Nutraceutical meal replacements: more effective than all-food diets in the treatment of obesity

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The prevalence of obesity continues to increase in many developed countries throughout the world and is now referred to as a pandemic. Obesity is a chronic, relapsing disease, with neurochemical changes that influence energy balance, often rendering traditional treatment interventions ineffective at restoring normal body weight. Therefore, obesity treatment interventions, including dietary strategies, are receiving increasing attention by investigators and clinicians. Hundreds of randomized, controlled trials examining various food diet interventions have found modest long-term weight loss. Meal replacements in the form of drinks, bars and entrees work to replace food, restrict caloric intake and blunt the rise of postprandial blood sugar, fatty acids and the resultant secretion of incretins, insulin and other factors. Thus, these agents have a significant neurohormonal impact that enables weight reduction and have therefore been referred to as nutraceuticals – nutrition with a pharmaceutical effect. There is accumulating evidence that meal-replacement dietary approaches are superior to all-food approaches for short- and long-term weight loss, as well as improvement of obesity comorbidities.

Keywords: disease biomarkers, glycemic index, meal replacement, nutraceutical, obesity, portion control, satiety, weight loss, weight maintenance

According to the Centers for Disease Control and Prevention, the prevalence of obesity (defined as a BMI ≥30 kg/m^2) continues to escalate in the USA and now comprises nearly a third of adults aged 20–74 years [1]. Unlike some other chronic disease states, effective interventions for obesity are lacking. Bariatric surgery has shown the highest success rates for obesity management and Type 2 diabetes recovery to date, with an average weight loss of 35–38% of initial total body weight and a 72–83% recovery from diabetes at 1-year post-roux-en-Y gastric bypass [2]. However, weight regain does occur and the data at 10 years post-roux-en-Y gastric bypass show a mean weight loss of 25–28% and 36% recovery from diabetes [2]. Overall, outcomes with dietary obesity interventions show a smaller percentage weight loss and are often associated with high attrition and low long-term maintenance [3].

Although unproven, several factors are believed to be fueling the obesity epidemic, including increasing availability of high caloric density convenience foods and growing portion sizes. These unhealthy dietary changes in combination with increasingly sedentary lifestyles have likely tipped the energy balance for most Americans (66%), and resulted in overweight or obesity [1]. Several terms are used to describe modern American culture including 'obesigenic society', 'toxic nutritional environment' and 'portion distortion.' Regardless of which term is used, it is evident that a multifactorial public health approach promoting and supporting healthy lifestyles will be necessary to halt and reverse current obesity trends.

Although obesity prevention initiatives are thought to be the greatest hope for combating the obesity epidemic, we are currently faced with addressing the millions of Americans suffering from obesity and related comorbidities. Therefore, evaluation of available dietary interventions, as well as behavior modification techniques and exercise programs, is necessary to determine optimal nonsurgical approaches. Weight-reduction diets range from fad diets, to evidence-based guidelines from medical or dietary associations, to medically supervised very low calorie diets (VLCDs). Over the past decade, the nutraceutical meal replacement (MR) approach has received increasing recognition as an effective weight-management intervention.

Meal replacements simplify portion control and calorie restriction and appear to provide a relatively high satiating effect per caloric density. Several randomized, controlled trials (RCTs) have demonstrated superior weight-management efficacy in comparison with all-food dietary approaches. This article will review the current data on meal replacements as a tool for weight management in obesity.

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Meal replacement nutraceutical diets

A unified definition of what constitutes a MR does not currently exist. However, the term 'meal replacement' is often used when referring to prepackaged, portion-controlled food products that are used to replace meals and/or snacks. MRs are available in a variety of forms including liquids/shakes, powders (that are combined with liquids), soups, meal/snack bars and shelf-stable or frozen entrees. Various combinations of all three macronutrients – carbohydrate, protein, and fat – are present in most MRs (Table 1). Most are vitamin and mineral fortified and designed to provide a balanced, low-calorie, low-fat diet when combined with one or more meals/snacks.

VLCDs are diet plans that result in an intake of 800 kcal/day or less. A VLCD is usually comprised solely of MRs, such as five 160 kcal MR shakes per day, and is also referred to as a 'full meal replacement diet'. Medical monitoring should always be part of a VLCD. More commonly, MRs are used by consumers to replace one to two meals and/or snacks per day and are often referred to as a 'partial meal replacement diet'. Two or more MR shakes (equating to ~400–600 kcal total) plus fruit/vegetable snacks and one portion-controlled, low-fat meal results in a low calorie diet (LCD), equating to approximately 1100–1300 kcal/day. A LCD refers to a dietary intake of 800–1500 kcal/day.

Safety of meal replacement diets

While many clinical trials on MR diets have found them safe and without adverse events, most of these trials involved overweight/obese individuals who were otherwise healthy (no comorbidities). For those trials that studied MR diets in diabetic subjects, the subjects with diabetes were also otherwise relatively healthy [4,5]. Use of insulin and diabetic complications were exclusion criteria. Additionally, most trial groups consisted of overweight or mildly obese subjects, with mean BMIs of approximately 30 kg/m^2, rather than moderate to severely obese individuals with BMIs of 35 or greater and 40 kg/m^2, respectively.

Evidence supports that use of a LCD of MRs plus food (a partial meal replacement diet) equating to approximately 1200 kcal/day or greater, is generally safe for healthy individuals with no major medical illnesses. However, VLCDs or LCDs in patients with certain medical problems can pose risk and medical monitoring is indicated. Chronic kidney disease, long QT syndrome, cardiac ischemia and congestive heart failure are conditions that may increase risk with an MR diet. As most MR diets are relatively low in sodium and carbohydrate content, diuresis can occur. This can lead to electrolyte abnormalities and dehydration, particularly in those taking diuretics, which can exacerbate chronic kidney disease and cardiac ischemia and can potentially provoke torsades de pointes for those with long QT syndrome. Among those on antidiabetic agents, there is a risk of significant hypoglycemia upon starting a MR diet. Therefore, certain medications may need adjustment or discontinuation during a VLCD/LCD with MRs, including diuretics, insulin, sulfonylureas and meglitinides. Additionally, some medications may need more frequent monitoring, such as warfarin, digoxin, phenytoin and carbamazepine.

Both obesity and weight loss increase risk of gallstone development. Studies have found varying degrees of gallstone development during weight loss, ranging from 10–12% after 8–16 weeks of a LCD, 28% after 16 weeks on a VLCD and 30% within 12–18 months after gastric bypass surgery [6,7]. Ursodeoxycholic acid, a bile salt that reduces cholesterol secretion into bile and improves biliary cholesterol solubility, has been shown to reduce risk of gallstone development during weight loss. A dose of 600 mg/day was associated with a 3% risk of gallstone development, compared with a 28% risk with placebo, during a 16-week trial of 1004 morbidly obese (mean BMI 44 kg/m^2) patients on a VLCD [7].

Proposed mechanisms of meal replacements

The effectiveness of a MR dietary approach is likely to be related to several factors, including portion control, satiety and convenience.

