, this fat emulsion may not elicit the GI responses manifested by an intragastric or intraduodenal administration. In the dynamic environment of the GI tract, resistance of the emulsion to digestion is crucial for stimulating an increase in satiety and a reduction in food intake.

The purpose of this study was to determine whether Olibra in conjunction with a healthy diet and exercise plan would result in weight loss that was associated with a reduction in food intake. The incidence of adverse effects of Olibra administration was also evaluated.

Methods

Subjects

Subjects of both sexes 18–60 years of age with a body mass index (BMI) between 25 and 40 kg/m^2, inclusive, were recruited from the communities surrounding the Pennington Biomedical Research Center (PBRC) in Baton Rouge, Louisiana. Subjects were eligible for the trial if they were determined to be healthy at a physical exam and had clinically normal findings in laboratory measurements. Questionnaires related to dietary restraint,[31] sandwich rating (to ensure that food used in the study was not disliked), and food selection[32] were completed. All subjects completed a 6-n-propylthiouracil (PROP)[33] test to determine if they were nontasters, medium tasters, or supertasters. Exclusion criteria included (1) a dietary restraint score of >13, (2) weight loss ≥4.5 kg in the preceding 3 months, (3) a medical condition or taking regular medication, (4) history of alcohol or other drug abuse in the preceding 1 year, and (5) pregnancy, lactation, or postpartum less than 6 months.

The study was approved by the Institutional Review Board of the PBRC, and participants provided written informed consent. The trial was registered on *ClinicalTrials.gov* under NCT01416051.

Study Design

The study followed a two-phased, randomized, placebo-controlled, double-blind, parallel design.

Phase I

At visit 1 (day -7 ± 2), qualified subjects arrived at the PBRC in the morning after a 12-hour overnight fast. Vital signs and weight were measured. Subjects were asked to consume an entire 382 kilocalorie (kcal) breakfast consisting of a serving of yogurt containing placebo (milk fat) followed by a cereal bar. Subjects returned 4 h later for a lunch meal consisting of a serving of yogurt containing placebo followed by more sandwiches, chips, and cookies than could reasonably be consumed. They returned 5 h later for a buffet dinner meal. The food intake at lunch and dinner was determined by subtracting the weight of the uneaten food from its original weight. The kcal and macronutrient intakes were calculated using product information and the United States Department of Agriculture (USDA) nutrient database.[34] Subjective ratings (appetite and satiety) were recorded through visual analog scales (VASs). Concomitant medications and any adverse events were assessed throughout the entire study to determine the feasibility of subjects' continuance with the study. One week later, at visit 2 (day 0 ± 2), the subjects arrived at the PBRC in the morning after a 12 h overnight fast and were randomized to the Olibra or placebo group. Vital signs, weight, waist and hip circumferences, and body fat measurements were taken. The food intake test conducted at visit 1 was repeated, except that subjects were given the yogurt with Olibra or the placebo added to it at breakfast and lunch.

Phase II

After the food intake test at visit 2, subjects were instructed by a registered dietitian to follow a 1500-kcal diet and encouraged to increase their current activity level. Olibra or the placebo was dispensed in a double-blind manner in ready-to-use portion packs. The subjects were instructed to consume the product twice daily, preferably with breakfast and lunch, for 12 weeks. Vital signs and weight measurements followed at visits 3–6 [days 14, 28, 56, and 84 (± 2)]. Subjects were considered compliant if they consumed the recommended dose at least 70% of the time. At visit 4, subjects repeated the food intake testing protocol followed at visit 2. At visit 6 (day 84 ± 2), subjects arrived at the PBRC after a 12 h overnight fast. Body fat, and waist and hip circumferences were measured. Blood tests and the physical exam performed at screening were repeated at visit 6. A schedule of assessments is presented in **Table 1**.

Test Products

One serving of the test product was 7.5 g (19 kcal), providing 2.1 g of the fat emulsion Olibra. One serving of the placebo was also approximately 7.5 g (18.5 kcal), providing 1.95 g of 100% milk fat and small amounts of carbohydrate (0.2 g) and protein (0.3 g). At the food intake tests, Olibra or the placebo was added to a 200 g carton of fruit-flavored yogurt—194 kcal, 1.8 g fat, 38.6 g carbohydrate, and 5.8 g protein.

Measurements

Anthropometry

Body weight was measured[35] at all visits. Fasting measurements were taken at screening and at visits 1, 2, 4, and 6. Height was measured[35] at screening to determine BMI [weight (kg)/height squared (m^2)]. Waist and hip circumferences were measured[35] and the waist-hip ratio was calculated.[36] Body composition was measured using bioelectrical impedance (RJL Systems, BIA101A, Clinton Township, MI).

Questionnaires

Each food intake test was preceded by a questionnaire about colds or allergies that might affect taste. Eating Inventory (EI)[31] was administered at screening and prior to the food intake test on day 28. The food intake tests were accompanied by VASs administered before and after breakfast, lunch, and dinner. Participants rated their degree of each subjective state by placing a hash mark on a 100-mm line. The 100-mm line was anchored using the descriptors "Not at all" to "Extremely." Hunger, fullness, desire to eat, food craving, desire for sweet, desire for salty, and desire for fatty foods were assessed. Visual analog scales were also used to assess hedonic (sensory) responses to the yogurt served at breakfast and lunch on all food-intake test days. The Food Selection Questionnaire[32] was used to rate the participants' food preferences from a wide variety of foods that were offered at the buffet dinner meals.

