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Structured Weight-Loss Programs: Meta-analysis of Weight Loss at 24 Weeks and Assessment of Effects of Intervention Intensity

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ABSTRACT

Obesity is increasing in epidemic proportions globally while current therapies continue to be suboptimal. In this investigation, weight loss in obese individuals after 24 weeks with different nutrition interventions was compared. The impact of intervention intensity was assessed. Inclusion criteria were established and a comprehensive literature review was performed. These nutrition interventions were identified and analyzable: meal replacements (MRs); energy-restricted (>1500 kcal/d) diets (ERDs); low-energy (800–1500 kcal/d) diets (LEDs); soy very low energy (<800 kcal/d) diets (VLEDs) referred to as SOYs; and VLEDs. Intensity was assessed using the following parameters: physician visits, clinic visits, and hours of class over 24 weeks; an intensity score represents an adjusted sum of the values. Weight losses at 24 weeks as percentage of baseline weights (95% confidence intervals) were as follows: MRs, 9.1% (5.7–12.5); ERDs, 8.5% (4.9–12.1); LEDs, 11.4% (8.9–13.1); SOYs, 16.5% (13.9–19.1); and VLEDs, 21.3% (20.1–22.5). Weight loss with SOYs was significantly greater than with MRs and ERDs; weight loss with VLEDs was significantly greater than with any other diet. Energy intake was the most significant ($P<.0001$) regression variable related to weight loss; however, the intensity of intervention ($P=.0003$) was significantly stronger than initial body weight or duration of treatment. Medically supervised VLEDs are

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the most effective intervention for facilitating substantial weight loss over 24 weeks. SOY may promote more rapid weight loss over the first 8 weeks than other interventions. MRs appear to be equally effective with ERDs and LEDs with lower levels of intervention intensity.

Keywords: obesity; weight loss; meal replacement; energy-restricted diet; low-energy diet; soy; very low energy diet

INTRODUCTION

Obesity has reached epidemic proportions and its prevalence is increasing globally.[1] In the United States, an estimated 34% of adults are overweight (body mass index [BMI] 25–30 kg/m^2) and 31% are obese (BMI >30 kg/m^2).[2] These are disturbing statistics, given that obesity may increase the risk for diabetes by 90-fold[3,4] and for coronary heart disease by up to 6-fold[5] and is an important risk factor for premature death.[6] Although there are many treatment regimens for obesity, successful weight loss and maintenance are suboptimal.[7]

Because of the high visibility of various weight loss regimens, healthcare professionals and consumers have difficulty discerning which programs are effective and promote good health.[8] An energy-restricted diet (ERD), ideally combined with exercise and behavior modification, is the initial treatment recommendation for most overweight and obese people seeking to lose weight.[9,10] However, while some ERDs are well balanced and nutritionally sound, others appear to encourage irrational and potentially harmful eating practices.[8] Self-help or community weight loss programs often produce short-term weight reduction, but the success rates for maintained weight loss are low.[11] Supervised weight loss programs include use of meal replacements (MRs), ERDs (providing >1500 kcal), low-energy diets (LEDs, providing 800–1500 kcal/day), and very low energy diets (VLEDs, providing ≤800 kcal/day). This review compared weight loss at 24 weeks with these supervised programs using meta-analysis techniques. Also evaluated was the impact of intervention intensity on weight loss. Responses were then compared with reported weight losses with community programs and pharmacotherapy.

MATERIALS AND METHODS

Study Identification

The primary purpose of this study was to compare weight loss of obese individuals with various nutrition interventions from previously published studies. The following inclusion criteria were identified. (1) Subjects participated in a structured weight loss program, not an unsupervised "self-directed" program. (2) Subjects had an initial BMI of at least 30 kg/m^2 or at least 120% of ideal body weight (the criteria used in some earlier studies). (3) Studies were at least 24 weeks in duration since many studies, including this review, find that maximal weight loss usually is achieved in approximately 6 months. (4) Results for adult subjects 18 years of age and older were included. (5) Studies using surgery were not included. (6) Studies selecting subjects based on other diagnoses such as diabetes, hypertension, and dyslipi-

demia were not included. (7) Studies serving as a "control" group for a more intensive intervention were not included since not receiving the "active" treatment may influence the weight loss.

