American Journal of Epidemiology
Vol. 137, No. 2
*Printed in U.S.A.*


# Does Body Fatness Modify the Effect of Dietary Cholesterol on Serum Cholesterol? Results from the Chicago Western Electric Study

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The hypothesis that lean persons are more responsive than fat persons to the effects of dietary cholesterol was investigated in 1,903 middle-aged employed men who were examined in 1958 and 1959 as participants in the Chicago Western Electric Study. Change in intake of dietary cholesterol was positively associated with change in serum cholesterol for men in the lowest tertile of body mass index (defined as weight (kg)/height (m)$^2$) (<24.2) but not for men in the highest tertile (>26.6) after adjustment for change in body mass index and change in intakes of energy and saturated and polyunsaturated fatty acids. A decrease of 150 mg/1,000 kcal in dietary cholesterol was associated with mean changes of −0.46, −0.18, and 0.13 mmol/liter in serum cholesterol for men with body mass indices of <24.2, 24.2–26.6, and >26.6, respectively. Body mass index was strongly correlated with subscapular skinfold thickness; thus, these differences in body mass index reflect true differences in adiposity. These results may help to explain inconsistencies that have occurred in feeding experiments with dietary cholesterol, and they suggest that a reduction in dietary cholesterol should have a more favorable effect on the serum cholesterol levels of fat persons after they have lost weight. *Am J Epidemiol* 1993;137:171–7.

body mass index; cholesterol; dietary fats; fatty acids, unsaturated; obesity

Individuals differ with respect to characteristic responses of serum cholesterol to a change in dietary cholesterol (1, 2). When changing from a low cholesterol diet to a moderately higher cholesterol diet, some individuals consistently show little change in serum cholesterol, while others show larger changes (1, 2). Mechanisms that account for individual differences in responsiveness have not been established, but an inverse association has been observed between responsiveness and body mass index (3). Per-

Received for publication April 10, 1992, and in final form September 3, 1992.

Abbreviations: BMI, body mass index; SD, standard deviation.

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The Western Electric Study is supported by grant HL 21010 from the National, Heart, Lung, and Blood Institute, and has also been supported by the American Heart Association, the Chicago Heart Association, the National Cancer Institute, and many private donors. Dr. Martijn B. Katan's participation was assisted by a travel grant, R90-040, from the Netherlands Heart Foundation.
The authors gratefully acknowledge Dr. Oglesby Paul for initiating the Western Electric Study and leading it during the early years; Dr. Mark Lepper for contributions to the study's design and conduct; Anne MacMillan Shryock for collecting the dietary data; Daniel Garside and Lois Steinfeldt for organizing data files; many physicians for conducting the examinations; and the officers and employees of the Western Electric Company for their support.

sons with lower body mass indices tended to be more responsive than persons with higher indices.

An association between change in dietary cholesterol and change in serum total cholesterol was observed in the Chicago Western Electric Study (4). The present analysis was designed to determine whether the magnitude of that association was modified by body mass index.

## PARTICIPANTS, MATERIALS, AND METHODS

### Participants

This analysis was based on 1,903 middle-aged men who were employed by the Western Electric Company in Chicago, Illinois, in 1957. Procedures for selection and examination of participants have been described elsewhere (4, 5). Briefly, 2,107 men were initially examined from October 1957 through December 1958, and men who continued to participate in the study were reexamined annually through 1969. The first and second examinations included a complete physical examination, a detailed medical history, measurement of serum cholesterol, and assessment of diet as well as other items. Excluded from the present study analysis were 204 men who had missing data for key variables—serum cholesterol, body mass index, or diet—at either the first or the second examination.

### Data collection

Information on foods and beverages consumed during the preceding 28 days was obtained at the initial examination and at the second examination 1 year later by two nutritionists who used standardized interviews and questionnaires based on Burke's diet history method (6). Data were analyzed according to a food table derived from several sources (7–10) to obtain each participant's usual daily intake of energy and nutrients. No therapeutic suggestions were made to participants, and no attempt was made to influence diet. However, some persons, particularly those with serum cholesterol concentrations of ≥7.82 mmol/liter (300 mg/dl) at the initial examination, did attempt to reduce their intakes of cholesterol and saturated fatty acids either on their own initiative or at the suggestion of their personal physicians (11).

Height and subscapular skinfold thickness were measured at the initial examination, and body weight was measured at both examinations. Body mass index was calculated as body weight (kg) divided by the square of height ($m^2$).

Serum cholesterol was measured at both examinations according to the method of Abell et al. (12). Lipoprotein cholesterol was not measured. The mean concentration of serum cholesterol declined by 0.305 mmol/liter from the first examination to the second. Modern procedures for standardization of cholesterol measurement had not been developed at that time, and it seems likely that the decline in mean serum cholesterol from 1958 to 1959 was due to baseline drift in the laboratory. Therefore, when each participant's change in serum cholesterol from the first examination to the second was calculated, 0.305 was added to the difference so that the mean difference would equal zero. This conversion did not change the substance of the results, but it facilitated their presentation in table 1.