Adverse Events

An adverse event was defined as any adverse change from baseline (pretreatment) condition that occurred during the course of the study after treatment had started, whether considered related to treatment or not. All adverse events, including intercurrent illnesses and an increase in severity or frequency of a concomitant sign/symptom of a concomitant illness, were documented.

Statistical Analysis

The food intake testing reported in the literature suggests that Olibra will reduce food intake by 20–30%.[23–25] From past experience, one can detect a 12% decrease in food intake in the eating laboratory with 30 subjects as their

Table 1.
Schedule of Study Procedures, from Screening Visit to the End of Study

Procedure	Phase I			Phase II			
	Screening visit	Visit 1, baseline, day -7 ± 2	Visit 2, day 0 ± 2	Visit 3, day 14 ± 2	Visit 4, day 28 ± 2	Visit 5, day, 56 ± 2	Visit 6, day 84 ± 2
Medical history	X						
Physical exam	X						X
Height	X						
Weight	X	X	X	X	X	X	X
Vital signs (blood pressure, pulse rate)	X	X	X	X	X	X	X
Body composition	X		X				X
Waist and hip circumference	X		X				X
Chemistry panel	X						X
Lipid profile	X						X
Complete blood count, with differential	X						X
Concomitant medications	X	X	X	X	X	X	X
β-hCG[a] pregnancy test—urine	X						
PROP taste-sensitivity test	X						
Visual analog scales		X	X		X		
Eating Inventory	X				X		
Food Selection Questionnaire	X						
Sandwich rating questionnaire	X						
Cold/allergy questionnaire		X	X		X		
Dietitian consultation			X				
Adverse events		X	X	X	X	X	X
Food intake tests with placebo		X					
Food intake tests (with test product or placebo)			X		X		

[a] β-hCG, β-human chorionic gonadotropin.

own controls.[37] The difference in food intake decreases with time on a diet.[37] Therefore, 82 subjects were randomized in this study. This allowed for 30 subjects per group to complete week 4 of the study assuming 30% maximum attrition. Assuming a standard deviation of 2.3 kg and an alpha of 0.05, the study was powered at 89% to detect a difference of 2 kg in weight loss between the groups at 12 weeks if 28 subjects finished per group.

Observations made during visit 1 of the study were considered as baseline measurements. A repeated measures analysis of covariance (ANCOVA) with baseline covariates was used to test if change in energy intake from baseline to week 4 differed significantly between the test and control groups. Body weight, waist circumference, waist-hip ratio, percent body fat, and EI scores were analyzed similarly. The changes from baseline for the scores for appetite and satiety assessed through VASs were analyzed by doubly repeated measures ANCOVA. Visual analog scales used to assess hedonic responses to the test and control yogurt were analyzed directly rather than as change scores in a repeated measures analysis of variance. Chi-square test was used to analyze the distribution of tasters. Food intake and body weight were analyzed by stratifying taster status. *Post hoc* tests when conducted followed the Tukey-Kramer adjustment. All analyses were carried out using SAS (v. 9.2; SAS Institute, Inc., Cary, NC). Subject characteristics are presented as mean ± standard deviation (SD) and efficacy endpoints are presented as mean ± standard error of the mean (SEM).