A thorough literature search was performed using MEDLINE (National Library of Medicine, Bethesda, Md) for the period of 1980–2001 and consulted the reference lists of retrieved articles and review articles. Of the 210 articles reviewed in detail, 47 met all inclusion criteria. Because most of the studies with MRs and ERDs included overweight (BMI, >25 kg/m^2) and obese patients, these reports were included in the analyses; however, in the LED, soy-based VLED (SOY), and VLED groups, only obese patients were included. SOY studies were separated from VLED studies because the treatment protocol differed (6–8 weeks of clinic visits for SOY and ≥16 weeks of clinic visits for VLED) and because the SOY supplement was soy protein-based and the VLED supplements were casein based. The effects of initial BMI and weight were also examined to assess appropriateness for inclusion of overweight patients in this analysis.

Definition of Diets

Diets were defined as follows: community programs that provide regular meetings and limited diet counseling (eg, Weight Watchers®); MRs that recommended at least 2 MRs daily (eg, Slim-Fast®); ERDs that recommended energy restriction but did not specifically limit energy intake to up to 1500 kcal/day; LEDs that recommended 800–1500 kcal/day; SOYs that provided up to 800 kcal/day from a soy product (Nutrilett®); and VLEDs that provided up to 800 kcal/day from widely used shakes, entrees, and bars (eg, Optifast® or HMR®).

Outcome Measures

The primary outcome measurement was weight loss at 24 weeks. All weight changes were expressed as percentage change from baseline. Changes in weight over time were recorded, where available, at 4, 8, 12, 16, and 24 weeks and mean values were calculated by the mixed model approach.

Intensity of Intervention Measurements

For each study, the duration of the weight loss intervention was recorded. Also determined were the number of physician (MD) visits, number of clinic visits, and hours of classroom instruction over the 24-week period for each study. For some studies these data were not clearly provided and were therefore estimated from similar studies from the same authors or from similar protocols with the same intervention. To estimate an overall intensity factor, the number of hours the subject was in the clinic over the 24-week period was calculated. Each MD visit and each clinic visit were assigned 0.5 hours. Thus the intensity factor, in hours, was calculated using the following formula: (MD visits × 0.5) + (clinic visits × 0.5) + class hours.

To assess factors affecting weight loss, multiple linear regression was performed. The dependent variable was percentage change from baseline in weight at 24 weeks (weight loss). The potential independent variables included initial weight in kilograms, duration of intervention, energy intake in kilocalories, and intensity factor. Initial testing indicated that baseline weight in kilograms and baseline BMI provided

almost identical results; kilogram values were used in this analysis. There were four possible regression variables in the model; this study employed the backward elimination model to identify significant variables. The backward elimination technique began by including all the independent variables. Variables continued to be eliminated from the model until all the remaining variables were significant ($P<.05$). At each step, the variable showing the smallest contribution to the model was deleted. The coefficient of determination for the stepwise regression was 0.7464, indicating that this model fit the data very well.

Meta-analysis

Estimates of effects were calculated by fixed-effects and random-effects models as previously described.[12,13] Because tests of homogeneity indicated significant heterogeneity across studies, only the random-effects model estimates were provided. All analyses were conducted using SAS-PC version 8.0 (SAS Institute, Inc., Cary, NC).

RESULTS

Attributes of Studies

Summary characteristics of the 47 studies fulfilling the selection criteria are presented in Table 1. Since only 1 community program study[11,14] met entry criteria, it was not included in the analysis. However, 4 MR,[15-18] 6 ERD,[19-24] 10 LED,[25-34] 8 SOY,[35-41] and 19 VLED[26,30-33,42-55] studies were included. The number of patients per study ranged from 6 to 621; most studies included women and men. The daily energy level reported was fairly consistent within dietary groups. Since diet instruction for ERDs usually did not provide specific energy intake instructions, intakes were variable. Most studies provided information regarding the number of patients who discontinued treatment before reaching the 24-week time point. The discontinuation rate ranged from 0% (for the smallest study) to 73% but was less than 50% for 40 of the 42 studies providing these data. The unweighted mean dropout rate with SOYs (10.7%) was distinctly lower than with other diets (18.9%–27%).

