Cholesterol-lowering effects of dietary fiber: a meta-analysis

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ABSTRACT

Background: The effects of dietary soluble fibers on blood cholesterol are uncertain.

Objective: This meta-analysis of 67 controlled trials was performed to quantify the cholesterol-lowering effect of major dietary fibers.

Design: Least-squares regression analyses were used to test the effect on blood lipids of pectin, oat bran, guar gum, and psyllium. Independent variables were type and amount of soluble fiber, initial cholesterol concentration, and other important study characteristics.

Results: Soluble fiber, 2–10 g/d, was associated with small but significant decreases in total cholesterol (−0.045 mmol·L⁻¹·g⁻¹ soluble fiber (95% CI: −0.054, −0.035)) and LDL cholesterol (−0.057 mmol·L⁻¹·g⁻¹ (95% CI: −0.070, −0.044)). The effects on plasma lipids of soluble fiber from oat, psyllium, or pectin were not significantly different. We were unable to compare effects of guar because of the limited number of studies using 2–10 g/d. Triacylglycerols and HDL cholesterol were not significantly influenced by soluble fiber. Lipid changes were independent of study design, treatment length, and background dietary fat content.

Conclusions: Various soluble fibers reduce total and LDL cholesterol by similar amounts. The effect is small within the practical range of intake. For example, 3 g soluble fiber from oats (3 servings of oatmeal, 28 g each) can decrease total and LDL cholesterol by ≈0.13 mmol/L. Increasing soluble fiber can make only a small contribution to dietary therapy to lower cholesterol. Am J Clin Nutr 1999;69:30–42.

KEY WORDS Meta-analysis, humans, controlled trials, total cholesterol, low-density-lipoprotein cholesterol, LDL cholesterol, high-density-lipoprotein cholesterol, HDL cholesterol, triacylglycerols, dose response, fiber

INTRODUCTION

Coronary artery disease is the major cause of death in the United States and in most Western countries (1), and blood cholesterol is a major risk factor (2). Dietary and pharmacologic reductions in total and LDL cholesterol decrease the risk of coronary events (3–6), and dietary intervention is the first-line approach (7). Increasing dietary fiber has been recommended as a safe and practical approach for cholesterol reduction (8).

Dietary fiber is a collective term for a variety of plant substances that are resistant to digestion by human gastrointestinal enzymes (9). Dietary fibers can be classified in 2 major groups depending on their solubility in water. In humans, the structural or matrix fibers (lignins, cellulose, and some hemicelluloses) are insoluble, whereas the natural gel-forming fibers (pectins, gums, mucilages, and the remainder of the hemicelluloses) are soluble. Studies have focused on soluble fibers such as oats, psyllium, pectin, and guar gum, and qualitative reviews suggested that these fibers lower total and LDL cholesterol (10, 11). Water-insoluble wheat fiber and cellulose have no effect unless they displace foods supplying saturated fats and cholesterol (12).

There is debate as to the degree of cholesterol reduction caused by soluble fibers. The range of effects on total cholesterol varies from −18% to 0% in trials of oat products, from −17% to 3% for psyllium, from −16% to −5% for pectin, and from −17% to 4% for guar gum (12). Reasons for such large variations include small sample sizes, different dosages of fiber, different background diets, concurrent changes in body weight, varying dietary control, and different types of subjects. It is also possible that certain fibers lower cholesterol more effectively than others. For example, Bell et al (13) examined the hypocholesterolemic effects of psyllium-and pectin-enriched cereals in a randomized, controlled study. They found that the psyllium-enriched cereal lowered cholesterol more effectively than the pectin-enriched cereal. Also, trials of oat products suggested that hypercholesterolemic patients are more responsive than normolipidemic persons (14, 15).

Concurrent changes in fat and cholesterol caused by inadequate dietary control can confound the relation between increased fiber intake and blood cholesterol concentrations. For this reason, quantifying the direct effect of fiber on cholesterol lowering, in addition to that attributed to displacement of saturated and trans-unsaturated fat in the diet, is difficult.
In this meta-analysis of controlled trials, we evaluated the cholesterol-lowering effects of several water-soluble fibers. We studied the influence on blood lipid changes of fiber type, dosage, initial cholesterol concentration, concurrent changes in dietary fat and cholesterol, and other aspects of the study designs.

MATERIALS AND METHODS

Trials of the effects of dietary fiber on blood cholesterol concentrations in adults were identified by a computerized literature search (MEDLINE; National Library of Medicine, Bethesda, MD) of articles published from 1966 to June 1996 and examination of cited reference sources. Only published trials reported in English were considered; however, we included one unpublished trial by Beling et al (1991; provided by Quaker Oats, Chicago), which has been previously referenced in the literature (15). Studies were selected for analysis if they met the following criteria: 1) they were controlled (insoluble fiber or low-fiber diet used for comparison with a high-fiber diet or a placebo used for comparison with a pure fiber supplement) and had either a randomized crossover or a parallel design; 2) they provided lipid changes in the fiber and control groups to permit calculation of the treatment effect; 3) they had an intervention period ≥14 d (16–18); 4) they used soluble fiber from a single source to permit analysis of differences between fiber types; 5) the amount of soluble fiber used was indicated or could be estimated from the published literature (19–21); 6) they had a minimum lead-in period of 14 d for studies administering the fiber with a low-fat, low-cholesterol diet to eliminate possible effects on plasma lipids due to overall dietary changes (16–18); and 7) dietary changes for both the fiber and control groups were made under isoenergetic conditions. This analysis was limited to primary sources of fiber for which there were >5 trials per type: oat products, psyllium, pectin, and guar gum.