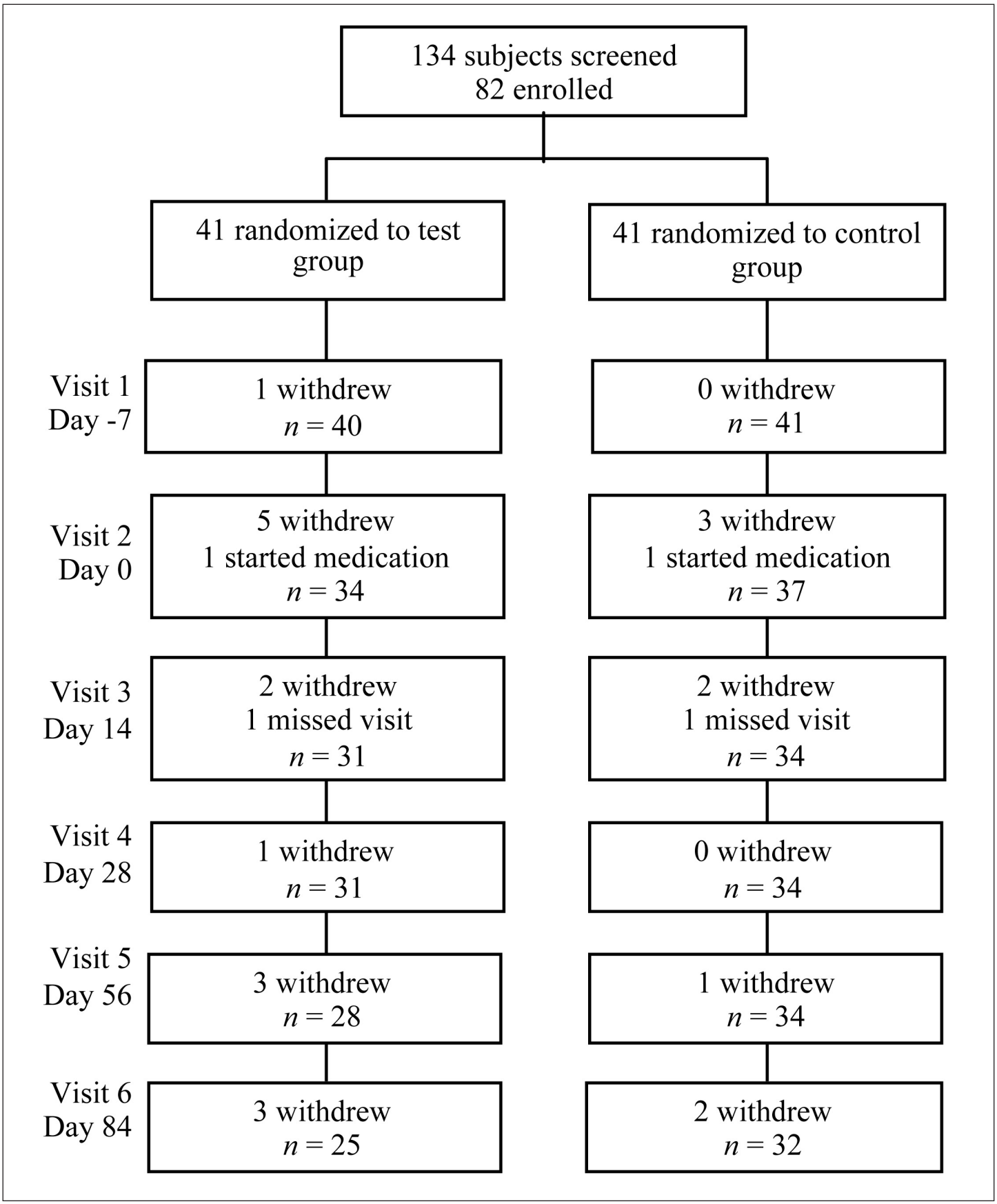

Figure 1. Subject recruitment, randomization, and continuance with the study.

Results

Data related to 71 subjects were analyzed, and 57 subjects completed the study (**Figure 1**). Descriptive characteristics of the subjects at baseline are summarized in **Table 2**.

Anthropometry

At the end of 12 weeks, body weight was significantly reduced in both groups (test group: 2.17 ± 0.46 kg, $p < .0001$) (control group: 1.68 ± 0.42 kg, $p < .0001$) with no significant difference between groups (**Table 3**). Waist circumference decreased by 2.93 ± 0.85 cm in the test group ($p = .001$) and by 1.78 ± 0.74 cm in the control group ($p = .02$), with no significant difference between the two treatment regimens. The waist-hip ratio decrease by 0.014 ± 0.007 in the test group and by 0.012 ± 0.006 in the control group was not significant, with no statistical difference between the groups. Neither group experienced a significant change in percent body fat or lean tissue as assessed by bioelectrical impedance.

Food and Energy Intake

There were no significant differences in the mean energy,

Table 2.
Subject Characteristics at Baseline, Including Demographics

	Total (n = 71)	Test (n = 34)	Control (n = 37)	p value
	Mean ± SD	Mean ± SD	Mean ± SD	
Age (years)	40.5 ± 12.1	38.4 ± 12.8	42.4 ± 11.2	.2
Height (cm)	166.4 ± 8.41	166.0 ± 8.2	166.7 ± 8.7	.7
Weight (kg)	89.3 ± 13.0	88.5 ± 14.6	90.0 ± 11.5	.6
BMI (kg/m^2)	32.3 ± 3.92	32.1 ± 4.5	32.4 ± 3.4	.7
Waist (cm)	97.6 ± 9.3	98.1 ± 10.5	97.2 ± 8.3	.7
Hip (cm)	112.6 ± 7.9	111.9 ± 8.7	113.3 ± 7.1	.5
Body fat (%)	40.7 ± 6.0	40.3 ± 6.9	41.1 ± 5.0	.6
Waist-hip ratio	0.9 ± 0.1	0.9 ± 0.1	0.9 ± 0.1	.7
	n (%)	n (%)	n (%)	
Sex				
Female	60 (84.5)	28 (82.3)	32 (86.5)	
Male	11 (15.5)	6 (17.7)	5 (13.5)	
Race				
White	47 (66.2)	22 (64.7)	25 (67.6)	
Black	24 (33.8)	12 (35.3)	12 (32.4)	

Table 3.
Body Weight and Body Composition Measurements, from Day -7 to 84, Including Change from Day 0 to 84 (Between-Group p value = Not Significant)[a,b]