Portion control

Marked increases in portion sizes and energy intake among Americans, both inside and outside the household, have been documented. Nielsen and Popkin examined change in portion sizes from 1977–1996 with three nationally representative surveys of more than 63,000 Americans [8]. They found increases in portion sizes for a variety of foods including snacks, desserts, soft drinks, fruit drinks, french fries and hamburgers. Portion size changes equated to calorie increases of 49–133 kcal per item for commonly consumed items.

Table 1. Macronutrient composition of common liquid meal replacements.

Meal replacement	kcal	Carbohydrate		Protein		Fat		Sodium		Potassium		Calcium		Phosphorous		Sugar (g)	Fiber (g)
		g	*% kcal**	*g*	*% kcal**	*g*	*% kcal**	*mg*	*% RDA†*	*mg*	*% RDA†*	*mg*	*% RDA†*	*mg‡*	*% RDA*		
Slim-Fast Original	220	40	73	10	18	3	12	220	9	600	17	400	40	280	40	24	5
Slim-Fast Optima	190	25	53	10	21	6	28	200	8	600	17	500	50	350	50	18	5
Slim-Fast High Protein	190	24	51	15	32	5	24	220	9	600	17	500	50	350	50	21	3
Slim-Fast Low Carb	190	6	13	20	42	9	43	260	11	550	15	400	40	280	40	13	5
Slim-Fast with Soy Protein	170	25	59	15	35	2	11	270	11	480	14	600	60	400	57	1	4
Optifast Ready to Drink	160	20	50	14	35	3	17	220	9	460	13	250	25	140	20	12	5
Health One	160	22	55	15	38	1	6	280	12	630	18	250	25	175	25	17	0
HMR 70 Plus	110	13	47	14	51	0.5	4	260	11	180	5	280	28	140	20	n/a	2
HMR 800	160	21	53	16	40	2	11	270	11	580	17	400	40	210	30	10	1
Procal	100	7	28	15	60	1.5	14	65	3	200	5	200	20	140	20	19	5
Scan Diet	160	21	53	18	45	3	17	540	23	700	20	400	40	200	29	7	0

**Percentage of kilocalories based on product nutrition label calories and macronutrient g.*

†%RDA based on RDAs of: sodium-2400 mg, potassium-3500 mg, calcium-1000 mg (for adults aged 20–50 years) [60].

‡mg of phosphorus derived from nutrition label %RDA, assuming RDA for phosphorus of 700 mg.

Meal replacements: Slim-Fast (Slim-Fast Foods Company, West Palm Beach, FL, USA), Optifast (Novartis Nutrition Corporation, MN, USA), Health One (Health and Nutrition Technology, Carmel, CA, USA), HMR (Health Management Resources Corp., Boston, MA, USA), Procal (R-Kane Products, Inc., Pennsauken, NJ, USA), Scan Diet Shakes (Nutri Pharma, ASA; Oslo, Norway).

n/a: Not available; RDA: Recommended daily allowance.

Another study by Nielsen and Popkin examining beverage intake in more than 73,000 Americans between 1977 and 2001 found an increase in energy intake from sweetened beverages of 135% and a reduction of energy intake from milk of 38%, resulting in a 278 total calorie increase per person per day [9]. These increases were associated with consuming larger portions as well as more servings per day of sweetened beverages.

Evidence suggests that the larger the portion size, the larger the energy intake. Rolls and colleagues found that subjects consumed 30% more energy when offered the largest portion than when offered the smallest portion [10]. The response to the variations in portion size was not influenced by who determined the amount of food on the plate (subject vs investigator) or by subject characteristics such as sex, BMI, or scores for dietary restraint or disinhibition. Likewise, Diliberti and colleagues found that when larger portion sizes are served at restaurants, more food is eaten [11]. Hence, it is easy to see how growing portion sizes in America have resulted in increased calorie consumption. Since an additional 100 kcal/day can lead to a weight gain of 10 pounds over 1 year, inappropriate portion size is likely to be a significant factor in promoting obesity.

As per the American Heart Association 2004 Scientific Statement on obesity, portion control is an important aspect of reducing energy intake [12]. Providing prepackaged prepared meals, either as frozen entrees of mixed foods or liquid-formula MRs, improves portion control and can enhance weight loss. MRs simplify portion control during weight loss by eliminating the need to measure or weigh food, or interpret food labels. However, education on appropriate portion sizes and self-monitoring of energy intake is crucial for long-term maintenance of weight loss.

Satiety

Investigators have examined appetite and satiety in relation to food macronutrient composition. Foods with high satiation per caloric density could presumably aid in limiting overall energy intake. Among the macronutrients of fat, carbohydrate and protein, fat was previously considered to have the strongest effect on satiety. Fat clears more slowly from the stomach so gastric transit time is prolonged with fat intake as compared with other macronutrients. More recent investigation, however, provides compelling evidence that fat is not the most satiating macronutrient. In fact, fat is likely to be the least satiating macronutrient [13]. Instead, protein appears to provide the highest satiety [14,15]. Studies examining both ratings of hunger following a protein preload as well as measurement of food intake have concluded that protein has the highest satiety.

Studies examining carbohydrates and satiety often reference glycemic index as a major stimulus for insulin release. Glycemic index is defined as the positive area under the glucose response curve after consumption of 50 g of available carbohydrate from a food test. Glycemic index values are expressed relative to the glucose response observed after the same amount of a reference food, typically glucose or white bread [16]. Although the evidence is inconclusive, some investigators have proposed that high glycemic-index-foods promote hunger and weight gain [17]. Shortly after ingestion of food, the gut secretes incretins, which work to signal the pancreas to produce glucagon-like-peptide 1 and to modulate the secretion of insulin in response to blood glucose. Ingestion of a high-glycemic-index food results in a prompt and large increase in plasma glucose. In response, there is a steep rise in insulin secretion, resulting in clearance of blood glucose and relative hypoglycemia. This, in turn, is believed to promote increased appetite.

Carbohydrates with a high glycemic index include refined grains and potatoes. Low glycemic index foods include high-fiber carbohydrates such as whole grains, most fruits, nonstarchy vegetables and legumes. However, other macronutrients ingested along with carbohydrates alter the glycemic index. Combining protein with a carbohydrate, for example, results in a lower glycemic index [18]. Foods with a lower glycemic index may help regulate satiety mechanisms [19] and body weight [20,21].

In congruence with the concept of glycemic index, fiber is also believed to have a high satiating effect relative to fat and refined carbohydrates. Proposed mechanisms include increased mastication time resulting in slower ingestion allowing satiety cues to take effect prior to over-eating, a direct neural effect of the mechanical act of chewing on central satiety centers [22], relatively low glycemic index and the resultant gastric distention that occurs with high-fiber foods.

