

Very-Low-Calorie Diets and Sustained Weight Loss

Wim H.M. Saris

Abstract

SARIS, WIM H.M. Very-low-calorie diets and sustained weight loss. *Obes Res.* 2001;9:295S–301S.

Objective: To review of the literature on the topic of very-low-calorie diets (VLCDs) and the long-term weight-maintenance success in the treatment of obesity.

Research Methods and Procedures: A literature search of the following keywords: VLCD, long-term weight maintenance, and dietary treatment of obesity.

Results: VLCDs and low-calorie diets with an average intake between 400 and 800 kcal do not differ in body weight loss. Nine randomized control trials, including VLCD treatment with long-term weight maintenance, show a large variation in the initial weight loss regain percentage, which ranged from -7% to 122% at the 1-year follow-up to 26% to 121% at the 5-year follow-up. There is evidence that a greater initial weight loss using VLCDs with an active follow-up weight-maintenance program, including behavior therapy, nutritional education and exercise, improves weight maintenance.

Conclusions: VLCD with active follow-up treatment seems to be one of the better treatment modalities related to long-term weight-maintenance success.

Key words: very-low-calorie diet, low-calorie diet, dietary treatment, weight loss, weight maintenance

Introduction

Nearly half a century ago Stunkard and McLaren-Hume (1) characterized the efficacy of the treatment of obesity as follows: "Most obese persons will not stay in treatment of obesity. Those that do stay in treatment, most will not lose weight, and of those who do lose weight, most will regain it." Nearly 50 years of research have yielded some progress in the treatment of obesity, especially how to lose weight. The use of very-low-calorie diets (VLCDs), providing 800

or fewer calories per day, has contributed significantly to this progress. Whether the above observation is outdated is not clear. This article reviews the long-term effectiveness of VLCDs in the treatment of obesity compared with other dietary treatments such as low-calorie diets (LCDs), ranging from 800 to 1200 kcal, or other types of treatment such as behavior treatment (BT) or physical activity (PA).

Definition of VLCD

Over the years the definition of VLCD and LCD have changed with regard to the energy-restriction level. In the early days more emphasis was given on the very-low-calorie level with values of 250 kcal/d or less. With the introduction of the international CODEX standardization and legislation by the U.S. Food and Drug Administration and the European Union on this type of food restriction, VLCDs are now defined as total diet replacements with <800 kcal and >400 to 450 kcal/d. Diets consisting of between 800 and 1200 kcal/d are classified as LCDs, whereas meal replacements are limited to 200 to 400 kcal. These types of definitions and regulations using fixed energy levels for all users ignore individual differences in body size and thus energy requirements. Therefore, the use of VLCDs and LCDs results in significantly different weight loss for different groups, for instance, between men and women.

Historical Perspective

The history of VLCDs goes back to 1929 when Evans and Strang (2) published their results of a diet, which is not too different in composition from those used today.

This diet made from food ingredients comprising ~ 400 kcal was used to get a more rapid weight loss. Instead of reducing the diets of the obese to 14 to 15 kcal/kg, resulting in weight losses of 2.5 to 3.5 kg/month, they reduced the energy intake to 6 to 8 kcal/kg to get a more rapid reduction. Based on their experience with hundreds of patients, the authors concluded that it was a safe and effective weight-reducing method.

In the 1970s, this dietary weight-loss concept was reintroduced with great success by Blackburn et al. (3) and Mclean Baird et al. (4) These studies attracted commercial interest, especially in the United States. Unfortunately the

Nutrition and Toxicology Research Institute Maastricht (NUTRIM), Maastricht University, Maastricht, The Netherlands.

Address correspondence to Wim H.M. Saris, Nutrition Research Institute (NUTRIM), Maastricht University, P.O. Box 616, 6200 MD Maastricht, Maastricht, The Netherlands. E-mail: W.SARIS@hb.unimaas.nl

Copyright © 2001 NAASO

commercial use of hydrolyzed collagen as the only protein source and no inclusion of adequate amounts of vitamins, minerals, and electrolytes in a “liquid-protein diet” seemed to be fatal as reported by the U.S. government (5).