The net changes in total cholesterol, LDL cholesterol, HDL cholesterol, and triacylglycerols are presented in units of mmol·L⁻¹·g soluble fiber⁻¹. For studies with parallel group designs, lipid effects were calculated by subtracting the mean change in the control (low fiber) group from that in the treatment (high fiber) group. In crossover studies, the estimate represents the change in the control (low-fiber) group from that in the treatment (high fiber) group. In crossover studies, the estimate represents the difference in posttreatment lipid concentrations for the high-fiber and low-fiber periods. The net change was divided by the daily dose of soluble fiber.

Individual studies were weighted by the inverse of the variance of the fiber effect. For each trial, we estimated the SE of the treatment effect for the lipid outcome measures by using the SDs of paired differences (follow-up minus initial) for the treatment and control groups. If the SDs were not provided, we used the SE values derived from the exact t ratios, P values, or 95% CIs (22). The within-study SE was divided by the average daily dose for each study to estimate the SE of the treatment effect per gram fiber.

We were unable to calculate the correct within-study SEs for more than two-thirds of the trials on the basis of the published data (few reported exact probability values or CIs for the group differences described above). As an alternative, we estimated the SE by using previously published methods and data from the Lipid Research Clinics (23–28; Appendix A).

We computed summary estimates (effect sizes) of the net lipid changes by combining the mean effect sizes reported by individual studies weighted by the inverse of the individual and between-study variance according to a random effects model (29). Summary estimates were computed for each type of soluble fiber separately and for all fibers combined. All effect sizes are presented with 95% CIs based on the estimated variances (Appendix A). We assessed the homogeneity of effect sizes by the Q test (29), where $Q > \chi^2_{k-1,0.05}$ indicated that the individual estimates for k studies were not estimators of one underlying effect.

For meta-analyses of each fiber type, we selected one set of lipid results per study to avoid undue weighting of a study. For instance, for the trial by Kestin et al (30), comparing oat bran, wheat bran, and rice bran, we selected the effect size comparing oat bran and wheat bran because wheat was the most often used control fiber in the studies included in the meta-analysis. When more than one dose was studied (31–33), the mean lipid change across all doses was used to provide an average effect size. However, each dose was represented separately in the dose-response analysis.

Weighted least-squares regression analyses were performed by using the general linear models procedure of the SAS program (34) to test for differences in lipid changes (without dividing by the dose of soluble fiber). In addition to the amount of soluble fiber, the following independent variables were included in the model: initial cholesterol concentration; type of dietary fiber; study design (parallel or crossover); health status of study population (healthy, hypertensive, or diabetic); mean age; background diet (low-fat, low-cholesterol diet compared with usual diet); dietary changes (change in the high-fiber period minus change in the low-fiber period) in total fat, saturated fat, and dietary cholesterol; type of control (low-fiber control product compared with diet only); and treatment length. All models were weighted by using the inverse of the variance of each effect estimate. Models of dose response (dose of specific fiber and dose response stratified by initial cholesterol concentration) were examined by forcing the intercept through zero. Further modeling was done to determine the effects of variability of these covariates among studies as predictors of changes in blood lipids after the amount of soluble fiber and initial lipid concentrations were controlled for. We did not assume a zero-intercept model to examine the influence of these other covariates. A two-sided significance level of 0.05 was used.

We calculated predicted changes in blood cholesterol from changes in dietary fatty acids and cholesterol by using the equations of Keys et al (18) and Mensink and Katan (35) when sufficient dietary data were included in the published reports. This calculation was used to determine whether lipid changes could be attributed to dietary changes other than the inclusion of soluble fiber in the diet. An adjusted effect size for soluble fibers was computed for each trial by subtracting the expected lipid changes from the observed lipid changes (the combined effect of fat and fiber). A new summary effect size was then calculated by using the adjusted values for each trial.

RESULTS

Characteristics of the studies

We reviewed 162 clinical studies reporting the effects of oat products, psyllium, pectin, or guar fiber on blood cholesterol. A description of the individual trials considered for this meta-analysis may be requested by contacting the corresponding author. Ninety-two studies were excluded: 81 were not sufficiently controlled, 8 had insufficient information, and 3 had a treatment
period <14 d. Seventy published reports were identified for a quantitative analysis. Three of these studies were included only in the dose-response analysis because they did not use a true low-fiber control but rather compared a high with a lower dose of the same intervention fiber (36–38). The 67 trials included in the analysis are summarized in Table 1 and included 25 trials of oat products (30–33, 39–59), 17 of psyllium (13, 60–74), 7 of pectin (13, 75–80), and 18 of guar gum (81–98). Not all trials of different fiber sources provided total cholesterol, LDL-cholesterol, HDL-cholesterol, and triacylglycerol concentrations.

