# Relative effects of weight loss and dietary fat modification on serum lipid levels in the dietary treatment of obesity

**Rianne Leenen,* Karin van der Kooy,* Saskia Meyboom,* Jaap C. Seidell,[1,*,†] Paul Deurenberg,* and Jan A. Weststrate[§]**

Department of Human Nutrition,* Wageningen Agricultural University, P.O. Box 8129, 6700 EV Wageningen, The Netherlands; National Institute of Public Health and Environmental Protection,† P.O. Box 1, 3720 BA Bilthoven, The Netherlands; and Unilever Research Laboratorium,§ P.O. Box 114, 3130 AC Vlaardingen, The Netherlands

**Abstract** The independent effects of weight loss and dietary fat modification on serum lipids were investigated in two groups of healthy moderately obese men and women. In one group (sequential group, n=19), a weight-stable low-fat, low-saturated-fat diet (Low-Sat) was given for 7 weeks (= dietary modification), followed by a 4.2 MJ/day deficit Low-Sat diet for 13 weeks (i.e., weight loss alone). Another group (simultaneous group, n=22) received a 4.2 MJ/day deficit Low-Sat diet for 13 weeks (i.e., weight loss + dietary fat modification). Each group was subject to an initial weight-stable high-fat, high-saturated fat diet for 3 weeks and a final weight stable Low-Sat diet for 3 weeks. Both groups lost similar amounts of body weight, about 13 kg, and had similar overall changes in total cholesterol, low density lipoprotein (LDL), cholesterol, high density lipoprotein (HDL) cholesterol, the HDL/LDL ratio, and triglycerides. Analysis of the separate effects of the Low-Sat diet without energy restriction and of weight loss in the sequential group showed that weight loss per se was responsible for about 50% of the total reduction in total cholesterol, and for about 60% and 70% of the fall in LDL cholesterol and triglycerides, respectively. Fat modification without weight loss reduced HDL cholesterol by 11.1% and the HDL/LDL ratio by 7.7%, while weight loss per se led to increases in HDL cholesterol of 12.5% and in the HDL/LDL ratio of 24.0%. We conclude that the effects of reduction in fat and saturated fat intake and weight loss are additive. The net favorable effect of weight loss seems to be greater than that of dietary fat modification in optimizing the serum lipid profile of obese subjects.—**Leenen, R., K. van der Kooy, S. Meyboom, J. C. Seidell, P. Deurenberg, and J. A. Weststrate.** Relative effects of weight loss and dietary fat modification on serum lipid levels in the dietary treatment of obesity. *J. Lipid Res.* 1993. **34:** 2183–2191.

**Supplementary key words** weight reduction • diet • lipids • cholesterol • triglycerides

One of the health hazards in affluent countries is obesity, which is associated with an increased risk of coronary heart disease (1, 2). Obese subjects tend to have elevated serum levels of total cholesterol, low density lipoprotein (LDL) cholesterol, and triglycerides, whereas their levels of high density lipoprotein (HDL) cholesterol tend to be reduced. Elevated total cholesterol levels as well as reduced HDL cholesterol levels are both risk factors for coronary heart disease (3, 4).

Obese subjects, especially when they are hypercholesterolemic, are usually advised to lose weight in order to improve their serum lipid profile. The effects of weight loss on serum lipid levels in obese subjects have been investigated extensively. However, differences in experimental design, type of diet, heterogeneity of the subjects studied, as well as lack of controlled dietary regimens in some studies, make comparison of these studies difficult. The most controversial issue in weight loss studies is whether or not there is a change in HDL cholesterol concentration after weight loss, although in most studies on weight loss in which patients were sufficiently weight-stable, weight reduction resulted in an increase in HDL cholesterol (5, 6). Recently, a meta-analysis of 70 weight loss studies has been published, which revealed beneficial effects of weight reduction on all serum lipid levels, including an increase in HDL cholesterol at a stabilized reduced weight (5). However, in this meta-analysis, it was not possible to distinguish between the independent effect of dietary alterations, usually accompanied by weight loss, and of weight reduction per se. It might be that the changes in lipid concentrations could, at least partly, be explained by changes in total fat intake and fatty acid composition of the diets.

Abbreviations: LDL, low density lipoprotein; HDL, high density lipoprotein; HDL/LDL, HDL cholesterol/LDL cholesterol.

[1]To whom correspondence should be addressed at: Department of Chronic Disease and Environmental Epidemiology, National Institute of Public Health and Environmental Protection, P.O. Box 1, 3720 BA Bilthoven, The Netherlands.

The current recommendations regarding the dietary management of hypercholesterolemia include a reduction in percent calories from fat of approximately 30% and no more than 250–300 mg of cholesterol per day. Caloric intake from saturated fat should be reduced to 10% or less and intake of polyunsaturated fat should be increased but to no more than 10% of total calories (7, 8).

To our knowledge, no previous studies have examined the independent effects of losing body weight on the one hand and of lowering the total and saturated fat intake of the diet as indicated by dietary guidelines on the other hand, on altering the serum lipid profile in obese subjects. The purpose of the present study was to evaluate the effects of these factors separately by introducing a change in nutrient composition either simultaneously with or preceding a period of energy restriction.