Although extensive research never revealed a direct link between the reported deaths and the use of this liquid-protein diet, the adverse publicity has marked VLCDs for many years. Nevertheless because of the success of a number of nutritionally complete commercial VLCDs, several million people have used VLCDs and lost tons of weight as calculated for the United Kingdom (6), without reported deaths. Also because of the efficacy of the method to lose weight, VLCD is by far the most extensively used weight-loss method in the scientific literature.

Most studies of VLCDs have used these diets as part of a more general weight-reduction program that also included other therapeutic forms, such as BT, nutritional counseling, PA programs, and drug treatment.

These combined therapy programs are aimed to have an effective weight loss at the start of the treatment using VLCD and the support therapies to promote long-term weight control.

Composition, Safety, and Beneficial Effects

VLCDs are intended to achieve a significant weight loss without the risk of a severe negative nitrogen balance and electrolyte unbalances associated with starvation.

Through the provision of enough protein (minimal 50 g) lean body mass (LBM) is preserved in a way that is comparable with LCDs. Several studies have shown that with the use of VLCD, the LBM:fat-mass ratio of the lost mass is approximately 25:75 (7). This is not the case in the first 2 weeks of VLCD use because much of the weight loss is fluid and glycogen.

Several mechanisms promote fluid loss early in a VLCD. Insulin, which causes sodium retention by the kidney, goes down and the natriuretic hormone glucagon goes up. Also, the increased excretion of ketones will lead to extra sodium and potassium loss together with water. Once a new mineral balance is achieved, weight loss is dependent on the energy deficit compensated by the release of fatty acids as energy substrate from the fat stores. Under those conditions the amount of lean body-mass loss is a fixed level of ~25% of the total-body weight loss. This lean mass is directly related to the adipose tissue such as supporting connective tissue and muscle. An important point of discussion in the past was the question of whether VLCD causes excessive loss of lean tissue because of the very energy-restricted protocol (8,9). From this it has been assumed that there is a greater health risk in slimming in the overweight (body mass index [BMI], 25 to 30 kg/m²) than in the obese (BMI, >30 kg/m²).

From a theoretical point of view, taking the second law of thermodynamics into consideration, a negative energy balance will lead to a higher proportional loss of protein in lean subjects than in obese subjects due to a relative lack of

available energy from the fat stores. However, the question remains: at which level of body fatness or leanness does the associated protein loss exceed the accepted 25:75 ratio?

Reexamination of the Forbes and Prentice graphs (8,9) demonstrates that if the data-points below 15-kg body fatness are excluded as well as those data-points based on energy restriction below 400 kcal/d, the trend for a disproportional loss of LBM is less clear. It is difficult to find much evidence that VLCDs have produced body composition changes where LBM accounted for more than ~25% of the total weight loss, unless the changes were reported in the initial phase of dieting (7).

A number of studies have addressed the question of whether the combination of a VLCD with an exercise program has a protective effect on the loss of LBM. The exercise triggers conservation of muscle. Meta-analysis evaluating this issue showed that there was a conservation of the LBM, although the effect is relatively small (9,10).

Besides the energy and protein level it is of importance that the VLCD provide ~50 g of carbohydrates and some grams of essential fatty acids (EFAs). Whereas some carbohydrate intake is necessary to maintain blood glucose levels and prevent loss of electrolytes and spare protein, the intake must be at a level that supports a mild physiological ketosis. Because several tissues, notably brain tissue, cannot use fatty acids for fuel there is a strict requirement for glucose as an energy source. Ketones can cross the blood-brain barrier and supply most of the brain's energy requirements if necessary. In the absence of ketones, there is a mandatory conversion of amino acids in glucose.

The need for EFA intake is not high because the adipose tissue releases enough for most, if not all, of what is required.

Because VLCD is a total diet replacement, it should contain all vitamins and minerals, especially potassium and magnesium, at recommended daily allowance levels.