### Data analysis

Participants were characterized by the difference between measurements made at the first and second examinations (e.g., change in body mass index (BMI) = $BMI_1 - BMI_2$) and by the mean of the two measurements (e.g., mean BMI = $(BMI_1 + BMI_2)/2$). We examined the relations between body mass index and height, weight, and subscapular skinfold thickness at the initial examination and between mean body mass index and change in dietary cholesterol by calculating product-moment correlation coefficients. Participants were sorted into nine groups according to tertile of change in dietary cholesterol and tertile of mean body mass index so that we could inspect the pattern of change in serum cholesterol for evidence of interaction. Linear regression analysis was used to test the null hypothesis that body mass index did not modify the association between change in dietary cholesterol and change in serum cholesterol. The cross-product term, mean body mass index × change in dietary cholesterol, was evaluated in a linear regression model which also included mean body mass index and change in dietary cholesterol, as well as change in percentage of calories derived from saturated fatty acids, change in percentage of calories derived from polyunsaturated fatty acids, and change in body mass index. We also performed regression analyses within tertiles of body mass index to estimate the effect of a change in dietary cholesterol on serum cholesterol at different levels of body mass index.

We used several other statistical methods in attempts to account for the potential influence of both baseline drift and regression to the mean from 1958 to 1959 on these results. In one analysis, serum total cholesterol measured at the second examination was regressed on serum total cholesterol measured at the first examination. The residuals from this regression analysis were examined as the dependent variables in further investigations of the interaction between dietary cholesterol and body mass index. The use of residuals has been proposed as an effective mechanism for removing the effect of regression to the mean on changes in lipoprotein values (13). This method also allowed us to account for the baseline drift through the use of a constant term in the regression model. Since the results regarding the presence of an effect modification agreed across statistical methods, the results presented here are from the method which provided for the greatest clarity.

## RESULTS

Serum cholesterol levels and intake of saturated fatty acids and cholesterol were high by current standards in this sample of 1,903 employed men who were 40–56 years of age at initial examination in 1958 (14). Mean values were 6.41 mmol/liter (standard deviation (SD), 1.41) for serum cholesterol, 16.7 percent (SD, 2.6) for percentage of calories derived from saturated fatty acids, and 240 mg/1,000 kcal (SD, 68) (753 mg/day; SD, 276) for dietary cholesterol. Intake of polyunsaturated fatty acids was low; the mean percentage of calories was 3.9 (SD, 0.9) (14). Mean body mass index was 25.4 (SD, 3.2).

The correlations of body mass index with height, weight, and subscapular skinfold thickness were −0.07, 0.85, and 0.71, respectively. When participants were stratified into tertiles according to body mass index, mean height was 175, 175, and 174 cm in the low, middle, and high tertiles, respectively. Corresponding mean weights were 68, 77, and 88 kg, and mean subscapular skinfold thicknesses were 13, 18, and 23 mm. The correlation between mean body mass index and change in dietary cholesterol for all 1,903 men was 0.00.

Mean serum total cholesterol measured at the second examination was 6.11 mmol/liter (SD, 1.16). Table 1 shows mean changes in serum cholesterol from the first annual examination to the second by mean body mass index and change in dietary cholesterol. For men who decreased their intake of dietary cholesterol by at least 27 mg/1,000 kcal,

**TABLE 1. Mean change in serum cholesterol (mmol/liter) from 1958 to 1959 among 1,903 middle-aged employed men in the Chicago Western Electric Study, by body mass index and change in intake of dietary cholesterol**

| Change in body mass index*,† | Change in dietary cholesterol (mg/1,000 kcal)‡ | | |
|---|---|---|---|
| | −282 to −27 | −26 to 12 | 13 to 326 |
| 16.9 to 24.1 | −0.27 | −0.01 | 0.10 |
| 24.2 to 26.6 | −0.11 | 0.09 | 0.08 |
| 26.7 to 40.6 | 0.06 | 0.07 | −0.02 |

* Weight (kg)/height (m)$^2$.

† Body mass index was calculated as mean body mass index at the first (1958) and second (1959) examinations. Mean values for the tertiles of body mass index were 22.2, 25.4, and 29.0, respectively. The number of men in each cell varied from 195 to 231.

‡ Change in dietary cholesterol was calculated as the difference between intake at the second examination (1959) and intake at the first examination (1958). Mean values for the tertiles of change in dietary cholesterol were −69.1, −7.7, and 51.7 mg/1,000 kcal, respectively.

leaner men had a greater decrease in serum cholesterol than fatter men, although they did not have a larger change in dietary cholesterol. Mean changes in dietary cholesterol were −65, −71, and −71 mg/1,000 kcal for the low, medium, and high body mass index groups.

