Effects of weight reduction on blood lipids and lipoproteins: a meta-analysis[1–3]

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ABSTRACT Studies designed to examine effects of weight reduction by dieting on total cholesterol (TC), low-density-lipoprotein cholesterol (LDL-C), high-density-lipoprotein cholesterol (HDL-C), very-low-density-lipoprotein cholesterol (VLDL-C), and triglycerides (TGs) have reported inconsistent results. The purpose of this study was to quantify effects of weight loss by dieting on lipids and lipoproteins through the review method of meta-analysis. Results from the 70 studies analyzed indicated that weight reduction was associated with significant decreases ($P \leq 0.001$) and correlations ($P \leq 0.05$) for TC ($r = 0.32$), LDL-C ($r = 0.29$), VLDL-C ($r = 0.38$), and TG ($r = 0.32$). For every kilogram decrease in body weight, a 0.009-mmol/L increase ($P \leq 0.01$) in HDL-C occurred for subjects at a stabilized, reduced weight and a 0.007-mmol/L decrease ($P \leq 0.05$) for subjects actively losing weight. Our results indicate that weight reduction through dieting can be a viable approach to help normalize plasma lipids and lipoproteins in overweight individuals. *Am J Clin Nutr* 1992;56:320–8.

KEY WORDS Body weight, obesity, weight reduction, lipids, lipoproteins

Introduction

Hypercholesterolemia is a major risk factor in the development of coronary heart disease (CHD) and in the progression of atherosclerosis (1). CHD morbidity and mortality is positively related to low-density-lipoprotein cholesterol concentrations (LDL-C) and inversely related to high-density-lipoprotein cholesterol concentrations (HDL-C) (2). Not only does lowering total cholesterol (TC) and LDL-C in asymptomatic individuals with hypercholesterolemia reduce CHD death and nonfatal coronary events (3–5), but lowering TC reduces risk of subsequent CHD events in people with established CHD (6) and may actually slow the progression of CHD (7).

In addition to high TC and LDL-C and low HDL-C, the 1988 National Cholesterol Education Program's Panel Report identified severe obesity, defined as ≥ 30% overweight, as another risk factor that should be considered when evaluating cholesterol concentrations and determining the course of treatment (4). Moreover, even mild-to-moderate overweight has been associated with increased risk of coronary disease (8). Thus, the Consensus Development Conference on Health Implication of Obesity (9) identified weight reduction as advantageous in normalizing blood lipids and lipoproteins for overweight individuals.

Although a strong relationship between obesity and CHD is likely, epidemiologic studies have not consistently reported an association (10, 11). Moreover, the literature supporting the effect of weight loss on lipid indices is inconclusive, and results have been inconsistent (12–15). Although several investigators have reported beneficial effects of weight loss on lipids and lipoproteins, many studies (16–18) have concluded that weight reduction by dieting was not associated with advantageous changes in plasma lipids and lipoproteins. In studies that have reported significant effects of weight loss on plasma lipids, there is little agreement about the magnitude of the effect and the circumstances under which the weight-reduction program is most effective in modifying plasma lipids.

The intent of the present investigation was to clarify results of existing studies designed to examine the effects of weight loss by dieting on lipids and lipoproteins through the research strategy of meta-analysis. Meta-analysis was chosen as a method to examine this literature for three reasons. First, meta-analysis provides an objective, quantitative means for summarizing the results of previous research (19–27). Second, meaningful and repeatable conclusions can be drawn from a meta-analysis that cannot be drawn from other types of research integration (28, 29). Third, meta-analysis has not been applied to analyze the effect of weight reduction, through dietary management, on plasma lipids and lipoproteins.

Methods

Studies used

All literature published in journals addressing the effects of weight reduction through dietary management of lipid or lipoprotein concentrations for adults were potential contributors to the database. A librarian trained in computerized searches of biological databases conducted the initial search of the literature from 1966 to 1989, using Medline for studies having the key

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words body weight, obesity, weight reduction, lipids, lipoproteins, cholesterol, diet-reducing, and combinations of these major or minor descriptors. The collection of references obtained by this procedure provided the initial base of potential studies. Because manuscript titles may not accurately describe study content, the introduction and discussion sections of each manuscript were read for additional references to secure the best representation of available studies.