Another factor that may affect satiety is meal frequency. It is speculated that long intervals between feedings results in hunger that requires a large energy intake to satiate, potentially larger than the total energy intake of more frequent feedings. Additionally, profound hunger may lead to impulsive and convenient food choices, which are often high in caloric density. Despite this rationale, studies have been inconclusive on whether food frequency plays a major role in satiety and overall energy intake [23]. However, physiologic benefits including improved lipid profiles and glucose tolerance have been associated with frequent, smaller-volume food intake [24].

MRs are thought to influence satiety through different mechanisms. Most MRs provide a combination of protein, carbohydrate and fat, therefore resulting in a relatively low glycemic index. Full- and partial-meal replacement diets often provide frequent significant protein intake, with a total daily protein intake of 70–110 g, equating to approximately 30–40% of total daily calories. This relatively high protein intake is thought to have a satiating effect. Additionally, although evidence is inconclusive, the frequent feeding that is an integral part of most MR diets is likely to attenuate extremes in hunger, subsequent poor food choices and overeating.

A few studies have examined MRs and satiety. In a randomized, crossover study, Ball and colleagues examined prolongation of satiety after a low-glycemic-index MR versus a low-glycemic-index whole-food meal versus a moderately high-glycemic-index MR in obese adolescents [25]. Significantly lower glucose and insulin responses were observed after both the low-glycemic-index MR and low-glycemic-index meal as compared with the relatively high-glycemic-index MR. Additionally, prolongation of satiety after the low-glycemic-index MR, based on time to request additional food, was observed.

Mattes and Rothacker examined the effect of thickness of MR shakes on hunger and found a direct and significant effect on hunger intensity during the first 2 h following ingestion [26]. Another study by Rothacker found that a MR bar with a glass of water resulted in hunger ratings and desire to eat ratings significantly below baseline for 5 h following consumption [27].

Table 2. Potential factors leading to increased consumption of unhealthy foods.

Unhealthy foods	Healthy foods
More accessible	Less accessible
More convenient	Less convenient
Less expensive	More expensive
Better tasting	Less preferred taste
Promoted heavily	Little promotion

Convenience

Over the past several decades, there has been an increase in the number and variety of portable and processed snacks and meals, both in grocery stores as well as restaurants and convenience stores. For many Americans, unhealthy foods became the preferred alternative over healthy foods for a variety of reasons, including availability, taste and time constraints (Table 2). Taste satisfaction rather than nutritional quality is the goal of most convenience food products. Therefore, these foods are usually high in fat, sugar and/or salt.

By contrast, healthy foods such as fresh produce are not as widely accessible, are not as convenient given their limited shelf-life, and many do not find them as palatable. Low-fat, low-sugar MRs provide a lower caloric density and healthier alternative to most convenience foods. During weight loss, MRs are more convenient than selecting, measuring and preparing food and can often be stored without refrigeration. During maintenance of weight loss, MRs can replace convenience food feedings, such as breakfast and a snack.

Short-term outcomes with meal replacement diets

We performed a Medline literature search for MR RCTs published within the past 10 years. We defined a control group as any group not using MRs during the intervention. Among those reporting short-term results, defined as less than 1 year, we identified seven RCTs (Table 3) and a single meta-analysis of RCTs. Short-term weight loss with MR diets was superior to control diets in four trials and similar to control diets in three studies. Some studies also demonstrated greater improvement of disease biomarkers with MR diets as compared with control interventions. Trial limitations include small sample sizes, ranging from 25 to 133 subjects, and substantial attrition, which was often greater than 25% at 3 months. However, there were no significant differences in attrition between the MR diet groups and the control groups. Reported outcomes were limited to completers only.

Table 3. Randomized, controlled trials: short-term (<1-year) weight loss and secondary outcomes with meal replacements.

Study	Duration	n	Baseline characteristics†		Dietary intervention		Weight loss and attrition		Secondary outcomes: MR vs control group	Ref.
			MR group	*Control*	*MR group*	*Control*	*MR group*	*Control*		
Allison *et al.*	12 weeks	100	Age 50.4 (8.9) BMI 35.1 (7.9) Wt 92.1 (14.8) 80% women	Age 50.0 (8.0) BMI 33.5 (3.5) Wt 91.4 (14.0) 80% women	1200 kcal: 5 shakes, F/V, 1 fat exchange (MR Scan Diet shakes)	1200 kcal: ADA exchange plan	*7.0 kg 7.7% Attrition: 26%	*2.9 kg 3.1% Attrition: 26%	*Greater improvements in TC, LDL, WC and fat mass	[28]
Ahrens *et al.*	12 weeks weight loss	95	Age 47.6 (7.9) BMI 29.5 (2.2) Wt 61.9 (11.1) 78% women	Age 47.8 (9.5) BMI 29.0 (2.6) Wt 78.3 (10.1) 73 % women	1200–1500 kcal: 2 shakes + 1 meal	1200–1500 kcal: ADA exchange plan	4.9 kg 6.4% Attrition: ‡28%	4.3 kg 5.5% Attrition: ‡28%	Similar improvements in WC, SBP, DBP, TG and HDL	[33]
	10 weeks maintenance				1 shake + 2 meals (MR Slim-Fast shakes)	Healthy diet of choice	6.7% Attrition: ‡42%	7.2% Attrition: ‡42%		
Hensrud	10 days	25	¶Age 54 BMI 33.6 Wt n/a 60% women		1000 kcal: 3 MR + F/V	1000 kcal: Type n/a			Similar improvements in fasting glucose and TG	[35]
	Until 10% weight loss				1000 kcal deficit: 2 MR + 1 meal + snacks	1000 kcal deficit: Type n/a				
	Total: 6 months				Maintenance: 1 MR + 2 meals + snacks (MR Slim-Fast shakes)	Maintenance: Type n/a	5.4 kg Attrition: n/a	4.6 kg Attrition: n/a		
Mattes	2 weeks	133	Group 1; n = 28 Age 43.0 (1.9) BMI 28.9 (0.4) Wt – n/a 78% women	Group 3; n = 26 Age 41.6 (2.4) BMI 29.3 (0.6) Wt – n/a 73% women	1573 kcal: 2 MR + 1 meal + 2 fruit (MR Kelloggs cereal + 2/3 cup skimmed milk)	2190 kcal: no intervention	*1.9 kg Attrition: 4.6%	*0.08 kg Attrition: 5.9%	*Greater improvement in fat mass	[30]

**Statistically significant between group difference.*

†Baseline characteristics: mean (standard deviation); age (years), BMI (kg/m²), weight (kg).

‡Per-group attrition not available.

¶Per-group baseline characteristics not available.

ADA: American Dietetic Association and American Diabetes Association; AHA: American Heart Association; DBP: Diastolic blood pressure; F/V: Fruit and vegetables; HbA1C: Glycosylated hemoglobin; HDL: High-density lipoprotein cholesterol; LDL: Low-density lipoprotein cholesterol; MR: Meal replacement; n/a: Not available; SBP: Systolic blood pressure; TC: Total cholesterol; TG: Triglycerides; VLCD: Very low calorie diet; WC: Waist circumference; Wt: Weight.

Table 3. Randomized, controlled trials: short-term (<1-year) weight loss and secondary outcomes with meal replacements. (cont.)