The meta-analyses included 2990 subjects (1733 men, 1011 women, 246 sex not specified) whose average age was 50 y. The average dose of 9.5 g soluble fiber was administered over a mean treatment period of 49 d. Fifty-seven of 67 (85%) studies included in the meta-analyses used a control fiber that was low in soluble fiber, such as wheat bran, cellulose-based placebo, or corn flakes. The remaining 10 trials (15%) compared the fiber intervention with a diet that excluded the fiber intervention (diet only).

In 38 studies the background diets were the subjects’ usual diets, which were most often similar to conventional Western diets in fat and cholesterol content; in 29 studies the background diets were low in fat and cholesterol (<30% of energy from fat and <300 mg cholesterol/d). During the high-fiber intervention, subjects consumed an average of 188 kJ more energy than during the control period. Dietary fat and cholesterol were slightly reduced during the high-fiber intervention: −2.8 g total fat, −0.34 g saturated fat, and −2.5 g cholesterol. Both groups receiving the high- and low-soluble-fiber interventions lost weight, 0.19 and 0.64 kg, respectively.

### Effect of soluble fiber

In the full dose range, soluble fiber significantly reduced both total and LDL cholesterol: −0.028 (95% CI: −0.035, −0.022) mmol·L⁻¹·g soluble fiber⁻¹ [−1.10 (−1.34, −0.87) mg/dL] and −0.029 (−0.035, −0.023) mmol·L⁻¹·g soluble fiber⁻¹ [−1.13 (−1.37, −0.89) mg/dL], respectively (Table 2). High-fiber diets also significantly reduced HDL cholesterol, but by a much smaller amount: −0.002 (−0.004, −0.0003) mmol·L⁻¹·g soluble fiber⁻¹ [−0.07 (−0.13, −0.01) mg/dL]. Soluble fiber intake did not significantly affect triacylglycerol concentrations: 0.001 (−0.004, 0.006) mmol·L⁻¹·g soluble fiber⁻¹ [0.07 (−0.35, 0.50) mg/dL]. The tests for heterogeneity were highly significant (all P < 0.001), indicating that the lipid changes may have been better characterized by separate estimates for studies similar in design or subject characteristics such as type of soluble fiber.

### Dose response

The net change in total and LDL cholesterol is plotted against the mean daily dose of soluble fiber in Figure 1. The plot suggests a nonlinear dose response. To test for nonlinearity, an exponential term for dose (natural log of the amount of soluble fiber) was used in the weighted least-squares regression models. We found significant nonlinearity with doses >10 g/d for total cholesterol and with doses >8 g/d for LDL cholesterol.

The meta-analyses in Table 2 were repeated for the practical dose range (≤10 g/d) and we found that the overall effects of fiber were greater compared with the results for the total dose range: 1 g soluble fiber/d produced a change in total and LDL cholesterol of −0.045 and −0.057 mmol/L (−1.73 and −2.21 mg/dL). There was no significant dose-response relation between soluble fiber and changes in HDL-cholesterol or triacylglycerol concentrations.

### Effect of initial lipid concentration

On the basis of weighted least-squares regression analyses, the initial total cholesterol concentration was not a significant predictor of lipid changes after adjustment for dose when entered into the models as either a continuous variable (P = 0.18) or a categorical (> compared with <6.20 mmol/L) variable (P = 0.91). There was a greater decrease in LDL cholesterol in studies in which subjects had an average initial LDL-cholesterol concentration >4.3 mmol/L [−0.034 mmol/L (−1.33 mg/dL), P = 0.02] compared with an average initial LDL-cholesterol concentration <4.3 mmol/L [−0.015 mmol/L (−0.58 mg/dL), P = 0.26]. However, this difference was only marginally significant (P = 0.05). Net lipid changes were not significantly related to initial concentrations for either HDL (P = 0.38) or triacylglycerols (P = 0.53) after adjustment for dose.

### Type of soluble fiber

Soluble fiber from oat products, psyllium, pectin, and guar gum each significantly lowered total cholesterol (Figure 2, Table 2). One gram of soluble fiber from oats, psyllium, pectin, or guar gum produced changes in total cholesterol of −0.037, −0.028, −0.070, and −0.026 mmol/L [−1.42, −1.10, −2.69, and −1.13 mg/dL], respectively, and in LDL cholesterol of −0.032, −0.029, −0.055, and −0.033 mmol/L [−1.23, −1.11, −1.96, and −1.20 mg/dL], respectively. These values were slightly higher when the meta-analysis was repeated for the practical dose range. Psyllium and guar gum lowered HDL cholesterol significantly but minimally (Table 2). None of the soluble fibers affected triacylglycerols. Type of soluble fiber was not a significant predictor of lipid changes after the initial lipid concentration was controlled for by linear regression. We were unable to compare effects of guar with those of the other fibers because of the limited number of studies using 2–10 g/d.