Any study published in a peer-reviewed journal designed to initiate weight reduction in adults through dietary manipulation that provided initial and final weights, as well as corresponding initial and final lipid or lipoprotein values, was included in the initial collection of articles. Of these 193 studies obtained, studies were excluded if test statistics or probability levels were not provided (n = 9), less than five subjects completed the study (n = 7), subjects engaged in planned exercise programs (n = 28), subjects had lost < 1.5 kg of weight (n = 6), subjects had insulin-dependent diabetes mellitus (n = 14), subjects were taking cholesterol-lowering medications (n = 3), the study duration was < 2 wk (n = 8), or the primary purpose of the study was not to initiate weight reduction through dietary manipulation (n = 4). The majority of studies (n = 44) were excluded for meeting at least two of the aforementioned exclusion criteria. A total of 70 studies that met final inclusion criteria was collected.

Coding studies

Lipid values included TG and TC; lipoprotein values included LDL-C, HDL-C, and VLDL-C. Thus, five separate meta-analyses were performed. The independent variables that may have influenced the effect of weight loss on these lipid and lipoprotein indices were methodological variables (date of publication, attrition rate, whether or not a control group was used, whether subjects were free living or housed in a metabolic ward, whether smoking was prohibited, whether alcohol was prohibited, whether blood was obtained and analyzed once at baseline and after weight reduction or at least twice at baseline and after weight reduction, whether serum or plasma was analyzed, study duration, and whether final blood was collected while subjects were actively losing weight or at a stabilized, reduced-weight). Studies of short duration (eg, 2–3 wk) in which subjects consumed a weight-reduction diet throughout the intervention period until final blood was collected, were coded as actively losing weight. Otherwise, studies must have specifically stated that subjects were actively losing weight or that a stabilized weight was achieved at final blood collection to be coded as such. Subject characteristics included weight loss (kg), baseline lipids and lipoproteins, age, sex, initial weight (kg), initial and final percent ideal body weight (%IBW), body mass index (BMI), final weight (within 10% of IBW or not), and rate of weight loss. A coding booklet was prepared to define and clarify each coded study feature and in accordance with recommendations (30), a reliability check for consistency in coding was conducted. The first author and a dietitian with a Master of Science degree in Nutrition served as independent raters. Agreement on inclusion and exclusion of studies among the two raters was 100%. The proportion of agreement between raters across all items was 92%. Disagreements between coders were resolved through further clarification of the variable definition and changes were incorporated into the coding process.

Statistical methods

Procedures followed the steps of meta-analysis as recommended by Glass et al (20), Hedges and Olkin (21), and Rosenthal (27). To test the hypothesis that there was no relationship between weight loss from dieting and changes in TG, TC, VLDL-C, HDL-C, and LDL-C, the Stouffer procedure of adding standard normal deviates (Zs) (27) was used. Both the methods of adding Zs and adding Zs weighted by the number of participants in each study were used to obtain overall estimates of probability. In addition, to determine the number of filed or unretrieved studies averaging null results required to bring the overall probability level to significance at 0.05, the equation by Rosenthal (27) given as $X = K\,[KZ^2 - 2.706]/2.706$ was used, where K is the number of studies combined, Z is the mean Z obtained from the K studies, and X is the number of filed or unretrieved studies known as the fail-safe-N.

Correlations between weight loss and changes in each lipid and lipoprotein were obtained for each study (20, 27, 31, 32). An overall correlation (effect size) for each lipid or lipoprotein category was calculated (21) and reported as a product-moment correlation. Mean unweighted and weighted correlations were calculated for each meta-analysis to determine whether the method of weighting produced results different from the unweighted method.

Before pooling correlations for each meta-analysis, statistical tests of homogeneity were applied to determine whether the series of sample correlations were more varied than would be expected on the basis of sampling variability if all the correlations were equal (21). Results from tests of homogeneity applied to the weighted and unweighted samples revealed that correlations associated with TC, LDL-C, VLDL-C, and TG were considered homogeneous and thus combined to achieve one overall effect size estimate for each meta-analysis. Homogeneity for the sample of HDL-C correlations was rejected. Therefore, studies were classified into subgroups and tested for within- and between-group homogeneity. Because the effect of weight loss on HDL-C depends, in part, on the period of weight stabilization (33–38), the subgrouping approach used to obtain homogeneity divided findings into those that analyzed HDL-C when subjects were actively losing weight and those that analyzed HDL-C after a stabilized, reduced weight was achieved. Within-group homogeneity was achieved for these subgroups and between-group homogeneity was rejected, which indicated that combining correlations within these subgroups was acceptable (21).