Recently more attention has been given to the fiber content of VLCDs. Because of the absence of nonenergy bulking agents in the products used in VLCDs, constipation is one of the most mentioned adverse effects. In the past, addition of fiber was a problem because of the technological problems involved in producing a palatable drink. Nowadays, several soluble and insoluble fibers are available without a taste problem. Levels of ~10 g are advisable.

There are a number of minor but bothersome side effects of VLCDs. Most cited are the following: dry mouth, constipation, headache, dizziness/orthostatic hypotension, fatigue, cold intolerance, dry skin, menstrual irregularities and hair loss. Most of these effects are directly related to the negative energy balance situation. In a study by Kirschner et al. (11), which analyzed 4026 dieters over more than 40,000 weeks with a 420-kcal VLCD, the most common problems were postural dizziness and tiredness. The most common complaint after prolonged use of VLCD was hair loss. More serious adverse events were exacerbation of gout (eight

Table 1. Short-term (4 to 6 weeks) weight-loss results of RCTs with VLCDs and LCDs

Reference	Diet (kcal/d)	Subjects (women/men)	Duration (weeks)	Δ Body weight		p Value
				(kg)	(kg/week)	
Ohno et al. 1989 (17)	240	7/4	4	8.9	2.2	NS
	420	6/4	4	7.6	1.4	
Foster et al. 1992 (18)	420	21 W	5	8.9	1.8	NS
	660	23 W	5	8.7	1.7	
	800	24 W	5	7.2	1.4	
Rossner and Flaten 1997 (19)	420	20/10	6	13.4	2.2	NS
	530	22/10	6	14.7	2.5	
	880	21/10	6	12.9	2.1	

NS, not significant.

cases) and acute psychosis (four cases). In recent years reports were published about a potential larger than normal prevalence of cholelithiasis during VLCD use (12). These reports were mostly from the United States, where relative low levels of additional EFAs were required. In contrast, this phenomenon was rarely seen in Europe, which has a required level of 7 g of EFA. The National Institute of Health (13) recommends an extra 10 g of fat to stimulate gall bladder contractions, which empties the bile and avoids stone formation. One has to take into consideration that obesity is one of the best known risk factors for cholelithiasis. Therefore, a somewhat higher level (7 g) than the required level of EFA seems to put people on VLCD at the same risk level for gall-stone problems as any other weight reduction program.

Cardiac complications have been a concern because fatal dysrhythmias were documented to occur with the use of the imbalanced VLCDs in the 1970s. Extensive evaluation of patients on modern VLCDs for 16 weeks or less has not shown an increased incidence of cardiac ventricular dysrhythmias or prolongation of the QT interval (14).

Also in the evaluation of large cohorts of patients using VLCDs, the cardiac complications were lower than expected based on the risk profiles of the obese population (15).

VLCD rapidly reduces the severity of a number of complications of obesity including diabetes mellitus, hypertension, hyperlipidemia, and some mechanical health problems like sleep apnea and joint problems.

Several studies have shown the dramatic improvements of glucose and insulin levels when diabetics start an energy restriction program including a VLCD. These effects are primarily caused by enhancement of the insulin-stimulated glucose oxidation, whereas the effect of nonoxidative glucose metabolism is less enhanced. Antidiabetic drugs or insulin intake can be reduced drastically or even stopped in patients with type 2 diabetes shortly after the start of the VLCD program. Blood pressure decreases rapidly with VLCD

and may reach normal levels with only modest weight loss. In general, blood pressure improves ~8% to 13% in hypertensive obese patients after a VLCD program is started (14).

Numerous studies have documented reductions in plasma lipids with VLCD. The reductions in triglyceride levels ranged from 15% to 50% in patients with hyper-triglyceridemia. The total serum cholesterol levels usually decrease 5% to 25%, especially in the first 4 weeks. Part of this reduction disappears after patients change to a normal food-based diet (16).

In general, the described improvements mostly disappear when the lost weight is regained (14).

Short-Term Weight Losses

The primary question in respect to weight loss is whether VLCD results in greater weight losses than LCD or other conventional diets.