Study	Duration	n	Baseline characteristics†		Dietary intervention		Weight loss and attrition		Secondary outcomes: MR vs control group	Ref.
			MR group	*Control*	*MR group*	*Control*	*MR group*	*Control*		
Heilbronn *et al.*	6 months	48	VLCD; n = 12 Age 38 (8) BMI 27.7 (1.8) Wt 82.0 (10.8) 58% women	Control; n = 12 Age 37 (7) BMI 27.8 (2.0) Wt 81.7 (8.9) 58% women	890 kcal: 5 shakes/day until 15% weight loss (MR HealthOne shakes)	Maintenance: AHA step 1	*13.9% Attrition: 8%	*1% Attrition: 8%	*Greater improvement in fat mass Similar improvements in fasting insulin	[31]
Noakes *et al.*	3 months	66	Age 49.3 (8.8) BMI 31.8 (2.8) Wt n/a 34% women	Age 47.1 (10.3) BMI 33.2 (3.1) Wt n/a 48% women	1433 kcal: 2 shakes + 1 meal + 5 F/V (MR Slim Fast products)	1433 kcal: low fat	6.3% Attrition: 27%	6.9% Attrition: 21%	*At 6 months, higher levels of serum folate and other micronutients *Dietary compliance and convenience were viewed more favorably Similar levels of β-carotene	[34]
	6 months						9.4% Attrition: 42%	9.3% Attrition: 30%		
Yip *et al.*	12 weeks	75	Age 59.2 (8.2) BMI 32.9 (4.6) Wt 94.2 (20.0) % women n/a diabetics	Age 59.2 (7.7) BMI 33.8 (4.8) Wt 95.7 (18.5) % women n/a diabetics	500 kcal deficit: 2 shakes + 1 meal (MR Slim-Fast shakes)	500 kcal deficit: ADA exchange plan	*6.1 kg Attrition: n/a	*4.2 kg Attrition: n/a	*Greater improvements in fasting glucose and TC Similar improvement in HbA1C and LDL	[32]

*Statistically significant between group difference.

†Baseline characteristics: mean (standard deviation); age (years), BMI (kg/m^2), weight (kg).

‡Per-group attrition not available.

¶Per-group baseline characteristics not available.

ADA: American Dietetic Association and American Diabetes Association; AHA: American Heart Association; DBP: Diastolic blood pressure; F/V: Fruit and vegetables; HbA1C: Glycosylated hemoglobin; HDL: High-density lipoprotein cholesterol; LDL: Low-density lipoprotein cholesterol; MR: Meal replacement; n/a: Not available; SBP: Systolic blood pressure; TC: Total cholesterol; TG: Triglycerides; VLCD: Very low calorie diet; WC: Waist circumference; Wt: Weight.

Short-term randomized trials of meal replacement diets versus all food diets

Allison *et al.* found greater short-term weight loss and cholesterol reduction with a MR diet compared with an all-food diet [28]. A total of 100 obese volunteers were randomized to either a soy-based MR program or a control diet derived from the American Dietetic Association and American Diabetic Association exchange list plan (ADA exchange plan) [29]. The MR plan consisted of five MRs a day (Scan Diet Shakes – Nutri Pharma, ASA; Oslo, Norway) with four exchanges of fruit, four exchanges of vegetables and one fat exchange. Caloric intake prescription and baseline characteristics were similar for both groups. Each group received a single dietary counseling session followed by 4-week interval assessments of anthropometric measurements, blood pressure, psychological evaluations and fasting lipid levels. A significantly greater weight loss of 7.0 kg was observed in the treatment group compared with a 2.9 kg loss in the control group at 12 weeks ($p = 0.001$). Additionally, the MR group had significantly greater reductions of fat mass (4.3 vs 1.4 kg; $p = 0.003$), waist circumference (6.0 vs 2.9 cm; $p = 0.003$), total cholesterol (22.5 vs 6.8 mg/dl; $p = 0.013$), and low-density lipoprotein (LDL) cholesterol (21.2 vs 7.1 mg/dl; $p = 0.009$). Attrition was similar between groups and no serious adverse events were observed among either group.

Mattes found that ready-to-eat cereal used as a portion-controlled MR promotes weight loss [30]. This trial randomized 133 subjects to four different groups. Group 1 utilized a single-variety, ready-to-eat cereal (Special K, Kellogg Co., Battle Creek, MI, USA) in a 100 kcal portion size. Group 2 incorporated a similar quantity, yet allowed for a variety of Kellogg ready-to-eat cereals. Each group used two MRs a day accompanied by a fruit and 2/3 cup of milk, along with a sensible all-food meal, for 2 weeks. Cereal meals were provided as part of the study. Control groups 3 and 4 were given no dietary intervention in the first 2 weeks. Group 3 continued as the no-intervention control group, while group 4 along with treatment groups 1 and 2, began the second phase of the study. This 4-week phase consisted of a 'volumetric diet', which has a high fiber and fluid content and a low energy density. All groups had a similar starting BMI and were similar with respect to race and gender. The 2-week cereal intervention resulted in a 640 ± 109 and 617 ± 105 kcal/day reduction of daily intake for MR groups 1 and 2, respectively.

Results from the cereal MR trial showed that participants in the single cereal group had a greater weight loss than the variety cereal group, $p = 0.025$. During the first 2-week phase, MR groups 1 and 2 experienced a significantly greater weight loss (1.9 and 1.1 kg, respectively) as compared with the control group (0.08 kg). Significant losses of fat mass were observed in MR groups only. Weight loss continued and was similar during the volumetric diet for all groups except the no intervention control group. Compliance and attrition rates were similar between groups.

A more recent study by Heilbronn and colleagues found greater short-term weight loss with a meal replacement VLCD versus an all-food diet [31]. Investigators examined 48 overweight (nonobese) sedentary men and women randomized to one of four groups for 6 months. Study groups included a weight-maintenance control group, a 25% calorie-restriction group, a 12.5% calorie-restriction plus 12.5% increase in energy expenditure group and a VLCD group. The VLCD group received 890 kcal/day via five MR shakes (Health One, Health and Nutrition Technology, Carmel, CA) until 15% weight reduction, at which point they switched to a weight-maintenance diet. The other three groups were placed on all-food diets based on American Heart Association recommendations (≤30% fat). Patients were weighed weekly, underwent body composition analysis via dual-energy x-ray absorptiometry (DXA), and laboratory testing including glucose, insulin, dehydroepiandrosterone sulfate and tri-iodothyronine levels. Metabolic testing to assess energy expenditure as well as DNA fragmentation studies to quantify DNA damage were performed.