Unstandardized regression coefficients were estimated by a modification of the generalized least-squares procedure (21) to address how independent variables predicted changes in each lipid or lipoprotein. The usual least-squares estimator for regression coefficients was not used because variances for each study were different because not all sample sizes of studies included in the meta-analysis were equal.

Results

Description of the sample

A total of 32 different journals was used to generate studies included in these meta-analyses. From the journals, 70 studies (3, 13, 15, 17–18, 33–97) met inclusion criteria. Because some of the studies provided information generating more than one probability level or correlation (eg, results for men and women

TABLE 1
Description of study characteristics for meta-analyses of effects of weight reduction on blood lipids and lipoproteins

Variable	*n* [%]*
Publication date (1951–1989)†	
1951–1960	2 [2]
1961–1970	3 [3]
1971–1980	41 [36]
1981–1989	68 [60]
Subjects per study (18.5 ± 7.9; 5–72)†‡	
5–10	32 [28]
11–20	44 [39]
21–30	18 [16]
31–40	7 [6]
41–50	6 [5]
≥51	7 [6]
Age (y) (38.2 ± 4.9; 25.8–53.4)†	
25–34	21 [18]
35–44	54 [47]
45–54	19 [17]
Not specified	20 [18]
Sex used in study	
Only males	31 [27]
Only females	33 [30]
Not specified	50 [44]
Study duration (wk) (32.1 ± 22.7; 2–216)†	
2–4	14 [12]
5–10	26 [23]
11–51	53 [46]
≥52	21 [18]
Final lipid or lipoprotein measurements taken during	
Active weight loss	63 [55]
Stabilized, reduced weight	42 [37]
Not specified	9 [8]
Attrition rate (%) (29.3 ± 21.7; 10–82)†	
10–30%	17 [15]
31–50%	5 [4]
>50%	5 [4]
Not specified	87 [76]
Control group	
Included	20 [18]
Not included	94 [82]
Smoking	
Prohibited	10 [9]
Allowed or not specified	104 [91]
Alcohol	
Prohibited	18 [16]
Allowed or not specified	96 [84]
Subject domicile	
Free living	83 [73]
Metabolic ward	21 [18]
Not specified	10 [9]
Blood analyzed at least twice before and after weight loss	
Yes	34 [30]
No	80 [70]
Lipid or lipoprotein determined with	
Serum	68 [60]
Plasma	46 [40]

* Number of findings that are defined as the results that summarize the effects of weight loss on plasma lipids in specific groups of subjects (eg, men, women . . .). Because of rounding, not all percentages equal 100.
† Variable is treated as quantitative in subsequent analysis.
‡ $\bar{x}$ ± SD; range.

TABLE 2
Initial body weight indices and change in body weight indices for effects of weight reduction on blood lipids and lipoproteins

Variable	Range	$\bar{x}$ ± SD	*n* [%]*
Initial weight (kg)	63.2–150.0	98.5 ± 17.6	114 [100]
Initial % ideal body weight	107.0–217.0	143.2 ± 25.8	39 [34]
Initial body mass index	22.4–46.0	34.8 ± 6.2	22 [19]
Weight loss (kg)	1.4–26.0	16.6 ± 12.6	114 [100]
Final % ideal body weight	105.0–163.0	125.8 ± 10.1	18 [16]
Final body mass index	23.1–33.5	27.8 ± 3.2	18 [16]
Final weight within 10% of ideal body weight			
Yes			2 [2]
No			59 [52]
Not specified			53 [46]
Rate of weight loss			
≤1 kg/wk			3 [2]
>1 kg/wk			4 [4]
Not specified			107 [93]

* Number of findings that are defined as results that summarize the effects of weight loss on plasma lipids in specfic groups of subjects (eg, men, women).

were presented separately), it was possible for a single study to provide more than one result. Thus, one or more findings, defined as results that summarize the effects of weight loss on plasma lipids in specific groups of subjects, could be generated from a respective study. Taking all of the findings together, a maximum of 114 findings were recorded. The maximum number of findings from any one study was four.

