

# Diet and Exercise in the Management of Hyperlipidemia

ROBERT B. KELLY, MD, MS, *Fairview Hospital/Cleveland Clinic Family Medicine Residency Program, Cleveland, Ohio*

Dietary factors that influence lipid levels include modification of nutritional components, consumption of specific foods, use of food additives and supplements, and major dietary approaches. The most beneficial changes result from reducing intake of saturated and *trans* fats; increasing intake of polyunsaturated and monounsaturated fats; fortifying foods with plant stanols or sterols; isocalorically adding tree nuts to the diet; consuming one or two alcoholic drinks per day; and adopting a Portfolio, Mediterranean, low-carbohydrate, or low-fat diet. Smaller but still beneficial effects result from reducing intake of dietary cholesterol, increasing intake of soluble fiber and soy protein, and eating fatty marine fish or taking marine-derived omega-3 fatty acid supplements. Red yeast rice supplements have effects similar to those of statin medications and are better tolerated in some patients. Regular aerobic exercise has beneficial effects on lipid levels, particularly if performed for at least 120 minutes per week. Brief physician counseling will have relatively small effects on unselected patients, so efforts should be concentrated on patients who are motivated and ready to make lifestyle changes. (*Am Fam Physician*. 2010;81(9):1097-1102, 1103-1104. Copyright © 2010 American Academy of Family Physicians.)

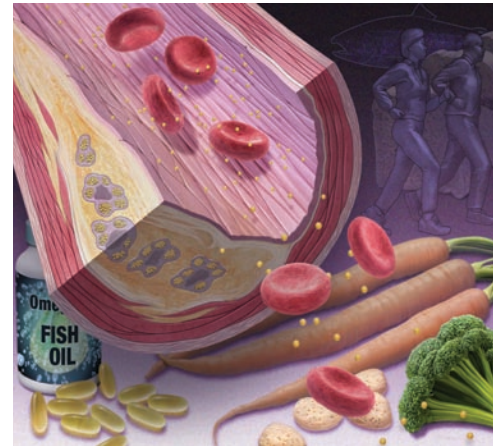


ILLUSTRATION BY SCOTT BOBEL

► **Patient information:** A handout on diet and exercise for hyperlipidemia, written by the author of this article, is provided on page 1103.

**H**yperlipidemia is a common risk factor for the development of cardiovascular disease. The Adult Treatment Panel III (ATP III) of the National Cholesterol Education Program has for the past decade recommended nonpharmacologic treatment as initial therapy in most patients with hyperlipidemia.<sup>1</sup> The Therapeutic Lifestyle Changes (TLC) approach was based on the panel's review of the available evidence in 1999 that concluded that diet and exercise can have a beneficial effect on serum levels of total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides. The TLC diet recommendations include obtaining 25 to 35 percent of daily calories from fats, and restricting saturated fats to less than 7 percent of total calories and cholesterol to less than 200 mg per day. However, physicians and patients are often unsure of how much change in blood lipid levels can be expected when the TLC diet is prescribed, and

wonder which lifestyle changes have the greatest effects. This article attempts to shed some light on these questions by examining recent literature that was not available at the time of the ATP III analysis. Because of the volume of published evidence in these areas, emphasis will be placed on meta-analyses, structured reviews, and randomized controlled trials (RCTs) that reported findings on serum lipid levels.

## Dietary Factors

A large number of dietary factors may influence lipid levels. These include modification of nutritional components, consumption of specific foods, use of food additives and supplements, and major dietary approaches.