	Day -7	Day 0	Day 14	Day 28	Day 56	Day 84	Δ Day 0–84	p value
Test	n = 34	n = 34	n = 31	n = 31	n = 28	n = 25	n = 25	
Control	n = 37	n = 37	n = 34	n = 35	n = 34	n = 32	n = 32	
Weight (kg)								
Test	88.4 ± 2.2	88.5 ± 2.2	87.1 ± 2.2	87.1 ± 2.2	86.6 ± 2.2	86.4 ± 2.2	-2.17 ± 0.5	<.0001
Control	90.0 ± 2.1	90.0 ± 2.1	90.0 ± 2.1	89.2 ± 2.1	88.9 ± 2.1	88.3 ± 2.1	-1.68 ± 0.4	<.0001
% Change in weight								
Test	.	0.2 ± 0.4	-1.4 ± 0.42	-1.4 ± 0.4	-1.9 ± 0.4	-2.1 ± 0.5	-2.2 ± 0.5	<.0001
Control	.	0.1 ± 0.4	-1.0 ± 0.4	-0.8 ± 0.4	-1.2 ± 0.4	-1.8 ± 0.4	-1.9 ± 0.4	<.0001
Waist (cm)								
Test	-	98 ± 1.6	-	-	-	95.0 ± 1.7	-2.9 ± 0.9	.001
Control	-	97.2 ± 1.5	-	-	-	95.5 ± 1.6	-1.8 ± 0.7	.02
Waist/hip ratio			-	-	-			
Test	-	0.87 ± 0.01	-	-	-	0.86 ± 0.01	-0.01 ± 0	.06
Control	-	0.86 ± 0.01	-	-	-	0.85 ± 0.01	-0.01 ± 0	.08
% Body fat			-	-	-			
Test	-	39.7 ± 1.0	-	-	-	38.8 ± 1.1	-0.9 ± 0.6	.13
Control	-	40.8 ± 1.0	-	-	-	40.2 ± 1.0	-0.6 ± 0.6	.31

[a] Values are mean ± SEM
[b] Waist, waist-hip ratio, and % body fat were measured on days 0 and 84

macronutrient, or amount of food consumed in the test group when compared with the control group (**Table 4**). Based on within-group analyses, on day 0, there was no significant change in the energy, macronutrient, or amount of food consumed in the test group as compared with their intake on day -7. The results were similar for the lunch, dinner, and total (lunch + dinner) meal intake.

Subjective Ratings

No significant treatment effects were found for any of the appetite and satiety measures over the various time periods. There was no significant difference in VAS ratings of pleasantness, palatability, desirability, and capacity to satiate between the test and control yogurt served at the food intake tests.

Adverse Events

Fifty-eight adverse events were reported (test group: 26, control group: 32). Forty adverse events were resolved (test group: 20, control group: 20). There were 18 adverse events ongoing at the end of the study. Six were reported in the test group and 12 in the control group (**Table 5**). There were no serious adverse events (life threatening, requiring hospitalization, or significantly disabling).

6-n-propylthiouracil Test

There were 24.2% supertasters, 57.6% medium tasters, and 18.2% nontasters in the test group as compared with 21.6% supertasters, 62.2% medium tasters, and 16.2% nontasters in the control group. Taster status did not indicate a differential response to food intake or an influence on body weight.

Eating Inventory

There were no significant changes in the scores for dietary restraint and disinhibition, however, hunger scores were significantly reduced in the test group as compared with the control group (p = .0082) (**Figure 2**).

Table 4.
Energy, Macronutrient, and Food Intake Determined at Lunch and Dinner, Including the Combined (Lunch + Dinner) Intake, Pre- and Postintervention (Between-Group p value = Not Significant)[a]

	Day –7		Day 0		Day 28[b]	
	Test	Control	Test	Control	Test	Control
Lunch	n = 34	n = 37	n = 34	n = 37	n = 30	n = 35
Energy intake (kcal)	654.2 ± 47.8	588.9 ± 45.8	639.5 ± 47.8	606.7 ± 45.8	639.2 ± 49.2	601.1 ± 46.4
Food intake (g)	700.4 ± 36.3	663.5 ± 34.8	661.4 ± 36.3	613.2 ± 34.8	637.2 ± 37.9	549.2 ± 35.5
Fat (g)	27.9 ± 2.7	23.4 ± 2.2	26.2 ± 2.7	23.7 ± 2.2	27.5 ± 2.3	25.7 ± 2.2
Carbohydrate (g)	70.8 ± 5.6	65.7 ± 5.4	71.5 ± 5.6	69.1 ± 5.4	69.5 ± 5.8	66. 8 ± 5.4
Protein (g)	28.4 ± 2.0	27.3 ± 1.9	27.9 ± 2.0	27.6 ± 1.9	27.0 ± 2.0	24.5 ± 1.9
Dinner	n = 34	n = 35[c]	n = 34	n = 35[c]	n = 29[d]	n = 32[c]
Energy intake (kcal)	948.9 ± 58.3	915.3 ± 57.4	838.0 ± 58.3	788.9 ± 57.4	720.2 ± 60.9	662.8 ± 58.9
Food intake (g)	419.7 ± 30.0	418.9 ± 29.6	383.3 ± 30.0	380.4 ± 29.6	342.0 ± 31.2	326.8 ± 30.2
Fat (g)	44.7 ± 3.3	46.6 ± 3.3	39.0 ± 3.3	39.5 ± 3.3	32.5 ± 3.5	32.2 ± 3.4
Carbohydrate (g)	102.4 ± 6.4	88.0 ± 6.3	91.3 ± 6.4	77.1 ± 6.3	80.5 ± 6.7	69.0 ± 6.5
Protein (g)	36.9 ± 2.7	36.5 ± 2.7	32.4 ± 2.7	31.9 ± 2.7	27.2 ± 2.8	25.0 ± 2.7
Lunch + dinner	n = 34	n = 35	n = 34	n = 35	n = 29	n = 32
Energy intake (kcal)	1603 ± 91.2	1484.1 ± 89.8	1477.5 ± 91.2	1376.1 ± 89.8	1350.7 ± 94.8	1239.7 ± 91.1
Food intake (g)	1120.1 ± 56.0	1074.8 ± 55.2	1044.7 ± 56.0	992.8 ± 55.2	988.6 ± 58.2	867.1 ± 56.4
Fat (g)	72.6 ± 4.8	69.4 ± 4.8	65.2 ± 4.8	62.5 ± 4.8	59.9 ± 5.0	57.0 ± 4.9
Carbohydrate (g)	173.2 ± 9.9	150.7 ± 9.8	162.9 ± 9.9	143.3 ± 9.8	148.7 ± 10.6	132.6 ± 10.0
Protein (g)	65.3 ± 3.9	63.3 ± 3.9	60.3 ± 3.9	59.1 ± 3.9	53.8 ± 4.1	48.7 ± 4.0