## SUBJECTS AND METHODS

### Subjects

This study was part of a project concerning the effects of weight loss on energy metabolism, serum lipids, body composition, and several hormones in relation to visceral fat accumulation (9, 10). Participants were recruited by means of advertisements in local newspapers. Fifty obese subjects (26 women and 24 men) were selected on the basis of their body mass index (between 28 and 38 kg/m$^2$), age (between 25 and 51 years), premenopausal state, smoking behavior (less than five cigarettes per day) and drinking behavior (less than two alcoholic consumptions per day). The selected subjects were apparently healthy, as evaluated by a medical history, a physical examination, an urine test for glycosuria and proteinuria, and a blood screening for serum levels of total cholesterol, triglycerides, and glucose. The levels of serum lipids of the subjects before the experiment ranged from 3.67 to 7.78 mmol/l (mean, 6.00 mmol/l) for total cholesterol and from 0.38 to 2.65 mmol/l (mean, 1.45 mmol/l) for triglycerides. Serum glucose levels ranged from 4.90 to 7.10 mmol/l (mean, 5.71 mmol/l) and systolic blood pressure from 110 to 180 mm Hg (mean, 141 mm Hg). Throughout the study, none of the volunteers received any medications known to affect serum lipids and the women did not use oral contraceptives. All women included in the study were premenopausal. The women were considered to be premenopausal if they reported regular normal menstrual cycles during the intervention. None of the subjects had been on a slimming diet for several months before the study.

Seven subjects did not complete the dietary treatment successfully: three subjects due to intercurrent illness, three subjects for personal reasons, and one subject was excluded from the analysis because of suspicion of poor dietary compliance. The lipid levels of this latter subject were unknown at the time of exclusion. In addition, data of one woman who was later diagnosed as having subclinical hypothyroidism and of one woman who was later found to have severe fasting hyperinsulinemia ($>$ 100 $\mu$U/ml) were also excluded, the latter because hyperinsulinemic patients are very likely to have abnormal lipoprotein metabolism. Results of 41 subjects (20 women and 21 men) remained for statistical analysis.

The protocol for the study, which had been approved by the Medical Ethical Committee of the Department of Human Nutrition, was fully explained to the volunteers and all subjects gave their written informed consent. No monetary incentive was given except for the free food.

### Diets and design

**Fig. 1** shows the experimental design of the study. Ten subjects per week entered the study over a period of 5 weeks. All subjects consumed a standardized affluent-type high-fat, high-saturated-fat diet (High-Sat) for 3 weeks, during which their body weight was kept stable. At weeks 1 and 3 of this run-in period, body composition and serum lipid levels were determined. After this period, the subjects were divided into two groups matched for age and body mass index within each sex.

One group (sequential group: 8 women, 11 men) was fed a weight-stable low-fat, low-saturated-fat diet (Low-Sat) for 7 weeks. This diet consisted of a low percentage of energy provided by total and saturated fat. At the end of week 7, all measurements were repeated. The subjects subsequently received a 4.2 MJ/day energy-deficit diet for 13 weeks with the same nutrient composition as the Low-Sat diet. The individual amount of energy provided equalled daily energy intake at the end of the weight-stable Low-Sat diet minus 4.2 MJ/day. Measurements of body composition were repeated after 7 and 13 weeks in this slimming period. After this period, the subjects were given a weight-stabilizing diet for 3 weeks with the same nutrient composition as the Low-Sat diet. At the end of this stabilization period, all measurements were repeated.

The other group (simultaneous group: 12 women, 10 men) received the energy-deficit Low-Sat diet immediately after the run-in period, followed by the 3 weeks stabilization period comparable with the sequential group. The 7-week period on a weight-stable Low-Sat diet was thus omitted in this group.

For both groups, the weight-stable diets were individually tailored to meet each person's energy requirement, which was estimated from resting metabolic rate and physical activity pattern at the beginning of the weight-stable periods as described elsewhere (11). Body weights were recorded twice a week by the subjects and energy intakes were adjusted by us to maintain individual weight stability.

The nutrient composition of the diets was calculated with the use of a Dutch computerized food-composition table (12). Ninety-five percent of the energy intake in each