In Table 1, three randomized control trials (RCTs) are presented with the short-term weight loss results over a 4- to 6-week period. The energy restriction varied from 240 to 880 kcal/d. Weight loss per week varied from 1.4 to 2.5 kg with a tendency for lower weight loss from LCDs compared with VLCDs. However, none of the differences were significant in the three studies. In Table 2, the intermediate (24 to 26 weeks) weight loss results of two RCTs using VLCDs or LCDs are presented. Again no significant differences or even a tendency to lower weight loss per week with VLCD could be observed.

A 400-kcal difference in energy deficit per day results in a theoretical total extra negative energy balance of 2800 kcal/week, representing ~0.4 kg of adipose tissue. Given the level of accuracy for the body composition methods, differences can only be detected over a relatively long period of time (months). However, both well-controlled RCTs did not show any difference in weight loss over a 6-month period. Also the 1-year results of the Rossner and

Table 2. Intermediate (16 to 26 weeks) weight-loss results of RCTs with VLCDs and LCDs

Reference	Diet (kcal/d)	Subjects (women/men)	Duration (weeks)	Δ Body weight		p Value
				(kg)	(kg/wk)	
Foster et al. 1992 (18)	420	21 W	24	19.5	0.8	NS
	660	23 W	24	22.6	0.9	
	800	24 W	24	90.6	0.8	
Rossner and Flaten 1997 (19)	420	20/10	26	18.9	0.7	NS
	530	22/10	26	20.2	0.8	
	880	21/10	26	17.7	0.7	

NS, not significant.

Flaten study were identical (19). These results indicate that compliance is better with a LCD. Based on these outcomes, Rossner and Flaten (19) suggested that one should take the fewer reported side effects with the LCD into consideration if the weight loss results are similar. As shown in their study, patients on LCD tended to report fewer adverse effects such as coldness, gastrointestinal discomfort, dizziness, and transient alopecia. Most authorities recommend that VLCDs may be used for only 2 weeks without medical supervision (14). Little available information documents the necessity for the safety precaution of frequent medical supervision. Such advice could lead to a strategy of intermittent VLCD treatment. Rossner (20) compared a 6-week continuous VLCD; three 2-week periods with 4-week intervals. Attrition and weight loss were similar in both groups after 14 and 26 weeks. Weight loss per week over a 26-week period was similar (0.8 kg/week) for the intermittent group compared with the results in Table 2. This study demonstrated that short-term (2 weeks) intermittent treatment with VLCD results in similar weight-loss results over short-term and intermediate periods of time.

Long-Term Weight Losses

A number of factors make it very difficult to evaluate the long-term weight loss efficacy of VLCD compared with LCD or other conventional diets. First of all, one can debate the definition of long-term. Is it only 1 year, or should a 5-year disease-free period, as accepted in general medicine, be considered? Also, the method used to calculate long-term success differs from study to study, making a comparison of weight-loss methods difficult. However, the most problematic aspect is the lack of RCTs comparing different weight-loss strategies. Published data are mostly based on long-term observations of those subjects who could be contacted without the rigorous measures to control for compliance. In most studies, control lack a persistent trend of increased body weights with increasing age.

In Table 3 an attempt is made to summarize the long-term weight-regain results (1 to 5 years) of RCTs including VLCD treatment. As an indicator of weight maintenance success, body-weight regain as a percentage of initial weight loss was selected. In this way, a comparison can be made between the relatively large and small initial weight losses often seen in RCTs with VLCD treatment. Of the nine RCTs including VLCDs, four studies have 1-year follow-up results. Only two RCTs report a 5-year follow-up. As stated before, it is difficult to compare the different studies because of the variety in design, treatment modalities, length of initial treatment, and follow-up activities. The lowest regain percentages are seen in the combination therapy of VLCD with BT and exercise. However, this observation is not consistent in all RCTs. The two 5-year follow-up studies showed remarkable differences in regain percentage. In the study by Wadden (22), there was a complete or even higher regain of the initial lost body weight. In the study by Pekkarinen and Mustajoki (29), subjects who were treated with VLCD and BT regained only 26% of their initial lost body weight. BT alone resulted in a relative low regain of 45%. The discrepancy between the favorable findings in some studies (23,29) and very disappointing results in others (22) is difficult to explain. One has to take into consideration, for instance, that there was an enormous rise in the mean weight of the population in the United States studies at the same that the United States' studies occurred. This makes it very difficult to keep reasonable long-term weight maintenance success rates.