[a] Values are mean ± SEM.
[b] One subject (control group) missed visit.
[c] Outliers in the data (all dinner records of 2 subjects and 1 dinner record of 1 subject that could not be verified) removed from analysis.
[d] One subject missed dinner.

Table 5.
Adverse Events Reported during the Study Period, Including Those Resolved and Those Ongoing at the End of the Study[a]

Effect	Resolved		Ongoing at end of study	
	Test group	Control group	Test group	Control group
Neurological				
Headache	6	4		2
Insomnia	1			
Musculoskeletal				
Muscle pain	1			
Back pain	2	2		1
Gastrointestinal				
Diarrhea	1	1		1
Abdominal pain	1	1		
Nausea/vomiting	1	1		
Heartburn/indigestion		1		2
Oral complaints	2		1	
Dermatologic				
Foot infection	1			
Rash			1	
Pruritus				1
Respiratory				
Cough /cold	1	2		1
Sinus infection		1	1	1
Allergy		2		1
Other		1		
Cardiovascular				
Hypertension				1
Chest pain				1
Dizziness		1		
Genitourinary				
Menstrual cramps		1		
Urinary tract infection		1		
Nonspecific				
Viral infection	1			
Fatigue		1		
Anxiety			1	
Special senses/other	2		2	
Total	20	20	6	12

[a] Four adverse events in the control group (2 indigestion, 1 diarrhea, and 1 dizziness) were reported as possibly related to the treatment. No treatment-related adverse events were reported in the test group.

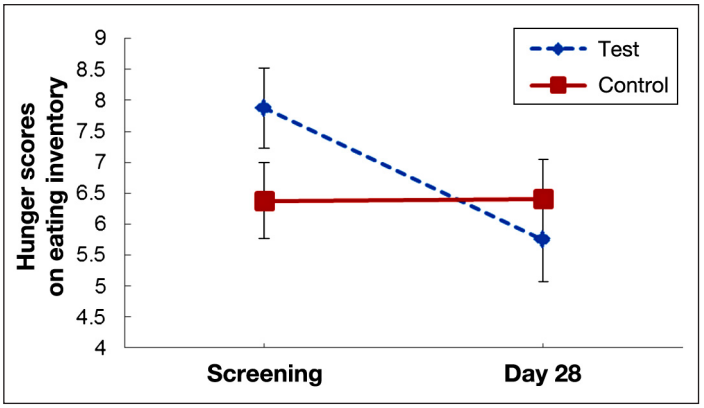

Figure 2. Hunger scores on EI collected at screening and prior to food intake test on day 28 (p = .0082). Values are mean ± SEM.

Discussion

At the end of 12 weeks, a reduction in body weight and waist circumference did occur but the differential reduction was not statistically significant between the groups. Eating Inventory scores for hunger, which reflect an individual's perception of hunger feelings, were significantly reduced in the test group as compared with the control group, however, no significant treatment effects were observed on energy intake, food intake, and appetite and satiety ratings after 4 weeks of Olibra consumption.

Earlier studies,[23–25] all crossover designs, reported a reduction in energy, macronutrient, and total weight of food intake following consumption of the Olibra emulsion. The suppressive effects on appetite ratings (hunger, desire to eat, and preoccupation with thoughts of food or perceived fullness) in the short term were only demonstrated in one study[24] and one part of another.[23] In the present study, there was no significant reduction in energy, macronutrient, or total weight of food intake 4 or 9 h after consumption of Olibra based on within- and between-group analyses. Crossover designs minimize the errors of individual variability, hence the present study was designed to evaluate the acute effects of Olibra using a within-subject analysis in addition to its effects on two different groups. Using self-reported food intake data, Burns and colleagues[25] concluded that the treatment effects of Olibra were maintained up to 36 hours. However, self-reported data are notorious for their susceptibility to misreporting and altered feeding behavior.