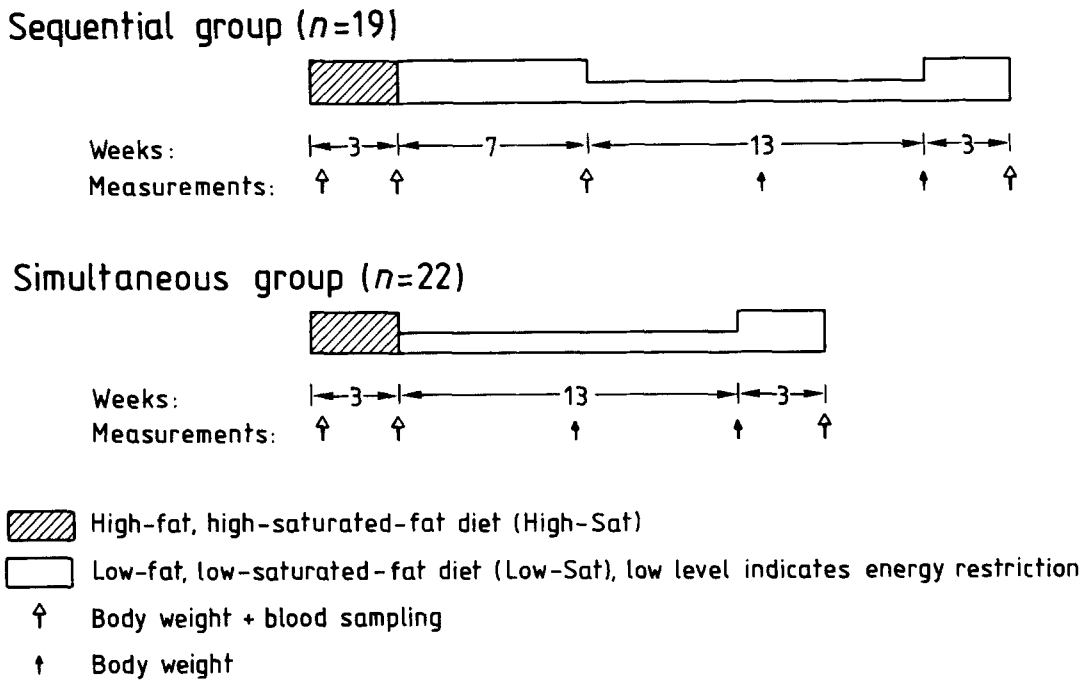


**Fig. 1.** Experimental design of the study.

dietary period was supplied individually to the volunteers. In addition, the participants were allowed to choose a limited number of food items, free of fat and cholesterol, that provided 5% of the total daily energy intake in order to give subjects some possibility to vary their choice and, thereby, to improve their cooperation. The weight-stable diets consisted of conventional foods and the energy-deficit diet was a combination of slimming products and conventional foods. The subjects were instructed to maintain their habitual pattern of physical activity and smoking habits during the study. They were asked to record in a diary any sign of illness, deviations from the diets, medications used, free-food choice, and changes in smoking and activity patterns. Compliance with the diets was checked by trained dieticians by means of interviews, checking the diary, and measuring body weight every 2 weeks.

Duplicate portions of each diet were collected on alternate days for three imaginary participants with different daily energy intakes on every 3 days, stored at −20°C, pooled per diet-period, and analyzed after the study. These chemically determined values were combined with the values calculated (12) for the free-food-choice items (**Table 1**).

### Blood sampling and analyses

Venous blood was drawn in the morning after an overnight fast of 11–13 h, twice with an interval of 2 days. The mean concentration of the two samples was used for statistical analysis. Serum was obtained by low-speed centrifugation within 1 h after venipuncture, stored at −80°C, and analyzed enzymatically for total and HDL cholesterol and triglycerides (13–15). The within-run coefficient of variation of control sera was 1.5% for total cholesterol, 1.8% for HDL cholesterol, and 1.2% for triglycerides. The coefficient of variation of control sera between runs was 0.7% for total cholesterol, 0.8% for HDL cholesterol, and 1.1% for triglycerides. The mean bias with regard to target values of serum pools provided by the U.S. Center for Disease Control (Atlanta, GA) was +0.11 mmol/l for total cholesterol and −0.07 mmol/l for triglycerides. The mean bias with regard to target values of serum pools obtained from the Solomon Park Research Laboratories (Kirkland, WA) was +0.10 mmol/l for HDL cholesterol. The LDL cholesterol concentration was calculated using the Friedewald equation (16). The ratio of HDL cholesterol to LDL cholesterol (HDL/LDL ratio) was calculated as an index of atherogenicity.

### Body composition

Body weight was determined to the nearest 0.05 kg using a digital scale (Berkel ED-60-T, Rotterdam, The Netherlands) with the subjects wearing only swimming gear or underwear. Body height was measured to the nearest 0.001 m using a wall-mounted stadiometer. Body mass index was calculated as weight (kg) divided by height squared ($m^2$). Whole-body density was determined by underwater weighing (17) with simultaneous measurement of the residual lung volume by a helium dilution

TABLE 1. Mean daily intake of energy and nutrient composition of the diets[a]

| | High Fat, High Saturated Fat | Low Fat, Low Saturated Fat | | |
|---|---|---|---|---|
| | | Weight Stable (7 weeks) | Energy Deficit | Weight Stable (3 weeks) |
| Energy (MJ/day) | 10.3 ± 1.7 | 10.8 ± 2.1 | 6.5 ± 1.7 | 9.5 ± 1.5 |
| (kcal/day) | 2458 ± 410 | 2572 ± 507 | 1561 ± 409 | 2272 ± 370 |
| Protein (% of energy) | 14.4 | 21.5 | 23.3 | 21.3 |
| Fat (% of energy) | 40.2 | 33.2 | 33.2 | 34.2 |
| Saturated fatty acids | 18.3 | 11.0 | 9.6 | 11.5 |
| C12:0 + C14:0 + C16:0 | 12.1 | 6.5 | 6.0 | 6.8 |
| C18:0 | 3.5 | 3.0 | 2.5 | 3.1 |
| Monounsaturated fatty acids | 15.2 | 11.5 | 11.5 | 11.7 |
| Polyunsaturated fatty acids | 5.0 | 9.2 | 10.8 | 9.6 |
| Carbohydrates (% of energy) | 44.7 | 44.9 | 43.2 | 44.0 |
| Alcohol (% of energy) | 0.7 | 0.5 | 0.3 | 0.6 |
| Cholesterol (mg/MJ)[b] | 27.8 | 24.2 | 30.6 | 25.1 |
| Dietary fiber (g/MJ)[b] | 3.7 | 3.0 | 3.8 | 3.1 |

[a] Based on chemical analysis of duplicate diets (95% of energy) and calculated nutrient composition of the free-choice items (5% of energy). Analysis of ancillary duplicate diets providing 7.8, 10.8, and 12.3 MJ per day in the weight-stable periods and 3.6, 6.6, and 8.1 MJ per day in the energy-deficit period showed that the variation between subjects in the composition of the diets was negligible, therefore, no standard deviations are given for the nutrients.
[b] To convert values for the intake of cholesterol to milligrams and dietary fiber to grams per 1,000 kcal, multiply by 4.184.

technique (18). Percentage body fat was calculated from total body density by the equation of Siri (17). One woman was afraid of complete immersion under water. Percentage body fat of this subject was determined from weight and total body water as assessed by the deuterium oxide dilution technique, assuming 73% of the fat-free mass to be water (19).