Timing of Weight Loss

Weight losses with the 5 diets over 24 weeks are illustrated in Figure 1. In the first 4 weeks, patients lost the most weight on SOYs, with percentage weight loss being significantly greater than with MRs, ERDs, or LEDs. At 4 and 8 weeks, respectively, weight losses with SOYs (9.0% and 13.1%) were greater than those with VLEDs (6.2% and 12.9%) but did not differ significantly. At 8 weeks and beyond, weight losses with SOYs and VLEDs were significantly greater than values for the other 3 diets. At 16 and 24 weeks, weight losses with VLEDs were significantly greater than with SOYs.

Table 1. Demographics

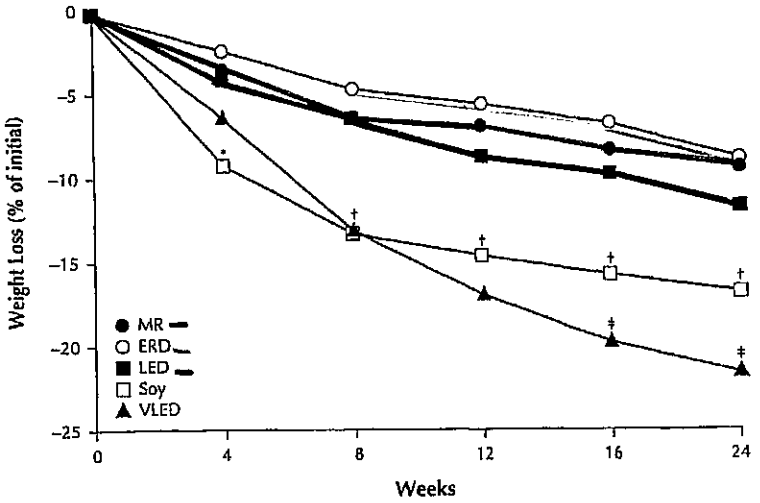
Reference	N	Sex	Diet	Energy, kcal/day	Initial BMI, kg/m²	Initial Weight, kg	Weight Loss, 24 wk % initial	Dropout Rate, %	VLED Source
Ashley[16]	26	F and M	MR	1200	30.1	83.5	9.3	15.8	NA
Bowerman[17]	252	F and M	MR	1350	33.2	94.0	8.9	52.4	NA
Ditschuneit[18]	50	F and M	MR	1350	33.6	92.6	9.4	10.0	NA
Herber[15]	301	F and M	MR	1100	28.4	79.1	9.0	29.9	NA
Burnett[19]	6	F	ERD	Variable	31.7	89.2	8.0	0.0	NA
Nicklas[24]	36	F	ERD	Variable	33.0	86.6	6.5	16.7	NA
Perri[20]	75	F and M	ERD	Variable	NA	96.7	13.2	25.5	NA
Perri[21]	16	F and M	ERD	Variable	NA	100.4	10.8	18.8	NA
Rigaud[22]	14	F and M	ERD	Variable	29.3	76.9	7.2	46.2	NA
Shah[23]	42	F and M	ERD	Variable	30.5	80.4	5.5	23.0	NA
Anderson[25]	16	F	LED	925	36.2	94.3	13.9	3.0	NA
Doherty[26]	8	F	LED	1250	36.5	102.8	11.4	11.1	NA
Fitzwater[27]	143	F and M	LED	1100	NA	103.0	7.3	73.0	NA
Foster[28]	8	F and M	LED	1200	NA	106.9	10.6	11.1	NA
Jeffrey[29]	81	F and M	LED	1250	31.0	90.9	8.5	11.0	NA
Wadden[30]	16	F and M	LED	1100	NA	112.2	12.7	15.3	NA
Wadden[31]	22	F and M	LED	1200	39.4	106.0	12.3	NA	NA
Wadden[32]	9	F	LED	1200	39.7	106.1	13.5	22.2	NA
Wadden[33]	21	F	LED	1200	38.8	105.4	11.2	14.3	NA
Wing[34]	41	F	LED	1250	32.8	87.4	13.7	9.0	NA
Fogelholm[35]	26	F	SOY	430	34.0	93.2	16.0	4.9	NA
Hoie[36]	18	F and M	SOY	430	33.9	98.8	16.3	11.1	NA
Hoie[37]	82	F and M	SOY	430	34.0	96.9	14.5	7.3	NA
Pekkarinen[38]	62	F and M	SOY	430	36.4	99.0	15.0	4.8	NA