Two subsequent studies failed to confirm the reduction in energy intake[26,27] although a suppressive effect on appetite ratings (hunger, fullness, desire to eat, and prospective intake or preoccupation with thoughts of food) was demonstrated.[27] No effect on body weight, body

composition, or waist circumference was observed after 3-weeks' consumption of Olibra.[26] A meta-analysis[38] of the short-term effects of Olibra on food intake attributed the differences in findings partly to the manufacture, processing, or preparation of Olibra. It has been speculated that the functional integrity of the Olibra emulsion structure is affected when it is subjected to processing such as homogenization and pasteurization along with the yogurt. The emulsion used in the present study was added after the yogurt, served at the food intake tests, was manufactured. It was therefore not subjected to further processing. The demonstrated efficacy of unprocessed as compared with processed Olibra in reducing energy and food intake[39] at 8 h was not observed. However, these investigators also found no effects on hunger, fullness, and satiety.

All of the studies that investigated the effects of oral ingestion of Olibra used between 4 and 5 g of the emulsion except for one study[25] that investigated the dose response using 2, 4, and 6 g and found no difference between the doses. Eating behavior is composed of a large learned and anticipatory component.[40] Behavioral and environmental factors can overcome physiological drives and influence feeding behavior.[41] Therefore, a physiological impetus would have to be sufficiently large to consistently correlate with altered energy and nutrient intakes. Additionally, the relatively small sample sizes used in all the studies resulted in divergent results since the actual difference was much smaller than the expected difference.

The beneficial effects of Olibra on body composition and weight maintenance after weight loss have been demonstrated,[28] however, Olsson and colleagues[29] observed no effect on weight although body fat mass decreased after an initial weight loss period. In these studies, the calorie restriction imposed during the weight loss period may have had a role to play in the demonstrated effects. In humans, it has been shown that exposure to a high-fat or high-energy diet decreases sensitivity to the GI mechanisms involved in appetite regulation.[18,42,43] High-fat diets have been shown to modify appetite perceptions, increasing hunger and decreasing fullness.[44] If the subjects in the present study usually consumed a high-fat or high-calorie diet, the effect of Olibra could have been attenuated. Nevertheless, the ultimate goal of altering appetite and satiety signals is to correct energy imbalance and reduce weight, which as demonstrated in this study, was far from accomplished with the consumption of Olibra.

A 45-minute delay in intestinal transit time following consumption of Fabuless (also known as Olibra) has been reported[30] but the computation of orocecal transit time has been questioned.[41] Using an intragastric administration technique to infuse Fabuless, Knutson and colleagues[22] concluded that the palmitic acid crystals observed in the jejunal samples of subjects caused a reduction in intestinal digestion and absorption rates. Both studies used a single dose of 8.5 g of Olibra to produce these effects, which is about twice the daily dose used in the present study. While it is important to demonstrate that Olibra produces conditions conducive to stimulation of the ileal brake mechanism, such manipulation must also produce the directional changes in feeding behavior consistent with the activation of this mechanism.

The present study is limited by the nonavailability of information related to subjects' usual intake, to determine if earlier patterns of nutrient exposure were related to the results of the study. A review of published human studies that investigated the effects of Olibra is presented in **Table 6**.

Conclusion

The Olibra emulsion had no significant effect on food intake, appetite and satiety ratings, body weight, or body composition. The results of studies indicating the beneficial effects of Olibra have not been confirmed in separate studies. A review of the available evidence indicates that further investigation of Olibra as a means of regulating appetite, satiety, food intake, and thereby body weight is not warranted.