Descriptive statistics for study characteristics coded in the meta-analyses are presented in **Table 1.** The average number of subjects per study was 18.5 ± 7.9 ($\bar{x}$ ± SD); the average age was 38.2 ± 4.9. The majority (44%) of studies provided findings from men and women combined. However, of studies reporting only one sex, 33 findings were recorded for women and 31 for men. The average study duration was 32.1 ± 22.7 wk. However, the range spanned from 2 wk to > 4 ys.

Several of the studies did not provide complete information for all study characteristics coded. For example, of the 114 findings 63 were from studies that recorded the lipid or lipoprotein measurement while subjects were actively losing weight; 42 were from studies that recorded the lipid or lipoprotein measurement while subjects were at a stabilized, reduced weight; and 9 did not provide adequate information to determine whether measurements were recorded during active weight loss or during stabilized weight. Mean initial weight (**Table 2**) for all subjects was 98.5 ± 17.6 kg; average weight loss was 16.6 ± 12.6 kg. The number of studies reporting initial and final %IBW, BMI, final weight (within 10% of IBW or not), and rate of weight loss was too few for further analysis.

Results from probability levels

When findings were treated independently and pooled together it was clear that weight reduction significantly decreased TC, LDL-C, VLDL-C, and TG ($P \leq 0.001$) (**Table 3**). Conclusions were identical if weighted or unweighted Z values were interpreted. The overall probability for determining whether a relationship between weight reduction and HDL-C existed, however,

TABLE 3
Average change in lipids and lipoproteins and overall probability for the change in lipids and lipoprotein concentrations (mmol/L) with body-weight (kg) loss*

	TC	LDL-C	HDL-C	HDL-C (active)	HDL-C (stable)	VLDL-C	TG
Number of studies	68	65	47	33†	21†	14	64
Number of findings‡	105	65	74	42	24	24	99
Before weight loss	5.93 ± 0.98§	3.44 ± 0.49	1.17 ± 0.23	1.11 ± 0.27	1.14 ± 0.26	1.09 ± 0.80	2.05 ± 1.07
Change with weight loss	−0.79 ± 0.67	−0.39 ± 0.64	0.03 ± 0.21	−0.09 ± 0.06	0.14 ± 0.11	−0.40 ± 0.70	−0.66 ± 0.76
Unweighted Z	15.81‖	9.33‖	−1.09	8.01‖	7.04‖	6.40‖	13.66‖
Weighted Z	14.11‖	8.80‖	−1.22	7.70‖	6.61‖	7.04‖	11.91‖
Fail-safe-N	11219	2029	—	687	278	354	8100

* TC, total cholesterol; TG, triglycerides; HDL-C, LDL-C, and VLDL-C high-density, low-density-, and very-low-density-lipoprotein cholesterol.
† Some studies provided data for both active and stable weight-loss periods.
‡ Findings are defined as results that summarize the effects of weight loss on plasma lipids in specific groups of subjects (eg, men, women).
§ $\bar{x}$ ± SD.
‖ $P \leq 0.001$.

was not significant for the total sample. When findings for HDL-C were subgrouped into those at active and stabilized weight-loss periods, significant results emerged. A decrease in HDL-C of 0.09 mmol/L was associated with active weight loss ($P \leq 0.001$) and a 0.14 mmol/L increase in HDL-C was associated with a reduced, stabilized weight ($P \leq 0.001$). The number of unretrieved studies with negative results required to overturn conclusions (fail-safe-N) that weight reduction significantly improved lipid and lipoprotein concentrations are also presented in Table 3.

The overall pooled average effect size for the relationships between weight loss and lipid and lipoprotein changes (**Table 4**) indicated that changes in TC, LDL-C, VLDL-C, TG, and HDL-C during stabilized weight loss were positive and significantly correlated ($P \leq 0.05$) with changes in body weight when both the weighted and unweighted methods for combining effect sizes were performed. However, a significant inverse relationship was found for the correlation between weight loss and HDL-C during active weight loss. In all cases, the unweighted and weighted effect sizes yielded generally the same results. With the exception of VLDL-C, weighted correlations were lower in magnitude and, therefore, more conservative.