### Effect of other variables

After dose of soluble fiber and initial lipid concentrations were controlled for, none of the following factors was a significant predictor of lipid changes in blood lipids: type of study design, type of control, treatment length, background diet, type of subject, weight change, or changes in dietary intake of fat and cholesterol.

### Dietary changes

For 22 of the 67 studies (33%), sufficient dietary data were provided to calculate predicted changes in total cholesterol by using equations from Keys et al (18) or Mensink and Katan (35). There were 13 oat, 6 psyllium, and 3 pectin studies with doses of soluble fiber ranging between 2.2 and 15 g. Most of the studies reported reductions in total cholesterol that were greater than predicted from changes in fatty acid or cholesterol intake. The effect of fiber before adjusting for expected change in total cholesterol was −0.039 (−0.042, −0.037) mmol/L [−1.51 (−1.58, −1.43) mg/dL] compared with −0.033 (−0.035, −0.032) mmol/L [−1.30 (−1.37, −1.23) mg/dL] after adjustment for expected change as estimated by the Keys equation. Expected change as estimated by the Mensink and Katan equation was −0.036 (−0.038, −0.034) mmol/L [−1.40 (−1.48, −1.32) mg/dL]. Thus, because the adjusted estimates were similar to the
<table>
<thead>
<tr>
<th>Fiber source</th>
<th>No. of trials</th>
<th>No. of subjects</th>
<th>Average dose of soluble fiber (g)</th>
<th>Average length of treatment (d)</th>
<th>Type of control (no. of trials)</th>
<th>Subject type (no. of trials)</th>
<th>Mean age (no. of trials)</th>
<th>Background diet mean lipid concentration (mmol/L)</th>
<th>Mean initial lipid concentration (mmol/L)</th>
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</thead>
<tbody>
<tr>
<td>Oat products</td>
<td>25: 13P, 12X</td>
<td>1600: 817M, 598C</td>
<td>5.0 (1.5–13.0)</td>
<td>39 (14–84)</td>
<td>10 Low-fiber control, 7 diet only</td>
<td>10 Healthy, 13 hyperlipidemic, 1 DM+hyperlipidemic, 1 other</td>
<td>48 (26–61)</td>
<td>12 LFLC, 13 usual TC: 6.31–0.84, LDL: 4.40–0.69, HDL: 1.28–0.15, TG: 1.82–1.98</td>
<td>3.89–3.31</td>
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<td>Parallel: 703T, 552C</td>
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<td>Crossover: 345T, 345C</td>
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<td>Psyllium</td>
<td>17: 11P, 6X</td>
<td>757: 515M, 242F</td>
<td>9.1 (4.7–16.2)</td>
<td>53 (14–112)</td>
<td>16 Low-fiber control, 1 diet only</td>
<td>5 Healthy, 12 hyperlipidemic</td>
<td>51 (44–59)</td>
<td>13 LFLC, 4 usual TC: 6.41–0.68, LDL: 4.37–0.70, HDL: 1.23–0.32, TG: 1.79–0.72</td>
<td>3.89–3.31</td>
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<td>Pectin</td>
<td>7: 3P, 4X</td>
<td>277: 216M, 61F</td>
<td>4.7 (2.2–9.0)</td>
<td>34 (28–42)</td>
<td>5 Low-fiber control, 2 diet only</td>
<td>4 Healthy, 1 hyperlipidemic, 1 DM, 1 other</td>
<td>50 (31–65)</td>
<td>1 LFLC, 6 usual TC: 5.62–0.73, LDL: 4.01–0.59, HDL: 1.48–0.36, TG: 1.45–0.44</td>
<td>3.89–3.31</td>
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<tr>
<td>Guar gum</td>
<td>18: 5P, 13X</td>
<td>356: 185M, 110F</td>
<td>17.5 (6.6–30.0)</td>
<td>66 (28–168)</td>
<td>18 Low-fiber control</td>
<td>2 Healthy, 4 hyperlipidemic, 8 DM, 4 DM+hyperlipidemic</td>
<td>52 (27–63)</td>
<td>3 LFLC, 15 usual TC: 6.49–0.88, LDL: 4.12–0.80, HDL: 1.27–0.21, TG: 1.76–0.64</td>
<td>3.89–3.31</td>
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<td></td>
<td>Parallel: 69T, 59C</td>
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<tr>
<td>Total</td>
<td>67: 32P, 35X</td>
<td>2990: 1733M, 1011F</td>
<td>9.5 (1.5–30.0)</td>
<td>49 (14–168)</td>
<td>57 Low-fiber control, 10 diet only</td>
<td>21 Healthy, 30 hyperlipidemic, 9 DM, 5 DM+hyperlipidemic, 2 other</td>
<td>50 (26–65)</td>
<td>29 LFLC, 38 usual TC: 6.23–0.88, LDL: 4.25–0.72, HDL: 1.27–0.21, TG: 1.76–0.64</td>
<td>3.89–3.31</td>
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1P, parallel; X, crossover; T, treated; C, control; hyperlipidemic, initial cholesterol >6.2 mmol/L (>240 mg/dL); DM, diabetes mellitus; LFLC, low-fat, low-cholesterol diet (typically 30% of energy from fat; ≤10% each from saturated, polyunsaturated, and monounsaturated fats; and <300 mg cholesterol); TC, total cholesterol; TG, triacylglycerol.