Cont'd

Table 1. Demographics *cont'd*

Reference	N	Sex	Diet	Energy, kcal/day	Initial BMI, kg/m²	Initial Weight, kg	Weight Loss, 24 wk % initial	Dropout Rate, %	VLED Source
Pekkarinen[39]	29	F	SOY	430	36.0	96.1	16.0	6.9	NA
Rossner[40]	30	F and M	SOY	420	38.6	112.1	18.9	16.7	NA
Rossner[40]	32	F and M	SOY	530	39.0	112.0	20.2	21.9	NA
Ryttig[41]	54	F and M	SOY	420	37.7	113.2	15.2	12.0	NA
Anderson[42]	100	F and M	VLED	420	36.8	100.4	19.1	42.0	HMR
Anderson[75,43]	80	F and M	VLED	520	45.6	129.2	27.2	28.0	HMR
Doherty[26]	12	F	VLED	420	40.4	111.2	20.1	11.1	Optifast
Foster[44]	68	F and M	VLED	660	37.5	102.3	20.2	10.5	Optifast
Gossain[45]	12	F and M	VLED	800	41.9	119.8	18.4	33.3	Optifast
Holden[46]	118	F and M	VLED	375	41.1	118.3	26.5	44.5	not stated
Molokhia[47]	25	F and M	VLED	NA	38.7	102.9	14.8	3.8	Lipotrim
Nunn[48]	60	F and M	VLED	470	38.1	104.3	23.4	18.3	not stated
Torgerson[49]	58	F and M	VLED	532	40.2	116.2	13.8	23.0	Modifast
Torgerson[50]	41	F and M	VLED	456	38.5	111.4	21.5	39.7	Modifast
Wadden[51]	17	F	VLED	450	NA	108.4	19.7	5.9	Optifast
Wadden[30]	19	F and M	VLED	450	39.1	108.0	17.9	15.3	PSMF
Wadden[31]	31	F and M	VLED	450	39.4	106.0	15.8	NA	PSMF
Wadden[32]	9	F	VLED	420	39.7	109.9	22.5	22.2	Optifast
Wadden[52]	517	F and M	VLED	610	38.1	107.8	19.3	44.0	Optifast
Wadden[33]	28	F	VLED	420	40.0	107.9	19.9	17.9	Optifast
Wadden[53]	621	F and M	VLED	610	38.8	110.3	23.1	NA	Optifast
Walsh[54]	143	F and M	VLED	610	37.7	107.7	19.9	NA	Optifast
Wise[55]	18	F and M	VLED	420	NA	106.4	20.8	NA	Optifast

Fig 1. Weight loss at 0, 4, 8, 12, 16, and 24 weeks.



Significant differences ($P<.05$) are indicated as follows:
*SOY vs MR, ERD, and LED.
†SOY and VLED vs MR, ERD, and LED.
‡VLED vs SOY, MR, ERD, and LED.

Weight Losses at 24 Weeks

The average energy intake, baseline weights and BMIs, and weight losses are presented in Table 2. The baseline weights are lower for the MR and ERD groups because these studies included overweight individuals. Weight losses at 24 weeks did not differ significantly for these diets—ERDs, 8.5% of initial weight; MRs, 9.1%; and LEDs, 11.4%. Average weight loss with SOYs (16.5%) was significantly greater than with MRs and ERDs but not with LEDs. VLEDs, with 21.3% average weight loss, were associated with significantly greater weight loss at 24 weeks than any other diet intervention. Dropout rates, at less than 10% at 24 weeks, were distinctly lower with SOYs than other diets and were significantly lower than with VLEDs ($P=.018$).

Three MR studies and 9 VLED studies provided adequate data to compare weight losses between women and men. The MR studies reported data for 470 women (mean initial weight, 85.2 kg) and 133 men (mean weight, 100.2 kg). At 24 weeks, women lost an average 9.3% of initial body weight (95% confidence intervals [CI], 9.2 to 9.4) while men lost an average 8.6% (95% CI, 8.3 to 8.8). This suggests that women lose a significantly larger percentage of initial weight with MRs than men. In VLED studies, data were reported for 1347 women (mean weight, 106.3 kg) and 396 men (mean weight, 129.8 kg). Women lost 20.8% of initial body weight (95% CI, 20.1 to 21.3) while men lost 25.0% (95% CI, 23.8 to 26.3). This suggests that men lose a significantly larger percentage of initial body weight with VLEDs than women.