Although not many conclusions can be drawn from the review of RCTs including VLCDs, at least it can be said that combination treatments including an initial phase of weight loss with VLCD give relatively good long-term results. However, further research is needed to assess the effectiveness of the different maintenance strategies after VLCDs.

Recently a study by Ayyad and Andersen (31) examined the long-term efficacy of the dietary treatment of obesity by

Table 3. Long-term (1 to 5 years) weight-regain results of RCTs, including VLCD treatment

Reference	Treatment	Duration (weeks)	Subjects (women/men)	Initial		Regain (%) of initial weight loss (years)				
				Weight (kg)	Weight loss (kg)	1	2	3	4	5
Sikand et al., 1988 (21)	VLCD + BT	16	10 W	106.6	17.5	95				
	VLCD + BT + exercise	16	11 W	105.6	21.8	58				
Wadden et al., 1989 (22)	VLCD + LCD	8 + 16	23 W	106.0	13.1	64				108
	BT + 1200 kcal	24	22 W		13.0	49				121
	VLCD + LCD + BT	8 + 16	31 W		16.8	37				117
Miura et al., 1989 (23)/ Ohno et al., 1990 (24)	VLCD	8	9/6		8.6	42	62	65		
	BT	16	27/12		4.5	122	129	131		
	VLCD + BT	8 + 8	10/6		10.7	-7	-5	9		
Wing et al., 1991 (25)	VLCD + diet	8 + 12	13/4	102.1	18.6	54				
	BT	20	12/4	104.5	10.1	33				
Wadden et al., 1994 (26)	Hypocaloric (1200 kcal)	52	21 W	105.4	14.4	15*				
	VLCD + hypocaloric	16 + 36	28 W	107.9	20.5	47*				
Torgerson et al., 1997 (28)	VLCD + diet	12 + 92	36/22	116.2	16.0	43				
	BT + diet	104	38/17	116.6	7.0	15				
Ryttig et al., 1997 (28)	VLCD + 1600 kcal + BT	8/92	30/23	113.2	19.2	69				
	VLCD + 1600 kcal + (a)	8/92				69				
	1600 kcal + BT	104				14/13	116.2	7.2	24	
Pekkarinen et al., 1997 (29)	VLCD + BT	8/8	16/11	131.2	22.9					
Torgerson et al., 1999 (30)	BT	16	18/14	134.2	8.9	45				
	VLCD + hypocal	16/36	31/10	111.4	-16.4	25				
	VLCD (b) + hypocal	16/36	31/8	107.2	-16.0	36				
	VLCD (c) + hypocal	16/36	32/9	109.3	-13.8	38				

*At 1, 5 year follow-up.

(a) One 420-kcal supplement in the evening. (b) First VLCD week metabolic ward. (c) Two small meals allowed weekly.

BT, behavior therapy; Exer, exercise therapy; Diet, general dietary advice; Hypocal, general energy restricted dietary advice; W, woman. Braces indicate that there is only a mean value for all treatment groups.

systematically reviewing studies published between 1931 and 1999. A total of 898 papers was identified. However, only 17 fulfilled the criteria set by others: a follow-up period ≥ 3 years and a follow-up rate $\geq 50\%$ of the original study group. The authors defined two alternative criteria for long-term success: no regain of initial weight loss (or further weight loss) and maintenance of at least 9 to 11 kg of the initial weight loss. In Figure 1, the success rate (%) is shown from the 17 identified studies with an observation

period between 3 and 14 years. From this graph, one can conclude that long-term success varies considerably between the different studies and treatments. The number of subjects within each study who could be considered successes varied between 5% and 30%, with some low (0%) and high (48%) extremes. Conventional diet with group therapy and VLCD with BT were the most efficacious treatment modalities. An active follow-up after an initial weight loss with VLCD gave the highest success rate (38%)