2To convert values for cholesterol to mg/dL, divide by 0.02586; to convert values for TG to mg/dL, divide by 0.01129. Not all studies of different fiber sources provided total, LDL-, and HDL-cholesterol and triacylglycerol concentrations.

3The number of male and female subjects does not equal the total number of subjects because some studies did not specify the sex of the subjects.

4Range in parentheses.

5Meta-analysis included 67 trials; however, studies did not necessarily report measurements of all 4 lipid changes (total cholesterol, LDL cholesterol, HDL cholesterol, and triacylglycerol).
<table>
<thead>
<tr>
<th>Lipid measured and fiber source</th>
<th>No. of studies</th>
<th>No. of subjects</th>
<th>Net change per gram soluble fiber</th>
<th>Heterogeneity (Q)</th>
<th>No. of studies</th>
<th>No. of subjects</th>
<th>Net change per gram soluble fiber</th>
<th>Heterogeneity (Q)</th>
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<tr>
<td><strong>Total cholesterol</strong></td>
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<tr>
<td>Oat products</td>
<td>25</td>
<td>1600</td>
<td>-0.037 (-0.051, -0.022)</td>
<td>62.6^d</td>
<td>22</td>
<td>1512</td>
<td>-0.040 (-0.054, -0.026)</td>
<td>43.4^d</td>
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<td>Psyllium</td>
<td>17</td>
<td>757</td>
<td>-0.028 (-0.037, -0.020)</td>
<td>27.5^c</td>
<td>12</td>
<td>535</td>
<td>-0.037 (-0.049, -0.025)</td>
<td>15.1</td>
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<td>7</td>
<td>277</td>
<td>-0.070 (-0.117, -0.022)</td>
<td>32.6^c</td>
<td>7</td>
<td>277</td>
<td>-0.070 (-0.117, -0.022)</td>
<td>32.6^c</td>
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<td>Guar gum</td>
<td>17</td>
<td>341</td>
<td>-0.026 (-0.038, -0.015)</td>
<td>180.5^c</td>
<td>2^a</td>
<td>4</td>
<td>-</td>
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<tr>
<td>All fibers^9</td>
<td>66</td>
<td>66</td>
<td>-0.028 (-0.035, -0.022)</td>
<td>260.4^i</td>
<td>43</td>
<td>43</td>
<td>-0.045 (-0.054, -0.035)</td>
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<td><strong>LDL cholesterol</strong></td>
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<td>Oat products</td>
<td>22</td>
<td>1439</td>
<td>-0.032 (-0.047, -0.017)</td>
<td>79.7^10</td>
<td>13</td>
<td>867</td>
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<td>-0.029 (-0.045, -0.025)</td>
<td>123.2^i</td>
<td>4</td>
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<td>117</td>
<td>-0.055 (-0.087, -0.022)</td>
<td>7.3^c</td>
<td>4</td>
<td>117</td>
<td>-0.055 (-0.087, -0.022)</td>
<td>7.3^c</td>
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<td>Guar gum</td>
<td>12</td>
<td>218</td>
<td>-0.033 (-0.048, -0.017)</td>
<td>76.6^i</td>
<td>1^c</td>
<td>16</td>
<td>-</td>
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<td>All fibers^9</td>
<td>55</td>
<td>55</td>
<td>-0.029 (-0.035, -0.023)</td>
<td>193.6^i</td>
<td>22</td>
<td>43</td>
<td>-0.057 (-0.070, -0.044)</td>
<td>35.6^i</td>
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<td><strong>HDL cholesterol</strong></td>
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<td>Oat products</td>
<td>24</td>
<td>1542</td>
<td>-0.002 (-0.007, 0.003)</td>
<td>70.0^c</td>
<td>18</td>
<td>998</td>
<td>-0.001 (-0.007, 0.008)</td>
<td>43.4^c</td>
</tr>
<tr>
<td>Psyllium</td>
<td>17</td>
<td>757</td>
<td>-0.002 (-0.004, -0.0003)</td>
<td>15.8</td>
<td>12</td>
<td>535</td>
<td>-0.004 (-0.008, -0.001)</td>
<td>10.0</td>
</tr>
<tr>
<td>Pectin</td>
<td>7</td>
<td>277</td>
<td>-0.004 (-0.028, 0.020)</td>
<td>84.7^c</td>
<td>7</td>
<td>277</td>
<td>-0.004 (-0.028, 0.020)</td>
<td>84.7^c</td>
</tr>
<tr>
<td>Guar gum</td>
<td>15</td>
<td>302</td>
<td>-0.003 (-0.005, -0.002)</td>
<td>11.3</td>
<td>2^a</td>
<td>16</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>All fibers^9</td>
<td>63</td>
<td>63</td>
<td>-0.002 (-0.004, -0.0003)</td>
<td>167.3^i</td>
<td>39</td>
<td>43</td>
<td>-0.003 (-0.006, 0.001)</td>
<td>134.8^i</td>
</tr>
<tr>
<td><strong>Triacylglycerol</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oat products</td>
<td>20</td>
<td>1374</td>
<td>0.008 (-0.005, 0.022)</td>
<td>24.1</td>
<td>16</td>
<td>882</td>
<td>0.006 (-0.006, 0.018)</td>
<td>17.5</td>
</tr>
<tr>
<td>Psyllium</td>
<td>16</td>
<td>720</td>
<td>0.003 (-0.007, 0.013)</td>
<td>17.6</td>
<td>11</td>
<td>498</td>
<td>0.003 (-0.013, 0.020)</td>
<td>13.8</td>
</tr>
<tr>
<td>Pectin</td>
<td>6</td>
<td>247</td>
<td>-0.021 (-0.066, 0.025)</td>
<td>17.6^i</td>
<td>6</td>
<td>247</td>
<td>-0.021 (-0.066, 0.025)</td>
<td>17.6^i</td>
</tr>
</tbody>
</table>