Regression analysis

Study characteristics that tended to consistently affect results included weight loss (kg) and initial values for lipids and lipoproteins (**Table 5**). Our results indicated that for every kilogram decrease in body weight there was a 0.05 mmol/L decrease in TC ($P \leq 0.01$), a 0.02 mmol/L decrease in LDL-C ($P \leq 0.001$), a 0.007 mmol/L decrease in HDL-C for active weight loss ($P \leq 0.05$), a 0.009 mmol/L increase in HDL-C for stabilized weight loss ($P \leq 0.01$), a 0.016 mmol/L increase in VLDL-C (NS), and a 0.015 mmol/L decrease in TG ($P \leq 0.05$).

Study duration also indicated an effect on HDL-C similar to that noted with active and stabilized weight-loss periods. Results indicated that for each week increase in duration, HDL-C was predicted to increase by 0.004 mmol/L ($P \leq 0.01$). Studies lasting $\approx$1 y (mostly stabilized weight-loss periods) were associated with a 0.18 mmol/L increase in HDL-C; in contrast, studies lasting $\leq$ 6 wk (mostly active weight-loss periods) were associated with a 0.09 mmol/L decrease in HDL-C (data not shown).

With the exception of LDL-C, initial lipids and lipoproteins followed a consistent pattern; the greater the initial concentration, the greater decrease expected with weight loss. Although initial HDL-C for stabilized weight loss was not significantly different from initial HDL-C for active weight-loss periods, each mmol/L change in initial HDL-C during active weight loss was associated with a 0.008 mmol/L decrease ($P \leq 0.05$). Each mmol/L change in initial HDL-C was associated with a 0.005 mmol/L increase ($P \leq 0.05$) with weight loss recorded at a stabilized, reduced weight.

Several variables were significantly related to the change in one or more lipids or lipoproteins, including initial weight, age, sex, publication date, smoking and/or alcohol consumption status (prohibited or not), time that blood was obtained and analyzed (at least twice at baseline and after the intervention period), and serum analysis (done or not). However, in several cases the number of findings were limited, and in some cases data were too few to provide confidence in the analysis. For example, only 9% of the findings included in these meta-analyses were from studies that specifically stated subjects did not smoke and only 16% of the findings reported that subjects abstained from alcohol.

Discussion

The purpose of this study was to summarize, via the review method of meta-analysis, the results of studies that examined the effect of weight reduction by dieting on TC, LDL-C, HDL-C, VLDL-C, and TG. Of particular interest was the practical and applied significance related to weight loss and changes in lipids and lipoproteins as well as examination of variables influencing the effectiveness of weight loss on lipid and lipoprotein values.

Of primary interest was the result that when findings from studies were treated independently and pooled together, weight reduction was associated with a decrease in TC, LDL-C, VLDL-C, and TG (Table 3). These results were not only convincing in terms of their probability level ($P \leq 0.001$), but also with respect to the number of negative findings needed to reverse the statistical significance. It is improbable that 11 219 studies with negative results for the effect of weight loss on TC have not been published.

TABLE 4
Effect sizes between weight loss (kg) and changes in lipid and lipoprotein concentrations (mmol/L)*

	TC	LDL-C	HDL-C	HDL-C (active)	HDL-C (stable)	VLDL-C	TG
Unweighted *r*	0.38†	0.33†	−0.07	−0.35†	0.33†	0.36†	0.39†
Weighted *r*	0.32†	0.29†	−0.11	−0.32†	0.30†	0.38†	0.32†
Confidence interval‡	(0.29, 0.47)	(0.24, 0.36)	(−0.02, −0.18)	(−0.48, −0.22)	(0.19, 0.40)	(0.29, 0.48)	(0.27, 0.45)

* TC, total cholesterol; TG, triglycerides; LDL-C, HDL-C, and VLDL-C, low-density, high-density, and very-low-density-lipoprotein cholesterol.
† $P \leq 0.05$.
‡ 95% confidence interval for weighted *r*.