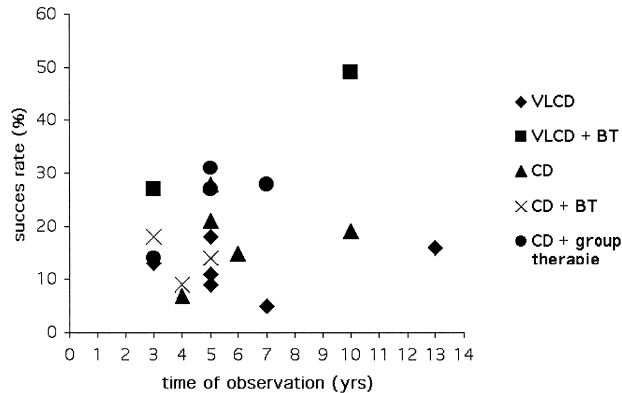


Figure 1: Success rate defined as maintenance of all weight (100%) initially lost, or maintenance of at least 9 to 11 kg of the initial weight loss and time of observation in 21 study groups. VLCD, very-low-calorie diet; BT, behavior therapy; CD, conventional diet. Adapted from Ayyad and Andersen (31).

compared with VLCD and BT with no support after initial treatment. This meta-analysis also clearly showed that it is an extremely demanding task to follow patients for extended periods of time and to maintain a sufficient number of subjects in the program. Knowing that 50% is the cut-off point for inclusion and that patients with a poor outcome are more likely to drop out, the overall long-term results are even more disappointing.

Gender

Recently, Mustajoki and Pekkarinen (32) suggested an interesting gender difference based on a number of RCTs including men. Both in the study of Torgerson et al. (27), which had a 2-year follow-up, and in the study of Pekkarinen and Mustajoki (29), which had a 5-year follow-up, results were considerably better in men than among women. Conversely, in the latter study weight maintenance was much better in women compared with men in the BT group (5-year mean weight loss: women, 7.9 kg; men, 1.9 kg) (29). Further research is needed to determine whether there is a gender difference in the long-term response of different treatment modalities.

Initial Weight Loss and Long-Term Results

Both among laymen and professionals it is believed that the initial greater weight losses achieved with VLCD is followed by larger weight regains ending in an even worse body-weight status. These ideas are partly based on the observation that, with a more profound energy restriction, adaptive mechanisms to preserve energy occur, such as the decline in resting metabolic rates (9). Therefore, the general advice is to achieve weight loss at a slow rate in order to preserve it. Jeffrey et al., (33) addressed this issue in a 30-month study initially treated with BT only. Initial weight losses were not related to the 30-month weight-maintenance

results. Also, the initial, more achievable weight-loss goals set by the patients did not correlate with long-term success.

In the study by Toubro and Astrup (34), the effect of weight-loss rate and absolute weight loss were separated. Patients were randomized for a VLCD (420 kcal/d) or a conventional diet (CD; 1250 kcal/d), aiming for the same weight loss of 13.6 and 13.8 kg, respectively. The VLCD resulted in a 1.6-kg body-weight loss per week for 8 weeks whereas the CD resulted in a 0.7-kg loss per week over a 17-week period. Randomization for a 1-year weight maintenance program with a 1-year follow-up resulted in extra weight-loss maintenance in the VLCD group compared with the CD group of 2.4 kg after 1 year and 3.0 kg after 2 years, respectively. Although the differences did not reach statistical significance, the outcome of this study with this special design at least does not support the idea that rapid weight loss negatively affects long-term success. Also, the RCTs shown in Table 3 do not indicate such an adverse effect. The study by Pekkarinen and Mustajoki (29), with an 8.9 kg and 22.2 kg initial weight loss, shows much better long-term results after 5 years (4.9 kg and 16.9 kg weight loss, respectively, or 4.5% and 26% regain of initial weight loss, respectively). Van Gaal (7) concluded in this review that the greater initial weight loss by VLCD produces better long-term results if the VLCD period is actively followed up with a program including nutritional education, BT, and increased PA.