### Statistical methods

Deviations from normality of the distributions of the variables were checked. Only the distribution of HDL cholesterol at week 3 of the High-Sat period was slightly skewed and natural logarithm-transformed values for this variable were used in statistical analysis. Differences in variables at week 3 of the High-Sat period and differences in responses between the simultaneous group and the sequential group were performed using unpaired Student's *t*-tests. Changes in variables due to the diets within each group were tested using Student's paired *t*-tests. Pearson's product–moment correlation coefficients were computed between the changes in body weight and the responses in serum lipids for both sexes. Two-sided *P*-values were considered statistically significant at $P < 0.05$. Results are expressed as means ± standard deviation (SD) unless otherwise indicated.

## RESULTS

**Table 2** presents the baseline characteristics of the 41 subjects who completed the study successfully. No

TABLE 2. Characteristics of the simultaneous group and the sequential group[a]

| | Simultaneous Group | | Sequential Group | |
|---|---|---|---|---|
| | Means ± SD | Range | Means ± SD | Range |
| N (females/males) | 22 (12/10) | | 19 (8/11) | |
| Age (yr) | 41 ± 6 | 31–51 | 40 ± 5 | 28–48 |
| Weight (kg) | 90.7 ± 8.5 | 70.7–103.9 | 89.7 ± 9.4 | 73.2–110.4 |
| Body mass index (kg/m²) | 30.6 ± 2.0 | 27.6–34.4 | 30.5 ± 2.3 | 27.1–36.5 |
| Body fat (%) | 39.3 ± 6.2 | 30.1–51.4 | 39.0 ± 7.8 | 25.9–50.7 |
| Fat mass (kg) | 35.5 ± 5.9 | 25.4–46.6 | 34.7 ± 6.5 | 24.1–48.5 |
| Serum lipids[b] | | | | |
| Total cholesterol (mmol/l) | 5.62 ± 0.71 | 4.34–7.08 | 5.57 ± 0.81 | 4.00–7.17 |
| LDL cholesterol (mmol/l) | 3.83 ± 0.65 | 2.74–5.28 | 3.85 ± 0.73 | 2.58–5.09 |
| HDL cholesterol (mmol/l) | 1.10 ± 0.22 | 0.69–1.69 | 0.99 ± 0.21 | 0.72–1.51 |
| HDL/LDL ratio | 0.30 ± 0.08 | 0.16–0.47 | 0.26 ± 0.07 | 0.18–0.40 |
| Triglycerides (mmol/l) | 1.53 ± 0.59 | 0.45–2.75 | 1.63 ± 0.62 | 0.58–2.83 |

[a] Characteristics were taken at week 3 on a high-fat, high-saturated-fat diet.
[b] To convert from mmol/l to mg/dl, multiply cholesterol values by 38.67 and triglyceride values by 88.54.

significant differences in variables were found between the simultaneous group and the sequential group. Comparison of the characteristics of women (n=20) with those of men (n=21) demonstrated that men had significantly lower levels of body fat ($P < 0.0001$), fat mass ($P < 0.01$), HDL cholesterol ($P < 0.0001$), and the HDL/LDL ratio ($P < 0.0001$), whereas the levels of body weight ($P < 0.0001$) and serum triglycerides ($P < 0.001$) were significantly higher in men than in women (data not shown).

Changes in body weight during the study are illustrated in **Fig. 2** for the two groups separately. During the High-Sat period, the mean body weight decreased by 1.4 ± 1.0 kg ($P < 0.0001$) in the simultaneous group, and by 1.6 ± 0.9 kg ($P < 0.0001$) in the sequential group. During the 7 weeks on a Low-Sat diet, body weight was reduced further by 1.5 ± 1.4 kg ($P < 0.001$) in the sequential group. No significant correlations were found between changes in body weight and changes in serum lipids in this period, calculated either for all subjects together or for men and women separately. Weight loss due to energy restriction was not statistically different between the simultaneous group and the sequential group ($P = 0.84$), and body weights remained stable during the following weight stabilization period. The total reductions in body weight and fat mass during the weight loss and final stabilization period together were 13.5 ± 3.3 kg ($P < 0.0001$) and 11.8 ± 3.4 kg ($P < 0.0001$), respectively, in the simultaneous group versus 13.2 kg ± 3.0 kg ($P < 0.0001$) and 10.9 kg ± 2.3 kg ($P < 0.0001$), respectively, in the sequential group.

**Table 3** shows the separate effects of change in dietary fat without energy restriction and of pure weight loss on serum lipids in the sequential group. As a result of the weight-stable Low-Sat diet as well as of weight loss, the levels of serum total cholesterol, LDL cholesterol, and triglycerides decreased significantly: −7.2%, −5.2%, and −12.9% after the Low-Sat diet, and −7.9%, −8.5%, and −33.1% after weight loss, respectively. The levels of HDL cholesterol and HDL/LDL ratio decreased significantly after the Low-Sat diet: −11.1% and −7.7%, respectively, whereas after weight loss a significant increase in HDL cholesterol and in HDL/LDL ratio could be observed, +12.5% and +24.0%, respectively. During the weight loss period, changes in body weight were positively associated with changes in serum total cholesterol ($r = 0.58$, $P < 0.01$), LDL cholesterol ($r = 0.42$, $P = 0.08$), and triglyceride levels ($r = 0.64$, $P < 0.01$). In contrast, no significant correlations could be observed with changes in levels of HDL cholesterol or the HDL/LDL ratio.