Continued on next page
unadjusted estimates, the observed lipid changes cannot be attributed primarily to the substitution of dietary fats and cholesterol for dietary fiber within this subset of trials.

DISCUSSION

This analysis of 67 controlled clinical trials indicated that diets high in soluble fiber decrease total and LDL cholesterol. These findings are generally consistent with individual published reports because high intakes of soluble fiber were associated with significant decreases in total and LDL cholesterol in 60–70% of the trials. Dietary fiber had a small HDL-lowering effect at the borderline of statistical significance and did not affect triacylglycerol concentrations.

There was substantial heterogeneity among individual studies, suggesting that effects of fiber are not uniform. Differences in the dose of soluble fiber accounted for some of the variability in study results. Type of fiber apparently did not account for a significant amount of variability; however, it is possible that small differences between fibers of −0.02 to −0.03 mmol·L⁻¹·g⁻¹ soluble fiber may not be detectable.

We found significant nonlinearity at higher doses, which may have been due to diminished adherence or a biological maximum being reached at higher doses (32). By analyzing lipid changes within the restricted dose range (≤10 g), we could assess lipid effects within more practical ranges of soluble fiber intake and within the range in which the dose response appeared linear.

Our primary dose-response analyses were conducted by assuming a zero intercept. Analyses allowing a nonzero intercept produced a slightly smaller effect of fiber because the intercepts were negative. This suggests that cholesterol would decrease in the treatment group even if there was no added fiber in the high-fiber group. This could result from nonlinearity of the relation between fiber intake and change in lipids or residual confounding by other important factors, such as body weight or dietary fat changes, for which we were unable to adequately control. For example, although we found that the changes in blood cholesterol could not be attributed to the substitution of fiber for dietary fats and cholesterol in most of the studies with available data, most of the published reports did not provide sufficient dietary data. This lack of sufficient data limits our ability to conclusively rule out this possibility. We also cannot rule out chance as an explanation because the intercepts were not significantly different from zero.

The mechanism by which fiber lowers blood cholesterol remains undefined. Evidence suggests that some soluble fibers bind bile acids or cholesterol during the intraluminal formation of micelles (99). The resulting reduction in the cholesterol content of liver cells leads to an up-regulation of the LDL receptors and increased clearance of LDL cholesterol. However, increased bile acid excretion may not be sufficient to account for the observed cholesterol reduction (100). Other suggested mechanisms include inhibition of hepatic fatty acid synthesis by products of fermentation (production of short-chain fatty acids such as acetate, butyrate, propionate) (101); changes in intestinal motility (102); fibers with high viscosity causing slowed absorption of macronutrients, leading to increased insulin sensitivity (103); and increased satiety, leading to lower overall energy intake (104).

Our data do not support previous findings that patients with hypercholesterolemia are more responsive to dietary fiber than are healthy individuals (14, 15). Subgroup analyses of initial cholesterol concentrations showed that persons with moderate or severe hypercholesterolemia (concentrations >6.20 mmol/L, or >240 mg/dL) showed only slightly larger decreases in total cholesterol than did those with lower cholesterol concentrations. We did, however, find that initial LDL cholesterol was a moderately
significant predictor of LDL-cholesterol changes, but the difference in responsiveness was small: 0.02 mmol/L (0.75 mg/dL) per gram of soluble fiber ($P = 0.05$).