Conclusions

VLCDs have been shown to be very effective in the treatment of obesity. An average weekly weight loss of approximately 2.0 kg in the first 4 to 6 weeks slows to an average weekly weight loss of approximately 0.8 kg over a 6-month period. VLCDS and LCDs with an average intake between 400 and 800 kcal/d do not result in differences in body weight loss, as shown in some RCTs. Therefore, the pessimistic 1958 view of Stunkard and McLaren-Hume (1), that most patients will not lose weight, is no longer true. However, their statement that most patients regain their lost weight is still true. Although there are difficulties in comparing studies because of large variations in the design and control of study variables, the overall picture is still very negative. VLCD in combination with active follow-up treatment seems to be one of the better treatment modalities for long-term weight maintenance success. Carefully controlled studies, however, are needed to determine more precisely the role of VLCD or other dietary treatments such as LCD in the treatment of obesity. Questions such as the rate and level of initial weight loss, as well as gender differences on weight-maintenance success, need further attention.

Acknowledgments

Dr. Saris has worked as a consultant and/or received research grants from food companies whose products are discussed in this article.

References

1. **Stunkard AJ, McLaren-Hume M.** The results of treatment for obesity. *Arch Intern Med.* 1959;103:79–85.
2. **Evans FA, Strang JM.** A departure from the usual methods of treating obesity. *Am Med Sci.* 1929;177:339–48.
3. **Blackburn GL, Flatt JB, Clowes GHA Jr, O'Donnel TF, Hensle TE.** Protein sparing therapy during periods of starvation with sepsis and trauma. *Ann Surg.* 1973;177:588–94.
4. **McLean Baird I, Parsons RL, Howard AN.** Clinical and metabolic studies of chemically defined diets in the management of obesity. *Metabolism.* 1974;23:645–57.
5. **Centers for Disease Control.** *Liquid Protein Diets.* Public Health Service Report. Atlanta, GA: Center for Disease Control; 1979, p. EPI 78-11-2.
6. **Kreitzman SN, Beeson V.** Obese patients in UK general practices lose 16 tonnes. *VLCD Update.* 1996;3:5–8.
7. **Van Gaal LF.** Dietary treatment of obesity. In: Bray GA, Bouchard C, James WPT, eds. *Handbook of obesity.* New York, NY: Marcel Dekker; 1978, 875–90.
8. **Forbes GB.** Lean body mass—body fat interrelationship in humans. *Nutr Rev.* 1987;45:225–31.
9. **Prentice AM, Goldberg GR, Jebb SA, Black AE, Murgatroyd PR, Diaz EOV.** Physiological responses to slimming. *Proc Nutr Soc.* 1991;50:441–458.
10. **Saris WHM.** The role of exercise in the dietary treatment of obesity. *Int J Obes Relat Metab Disord.* 1993;17:S17–21.
11. **Kirschner MA, Schneider G, Ertel NH, Gorman J.** An eight year experience with a very-low-calorie-formula diet for control of major obesity. *Int J Obes Relat Metab Disord.* 1988;12:69–80.
12. **Weinsier RL, Ullman DO.** Gallstone formation and weight loss. *Obes Res.* 1993;1:51–56.
13. **United States Public Health Service.** Very Low Calorie Diets. Bethesda, MD: NIH Publications; 1993, 94-3677, pp. 1–4.
14. **National Task Force on the Prevention and Treatment of Obesity.** Very-low-caloric-diets. *JAMA.* 1993;270:967–74.
15. **Atkinson RL, Kaiser DL.** Non-physician supervision of a very-low-calorie-diet: results over 200 cases. *Int J Obes Relat Metab Disord.* 1991;5:237–41.
16. **Saris WHM, Koenders MC, Pannemans DLE, van Baak MA.** Outcome of a multicenter outpatient weight-management program, including very-low-caloric-diet and exercise. *Am Clin Nutr.* 1992;56:2945–65.