The combined effects of change in dietary fat and weight loss for both groups as well as the separate effects for the sequential group on serum lipid levels are illustrated in **Fig. 3.** As a result of the combined effects of change in diet composition and weight loss, the serum levels of total cholesterol, LDL cholesterol, and triglycerides fell to the same extent in both groups: −0.82 ± 0.50 mmol/l, −0.51 ± 0.35 mmol/l, and −0.68 ± 0.52 mmol/l, respectively, in the sequential group, and −0.81 ± 0.40 mmol/l, −0.59 ± 0.38 mmol/l, and −0.55 ± 0.44 mmol/l, respectively, in the simultaneous group. All these reductions were statistically significant ($P < 0.0001$). In the sequential group, the weight-stable Low-Sat diet produced a decrease in HDL cholesterol, while weight loss per se led to a comparable increase in HDL cholesterol, resulting in an overall unchanged HDL cholesterol level (−0.002 ± 0.10 mmol/l). In the simul-

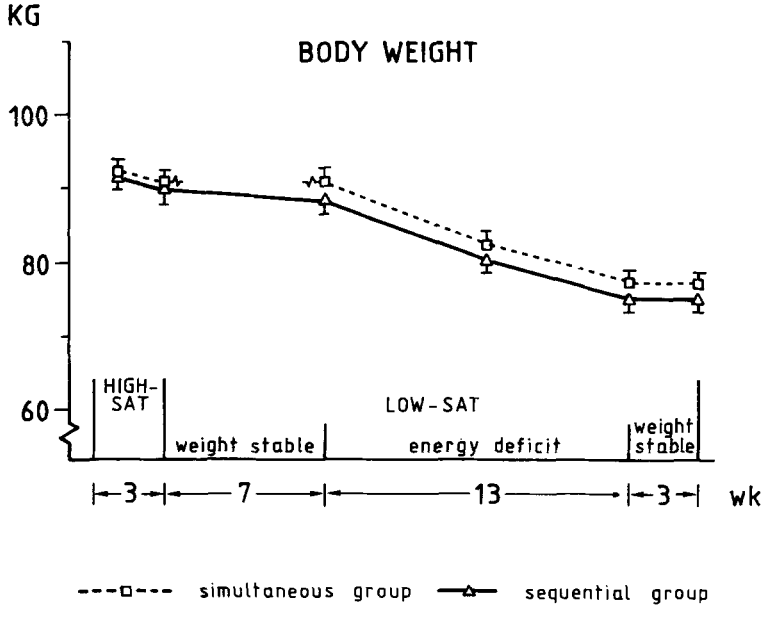


**Fig. 2.** Body weight (means ± SEM) for the simultaneous group (n=22) and the sequential group (n=19) during the study. High-Sat, high fat, high saturated fat; Low-Sat, low fat, low saturated fat.

TABLE 3. The separate effects of change in dietary fat and weight loss on serum lipids in the sequential group (n = 19) and the combined effects in the simultaneous group (n = 22)

| | Sequential | | |
|---|---|---|---|
| | Change in Dietary Fat | Weight Loss | Simultaneous Change in Dietary Fat + Weight Loss |
| Total cholesterol (mmol/l) | | | |
| Before | 5.57 ± 0.81 | 5.16 ± 0.87 | 5.62 ± 0.71 |
| After | 5.16 ± 0.87 | 4.75 ± 0.71 | 4.81 ± 0.64 |
| Change | −0.40 ± 0.30[a] | −0.41 ± 0.53[b] | −0.81 ± 0.40[a] |
| LDL cholesterol (mmol/l) | | | |
| Before | 3.85 ± 0.73 | 3.65 ± 0.81 | 3.83 ± 0.65 |
| After | 3.65 ± 0.81 | 3.34 ± 0.65 | 3.24 ± 0.54 |
| Change | −0.20 ± 0.25[b] | −0.31 ± 0.42[b] | −0.59 ± 0.38[a] |
| HDL cholesterol (mmol/l) | | | |
| Before | 0.99 ± 0.21 | 0.88 ± 0.16 | 1.10 ± 0.22 |
| After | 0.88 ± 0.16 | 0.99 ± 0.19 | 1.13 ± 0.20 |
| Change | −0.11 ± 0.08[a] | +0.11 ± 0.07[a] | +0.03 ± 0.14 |
| HDL/LDL ratio | | | |
| Before | 0.26 ± 0.07 | 0.25 ± 0.06 | 0.30 ± 0.08 |
| After | 0.25 ± 0.06 | 0.31 ± 0.08 | 0.36 ± 0.08 |
| Change | −0.02 ± 0.03[c] | +0.06 ± 0.04[a] | +0.06 ± 0.05[a] |
| Triglycerides (mmol/l) | | | |
| Before | 1.63 ± 0.62 | 1.42 ± 0.51 | 1.53 ± 0.59 |
| After | 1.42 ± 0.51 | 0.95 ± 0.30 | 0.98 ± 0.38 |
| Change | −0.21 ± 0.33[c] | −0.47 ± 0.40[a] | −0.55 ± 0.44[a] |

Values are means ± SD. To convert from mmol/l to mg/dl, multiply cholesterol values by 38.67 and triglyceride values by 88.54.
[a] $P < 0.0001$; [b] $P < 0.01$; [c] $P < 0.05$; before versus after diet or weight loss.

taneous group, the HDL cholesterol level also did not change significantly (+0.03 ± 0.14 mmol/l). As a consequence, the HDL/LDL ratio increased significantly within each group: +0.04 ± 0.05 in the sequential group ($P < 0.01$) and +0.06 ± 0.05 in the simultaneous group ($P < 0.0001$). The differences in the overall responses between both groups were not statistically significant for any of the serum lipids.