The smallest fail-safe-N value of 278 (for HDL-C during stabilized weight) was also large enough to indicate that results obtained from this meta-analysis could not be easily overturned. Weight loss was associated with a small and nonsignificant increase in HDL-C when results from the total sample were pooled (Table 3). However, when results from subjects actively losing weight were analyzed, HDL-C significantly decreased by 0.09 mmol/L (8.0%) ($P \leq 0.001$). In contrast, HDL-C significantly increased by 0.14 mmol/L (12.3%) ($P \leq 0.001$) when subjects were at a stabilized, reduced weight.

Overall correlations for the relationship between weight loss and change in various lipids and lipoproteins were also of primary interest (Table 4). Taking the data as a whole, the average weighted effect size between weight reduction and change in TC was 0.32. Thus, weight reduction was associated with ≈10% of the variance in change in TC. In contrast with results from the meta-analyses on TC, LDL-C, VLDL-C, and TG, the weighted effect size for the relationship between change in HDL-C and weight loss was nonsignificant. Because these data were obtained from a nonhomogeneous group, results should be interpreted cautiously. However, once correlations were subgrouped into active and stabilized weight-reduction periods, effect sizes were moderate and significant ($r = -0.32$, $P \leq 0.05$; $r = 0.30$, $P \leq 0.05$), respectively.

Although the authors are aware of no other meta-analysis addressing the effects of weight reduction by dietary measures, reported change in Metropolitan Relative Weight for > 5000 participants in the Framingham study accounted for only 3.9 and 2.0% (in men and women, respectively) of the variance in serum cholesterol with weight loss (98). The use of kilogram weight in this meta-analysis, rather than % IBW, may explain the different results. If selection criteria in these meta-analyses for weight index were different (eg, allowing studies that did not provide initial and final weight in pounds or kilograms, but instead pro-

TABLE 5
Unstandardized B values from zero-order regression of study characteristics on change in lipids and lipoproteins with weight loss*

Variables	TC	LDL-C	HDL-C	VLDL-C	TG
Weight loss (kg)	−0.05†	−0.02‡	—	0.016	−0.015§
Actively losing weight			−0.007§		
Reduced, stabilized weight			0.009†		
Initial TC	−0.019†	—	—	—	—
Initial HDL	—	—	—	—	—
Actively losing weight			−0.008§		
Reduced, stabilized weight			0.005§		
Initial LDL	—	−0.009	—	—	—
Initial VLDL	—	—	—	−0.018†	—
Initial TG	—	—	—	—	−0.005†
Initial weight (kg)	−0.01§	−0.016‡	0.004	0.004	−0.005
Age	−0.04	0.036§	0.005	−0.075	−0.025
Sex (male)	−0.201	−0.116	0.07§	−0.116	−0.130§
Publication date	0.015	0.021	0.019§	0.078	0.012
Control group used	0.118	−0.237	0.01	−0.489	0.279
Free-living subjects	0.127	0.054	0.017	0.05	0.151
Smoking prohibited	−0.076	−0.336	0.131†	−0.287	−0.06
Alcohol prohibited	−0.095	−0.274	−0.091§	0.189	−0.004
Blood analyzed (≥ 2 times)	0.172	−0.295	0.034	1.102§	0.677†
Serum analyzed	−0.212§	−0.468‡	0.086‡	0.518	−0.084
Study duration (wk)	0.0003	−0.007	0.004†	0.002	−0.001

* TC, total cholesterol; TG, triglycerides; LDL-C, HDL-C, and VLDL-C, low-density, high-density, and very-low-density-lipoprotein cholesterol.
† $P \leq 0.01$.
‡ $P \leq 0.001$.
§ $P \leq 0.05$.

vided weight as BMI or %IBW), additional studies would have been included, and perhaps results would have been different. Although it is possible to estimate kilograms from BMI or %IBW (99), many assumptions are made in the conversion. Because weight was such an important variable in these meta-analyses, extrapolation procedures appeared too imprecise to be used routinely. Thus, studies not providing kilogram weight, or weight in pounds, were excluded.

Because subjects in these meta-analyses lost weight, it is possible that total dietary fat, saturated fatty acid, and cholesterol intakes simultaneously decreased; these dietary alterations could partially explain reported changes in lipids and lipoproteins. However, few studies in these meta-analyses presented dietary data on fat quantity or quality. Thus, it was impossible to identify the independent influence of dietary fat on changes in lipids and lipoproteins.