Most of the available epidemiologic studies suggest that dietary fiber is inversely related to coronary artery disease (5, 105–109). Earlier studies suggested that the effects of fiber may be larger than those shown in this meta-analysis. However, methodologic problems including small sample sizes, incomplete dietary measures, and inadequate control of important confounders made it difficult to determine the effects of dietary fiber independently of other dietary components and, more specifically, the contribution of soluble compared with insoluble fiber. The modest reductions in cholesterol expected from intakes of soluble fiber within practical ranges may exert only a small effect on the risk of heart disease. For example, daily intake of 3 g soluble fiber from either 3 apples or 3 bowls (28-g servings) of oatmeal can decrease total cholesterol by $\approx 0.129$ mmol/L (5 mg/dL), a $\approx 2\%$ reduction. On the basis of estimates from clinical studies of cholesterol treatment (110), this could lower the incidence of coronary artery disease by $\approx 4\%$. These findings are consistent with an earlier summary of the cholesterol-lowering effects of oat products (15).

Publication bias toward studies that showed positive results is always a potential issue in meta-analyses and could be operating in this study. If this were true, then the small effect estimates associated with intake of dietary soluble fiber would be further attenuated, further highlighting the need for conservative public health claims. The major benefit from eating fiber-rich foods

FIGURE 1. Relation between dose of soluble fiber and mean lipid changes. For each study, the net change in total cholesterol and LDL cholesterol (expressed as the change during the high-soluble-fiber period minus the change during the low-soluble-fiber period) is plotted against the mean daily dose of soluble fiber. All models were weighted by using the inverse of the variance of each effect size and forcing the intercept through zero. Plots show an inverse association between dose of soluble fiber and mean changes in total and LDL cholesterol ($P < 0.001$). Individual studies with low variance in the meta-analysis are denoted with circles around the point estimates.
FIGURE 2. Net change in total cholesterol. The net effect of consumption of different dietary fibers on total cholesterol concentrations for oat products, psyllium, pectin, and guar gum. Note that one guar study (85) did not include measures for total cholesterol. The bars represent the width of the 95% CIs for each study. The overall effect estimates and 95% CI are provided for each fiber.
may be a change in dietary pattern, resulting in a diet that is lower in saturated and trans-unsaturated fats and cholesterol and higher in protective nutrients such as unsaturated fatty acids, minerals, folate, and antioxidant vitamins.

We are indebted to Peter Goldman, Endel J Orav, Ingrid J Anderson, and Joseph McDevitt for their contributions to the early development of this research and their continued support.

REFERENCES


APPENDIX A

1. TREATMENT EFFECT CALCULATION

Parallel studies: \[ \Delta_p = [X_{tf} - X_{cb}] - [X_{cf} - X_{cb}] \] (A1)
where \( X_{tf} \) is the lipid value at the end of follow-up in the treatment group, \( X_{cf} \) is the lipid value before intervention in the treatment group, \( X_{cb} \) is the lipid value at the end of follow-up in the control group, and \( X_{cb} \) is the lipid value before intervention in the control group.

Crossover studies: \[ \Delta_c = [X_1 - X_2] \] (A2)
where \( X_1 \) is the lipid value at the end of follow-up and \( X_2 \) is the lipid value before intervention. The treatment effect was divided by the average daily amount (dose in grams) of soluble fiber. A negative effect size indicates a reduction during the intervention phase.

2. CALCULATION OF WITHIN-STUDY VARIANCE

The primary endpoint is the change in total cholesterol, LDL cholesterol, HDL cholesterol, and triacylglycerol from the end of the dietary run-in period (if applicable) or the concentration before the intervention was initiated (total cholesterol 1) to the end of the intervention period (total cholesterol 2).

To derive a model for the variance of total cholesterol change, we first assumed the following variance component model of Rosner and Polk (1), which includes day-to-day variability and subject-to-subject variability. (Within-day variability is also included but it does not apply in our model because lipids were measured once per visit.)

Total cholesterol = \( \alpha + \gamma + \beta \) (A3)
where \( \alpha \) is a fixed constant describing the true mean total cholesterol concentration in the population, \( \gamma \sim N(0, \sigma_\gamma^2) \) is the true individual deviation about this population mean at the time of the measurements, and \( \beta \sim N(0, \sigma_\beta^2) \) reflects the day-to-day variation.

If we assume that both total cholesterol 1 and total cholesterol 2 are computed as the mean of \( k \) measurements, then the variance of each of these measures is given by

\[ V(x) = \sigma^2 = \sigma_p^2 + \sigma_d^2/k \] (A4)
The variance of the difference, \( \Delta = \text{total cholesterol 2} - \text{total cholesterol 1} \), may then be expressed as

\[ \text{Var}(\Delta) = 2\sigma^2 (1 - r) \] (A5)
where \( r \) is the observed tracking correlation between the cholesterol measures at baseline and follow-up. This quantifies the association between initial and subsequent cholesterol concentrations.

Calculation of variance components

**Total cholesterol**

By using estimates from the Lipid Research Clinics (2–4) and the above formula, we obtained the following estimates for the variance components, assuming that \( k = 2 \) (baseline and follow-up).