## DISCUSSION

The main findings of this strictly controlled study in moderately obese subjects are that the net favorable effect of body weight loss on serum lipids as a result of energy restriction seems to be greater than that of reduction in calories from total fat and saturated fat. Furthermore, the separate effects of weight loss and dietary fat modification appear to be additive. The HDL cholesterol-lowering effect of a low-fat low-saturated-fat diet effectively counteracted the effect of losing body weight.

The design of the present study made it possible to distinguish the effects of weight loss per se from the effects of dietary fat modification. Switching from an affluent-type diet to a diet with a decreased percent of energy provided by total and saturated fat without energy restriction by obese subjects resulted in reductions of all serum lipid levels, including HDL cholesterol. Dietary guidelines recommend a decrease in intake of total fat from the current average of 40% of energy in most affluent societies down to about 30%. In particular, the intake of saturated fatty acids should be reduced (7, 8). However, it has been suggested that a reduction in total fat intake may lower HDL cholesterol levels (20–22). In the present study, HDL cholesterol was significantly reduced on a weight-stable low-fat, low-saturated-fat diet both in males and in females. The reduction in women was significantly greater ($P < 0.05$) than that in men (−0.16 ± 0.08 mmol/l (14.5%) and −0.07 ± 0.05 mmol/l (7.8%), respectively). Whether or not this is a real gender difference in response to a low-fat, low-saturated-fat diet remains to be established. Results from a meta-analysis suggest that the change in HDL cholesterol is twice as large in men compared to women. In addition, triglycerides would be reduced more in men compared to women (5). Similar larger responses in HDL cholesterol and triglycerides in males versus females were observed in trials reported by Mensink and Katan (20, 23), Ernst et al. (24), and Wood et al. (25).

In the present study, the change in serum total cholesterol as a result of the change from the High-Sat diet to the Low-Sat diet without energy restriction was

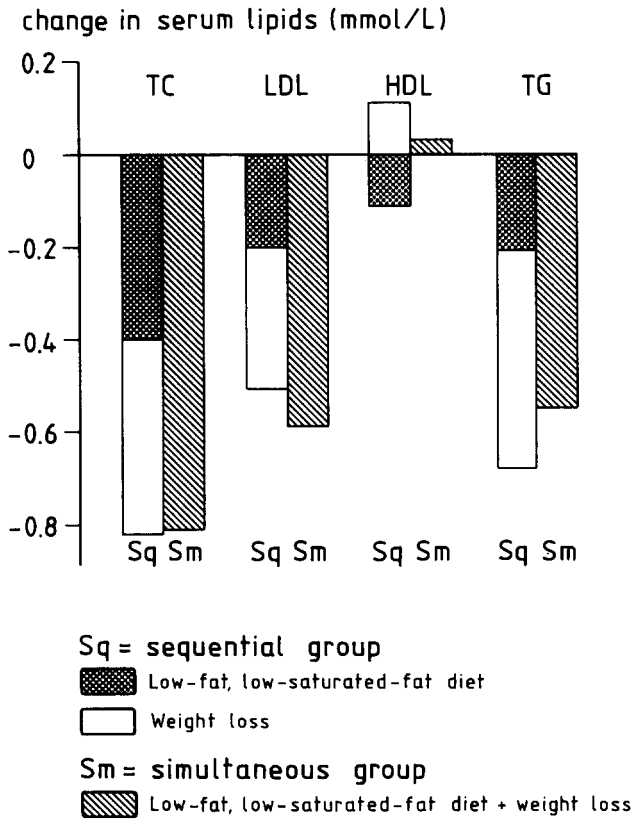


**Fig. 3.** Changes in serum lipid levels for the sequential group (n=19) and the simultaneous group (n=22) during the study. Changes are expressed as after minus before diet and/or weight loss. TC, total cholesterol; LDL, low density lipoprotein cholesterol; HDL, high density lipoprotein cholesterol; TG, triglycerides.

less than the 0.58 mmol/l predicted from the Keys' equation (26). Cole et al. (27) also demonstrated smaller decreases than predicted by the Keys' equation in obese subjects. They speculated that obesity may diminish the responsiveness to dietary change. This is in accordance with the observations of Goff and colleagues (28), which indicated that fatter men apparently do not benefit from a diet lower in cholesterol. In the present study, the subjects were highly motivated and the average weight loss was of a magnitude expected from a 4.2 MJ/day deficit diet. Distortion of the results due to lack of dietary compliance is, therefore, thought to be minimal.

It should be noted that isocaloric replacement of dietary fat by carbohydrates, as advocated by the dietary guidelines instead of by protein in this study, might produce a less favorable serum lipid profile than observed in the present study. In a study with moderately hypercholesterolemic subjects, it was demonstrated that isocaloric substitution of dietary protein for carbohydrate lowered total cholesterol, LDL cholesterol, and triglycerides and increased HDL cholesterol (29), while the findings of Lithell et al. (30) indicated that carbohydrates increase the level of very low density lipoprotein and slightly decrease HDL cholesterol compared with dietary protein.