## NUTRITIONAL COMPONENTS

Comprehensive reviews of the evidence for dietary influences on levels of serum lipids and cardiovascular disease have been published.<sup>2,3</sup> Decreasing total fat intake and replacing saturated and *trans* fats with

## Diet and Exercise in Hyperlipidemia

### SORT: KEY RECOMMENDATIONS FOR PRACTICE

<i>Intervention</i>	<i>Comments, examples</i>	<i>Evidence rating*</i>	<i>References</i>	<i>Additional resources</i>
Reduce intake of saturated fats and <i>trans</i> fats	Limit saturated fats to less than 7 percent of calories; eliminate <i>trans</i> fats	C	2-5	<a href="http://www.americanheart.org/presenter.jhtml?identifier=532">http://www.americanheart.org/presenter.jhtml?identifier=532</a> <a href="http://content.nejm.org/cgi/content/full/354/15/1601">http://content.nejm.org/cgi/content/full/354/15/1601</a>
Increase intake of poly- and monounsaturated fats	Replace saturated fats and <i>trans</i> fats with poly- and monounsaturated fats	C	2-5	<a href="http://www.mayoclinic.com/health/fat/NU00262">http://www.mayoclinic.com/health/fat/NU00262</a>
Increase intake of soluble fiber	3 oz oats per day; psyllium supplement	C	2, 3, 6	<a href="http://www.mayoclinic.com/health/cholesterol/CL00002">http://www.mayoclinic.com/health/cholesterol/CL00002</a> <a href="http://www.americanheart.org/presenter.jhtml?identifier=4574">http://www.americanheart.org/presenter.jhtml?identifier=4574</a>
Isocalorically increase consumption of tree nuts	1.5 oz almonds, walnuts, or pecans per day	C	3, 10, 11	<a href="http://www.nuthealth.org/consumer/gonuts.pdf">http://www.nuthealth.org/consumer/gonuts.pdf</a> <a href="http://www.vegan.org.nz/nuts.php">http://www.vegan.org.nz/nuts.php</a>
Increase intake of soy protein	1.5 oz soy protein per day; tofu and soy foods to replace meat	C	2, 3, 12	<a href="http://www.medicinenet.com/script/main/art.asp?articlekey=56308">http://www.medicinenet.com/script/main/art.asp?articlekey=56308</a> <a href="http://www.webmd.com/cholesterol-management/features/low-cholesterol-soy-protein">http://www.webmd.com/cholesterol-management/features/low-cholesterol-soy-protein</a>
Limit alcoholic drinks to one or two per day	One drink per day for women; two per day for men	C	2, 3, 13	<a href="http://www.americanheart.org/presenter.jhtml?identifier=4422">http://www.americanheart.org/presenter.jhtml?identifier=4422</a>
Increase intake of plant stanols and sterols	1 oz Promise Activ or Benecol spread per day	C	2, 3, 15	<a href="http://my.clevelandclinic.org/heart/women/sterolstamol.aspx">http://my.clevelandclinic.org/heart/women/sterolstamol.aspx</a> <a href="http://www.webmd.com/cholesterol-management/features/low-cholesterol-diet-plant-sterols-stanols">http://www.webmd.com/cholesterol-management/features/low-cholesterol-diet-plant-sterols-stanols</a>
Increase intake of omega-3 fatty acids from marine sources	6 oz of salmon or tuna twice per week; EPA/DHA supplement on other days	C	2, 3, 16	<a href="http://www.webmd.com/diet/guide/good-fat-bad-fat-facts-about-omega-3">http://www.webmd.com/diet/guide/good-fat-bad-fat-facts-about-omega-3</a>
Follow a Mediterranean diet	Olive oil is main dietary fat; moderate wine consumption; limited amounts of red meat, dairy products, eggs, and poultry; increased amounts of vegetables, whole grains, fish, and tree nuts	C	2, 26	<a href="http://www.mayoclinic.com/health/mediterranean-diet/CL00011">http://www.mayoclinic.com/health/mediterranean-diet/CL00011</a> <a href="http://www.americanheart.org/presenter.jhtml?identifier=4644">http://www.americanheart.org/presenter.jhtml?identifier=4644</a>
Follow the Portfolio Diet	Mainly vegetarian diet with soy and other vegetable proteins, plant sterols, almonds, and soluble fiber	C	2, 3, 28	<a href="http://preventdisease.com/home/tips34.shtml">http://preventdisease.com/home/tips34.shtml</a> <a href="http://www.webmd.com/cholesterol-management/features/portfolio-diet-recipe-for-lower-cholesterol">http://www.webmd.com/cholesterol-management/features/portfolio-diet-recipe-for-lower-cholesterol</a>
Engage in aerobic exercise	At least 120 minutes per week	C	2, 3, 29-31	<a href="http://www.webmd.com/cholesterol-management/features/exercise-to-lower-cholesterol">http://www.webmd.com/cholesterol-management/features/exercise-to-lower-cholesterol</a>