Day-to-day variation:

\[ \sigma^2_p = \sigma^2_{p \text{ observed}} - \sigma^2_d = 35^2 - 15.7^2 = 978.5 \]

Between-person variation:

\[ \sigma^2_p = \sigma^2_{p \text{ observed}} - \sigma^2_d = 35^2 - 15.7^2 = 978.5 \]

**LDL cholesterol, HDL cholesterol, and triacylglycerol (mg/dL)**

<table>
<thead>
<tr>
<th>Day-to-day variation</th>
<th>Between-person variation</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \sigma^2_{p} ) (2, 4)</td>
<td>( \sigma^2_{p \text{ observed}} - \sigma^2_d = \sigma^2_{p} )</td>
</tr>
</tbody>
</table>

| LDL cholesterol | 15.5^2 = 240.3 | 35^2 - 15.5^2 = 848.8 |
| HDL cholesterol | 6.4^2 = 41.0 | 11.25^2 - 6.4^2 = 85.6 |
| Triacylglycerol  | 51.0^2 = 2601.0 | 121.0^2 - 51.0^2 = 12040.0 |

Calculation of within-study variance

**Total cholesterol**

The observed tracking correlation between the initial and follow-up total cholesterol equaled 0.815 (4). This value was corrected for within-person variation by using the following formula (5) and the variance components as calculated above. This model assumes that the variance components remain constant over time. The true mean for an individual is allowed to vary over time with a correlation \( P_{ts} \) for measurements at time \( t \) and \( s \).

\[ P_{ts} = P_{ts} \times \frac{\sqrt{(\sigma_p^2 + \sigma_w^2)(\sigma_p^2 + \sigma_w^2)}}{\sigma_p^2} \] (A6)

where \( P_{ts} \) is the true tracking correlation between cholesterol measures at times \( t \) and \( s \) where \( s > t \).
times \( t \) and \( s \) (0.815), \( \sigma_p^2 \) is the between-person variance as calculated on the previous page (978.5), \( \sigma_{w_i}^2 \) is the within-person variance at time \( t \) (baseline), and \( \sigma_{w_s}^2 \) is the within-person variance at time \( s \) (follow-up).

Thus,

\[
P_{ts} = 0.815 \times \sqrt{\frac{(978.5 + 246/1) (978.5 + 246/1)}{978.5}}
\]

\( P_{ts} = 1 \) if the true tracking correlation is 1; eg, if for a short-term period, the only source of variation is within-person variability.

Thus, we estimated that the SD of the change in total cholesterol would be 15.7 mg/dL for one measure taken at baseline and one at the end of treatment as calculated below.

\[
\text{Var} (\Delta) = 2[\sigma_p^2 (1 - r) + (\sigma_{w_i}^2/2)]
\]

\( \text{Var} (\Delta) = 2[978.5 (0) + (246/2)] = 246.\ SD = \sqrt{246} = 15.7 \text{ mg/dL (0.41 mmol/L).}
\]

LDL cholesterol, HDL cholesterol, and triacylglycerol (mg/dL)

<table>
<thead>
<tr>
<th>Observed tracking correlation (4,6)</th>
<th>After correction for within-person variation</th>
<th>Estimated pre – post SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL cholesterol</td>
<td>( P_{ts} )</td>
<td>0.012</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>0.99</td>
<td>0.01</td>
</tr>
<tr>
<td>Triacylglycerol</td>
<td>0.91</td>
<td>0.09</td>
</tr>
</tbody>
</table>

3. CALCULATION OF \( Q \)

\( Q \) is used to assess homogeneity of study estimates of effect (7).

\[
Q = \sum w_i (y_i - \bar{y}_w)^2
\]

\[
y_w = \sum w_i y_i / \sum w_i
\]

4. CALCULATION OF BETWEEN-STUDY VARIANCE

\[
\sigma^2 = \frac{(Q - (k - 1)) / \sum w_i - (\sum w_i^2 / \sum w_i)}{\sum w_i}
\]

where \( y_i \) is the outcome measure for the \( i \)th study, \( \sigma^2 \) is between-study variance, \( s_i^2 \) is within-study variance (SE/daily dose of soluble fiber in grams), \( w_i = 1/(s_i^2) \) for \( i \)th study (1/SE), \( y_w \) is the weighted mean, and \( k \) is the number of studies. \( Q > \chi^2_{1-0.95} \) indicates that individual estimates for \( k \) studies are not estimated by one underlying effect.

5. CALCULATION OF SUMMARY ESTIMATE OF EFFECT AND 95% CIs (EFFECT SIZE PER GRAM SOLUBLE FIBER)

Summary estimate: random effects model

The weighted estimate of the overall mean \( y_w \) is

\[
\bar{y}_w = \frac{\sum_{i=1}^{k} w_i y_i}{\sum_{i=1}^{k} w_i}
\]

\( 95\% \ CI \)

\[
\bar{y}_w \pm 1.96 \sqrt{\text{var} (\bar{y}_w)}
\]

where \( w_i = 1/(s_i^2 + \sigma^2)(d^2) \), \( d^2 \) is the daily amount of soluble fiber in grams squared, and \( \text{var} y_w = 1/\sum w_i \).

REFERENCES