Weight loss of approximately 13 kg, of which 83% was body fat, had beneficial effects on all serum lipid levels. During this weight loss period, changes in body weight were positively associated with changes in serum total cholesterol, LDL cholesterol, and triglyceride levels, whereas no significant correlations were observed with changes in HDL cholesterol or the HDL/LDL ratio. This latter result could possibly be explained by the relatively small variation in the responses of HDL cholesterol in this study. Another explanation could be that the amount of weight loss per se might not entirely be responsible for changes in HDL cholesterol concentrations. Previous studies have reported that significant increases of serum HDL cholesterol may occur in obese subjects in response to weight loss after their body weight has been stable for some time (5, 31). In agreement with these findings, Schwartz and Brunzell (32) found an enhanced activity of adipose tissue lipoprotein lipase after weight stabilization at a reduced body weight, resulting in increased HDL cholesterol levels, whereas during active weight loss a decreased lipoprotein lipase activity has been observed (33).

We also measured fat distribution by means of circumference ratios and magnetic resonance imaging in the group of subjects of which the group included in this paper was a subsample (10). Changes in visceral fat were not correlated to changes in serum lipids except for HDL cholesterol in women (10). The groups that were compared in the present study were not different with respect to baseline values and changes in waist/hip ratio and visceral fat area.

In the present study, the average weight losses per se in men and women were similar, 12.8 ± 3.0 kg and 13.8 ± 3.1 kg, respectively. Comparing the responses of serum lipids to the weight losses of obese men with those of women clearly demonstrated no sex-specific pattern: decreases in serum levels of total cholesterol, LDL cholesterol, and triglycerides were −9.2%, −9.8%, and −33.5% in men and −6.3%, −6.6%, and −33.3% in women, respectively. There were considerable increases in average HDL cholesterol and the HDL/LDL ratio in men (+13.3%, +25.0%, respectively) as well as in women (+11.7%, +19.2%, respectively).

The present study shows that the effects of weight loss and that of change to a low-fat, low-saturated-fat diet were additive: the total effect of slimming on reducing serum levels of total cholesterol, LDL cholesterol, and triglycerides could be ascribed for 50%, 61%, and 69%, respectively, to weight loss per se. The unfavorable reductions in HDL cholesterol and the HDL/LDL ratio in response to the recommended dietary fat modification without energy restriction were compensated by weight loss. In conclusion, our findings support beneficial effects of a diet low in total and saturated fat on some serum lipid levels in

obese subjects. The considerable additive effects of weight loss per se underscore the importance of establishing successful dietary treatment and weight maintenance programs for obesity.

The authors thank the participants for their enthusiastic cooperation and interest in the study. They are indebted to the students, the dietician A. Droop, and the members of the laboratory of the Department of Human Nutrition for help in conducting the study. They also thank Prof.dr. M. B. Katan and Prof.dr. J. G. A. J. Hautvast for their helpful comments on earlier versions of this manuscript, and the physicians A. F. X. Giesen and H. G. Martijn for the medical examinations. This study was supported by a research grant No. 87.067 from the Netherlands Heart Foundation and by slimming products of Wander AG/Sandoz Nutrition Ltd., Bern, Switzerland. J. C. Seidell is a research fellow of the Royal Netherlands Academy of Sciences (KNAW).