Results from Heilbronn's trial showed the mean weight reduction at 6 months was greater in the three intervention groups compared with the control group. Percent weight reduction was 1.0% for the control group, 10.4% for the calorie restriction group, 10.0% for the calorie restriction with exercise group and 13.9% for the VLCD group ($p < 0.001$ between all groups). Fasting insulin and DNA damage were reduced from baseline among all intervention groups. After adjustment for body composition change, sedentary 24-h calorie expenditure decreased in all intervention groups, with a decrease of 135 kcal/day in the calorie restriction group, 117 kcal/day in the calorie restriction plus exercise group and 125 kcal/day in the VLCD group. The calorie restriction and calorie restriction plus exercise groups experienced reductions in core body temperature, while the VLCD and control groups did not. The authors suggested that prolonged calorie restriction decreases two biomarkers of longevity (fasting insulin and body temperature) and could attenuate the aging process.

Yip and colleagues found greater weight loss, glucose control and total cholesterol reduction with a MR diet compared with an all-food diet over 12 weeks [32]. A total of 75 diabetic subjects were randomized to three different intervention groups: a MR containing lactose, sucrose and fructose (Slim-Fast; Slim-Fast Foods, NY, USA), a MR in which fructose and sucrose were replaced with oligosaccharides (sugar-free Slim-Fast) or an ADA exchange plan. An individualized caloric target was calculated to achieve a 500 kcal/day deficit according to estimated resting metabolic rates. Over the course of the study, there were no significant differences between the MR groups with regards to change in weight or disease markers; therefore, data from the MR groups were pooled and compared with the all-food diet group. At 12 weeks, subjects in the MR group had greater weight loss compared with the all-food diet group, with mean losses of 6.1 versus 4.2 kg, respectively ($p = 0.009$). Additionally, serum glucose levels were significantly lower in the MR group versus the all-food diet group over time ($p = 0.012$) and the MR group experienced a significant reduction in total cholesterol (12.6%; $p < 0.05$) that was not observed in the all food group. Similar significant improvements in LDL cholesterol were observed with both the MR group and the all-food diet group.

While most short-term RCTs found a greater weight loss with MR diets versus controls, three studies found similar weight loss between treatment and control groups. Ahrens *et al.* evaluated 95 overweight and obese subjects in a pharmacy setting [33]. Patients were randomized to a traditional reduced-calorie diet (RCD) or a MR diet. The RCD was self-selected based on the ADA exchange plan. The MR group followed a similar self-selected diet, except that two meals were replaced with a liquid MR shake (Slim-Fast). Recommended calorie intake for women and men in both groups was approximately 1200 kcal/day and approximately 1500 kcal/day, respectively. Baseline characteristics were similar between groups with respect to age, gender, BMI and biomarkers of disease. Patients were followed bimonthly by a pharmacist through an active 3-month period on their respective diets, at which point both groups initiated a weight maintenance plan for an additional 10-week period. For the maintenance diet, the control group was advised to return to healthy eating and to adjust calorie intake as desired. The MR group was advised to consume a single shake along with two sensible meals per day.

Results from Ahrens' trial showed that mean weight loss and percent weight loss was significant and similar for both groups. At 12 weeks the mean weight loss was 4.90 and 4.30 kg ($p = 0.16$), and the percent weight loss was 6.4 and 5.5% ($p = 0.30$), in the MR and control groups, respectively. Both groups continued to lose a similar amount of weight in the maintenance phase of the study, totaling 6.86% and 7.15% in the RCD and MR groups, respectively. Similar improvements in systolic and diastolic blood pressure, as well as waist circumference, were noted. The initial improved LDL cholesterol noted during the active portion of weight loss returned toward baseline in the maintenance phase.

Similarly, Noakes *et al.* did not find an appreciable difference in weight loss between a MR diet and a control group [34]. This study enrolled 66 subjects and randomized them to a structured low-fat all-food diet or a MR plan for 6 months. The MR diet consisted of two shakes (Slim-Fast) with five servings of fruits and vegetables and one low-fat meal daily. Baseline characteristics were similar in both groups. Subjects were weighed every other week and underwent micronutrient assessment at 3 and 6 months. Food vouchers were provided to the control group and the MR group was supplied with Slim-Fast products for two meals. No professional dietary counseling was given to either group. Percent weight loss was similar between groups at both 3 and 6 months. At 6 months, the percent weight loss was 9.4 and 9.3% for the MR and control groups, respectively. The MR treatment group had significantly greater intake of magnesium calcium, iron, zinc and niacin at both 3 and 6 months. Serum folate and plasma β-carotene were higher in the MR group. Convenience and dietary compliance, assessed by 3-day weighed food records, were determined to be more favorable by the MR group than the low-fat conventional diet group.

Hensrud found similar weight loss and glucose control at 6 months with a MR diet compared with an all-food diet [35]. A total of 25 overweight and obese subjects with noninsulin-dependent diabetes were randomized to an intake of 1000 kcal/day for 10 days via either an all-food diet or three liquid MRs (Slim-Fast) plus fruit and vegetable snacks. This was followed by an energy deficit diet of 1000 kcal/day until a weight loss of 10% of baseline body weight was achieved, at which point a weight maintenance diet was prescribed. The 1000 kcal/day deficit diet for the MR group consisted of two liquid MRs, one meal and snacks. The MR weight maintenance diet consisted of one liquid MR, two meals and two snacks. Weight loss at 6 months was similar between the all-food and MR groups, with losses of 4.6 and 5.4 kg, respectively. Similar improvements of fasting glucose at 6 months were observed, with a 14 mg/dl reduction in the all-food group and a 26 mg/dl reduction in the MR group. Interestingly, mean triglyceride value decreased by 22 mg/dl in the MR group but increased in the all-food group by 16 mg/dl at 6 months. However, this between-group difference was not significant.

Short-term outcomes of meta-analysis

In 2003, Heymsfield *et al.* compiled a meta-analysis of six RCTs assessing the utility of partial MR diets compared with all-food RCDs [36]. Three of these RCTs [32,33,35] are reviewed above and three are reviewed below under 'Long-term outcomes'. Inclusion criteria were use of low-calorie commercially available liquid MR(s) with at least one all-food meal daily, equivalent prescribed caloric intake between control and MR groups and 3 months or longer study duration. Demographic requirements included minimum age of 18 years and a BMI of 25 kg/m^2 or greater. Data from a total of 487 subjects was evaluated. All methods of analysis indicated a significantly greater weight loss for those receiving MR diets compared with those on RCD plans. A pooling analysis for completers and a random effects meta-analysis each revealed a weight loss in the MR group of 2.54 kg greater than the RCD group ($p < 0.01$; each) at 3 months. Percent weight loss at 3 months was 7 and 4% in the partial MR and RCD groups, respectively, with similar attrition noted between study groups.

The meta-analysis also evaluated the effect of MR diets versus RCD plans on disease biomarkers. Significant improvements in plasma insulin levels were noted in the MR group compared with the control group ($p < 0.001$). Other metabolic improvements, which were similar in both groups, included blood glucose, triglyceride level and systolic blood pressure. The authors concluded that an MR diet appears to have greater weight-loss efficacy than a RCD plan and is associated with improvements in biomarkers.