To determine which study characteristics influenced change in lipids and lipoproteins, regression analyses were performed. However, because the number of independent variables (study characteristics) was large (eg, 13) relative to the number of findings (eg, 24–105), zero-order regression rather than multiple regression was used to provide insight into which variables influenced the results. Although it can be speculated that some variables were interrelated, when variables were individually regressed on the change in lipids or lipoproteins, several interesting results emerged.

Each kilogram weight loss was associated with a 0.05 mmol/L decrease in TC ($P \leq 0.01$) and a 0.02 mmol/L decrease in LDL-C ($P \leq 0.001$). Mechanisms to explain how changes in body weight influence change in lipid and lipoprotein results have not been clearly defined; however, body weight is perhaps the most important determinant of increased cholesterol synthesis often associated with obesity (100). Daily cholesterol production rate has been directly and significantly correlated with excess body weight (101). An estimated cholesterol synthetic rate of $\approx$20 mg/d for each kilogram body fat has been reported (102). Although the liver is the predominant organ responsible for cholesterol synthesis, adipose tissue can synthesize cholesterol. However, because in vitro quantification of cholesterol synthesis in human adipose tissue has a limited capability for converting labeled precursors into sterols, it has been concluded that excess cholesterol synthesis found in obesity is most likely from hepatic or intestinal origin instead of from adipose tissue (102).

Considerable support exists for the hypothesis that after energy restriction β-hydroxy-β-methylglutaryl coenzyme A reductase (HMG-CoA reductase) activity is decreased (100). In addition, mobilization of adipose tissue stores of cholesterol may accentuate the inhibition of hepatic cholesterol synthesis (100). Another likely hypothesis proposed to explain decreases in TC with weight reduction (103) is the enhancement of cholesterol excretion in bile with weight loss.

In addition to obesity being associated with hypercholesterolemia, obesity is often associated with hypertriglyceridemia, thought to result from either an increase in TG production rate and/or impaired removal (104). Results from these meta-analyses indicated that each kilogram weight lost was associated with a 0.015 mmol/L decrease in TG ($P \leq 0.05$).

Lipoprotein lipase activity generally increases with weight loss, particularly once weight stabilizes (82). However, during acute energy restriction, tissue concentrations of lipoprotein lipase have been reported to decrease by 50% to 80% (105). Because of the decrease in lipoprotein lipase during active weight loss, TG-rich lipoprotein synthesis is likely diminished and VLDL-C catabolism impaired. Thus, transfer of lipids to HDL-C is limited, resulting in decreased HDL-C concentrations. In agreement with our results, HDL-C decreased during active weight loss ($P \leq 0.05$). However, when weight stabilizes at a reduced level, lipoprotein lipase has been reported to increase with an associated increased hydrolysis of VLDL-C and transfer of lipids to HDL-C. In the present study, when subjects were at a reduced but stabilized weight, HDL-C increased ($P \leq 0.05$).

Regression analysis also indicated that sex was significantly related to the change in HDL-C and TG with weight loss. HDL-C was expected to increase by approximately twice as much in males as in females. In addition, TG in males was expected to decrease by $\approx$0.13 mmol/L more than for females. These results indicated that males may show greater changes in TG and HDL-C but the predicted changes for females none-the-less were still beneficial.

Age of subjects was related to the change in LDL-C with weight loss but no other lipid or lipoprotein. Results revealed an approximate fourfold difference in the predicted decrease in LDL-C with weight reduction. Younger subjects (eg, 34 y) were expected to decrease LDL-C by 0.65 mmol/L but older subjects (eg, 46 y) were expected to decrease LDL-C by only 0.21 mmol/L (data not shown). These findings are particularly interesting because as individuals age, LDL-C usually increases. However, initial LDL-C was not related to the change in LDL-C with weight loss. Therefore, individuals with lower initial LDL-C concentrations may receive equal benefit from weight reduction as those with higher initial LDL-C.