Table 2—Weight Loss Comparisons with Different Diets

Group	No. of Studies	No. of Subjects	Energy, kcal/d	Initial BMI, kg/m²	Initial Weight, kg	Weight Loss 24 wk % Initial	95% CI %	Dropout Rate, %*	Significance†
MR	4	579	1250	31.3	87.3	9.1	5.7–12.5	36.7	A
ERD	6	200	Variable	31.1	88.4	8.5	4.9–12.1	23.4	A
LED	10	365	1148	36.3	101.5	11.4	8.9–13.9	36.9	A,B
SOY	8	333	468	36.2	102.7	16.5	13.9–19.1	9.8	B
VLED	19	1968	434	39.6	109.9	21.3	20.1–22.5	35.2	C

*Weighted for number of subjects per study.
†Weight loss significantly different if letters different.

Intensity of Intervention

Measures of intervention intensity are presented in Table 3. The duration of diet intervention was shortest for SOYs, with supervised dieting lasting up to 8 weeks, on average. The duration of supervised diet intervention was intermediate for VLEDs and MRs. Usually patients were followed in a maintenance program after completion of the VLEDs with continued clinic visits and classes. For the MR studies, patients were encouraged to use 2 MRs daily after completing clinic visits; most studies suggested use of 2 MRs daily for a total of 6–12 months. Most studies using ERDs or LEDs continued classes and instruction for the entire 6 months of observation. The number of MD visits varied widely. For all the ERD studies, only an initial MD visit was required. For LED studies, MD visits were usually scheduled at the beginning and end of the treatment. MR and SOY studies had intermittent MD visits. Only the VLED studies had almost weekly MD visits; most studies had weekly or biweekly classes. Although most programs also included group classes, the MR studies tended to have short counseling sessions with a dietitian. The SOY studies also used fewer classes of shorter duration. However, the other 3 interventions—ERDs, LEDs, and VLEDs—usually had weekly classes of 60–90 minutes in duration. The intensity factor, which aggregated MD visits, clinic visits, and class hours, had a 4-fold range. The MR studies employed the lowest intensity, with the SOY studies using the next lowest intensity. The LEDs and VLEDs were high intensity, requiring almost 2 hours weekly for 24 weeks.

Table 3. Intensity of Intervention for Various Diets

Diet	No. of Studies	Duration Weeks	MD Visits	Clinic Visits	No. of Classes	Class Hours	Intensity Factor*
MR	4	17.5	4.4	10.6	10.3	3.6	11.2
ERD	6	23	1	16.4	16.3	24.7	33.4
LED	10	23.9	1.9	21.9	21.9	32.8	44.8
SOY	8	7.8	2.8	17.5	10.7	9.2	19.4
VLED	19	13.6	18.4	22.1	22.0	26.8	47.1

*Intensity factor = (MD visits × 0.5) + (clinic visits × 0.5) + class hours.

All of the independent variables were closely interrelated. For example, duration of treatment was closely related to number of clinic visits. The multiple linear regression model was used to assess the impact of these variables on weight loss. With all independent variables in the model, the initial regression significance values were as follows: initial weight in kilograms (P=.076); duration of treatment (P=.574); intensity factor (P=.006); and energy intake (P<.0001). With stepwise backward elimination, initial body weight and duration of treatment, not significant variables, were eliminated. Energy intake remained the strongest regression variable (P<.0001), with intensity showing a stronger correlation (P=.0003) than with the initial regression. Although MD visits, clinic visits, and class hours were significantly correlated to weight loss,

the intensity factor that aggregates these variables was the strongest predictor of weight loss in the model.

DISCUSSION

Structured nutrition intervention programs were associated with weight losses of 8.5%–21% of initial body weight over a 24-week period. VLEDs were associated with significantly more weight loss than other nutrition interventions, as previously documented.[7] VLEDs using 420–800 kcal/day were well tolerated and, with appropriate medical monitoring, were associated with minimal side effects.[7,43,56] In clinical practice, many intensive medical intervention programs now recommend 800–1000 kcal/day. Clinical experience[72] and research[40,44,57,58] indicate that the intake of higher energy levels combined with behavioral intervention and medical monitoring are associated with similar weight losses to that observed previously with energy intakes of approximately 500 kcal/day. The most frequent side effect of consequence is development of gall stones.[59]

MRs are emerging as very effective tools for promoting weight loss.[15-18,60-62] The weight loss observed with MR use did not differ significantly from that seen with interventions that provided much more intensive behavioral training and classes. Perhaps of greatest interest is the effectiveness of MR use with a rather low intensity intervention.