For men who increased their intake of dietary cholesterol by 13 mg/1,000 kcal or more, leaner men had a greater increase in serum cholesterol than fatter men. Again, this trend cannot be explained by differences in change in dietary cholesterol. Mean changes in dietary cholesterol in the low, medium, and high body mass index groups were 48, 53, and 54 mg/1,000 kcal, respectively.

To test statistically the null hypothesis that body mass index did not modify the effect of change in dietary cholesterol on serum cholesterol, we regressed change in serum cholesterol on mean body mass index, change in dietary cholesterol, and the product of the two variables. Other variables in this analysis were change in body mass index and change in percentages of energy derived from saturated fatty acids and polyunsaturated fatty acids. The correlation between change in dietary cholesterol and change in saturated fatty acids was 0.37. Correlations between other variables were all less than 0.20.

Results of the regression analysis are shown in table 2. The regression coefficient for the product of mean body mass index and change in dietary cholesterol was negative ($p < 0.001$), indicating that the effect of change in dietary cholesterol on serum cholesterol was less for fat men than for lean men. For example, assuming no change in body mass index or in intakes of saturated fatty acids and polyunsaturated fatty acids, the model indicates that a decrease in intake of dietary cholesterol of 150 mg/1,000 kcal would be associated with mean changes in serum cholesterol of −0.51, −0.18, and 0.14 mmol/liter for men with body mass indices of 20, 25, and 30, respectively.

To check this result, we divided the study group into thirds according to body mass index. Mean body mass indices for the lower, middle, and upper groups were 22.2, 25.4, and 29.0, respectively. For each group, change in serum cholesterol was regressed on change in dietary cholesterol, change in saturated fatty acids, change in polyunsaturated fatty acids, and change in body mass index. The resulting coefficients were used to calculate the mean change in serum cholesterol associated with a decrease of 150 mg/1,000 kcal in intake of dietary cholesterol. The results, shown in table 3, indicate that mean changes in serum cholesterol were −0.46, −0.18, and 0.13 mmol/liter for men in the lower, middle, and upper thirds of the body mass index distribution, respectively.

Further regression analyses indicated that body mass index did not appear to modify the association between change in percentage of energy from saturated fatty acids and change in serum cholesterol or the association between change in percentage of energy

**TABLE 2. Linear regression analysis of change in serum cholesterol (mmol/liter) from 1958 to 1959 among 1,903 middle-aged employed men in the Chicago Western Electric Study**

| Independent variable* | $\beta$ | SE† | $p$ |
|---|---|---|---|
| Change in dietary cholesterol (mg/1,000 kcal) | 0.01203 | 0.00335 | <0.001 |
| Body mass index‡ | 0.00031 | 0.00100 | 0.752 |
| Product of body mass index and change in dietary cholesterol | −0.00043 | 0.00013 | <0.001 |
| Change in saturated fatty acids (% energy) | 0.03862 | 0.01002 | <0.001 |
| Change in polyunsaturated fatty acids (% energy) | −0.00940 | 0.02300 | 0.683 |
| Change in body mass index | 0.14133 | 0.02601 | <0.001 |

* Change was calculated as the second examination (1959) value minus the first examination (1958) value. The body mass index value was the mean value for the first and second examinations. Mean values for the regressors were −8.2 mg/1,000 kcal for change in dietary cholesterol (standard deviation (SD), 61.1); 25.6 for body mass index (SD, 3.2); −0.6 percent for change in percentage of energy derived from saturated fatty acids (SD, 2.6); 0.0 percent for change in percentage of energy derived from polyunsaturated fatty acids (SD, 1.1); and 0.2 for change in body mass index (SD, 0.9). $R^2$ for this model was 0.038.

† SE, standard error.

‡ Weight (kg)/height (m)$^2$.

**TABLE 3. Mean change in serum cholesterol* associated with a decrease in dietary cholesterol of 150 mg/1,000 kcal from 1958 to 1959 among 1,903 middle-aged employed men, by tertile of body mass index: Chicago Western Electric Study**

| Body mass index† | No. of men | Predicted mean change in serum cholesterol (mmol/liter)‡ | 95% confidence interval |
|---|---|---|---|
| 16.9–24.1 | 631 | −0.46 | −0.69 to −0.22 |
| 24.2–26.6 | 645 | −0.18 | −0.39 to 0.04 |
| 26.7–40.6 | 627 | 0.13 | −0.08 to 0.36 |

* Adjusted for change in body mass index and intake of saturated and polyunsaturated fatty acids.

† Weight (kg)/height $(m)^2$.