Long-term outcomes with meal replacement diets

A Medline search for long-term outcome (≥1 year) RCTs of MR diets over the past 10 years yielded six RCTs, one controlled but not randomized trial and one meta-analysis. Among the RCTs, four compared MR diets with all-food diets (Table 4), one compared a MR diet with medication, and one compared a MR diet plus medicine with an all-food diet. Although the kilocalories/day were often the same or similar for both the MR diet plans and the all-food diets, every trial that compared these two diets found significantly greater weight loss at 1 year or longer with MR diets. This is potentially due to greater compliance with MR plans, possibly related to the proposed mechanisms of portion control, satiety and convenience with MR diets. However, dietary compliance was not reported in the majority. A few trials measured dietary compliance based on self-reported food diaries, but did not include assessment of between-group energy intake differences. Similar to the short-term MR trials, the sample sizes for long-term outcomes were small, ranging from 75–113.

1-year attrition was surprisingly similar to the 3-month attrition rates observed in short-term trials, ranging from 14–35%. Some of the trials provided grocery vouchers or meal replacement products. For other trials it was unclear whether any products or financial incentives were given. It is conceivable that the relatively low attrition rates may be related to these incentives. Similar to the short-term trials, there were no significant differences in attrition between the MR diet groups and control groups.

Two of the RCTs included pharmaceutical intervention. A MR diet and orlistat were found to be equally effective at maintaining weight loss for 1 year. Superior 1-year weight loss was found with a MR diet plus sibutramine versus a reduced calorie all-food diet.

Long-term randomized trials of meal replacement diets versus all-food diets

Rothacker and colleagues evaluated 75 healthy overweight and obese women and found superior weight loss with a MR diet versus a traditional low-calorie, low-fat diet at 1 year [37]. Subjects were randomized to a 1200 kcal/day

Table 4. Randomized, controlled trials: long-term (>1-year) weight loss and secondary outcomes with meal replacements.

Study	Duration	n	Baseline characteristics†		Dietary intervention		% Weight loss and attrition		Secondary outcomes: MR vs control group	Ref.
			MR group	*Control*	*MR group*	*Control*	*MR group*	*Control*		
Ashley *et al.*	1 year weight loss	113	Group B; n = 26 Age 41.0 (4.3) BMI 30.1 (2.9) Wt 83.5 (9.5) 100% women	Group A; n = 23 Age 42.3 (4.1) BMI 29.9 (2.6) Wt 82.9 (9.1) 100% women	Kcal n/a; 2 MR + 1 meal, snacks	1200 kcal: USDA pyramid	*7.7 kg *9.1% Attrition: ‡35%	*3.4 kg *4.1% Attrition: ‡35%	*Greater improvement in BMI	[38]
	1 year maintenance				Kcal n/a; 1 MR + 2 meals, snacks (MR Slim-Fast shakes and bars)	1200 kcal: USDA pyramid	*9.2% Attrition: ‡66%	*2.2% Attrition: ‡66%		
Flechtner-Mors *et al.*	3 months weight loss	100	Women: Age 44.3 (9.8) BMI 33.1 (4.1) Wt 89.1 (12.1)	Women: Age 46.8 (11.2) BMI 33.9 (3.0) Wt 90.6 (9.4)	1200–1500 kcal; 2 MR + 2 snack replacements + 1 meal	1200–1500 kcal: dietitian-directed balanced diet	*7.8%* Attrition: 0%	*1.5% Attrition: 0%	*Greater improvements in SBP, TG, glucose and insulin	[39]
	4 years maintenance		Men: Age 46.5 (9.5) BMI 33.0 (3.7) Wt 103.7 (12.9) 76% women	Men: Age 45.5 (12.0) BMI 33.1 (4.1) Wt 101.7 (12.3) 82% women	1 MR and 1 snack replacement + 2 meals and snacks (MR: Slim-Fast shakes and bars)		*8.4% Attrition: ‡25%	*3.3% Attrition: ‡25%	*Greater improvements in SBP and TG Similar improvements in glucose and insulin	
Li *et al.*	1 year	104	Age 54.4 BMI 32.8 (3.7) Wt n/a 41.3% women	Age 56.6 BMI 33.7 (3.6) Wt n/a 33.3% women	500 kcal/day deficit: Phase 1 (5 days): 3 MR + F/V; Phase 2 (3 months): 2 MR + F/V + 1 meal; Phase 3 (9 months): 1–2 MR + F/V + 1–2 meals (MR Soy Slim-Fast)	500 kcal/day deficit: ADA exchange plan	*4.57% Attrition: 14%	*2.25% Attrition: 21%	Greater improvement in diabetic medication requirement Similar improvements in HbA1C, TC, TG, LDL, HDL and hsHCRP	[40]
Rothacker *et al.*	1 year	75	Age 36.1 (7.2) BMI 28.6 (1.7) Wt 75.2 (6.9) 100% women	Age 37.5 (6.2) BMI 29.2 (1.7) Wt 77.5 (7.5) 100% women	1200 kcal 1–3 MR + 0–2 meals + F/V (MR Slim-Fast shake)	1200 kcal traditional food diet	*6.4 kg 8.5% Attrition: 21%	*1.2 kg 1.5% Attrition: 15%	*Greater improvements in fat mass and percent fat	[37]

**Statistically significant between-group difference.*

†Baseline characteristics: mean (standard deviation); age (years), BMI (kg/m^2), weight (kg).

‡Per group attrition not available.

ADA: American Dietetic Association and American Diabetes Association [26]; AHA: American Heart Association; DBP: Diastolic blood pressure; F/V: Fruit and vegetables; HbA1C: Glycosylated hemoglobin; HDL: High-density lipoprotein cholesterol; hs-CRP: High-sensitivity; LDL: Low-density lipoprotein cholesterol; MR: Meal replacement; n/a: Not available; SBP: Systolic blood pressure; TC: Total cholesterol; TG: Triglycerides; USDA Pyramid: United States Department of Agriculture Food Guide Pyramid; WC: Waist circumference; Wt: Weight.

traditional food diet or an equal energy MR diet. Women randomized to the traditional food diet received literature on healthy eating and sample diets. The meal-replacement group was instructed to replace up to three meals per day with an approximately 220 kcal MR shake (Slim-Fast) plus supplemental fruits and vegetables. No counseling was given to either group. Subjects received groceries at the beginning of the study, were paid for their participation and came to the research facility for brief monthly follow-up. The MR group received free powder packets throughout the study. Physical activity and dietary compliance were not monitored.

The 3-month results from Rothacker's trial found that the MR group had significantly greater weight loss than the traditional food diet group, with mean losses of 6.3 and 3.8 kg, respectively. After 1 year, the MR group had significantly greater reductions in weight (6.4 vs 1.2 kg), fat mass (5.3 vs 0.9 kg) and percentage fat (4.3 vs 0.3%) than the traditional food diet group. There was no difference between groups for changes in lean body mass. The authors concluded that MRs may be a useful tool for weight control for those unable to permanently change eating habits.