Table 6.
Review of Published Studies That Investigated the Effects of Olibra

Source	Study overview	Summary of results	Conclusions
Burns *et al*., 2000[23]	*Aim:* To investigate the short-term effects of Olibra on energy and macronutrient intake in nonobese subjects. *Subjects*: 59 total participants Study 1: 15 females, 14 males Study 2: 16 females, 14 males Age: 18–65 years BMI: ≤30 *Study design*: Two RDBPC[a] WS[b] crossover studies 3 months apart. *Intervention*: An emulsion in yogurt to provide 5 g of fat as Olibra (1 treatment). *Length of each study:* Two visits with a 1-week interval between crossover. *Food intake test:* Four hours after consumption of test or placebo product. Free living weighed intake recorded in food diaries for rest of day. *Subjective ratings:* VASs[c] before and after eating yogurt and at hourly intervals until 9 p.m. on test days.	*Food intake*: Lower mean energy, macronutrient, and total weight of food intake after consuming test product. *Energy intake:* $p < .001$ (study 1) $p < .001$ (study 2) $p < .001$ (combined studies) *Subjective ratings*: Reduced hunger, desire to eat, and preoccupation with food in study 1 but not in study 2 or combined studies. *Study 1:* $p = .002$ (hunger) $p = .006$ (desire to eat) $p < .001$ (preoccupation with food)	The physicochemical characteristics of small amounts of dietary fat affect short-term satiety.
Burns *et al*., 2001[24]	*Aim:* To investigate the effects of Olibra on energy and macronutrient intakes up to 8 h in nonoverweight, overweight, and obese subjects. *Subjects*: 60 total participants Nonoverweight: 20 (10 females, 10 males Overweight: 20 (10 females, 10 males) Obese: 20 (13 females, 7 males) Age: 18–65 years BMI: 20–30+ *Study design*: RDBPC, WS, crossover *Intervention*: An emulsion in yogurt to provide 5 g of fat as Olibra (1 treatment). *Length of study:* Two visits with a 1-week interval between crossover. *Food intake test*: Four and 8 h after consumption of test or placebo product. Free living weighed intake recorded in food diaries for rest of day and following day to 9 p.m. *Subjective ratings:* VASs before and after eating yogurt and at hourly intervals until 9 p.m. on test days.	*Food intake*: Lower mean energy and macronutrient intake in nonoverweight and overweight after consuming test product at 4 h, and in all groups after consuming test product at 8 h. No overcompensation in next 24 h. *Energy intake, 4 h / 8 h:* $p < .01$ / $p < .001$ (nonoverweight) $p < .001$ / $p < .001$ (overweight) $p > .05$ / $p < .01$ (obese) $p < .001$ (total group at 24 h) *Subjective ratings:* Reduced hunger, desire to eat, and preoccupation with food, and greater perceived fullness. $p < .05$	Effects of Olibra were maintained at least until 8 h and were evident in nonoverweight, overweight, and obese subjects.
Burns *et al*., 2002[25]	*Aim:* To investigate if the energy and macronutrient intake responses to Olibra are dose-dependent and maintained up to 36 h. *Subjects*: 50 total participants 30 females, 20 males Age: 18–65 years BMI: 20–25 kg/m^2 *Study design*: RSBPC,[d] WS, crossover *Intervention*: Five, 10, and 15 g emulsions in yogurt to provide 2, 4, and 6 g of fat, respectively, as Olibra (3 treatments). *Length of study:* Four visits with a 1-week interval between visits. *Food intake test*: Four hours after consumption of test or placebo product. Free living weighed intake recorded in food diaries for rest of day and following day to 9 p.m. *Subjective ratings:* VASs before and after eating yogurt and at hourly intervals until 9 p.m. on test days.	*Food intake*: Lower mean energy (21, 25, and 30% with 2, 4, and 6 g of Olibra fat emulsion, respectively) macronutrient, and total weight of food intake after consuming test product. Lower energy and macronutrient intakes up to 36 h. *Energy intake:* $p < .001$ (at each dose) $p < .001$ (at each dose at 36 h) *Subjective ratings:* No effect between doses and with control.	Effects of Olibra were dose-dependent but results were not consistent across gender or proportional across dose levels. Effects were maintained at 36 h.

Continued →

Table 6. Continued

Source	Study overview	Summary of results	Conclusions
Logan *et al.*, 2006[26]	*Aim:* To investigate the medium-term effects of Olibra on appetite and food intake in nonobese subjects. *Subjects:* 28 total participants 14 females, 14 males Age: 20–55 years BMI: <30 kg/m^2 *Study design:* RDBPC, WS, crossover *Intervention:* A 12.5-g emulsion in yogurt drink to provide 5 g of fat as Olibra (22 treatments). *Length of study:* Two × 3-week study phases separated by a 3-week wash out phase. *Food intake test*: Four hours after consumption of test or placebo product on days 1, 8, and 22. Free living weighed intake recorded in food diaries for rest of day and following day. *Anthropometry:* Body weight and body composition measured on days 1, 8, and 22. *Subjective ratings:* VASs before and after eating yogurt and at hourly intervals until 9 p.m. on test days.	*Food intake:* No treatment effect on energy, macronutrient, and total weight of food intake 4 h after consuming test product. No treatment effect on intake during remainder of day and posttest day. *Anthropometric indices*: No treatment effect on body weight, body composition, or waist circumference. *Subjective ratings*: No treatment effect. *Blood parameters:* No effect on lipid levels but reduction in fasting blood glucose during test treatment. $p = .018$	There was no evidence of short- or medium-term effects of Olibra on food intake or appetite.
Diepvens *et al.*, 2007[28]	*Aim*: To investigate the effects of Olibra on weight maintenance after a very low-calorie diet. *Subjects*: 50 female participants Age: 18–58 years BMI: 25–32 kg/m^2 *Study design*: RDBPC, parallel *Intervention*: A 5-g emulsion in yogurt to provide 2 g fat as Olibra (twice daily = 252 treatments). *Length of study*: Twenty-six weeks; 6-week weight-loss period with a very low-energy diet, followed by 18-week weight maintenance period with test product or placebo. *Anthropometric measurements*: Weeks 2, 8, and 26. *Satiety tests:* Test or placebo product consumption in the morning. VASs recorded hourly until 1 p.m. in weeks 1, 7, and 25 *Blood tests:* Fasting, and 90 and 180 minutes after test or placebo product consumption at satiety tests. *REE^e measurement*: Weeks 2, 8, and 26.	*As compared with placebo group:* *Weight*: There was no significant increase in body weight in test group. $p < .001$ *Body composition:* Decrease in fat mass and increase in fat free mass in test group. $p < .05$ *BMI/waist circumference:* No increase in test group. $p < .05$ *REE:* Measured REE as a function of fat free mass was higher than predicted REE in test group. $p < .05$ *Blood parameters*: Increase in GLP-1 values 180 min after test product consumption. $p < .05$ *Subjective ratings*: Decrease in hunger 4 h after test product consumption. $p < .05$	Long-term consumption of Olibra had beneficial effects on weight maintenance and body composition after initial weight loss.
Diepvens *et al.*, 2008[27]	*Aim:* To investigate the short-term effects of Olibra on satiety and energy intake. *Subjects*: 41 female participants 21 junior normal weight 20 senior overweight Age: 18–50 years BMI: 20–30 kg/m^2 *Study design:* RDBPC, WS, crossover *Intervention:* Ten-gram emulsion in yogurt to provide 4 g fat as Olibra (1 treatment). *Length of study*: Two visits with a 1-week interval between crossover. *Food intake test*: Four hours after consumption of test or placebo product. *Subjective ratings*: VASs at hourly intervals four times after consumption of test or placebo product.	*Food intake:* No treatment effect. *Subjective Ratings:* Suppressive effect over appetite ratings at 3 h, and lower return to baseline hunger in normal-weight women aged between 18 and 30 years. $p < .05$ (hunger) $p < .05$ (desire to eat) $p < .05$ (return to baseline hunger)	Olibra exerted a suppressive effect on appetite ratings in the short term and may prevent overeating.