Serum HDL-C concentrations have been reported in several population studies to be lower in cigarette smokers than in nonsmokers (106–108). Smoking was a significant variable when regressed on change in HDL-C; however, smoking had no effect on other lipids and lipoproteins. This finding is particularly interesting in view of the negative association between cigarette smoking and body weight (109–110). Although initial weight may have been an interfering variable not controlled for in this zero-order regression, and the number of findings reporting abstinence from cigarettes was severely limited, results indicated that the increase in HDL-C associated with weight reduction was attenuated with smoking.

Alcohol is associated with increased TG and HDL-C concentrations in the general population (111). Results from these meta-analyses indicated that alcohol was related to the change in HDL-C but not to change in TG or any other lipid or lipoprotein. If alcohol was prohibited, HDL-C was estimated to decrease. The findings that alcohol did not significantly influence the change in TG is especially intriguing because alcohol has been shown to increase TG concentrations. However, there were few studies reporting that alcohol was prohibited.

Serum is the preferred blood fraction to analyze for lipids and lipoproteins (4). Although 60% of the findings reported analyzing serum, 40% analyzed plasma. Serum values are typically 3% higher than plasma values (4). Therefore, findings from studies that analyzed plasma should have lower initial lipid and lipoprotein values and demonstrate less absolute change in the lipid and lipoprotein concentration with weight reduction than findings from studies that analyzed serum. The difference between findings that analyzed serum verses plasma were greater than the 3% as noted by The Expert Panel (4). Therefore, other ex-

traneous factors may have influenced results. However, in those lipids and lipoproteins where blood fraction analysis was significant, results were consistent; specifically, serum values predicted a greater change in lipids and lipoproteins than did plasma values.

Of the 114 findings, 60% were from studies published between 1981 and 1989 (Table 1). Apparently, little research addressing the effects of weight reduction on lipids and lipoproteins was published before 1971, as evident by the limited number of findings (5%). Publication date was significantly related to change in HDL-C over time. Studies published in 1973 were associated with an estimated decrease of 0.09 mmol/L whereas studies published in 1987 indicated an increase HDL-C by 0.07 mmol/L. The reason for such variability in estimated HDL-C change is not known. Perhaps, laboratory techniques for HDL-C have become more sensitive in recent years.

Because the majority of findings included in these meta-analyses were from studies lacking control groups (82%), we compared Z values for the degree of change achieved for TC, LDL-C, HDL-C, VLDL-C, and TG from studies with experimental and control groups and compared these values with the degree of change from studies without control groups to determine whether results from studies of the two experimental designs differed. No significant differences for Z values between the groups were determined. Furthermore, regression coefficients associated with each kilogram weight loss for lipids and lipoproteins were quantitatively similar regardless if they were from comparisons between degree of change in experimental and control groups, or experimental groups alone. Apparently, whether or not a control group was included in the study design did not influence results. Furthermore, it appears that results from these meta-analyses reflect the influence of weight loss on lipids and lipoproteins and not regression toward the mean.

In conclusion, results from these metaanalyses indicated a strong effect of weight reduction on decreasing TC, LDL-C, and TG. Every 1 kg decrease in weight was associated with a 0.05 mmol/L, a 0.02 mmol/L, and a 0.015 mmol/L decrease, respectively. In addition, results indicated that HDL-C significantly increased (0.009 $mmol \cdot L^{-1} \cdot kg\ wt\ loss^{-1}$) when weight reduction was maintained, but decreased (0.007 $mmol \cdot L^{-1} \cdot kg\ wt\ loss^{-1}$) while subjects were actively losing weight. Because TC, LDL-C, and HDL-C affect the risk of CHD, weight control is important in CHD risk management. Therefore, it appears that weight reduction, when maintained, has beneficial effects on the lipid profile of overweight individuals. Current recommendations to decrease weight in overweight individuals with elevated lipids and lipoprotein concentrations are supported by results from these meta-analyses.

In addition to weight loss, several variables may have influenced the change in one or more lipids or lipoproteins. However, the number of studies that included a control group, prohibited alcohol and smoking, and obtained and analyzed blood samples at least twice before and after weight loss, was limited. In addition, the number of studies that reported attrition rate and rate of weight loss were too few to analyze. As future research in the area of weight reduction and lipids occurs, it may be possible to identify these and other explanatory variables that influence the effect of weight reduction on lipids and lipoproteins.

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