Likewise, Ashley and colleagues also found greater weight loss and weight maintenance with MR diets (Slim-Fast) versus an all-food diet during a 2-year study of 113 overweight and obese premenopausal women [38]. Their three-arm randomized study consisted of a 1-year weight loss phase followed by a 1-year weight maintenance phase. Subjects were randomized to a dietitian-led low-calorie (~1200 kcal/day) all-food diet intervention (Group A), a dietitian-led intervention with similar dietary advice except replacement of two meals per day with MR shakes or bars (Group B), or a primary care office-based intervention with the same MR diet prescription as group B (Group C). Groups A and B attended a total of 26 small group classes during the first year. Group C also attended 26 sessions, but the sessions were 10–15-min individual visits with a primary care physician or nurse. For weight maintenance, groups B and C were instructed to consume one MR per day and reinitiate two MRs if their weight increased. Group A was instructed to continue to follow a traditional all-food diet during maintenance. All groups attended monthly dietitian seminars as well as individual monthly treatment center visits during year 2.

Ashley's results at 1 year found that group B, the dietitian-led MR diet with group sessions, lost significantly more weight (7.7 kg; 9.1%) than the all-food diet group A (3.4 kg; 4.1%) and the MR diet group C (3.5 kg; 4.3%). The 2-year results found that group B again had a significantly larger weight loss. Among women evaluated at all three time points of the study (n = 39), the mean weight loss at 2 years was 9.2% for MR group B, 3.4% for MR group C and 2.2% for all-food diet group A. The authors concluded that in premenopausal women, weight loss can be achieved and maintained over a 2-year period with lifestyle counseling and a MR diet strategy.

Flechtner-Mors *et al.* found superior weight loss and weight maintenance with a MR diet versus a conventional reduced-calorie diet during a prospective 4-year trial [39]. The study consisted of a two-arm randomized 3-month intervention followed by a single-arm 4-year trial. Participants randomized to group A were instructed on a 1200–1500 kcal/day all-food diet and Group B subjects were instructed to follow the same kilocalorie amount with a MR diet. The MR group consumed two MRs (Slim-Fast) and two snack replacements (Slim-Fast) plus one meal high in fruits and vegetables. After the 3-month intervention, both groups were placed on a 4-year maintenance diet that included replacement of one meal and one snack with a MR and a snack replacement. The MR group had a greater 3-month percent weight loss of 7.8% compared with a 1.5% weight loss in the reduced calorie diet group. Only the MR group had improvements in biomarkers of disease at 3 months. At the end of the trial (>4 years), the MR group was found to have superior weight loss results compared with the reduced calorie diet group, with mean percent losses of 8.4 and 3.3%, respectively. Both groups showed significant improvements in blood glucose and insulin ($p < 0.001$), but only the MR group showed significant improvement in triglyceride level and systolic blood pressure compared with baseline ($p < 0.001$).

Li *et al.* found greater weight loss at 12 months in diabetic subjects randomized to a MR diet versus an individualized all-food diet plan [40]. A total of 104 obese male and female subjects with Type 2 diabetes were recruited and randomized. The MR group was instructed to replace three meals per day with a soy MR shake (Slim-Fast), as well as fruits and vegetables, for the first 5 days. Thereafter, they replaced two meals per day with MRs, continued the fruits and vegetables and added a sensible third meal for 3 additional months. For the remainder of the study, the MR group was instructed to replace one to two meals daily with the MR shake and consume correspondingly one to two sensible meals. The all-food diet group was instructed on ADA exchange plan. For both groups, diets prescribed aimed to achieve a 500 kcal/day deficit based on estimated basal metabolic rate. Results at 12 months showed a significantly greater percentage weight loss in the MR group of 4.57% as compared with 2.25% in the all-food diet group. Additionally, significant reductions in diabetic medications were seen in the MR group but not the all-food group.

Long-term randomized trial of meal replacement diet versus medication

LeCheminant *et al.* evaluated the utility of a MR diet versus orlistat for weight maintenance following weight loss and found that both were effective in maintaining weight significantly below baseline over a 1-year period [41]. Obese women and men followed a VLCD (~520 kcal) of liquid MRs (Health Management Resources, Boston, MA, USA) for 12 weeks, followed by reintroduction of solid foods over 4 weeks. Following this 16-week period, they were randomized to receive either MRs or orlistat along with a structured meal plan at a kilocalorie level designed to maintain weight loss. The maintenance program included weekly behavioral weight management clinics on healthy lifestyle topics for 26 weeks, then biweekly for the remaining 26 weeks.

LeCheminant and colleagues found that attrition and adherence were similar for both groups. A total of 92 out of the original 157 completed all testing and clinic measures. At 16 weeks prior to randomization, women and men had a 21 and 22% decrease in initial body weight, respectively. During weight maintenance, women in the MR group and orlistat group experienced a 2.9 and a 1.6% increase in body weight, respectively, over 1 year. This increase was not statistically significant and women were still considerably below their baseline weight (18.9 and 18.7% below baseline for the MR and orlistat groups, respectively). Conversely, men in both the MR group and orlistat group experienced a significant weight gain at 1 year of 4.4 and 5.7%, respectively. Their percentage weight loss from baseline at the end of the trial, however, was also still considerably below baseline at 18.0% in the MR group and 17.3% in the orlistat group. There were no significant between-group differences for the MR group versus the orlistat group in body fat percentage, fat-free mass or waist circumference at baseline or 1 year. While 41% of the orlistat group reported gastrointestinal side effects ranging from flatus to oily spotting, no adverse events for the MR group were reported.

Long-term randomized trial of meal replacement diet plus medication versus all-food diet

Redmon *et al.* found greater 1-year weight loss and improved diabetes control in subjects with diabetes randomized to a MR plan with daily sibutramine versus a reduced-calorie all-food diet [4]. A total of 61 overweight or obese subjects with Type 2 diabetes were randomized to two groups. The MR group was prescribed sibutramine 10–15 mg daily and a LCD (900–1300 kcal/day) using four to six MR products (Slim-Fast) per day for 7 consecutive days every 2 months. Between the MR weeks, use of MR products and snack bars to replace one usual meal and one snack was advised. Subjects in the all-food ‘standard therapy’ group received an individualized 500–1000 kcal/day deficit diet based on their calculated basal energy requirement. Both groups received an educational program of dietary, exercise and behavioral strategies. 1-year outcomes revealed significantly greater weight loss in the MR plus sibutramine group of 7.3 versus 0.8% in the standard therapy group. Additionally, there were greater reductions in body fat, glycosylated hemoglobin and fasting triglyceride level in the MR plus sibutramine group compared with the standard therapy group.

Long-term controlled trial of meal replacement diet versus no intervention

A second study by Rothacker *et al.*, with a longer 5-year duration, found superior weight loss results with a MR diet as compared with a control group [42]. This study was not randomized. Overweight and obese (but otherwise healthy) men and women (n = 158) were given milk-based MR shakes (Slim-Fast) and instructed to follow label instructions. For the first 3 months, the MR intervention group was instructed to replace two meals per day with a MR and weigh in weekly. After 3 months, they were to replace one to two meals per day until they reached their ideal weight. Participants weighed in twice a year for the duration of the study. For maintenance, subjects were advised to replace one meal per day with a MR or self-monitor weight daily and incorporate MRs into their diet for weight increases. Three control subjects per MR subject were selected from the surrounding area and matched for age, gender, BMI and race. There was no intervention by the investigators with the control group.