‡ Mean changes in serum cholesterol and their 95% confidence intervals were calculated from the following linear regression coefficients for the three groups in the order listed above: 0.00304 ± 0.00080 (standard error), 0.00117 ± 0.00072, and −0.00091 ± 0.00075.

from polyunsaturated fatty acids and change in serum cholesterol. When the interaction term was added to the model shown in table 2, the regression coefficient for mean body mass index × change in saturated fatty acids was 0.00087 ± 0.0029 (standard error) ($p$ = 0.77). The comparable result for mean body mass index × change in polyunsaturated fatty acids was 0.0037 ± 0.0080 ($p$ = 0.64).

## DISCUSSION

These results support the hypothesis that body fatness modifies the effect of change in dietary cholesterol on serum cholesterol concentration. After adjustment for change in body mass index and change in intakes of saturated and polyunsaturated fatty acids, a decrease of 150 mg/1,000 kcal in dietary cholesterol was associated with changes of −0.46, −0.18, and 0.13 mmol/liter in mean serum cholesterol for men with body mass indices of <24.2, 24.2–26.6, and >26.6, respectively. An absence of correlation between body mass index and height, combined with strong positive correlations of body mass index with weight and subscapular skinfold thickness, support the inference that these differences in body mass index reflect differences in body fatness.

The absolute values for these changes in serum total cholesterol should be interpreted with caution, since both baseline drift in laboratory measurements of serum total cholesterol and the phenomenon of regression to the mean could have been related to changes in a participant's serum total cholesterol from 1958 to 1959. However, neither of these factors could have been responsible for the observed pattern, which showed an attenuation of the effect of dietary cholesterol on serum total cholesterol in fatter persons as compared with leaner persons. The effect modification shown here persisted when several other analytic methods were used.

Chance is an unlikely explanation for these differences in effect. The coefficient for the interaction between body mass index and change in dietary cholesterol was associated with a $p$ value less than 0.001. Confounding by changes in body weight or changes in intake of saturated or polyunsaturated fatty acids are also unlikely explanations, since the differences persisted after adjustment for these variables. Changes in diet were estimated from 28-day dietary histories, and it is possible that changes reported by fatter men were less valid than those reported by leaner men. For example, the observed results could have occurred if fatter men, in comparison with leaner men, had exaggerated decreases in consumption of foods rich in cholesterol and saturated fatty acids. Motivation for this kind of bias is not readily apparent in the present investigation, because it was strictly an observational study, and no attempts were made to influence what participants were eating. Moreover, if that kind of bias had occurred, we would expect body mass index to have modified the association of change in intake of saturated fatty acids with change in serum cholesterol in the same way that it modified the association of change in dietary cholesterol with change in serum cholesterol, but that was not the case. Coefficients for the interactions of body mass index with change in saturated fatty acids and change in polyunsaturated fatty acids were not statistically significant and did not appreciably change the fit of the regression model. Since body mass index was strongly associated with subscapular skinfold thickness, we conclude that these results support the hypothesis that lean men are more responsive than fat men to the hypocholesterolemic effects of reduced dietary cholesterol intake.

These results indicate that a decrease of 150 mg/1,000 kcal in dietary cholesterol was associated with a small increase in serum cholesterol in the sample of men with a body mass index greater than 26.6, but the existence of the baseline drift in laboratory measurements of serum total cholesterol limited our ability to examine this issue precisely in this study. Further research is needed to resolve this question.

Increases in either body mass index or dietary cholesterol were associated with increases in serum total cholesterol levels, but the effect of increases in both was less than additive. Obesity has been associated with decreased absorption of cholesterol (15) and increased secretion of bile acids and biliary cholesterol (16). Both would tend to make fat persons appear to be less responsive than lean persons to the hypercholesterolemic effects of dietary cholesterol. Further research is needed to establish how adiposity modifies the effect of dietary cholesterol on plasma lipids and apoproteins.

The apparent effect of body fatness on the relation between dietary cholesterol and serum cholesterol may help to explain some of the inconsistencies that have been observed in experiments on the effects of dietary cholesterol on serum cholesterol. Investigators who study fatter persons would tend to observe smaller effects than those who study leaner persons. In this study, body mass index did not modify the effect of change in intake of saturated fatty acids on change in serum cholesterol; thus, the relation between dietary saturated fatty acids and serum cholesterol should be apparent regardless of the body mass index distribution of the study population.

These results support the idea that fatter persons are less responsive than leaner persons to changes in dietary cholesterol. This should not be taken to indicate that obesity is a protective factor. In fact, change in body mass index was positively associated with change in serum total cholesterol. Furthermore, a large body of evidence indicates that obesity has an important role in the development of atherosclerosis, diabetes, hypertension, cholelithiasis, and other adverse health outcomes (17). Rather, these results suggest that reduction in dietary cholesterol should produce a more favorable effect on the serum cholesterol concentration of fat persons after they have lost weight. This expectation should be investigated experimentally.

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