17. **Ohno M, Miura J, Araik, Tsukahara S, Ikeda V.** The efficacy and metabolic effects of two different regimens of very-low-calorie diets. *Int J Obes Relat Metab Disord.* 1989; 13(suppl 2):79–85.
18. **Foster GD, Wadden TA, Peterson FJ, Letizia KA, Barlett SJ, Conill AM.** A controlled comparison of three very-low-calorie-diets: effects on weight, body composition and symptoms. *Am Clin Nutr.* 1992;55:811–7.
19. **Rössner S, Flaten H.** VLCD versus LCD in long-term treatment of obesity. *Int J Obes Relat Metab Disord.* 1997;21: 22–6.
20. **Rössner S.** Intermittent vs continuous VLCD therapy in obesity treatment. *Int J Obes Relat Metab Disord.* 1998; 22:190–2.
21. **Sikand G, Koudo A, Foreyt JB, Jones PH, Gotto AM.** Two year follow-up of patients treated with a very-low-calorie-diet and exercise training. *J Am Diabetes Assoc.* 1988;88:487–91.
22. **Wadden TA, Sternberg JA, Letizia KA, Stunkard AJ, Foster GD.** Treatment of obesity by very-low-calorie diet. Behaviour therapy and their combination: a five year perspective. *Int J Obes Relat Metab Disord.* 1989;13(suppl 2):39–46.
23. **Miura J, Arcu K, Tsukahara S, Ohno M, Ikeda Y.** The longterm effectiveness of combined therapy by behaviour modification and very-low-calorie diet: two year follow up. *Int J Obes Relat Metab Disord.* 1989;13(suppl. 2):73–7.
24. **Ohno M, Arai K, Tsukahara S, Miura J, Yokoyama J, Ikeda Y.** Longterm effectiveness of combined therapy by behaviour modification and VLCD: a three year follow up. In: Oomura Y, ed. *Progress in Obesity Research.* Eds. London, UK: John Libbey; 1990, pp. 523–9.
25. **Wing RR, Marcus RD, Salata R, Epstein LH, Maskiewicz S, Blair EH.** Effects of a very-low-calorie diet on long term glycemic control in obese type 2 diabetic subjects. *Arch Intern Med.* 1991;151:1334–40.
26. **Wadden TA, Foster GD, Letizia KA.** One-year behavioral treatment of obesity: comparison of moderate and severe caloric restriction and the effects of weight maintenance therapy. *J Cons Clin Psych.* 1994;62:165–71.
27. **Torgerson JS, Lissner L, Lindroos AK, Kruijer H, Sjöström L.** VLCD plus dietary and behavioural support versus support alone in the treatment of severe obesity. A randomized two-year clinical study. *Int J Obes Relat Metab Disord.* 1997; 21:987–94.
28. **Ryttig KR, Flaten H, Rössner S.** Longterm effects of a very-low-calorie diet (Nutrilett[®]) in obesity treatment. A prospective randomized comparison between VLCD and a hypocaloric diet plus behaviour modification and their combination. *Int J Obes Relat Metab Disord.* 1997;21:574–9.
29. **Pekkarinen T, Mustajoki P.** Comparison of behaviour therapy with and without very-low-energy diet in the treatment of obesity. A 5-year outcome. *Arch Intern Med.* 1997; 157:1581–5.
30. **Torgerson JS, Agren L, Sjöström L.** Effects on body weight of strict or liberal adherence to an initial period of VLCD treatment. A randomized, one year clinical trial of obese subjects. *Int J Obes Relat Metab Disord.* 1999;23:190–7.
31. **Ayyad C, Andersen T.** Long term efficacy of dietary treatment of obesity: a systematic review of studies published between 1931 and 1999. *Obes Rev.* 2000;1:113–9.
32. **Mustajoki P, Pekkarinen T.** Very low energy diets in the treatment of obesity. *Obes Rev.* 2001;2:61–72.
33. **Jeffrey RW, Wing RR, Mayer RR.** Are smaller weight losses or more achievable weight loss goals better in the long term for obese patients? *J Cons Clin Psych.* 1998;66:641–5.
34. **Toubro S, Astrup A.** Randomized comparison of diets for maintaining obese subjects weight after major weight loss: ad lib, low fat, high carbohydrate diet vs. fixed energy intake. *Brit Med J.* 1997;314:29–34.