Continued →

Table 6. Continued

Source	Study overview	Summary of results	Conclusions
Haenni *et al.*, 2009[30]	*Aim:* To investigate the effects of Fabuless[f] on orocecal transit time. *Subjects*: 15 male participants Age: 20–59 years BMI: 22–28 kg/m^2 *Study design:* RDBC,[g] crossover *Intervention:* An emulsion in yogurt to provide 8.5 g of fat as Fabuless (1 treatment). *Length of study*: Two visits with a 1-week interval between crossover. *Food intake:* Nutritional drink with 1000 mg salazopyrine 3 h after consumption of test or control product, followed by lunch 4 h later. Dinner was served 4 h after lunch. *Blood tests:* Before lunch and every hour until 11 h after lunch.	*Blood parameters*: A delay in the appearance of serum sulfapyridine (a metabolite of salazopyrine) in the test group compared with the control group corresponded to a 45-minute delay in orocecal transit time. $p < .05$	Fabuless may stimulate the ileal brake mechanism by increasing GI transit time.
Knutson *et al.*, 2010[22]	*Aim*: To investigate the differences in digestion and absorption of Fabuless compared with milk fat. *Subjects:* 16 total participants 12 females, 4 males Age: 23–36 years BMI: 19–29 kg/m^2 *Study design:* RDBPC, crossover *Intervention:* An emulsion in yogurt to provide 8.5 g of fat as Fabuless (1 treatment). *Length of study*: Three months; 2 visits with ≥5-day interval between crossover. *Route of administration*: Intragastric perfusion of test or control yogurt. *Intestinal samples:* Collected every 30 minutes following intragastric perfusion of test or control yogurt.	*Jejunal sample:* Test group had higher lipids, mainly as free fatty acids, than control group. Needle-shaped palmitic acid crystals were observed only in test group. $p < .05$ (total lipids) $p < .05$ (free fatty acids)	Higher amount of lipids in the proximal jejunum and crystallization of lipids after infusion of Fabuless makes it possible for sufficient lipids to reach the ileum and activate the ileal brake.
Olsson *et al.*, 2011[29]	*Aim:* To investigate the effects of Fabuless on body weight and body composition after initial weight loss. *Subjects:* 43 females Age: 18–60 years BMI: 26–31 kg/m^2 *Study design:* RDBC, parallel *Intervention*: A 12.5-g emulsion in ready-to-use portion packs, added to meal replacement drink to provide 5.2 g of fat as Fabuless (84 treatments). *Length of study*: Eighteen weeks; 6-week weight loss period with calorie-restricted diet, followed by 12-week weight maintenance period with test or control product. *Anthropometric measurements:* Baseline and weeks 4, 8, and 12.	*Weight*: Significant reduction in both groups but no difference between groups. *Body fat mass:* Decrease in body fat mass in test group as compared with control group. $p < .05$ *Waist circumference*: Significant reduction in test group but no differences between groups. *Muscle mass and hip circumference:* No treatment effects.	The addition of Fabuless to a meal-replacement diet plan resulted in a 0.9% decrease in body fat mass with no change in body weight between the groups.
Smit *et al.*, 2011[39]	*Aim:* To investigate the effects of Fabuless on appetite and food intake and to establish the impact of processing on its efficacy. *Subjects*: 24 total participants 16 female, 8 male Age: 18–43 years BMI: 18–37 kg/m^2 *Study design*: RDBPC, crossover *Intervention:* A 12.5-g emulsion in yogurt-based beverage to provide 5 g of fat as Fabuless (2 treatments; 1 processed,1 unprocessed). *Length of study:* Four weeks; 3 testing days over a 2-week period. *Food intake test*: Four and 8 h after consumption of test or placebo product. *Subjective ratings*: VASs at baseline and every 30 minutes posttreatment until after dinner on test days.	*Food intake:* Reduced food intake 8 h after treatment only if active ingredient was added at the end of manufacture. $p < .01$ *Subjective ratings:* No treatment effect on appetite and satiety.	Unprocessed Fabuless had a modest effect on food and energy intake. No effect when active ingredient was added to yogurt prior to homogenization and pasteurization.

[a] RDBPC = randomized double-blind placebo-controlled
[b] WS = within-subject
[c] VASs = visual analog scales
[d] RSBPC = randomized single-blind placebo-controlled
[e] REE = resting energy expenditure
[f] Also known as Olibra
[g] RDBC = randomized double-blind controlled

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