Behavioral programs traditionally have used ERDs or LEDs. Both approaches generally provide weekly behavioral classes. However, weight loss with the lower energy intakes (LEDs) appears better than with higher energy intakes (ERDs), suggesting that behavioral programs may be more effective with use of lower energy intakes. Overall, the recommended energy intake was the strongest predictor ($P<.0001$) of weight loss, followed by intensity ($P=.0003$) of the program. Weight loss usually falls short of predictions based on calculated energy needs and prescribed energy intakes. For example, a woman between 30 to 60 years of age with a weight of 100 kg and an inactive activity level would have an estimated energy requirement of approximately 1977 kcal/day.[63] With a weight loss of 11 kg her energy needs would decrease to approximately 1853 kcal/day. After averaging these 2 for an average energy requirement of approximately 1915 kcal/day, it can be estimated that using an LED (average of 1168 kcal/day), the woman would have an energy deficit of approximately 747 kcal/day. Over a 24-week period (168 days), she would have an energy deficit of 125,496 kcal, which should allow her to lose 16.3 kg or 16.3% of her initial body weight. Patients treated with LED lost only 11.4% of initial body weight (Table 2) or 11.6 kg. This suggests that the prescribed energy intake is one important factor but the "intensity" of the intervention also has a very important role to success.

Responses to behavioral weight loss programs have been reviewed previously. Faith and colleagues[64] recently summarized weight loss with behavior therapy and LEDs; they reported an average weight loss of 5.6 kg after 1 year of therapy. However, Wadden and colleagues[65] reported average losses of more than 11 kg.

The SOY interventions were associated with the greatest rate of weight loss during the first 8 weeks. During the first 4 weeks, patients on SOYs lost 2.3% of initial body weight while patients on VLEDs lost 1.6% of initial weight. The intensity of the inter-

vention used with the SOY diet was less than half that used by the VLED intervention. This may indicate that the SOY formulation, which included isolated soy protein and soy fiber, may in some way enhance weight loss. Animal studies suggest that soy protein or soy protein hydrolysates may specifically promote visceral adipose tissue loss with reduced-energy diets.[66-68] However, the limited data from human clinical studies are inconclusive regarding the specific benefits of soy protein for weight loss.[69] Another potential advantage of soy protein intake with weight loss interventions may relate to its specific effects on reducing serum cholesterol and low-density lipoprotein cholesterol values.[12,62,70]

The effects of pharmacotherapy were not included in this analysis but several recent reviews provide comparative values.[71] Haddock[72] recently performed an exhaustive literature review and meta-analysis of weight loss outcomes with a large number of pharmacologic agents. Their meta-analysis indicated that weight loss (after subtraction of the placebo effect) never exceeded 4 kg or approximately 4% of initial body weight. The current review and meta-analysis of 6 studies with orlistat and 5 with sibutramine indicate that weight loss may be somewhat higher than the values reported by Haddock.[72] Nevertheless, it was estimated that weight losses at 24 weeks with LED plus orlistat (5.6%) or LED plus sibutramine (8.0%) appear lower than with behavioral intervention and LED without medication. It was recently reported that a fairly intensive behavioral intervention plus use of bupropion SR 400 mg/day was associated with a 24-week weight loss of 10.1%.[73] The results suggested that the behavioral intervention including frequent office visits, lifestyle diaries, use of 2 MRs daily, and use of pedometers to assess and record miles walked daily, enhanced the weight loss achieved in this pharmacotherapy trial. Phelan and Wadden[74] also suggested that behavioral therapy and pharmacotherapy may have additive effects.

This report indicates that VLEDs are the most effective nutrition interventions for facilitating weight loss over a 24-week period. SOYs may be even more efficacious because of more rapid weight loss and favorable effects on serum cholesterol and low-density lipoprotein cholesterol values. Men appear to lose significantly more weight than women with VLEDs. MRs appear very effective in promoting weight loss and are effective with a lower level of behavioral intervention than traditional behavioral programs. Women appear to lose significantly more weight than men using MRs. Initial body weight, BMI, and duration of therapy did not have a strong effect with multiple linear regression analysis. The prescribed energy intake and the intensity of intervention were significantly associated with weight loss. Most nutrition interventions appear more effective than pharmacotherapy for facilitating weight loss.

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