*Manuscript received 13 May 1993 and in revised form 26 July 1993.*

## REFERENCES

1. Manson, J. E., G. A. Colditz, M. J. Stampfer, W. C. Willett, B. Rosner, R. R. Monson, F. E. Speizer, and C. H. Hennekens. 1990. A prospective study of obesity and risk of coronary heart disease in women. *N. Engl. J. Med.* **322:** 882–889.
2. Seidell, J. C., P. Deurenberg, and J. G. A. J. Hautvast. 1987. Obesity and fat distribution in relation to health—current insights and recommendations. *Wld. Rev. Nutr. Diet.* **50:** 57–91.
3. Gordon, D. J., and B. M. Rifkind. 1989. High-density lipoprotein—the clinical implications of recent studies. *N. Engl. J. Med.* **321:** 1311–1316.
4. Stamler, J., D. Wentworth, and J. D. Neaton. 1986. Is relationship between serum cholesterol and risk of premature death from coronary heart disease continuous and graded? Findings in 356,222 primary screenees of the Multiple Risk Factor Intervention Trial (MRFIT). *J. Am. Med. Assoc.* **256:** 2823–2828.
5. Dattilo, A. M., and P. M. Kris-Etherton. 1992. Effects of weight reduction on blood lipids and lipoproteins: a meta-analysis. *Am. J. Clin. Nutr.* **56:** 320–328.
6. Wood, P. D., M. L. Stefanick, D. M. Dreon, B. Frey-Hewitt, S. C. Garay, P. T. Williams, H. R. Superko, S. P. Fortmann, J. J. Albers, K. M. Vranizan et al. 1988. Changes in plasma lipids and lipoproteins in overweight men during weight loss through dieting as compared with exercise. *N. Engl. J. Med.* **319:** 1173–1179.
7. Consensus Conference. 1985. Lowering blood cholesterol to prevent heart disease. *J. Am. Med. Assoc.* **253:** 2080–2086.
8. Erkelens, D. W. 1989. Cholesterol consensus in the Netherlands. *Eur. J. Clin. Nutr.* **43:** 89–96.
9. Leenen, R., K. van der Kooy, P. Deurenberg, J. C. Seidell, J. A. Weststrate, F. J. M. Schouten, and J. G. A. J. Hautvast. 1992. Visceral fat accumulation in obese subjects: relation to energy expenditure and response to weight loss. *Am. J. Physiol.* **263:** E913–E919.
10. Leenen, R., K. van der Kooy, A. Droop, J. C. Seidell, P. Deurenberg, J. A. Weststrate, and J. G. A. J. Hautvast. 1993. Visceral fat loss measured by magnetic resonance imaging in relation to changes in serum lipid levels of obese men and women. *Arterioscler. Thromb.* **13:** 487–494.
11. Weststrate, J. A., and J. G. A. J. Hautvast. 1990. The effects of short-term carbohydrate overfeeding and prior exercise on resting metabolic rate and diet-induced thermogenesis. *Metabolism.* **39:** 1232–1239.
12. Commissie UCV. 1985. UCV tabel. Voorlichtingsbureau voor de Voeding, The Hague, The Netherlands.
13. Siedel, J., E. O. Hägele, J. Ziegenhorn, and A. W. Wahlefeld. 1983. Reagent for the enzymatic determination of serum total cholesterol with improved lipolytic efficiency. *Clin. Chem.* **29:** 1075–1080.
14. Warnick, G. R., J. Benderson, and J. J. Albers. 1982. Dextran sulfate-$Mg^{2+}$ precipitation procedure for quantitation of high-density-lipoprotein cholesterol. *Clin. Chem.* **28:** 1379–1388.
15. Sullivan, D. R., Z. Kruijswijk, C. E. West, M. Kohlmeier, and M. B. Katan. 1985. Determination of serum triglycerides by an accurate enzymatic method not affected by free glycerol. *Clin. Chem.* **31:** 1227–1228.
16. Friedewald, W. T., R. I. Levy, and D. S. Fredrickson. 1972. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin. Chem.* **18:** 499–502.
17. Siri, W. E. 1956. The gross composition of the body. *In* Advances in Biological and Medical Physics. IV. C. A. Tobias and J. H. Lawrence, editors. Academic Press, New York. 239–280.
18. Comroe, J. H., R. E. Forster, A. B. Dubois, W. A. Briscoe, and E. Carlsen, editors. 1977. The Lung—Clinical Physiology and Pulmonary Function Tests. Year Book Medical Publishers, Chicago.
19. Pace, N., and E. N. Rathbun. 1945. Studies on body composition. III. The body water and chemically combined nitrogen content in relation to fat content. *J. Biol. Chem.* **158:** 685–691.
20. Mensink, R. P., and M. B. Katan. 1987. Effect of monounsaturated fatty acids versus complex carbohydrates on high-density lipoproteins in healthy men and women. *Lancet.* **i:** 122–125.
21. Sacks, F. M., G. H. Handysides, G. E. Marais, B. Rosner, and E. H. Kass. 1986. Effects of a low-fat diet on plasma lipoprotein levels. *Arch. Intern. Med.* **146:** 1573–1577.
22. Grundy, S. M. 1986. Comparison of monounsaturated fatty acids and carbohydrates for lowering plasma cholesterol. *N. Engl. J. Med.* **314:** 748–748.
23. Mensink, R. P., and M. B. Katan. 1989. Effect of a diet enriched with monounsaturated or polyunsaturated fatty acids on levels of low-density and high-density lipoprotein in healthy women and men. *N. Engl. J. Med.* **321:** 436–441.
24. Ernst, N., M. Fisher, P. Bowen, E. J. Schaeffer, and R. I. Levy. 1980. Changes in plasma lipids and lipoproteins after a modified fat diet. *Lancet.* **ii:** 111–113.
25. Wood, P. D., M. L. Stefanick, P. T. Williams, and W. L. Haskell. 1991. The effects on plasma lipoproteins of a prudent weight-reducing diet, with or without exercise, in overweight men and women. *N. Engl. J. Med.* **325:** 461–466.
26. Keys, A., J. T. Anderson, and F. Grande. 1965. Serum cholesterol response to changes in the diet. IV. Particular saturated fatty acids in the diet. IV. Particular saturated fatty acids in the diet. *Metabolism.* **14:** 776–787.
27. Cole, T. G., P. E. Bowen, D. Schmeisser, T. E. Prewitt, P. Aye, P. Langenberg, T. A. Dolecek, L. D. Brace, and S. Kamath. 1992. Differential reduction of plasma cholesterol by the American Heart Association Phase 3 Diet in moderately hypercholesterolemic, premenopausal women with

different body mass indexes. *Am. J. Clin. Nutr.* **55:** 385–394.
28. Goff, D. C., R. B. Shekelle, M. B. Katan, A. M. Gotto, and J. Stamler. 1992. Does body fatness modify the association between dietary cholesterol and risk of coronary death? Results from the Chicago Western Electric study. *Arterioscler. Thromb.* **12:** 755–761.
29. Wolfe, B. M., and P. M. Giovannetti. 1991. Short-term effects of substituting protein for carbohydrate in the diets of moderately hypercholesterolemic human subjects. *Metabolism.* **40:** 338–343.
30. Lithell, H., B. Karlström, I. Selinus, B. Vessby, and B. Fellström. 1985. Is muscle lipoprotein lipase inactivated by ordinary amounts of dietary carbohydrates? *Hum. Nutr.: Clin. Nutr.* **39C:** 289–295.
31. Zimmerman, J., N. A. Kaufmann, M. Fainaru, S. Eisenberg, Y. Oschry, Y. Friedlander, and Y. Stein. 1984. Effect of weight loss in moderate obesity on plasma lipoprotein and apolipoprotein levels and on high density lipoprotein composition. *Arteriosclerosis.* **4:** 115–123.
32. Schwartz, R. S., and J. D. Brunzell. 1981. Increase in adipose tissue lipoprotein lipase activity with weight loss. *J. Clin. Invest.* **67:** 1425–1430.
33. Taskinen, M-R., and E. A. Nikkilä. 1979. Effects of caloric restriction on lipid metabolism in man. Changes of tissue lipoprotein lipase activities and of serum lipoproteins. *Atherosclerosis.* **32:** 289–299.