5-year results found the MR group had a significantly lower weight than their baseline, with a mean weight loss of 5.8 and 4.2 kg for men and women, respectively. Conversely, the matched controls experienced a weight gain of 6.7 and 6.5 kg for men and women, respectively. The authors concluded that a self-managed weight-control program using MR shakes was successful in weight control and prevention of weight gain over a 5-year period in an overweight to obese adult population.

Long-term outcomes of meta-analysis

The meta and pooling analysis by Heymsfield *et al.*, described in more detail above, also examined 1-year outcomes [36]. A random effects meta-analysis estimate indicated a 2.43 kg greater weight loss in the MR group at 1 year compared with the RCD group. However, this difference did not reach statistical significance ($p = 0.14$). A pooling analysis of completers, however, showed a significantly greater weight loss in the MR group compared with the RCD group at 1-year, with losses of 6.97 versus 4.35 kg, respectively ($p = 0.003$). Additionally, the attrition rate at 1-year was significantly less for the MR group compared with the RCD group.

Optimal therapy

Optimal nonsurgical treatment for weight reduction in overweight and mildly to moderately obese individuals includes a MR diet that creates a caloric deficit of 500–1000 kcal/day or greater. Although restoration of a normal body weight may not occur, significant weight loss of 5–7% at 3 months and 8–10% at 1 year is likely, resulting in improvement or resolution of obesity comorbidities. These outcomes are similar or superior to the currently available anti-obesity pharmaceutical interventions, but without the risk of adverse events and medication interactions. Overall, the use of meal replacements can help obese subjects with low energy expenditure sufficiently reduce energy intake while maintaining adequate nutrient intake. Evidence suggests that success rates are higher for those attending regular group behavior modification/educational sessions [43,44] and participating in physical activity [44,45]. MR diets are also useful for weight maintenance.

Summary & conclusions

As the prevalence of obesity continues to rise, data on obesity treatment is gradually increasing. Several RCTs now support MR dietary approaches as more effective than all-food diets for weight loss, weight maintenance and improvement in disease biomarkers. The success of MR interventions is likely related to convenience, portion control and satiety.

Overall, partial MR diets of approximately 1200 kcal/day or greater are safe for otherwise healthy adults with mild to moderate obesity (BMI <40 kg/m^2) [36]. Risk of a MR diet can increase with certain medical conditions, degree of obesity, severity of relative caloric restriction and rate of weight loss. Therefore, medical monitoring, medication adjustment and ursodiol for gallstone prevention may be indicated.

Expert commentary

A combined intervention involving a MR diet, behavior modification, nutrition education and physical activity is a comprehensive approach for obesity management. Evidence suggests that frequent accountability, particularly face-to-face accountability, increases success for both weight loss and weight maintenance [46]. While this comprehensive approach is thought to be the best nonsurgical intervention to date, it is not readily available to most obese Americans. Currently, obesity is not recognized as a disease entity by most third-party payers, despite the fact that a comprehensive MR approach would ultimately reduce healthcare expenses. Therefore, the expense of treatment, particularly nonsurgical treatment, is usually the responsibility of the individual. As research on health economics evolves, however, and the currently underestimated costs of obesity become known, it is likely that healthcare plans and employers will begin to provide coverage for nonsurgical obesity interventions.

Future perspective

Unlike hypertension and hyperlipidemia, in which medications can effectively restore normal levels for most, interventions to restore normal BMI in most obese individuals do not exist. Newer medications found to have anorexigenic effects, such as pramlintide [47,48] (now undergoing trials in nondiabetic obese individuals) and exenatide [49], are likely to be more efficacious than our current pharmaceutical armamentarium. Investigational interventions include appetite-regulating hormones and endoscopic procedures. As knowledge regarding the interplay between genetics, diet and disease evolves, the arena of functional foods, including foods developed to regulate appetite, are likely to play a part in obesity management.

Administration of peptides that regulate appetite such as leptin [50,51], peptide YY [52], and oxyntomodulin [53], as well as a vaccine against ghrelin (a gastrointestinal hormone that promotes hunger) [54], are under investigation. Endoscopic procedures for obesity continue to be explored. A variety of endoscopically placed intragastric devices, primarily balloons, have been evaluated for weight loss [55]. More recently, attempts at endoscopically duplicating gastric restrictive and bypass surgeries are undergoing investigation [56].

Advances in nutrition for prevention and treatment of disease states, including obesity, are likely to be influenced by nutritional genomics over the next decade. There is evidence that common dietary chemicals can act on the human genome, either directly or indirectly, to alter gene expression or structure [57]. Nutritional genomics is concerned with the degree to which diet influences the balance between health and disease based on a person's genetic makeup. As knowledge about the roles of various food components on metabolic pathways and disease risk evolves, production of nutritional supplements and functional foods is expected to grow [58]. 'Functional foods' refer to foods that, by virtue of physiologically active food components, provide health benefits beyond basic nutrition [59]. It is plausible that functional foods, targeting genes involved with neurochemical pathways of satiety and food intake, may be part of our obesity prevention and treatment armamentarium in the future.

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Executive summary

- The prevalence of obesity continues to escalate in many developed countries and is considered a pandemic. Environmental factors involved include increasing availability of high caloric density convenience foods, growing portion sizes and increasingly sedentary lifestyles.
- Randomized clinical trials on obesity treatment, including dietary interventions, are accumulating. Overall, trial outcomes support meal replacement approaches as more effective than all-food diets for short-term weight loss, long-term weight maintenance and improvement in disease biomarkers.
- The term 'meal replacement' refers to prepackaged, portion-controlled, food products that are used to replace meals and/or snacks. Beneficial effects on calorie restriction and weight loss are thought to be related to portion control, satiety and convenience.
- Overall, partial meal replacement diets of approximately 1200 kcal/day or greater are safe for otherwise healthy adults with mild to moderate obesity. Risk of a meal replacement diet can increase with certain medical conditions, degree of obesity, severity of relative caloric restriction and rate of weight loss.
- A comprehensive obesity treatment approach involving a meal replacement diet, behavior modification, nutrition education and physical activity appears to be the most effective nonsurgical intervention. Unfortunately, this intervention is not available to most due to the out-of-pocket cost of most such programs.
- As research on health economics evolves and the currently underestimated costs of obesity become known, it is likely that healthcare plans and employers will begin to provide coverage for nonsurgical obesity interventions.
- New and emerging obesity medications are likely to be more efficacious than our current pharmaceutical armamentarium. Investigational interventions include appetite-regulating hormones and endoscopic procedures. As knowledge regarding the interplay between genetics, diet and disease evolves, the arena of functional foods, including foods developed to regulate appetite, is likely to play a part in obesity management.

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