DHA = *docosahexaenoic acid*; EPA = *eicosapentaenoic acid*.

\*—Evidence is rated C rather than A because the outcomes are not patient oriented.

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to <http://www.aafp.org/afpsort.xml>.

polyunsaturated and monounsaturated fats, along with limiting dietary cholesterol, lower total cholesterol, LDL cholesterol, and triglyceride levels. Compared with a baseline or Western diet, reducing saturated fat intake

to 7 percent of total calories and limiting cholesterol to 200 mg per day reduce LDL cholesterol levels by 9 to 12 percent.<sup>3</sup> A meta-analysis of 224 studies of dietary interventions showed that changes in total cholesterol

levels were affected primarily by changes in intake of saturated and polyunsaturated fats, and dietary cholesterol.<sup>4</sup> A more recent meta-analysis of 60 controlled trials showed that replacing *trans* fats with polyunsaturated fats from unhydrogenated oils is the most effective measure for improving blood lipid profiles.<sup>5</sup>

A meta-analysis of 67 controlled trials of dietary soluble fiber as a single intervention showed that the effects on total cholesterol and LDL cholesterol levels were modest. For example, the addition of three 28-g servings of oats per day decreases LDL cholesterol levels by 5 mg per dL (0.13 mmol per L).<sup>6</sup>

Some persons have little change in lipid levels despite significant changes in fat and cholesterol intake.<sup>7</sup> This observed variation may be explained by genetic factors<sup>8</sup> or insulin resistance.<sup>9</sup>

#### SPECIFIC FOODS

Tree nuts are high in unsaturated fats and low in saturated fats. Recent reviews of published data conclude that consumption of tree nuts can reduce LDL cholesterol levels by 2 to 19 percent compared with lower-fat and Western diets.<sup>10,11</sup> Nuts are calorie-dense and therefore should be isocalorically substituted for other foods. Recommended amounts range from 1 to 3 oz per day, at least five days per week.<sup>3,11</sup>

Soy protein can also be used to replace foods high in saturated fats and *trans* fats. A meta-analysis of 41 RCTs concluded that soy protein supplementation leads to small reductions in total cholesterol and LDL cholesterol levels (about 5 and 4 mg per dL [0.13 and 0.10 mmol per L], respectively), as well as small increases in HDL cholesterol levels (about 0.8 mg per dL [0.02 mmol per L]).<sup>12</sup> The typical amount of soy protein used in studies has been 1.0 to 1.5 oz per day.

Alcohol consumption is associated with an increase in HDL cholesterol levels of as much as 9 to 13 mg per dL (0.23 to 0.34 mmol per L) when nondrinkers are compared with the highest consumers.<sup>13</sup> In an eight-week controlled study of postmenopausal women, alcohol consumption (15 g per day, equivalent to one drink) lowered LDL cholesterol levels by 7.8 mg per dL (0.20 mmol per L), but HDL cholesterol levels only increased significantly when alcohol consumption was increased to 30 g per day.<sup>14</sup>

#### ADDITIVES AND SUPPLEMENTS

A comprehensive review of plant stanols and sterols showed that these substances lower LDL cholesterol levels in persons at risk of coronary heart disease.<sup>15</sup> This review included a meta-analysis of 41 trials showing that 2 g per day of either stanols or sterols reduces LDL cholesterol

levels by 10 percent. These effects are additive with other diet or drug interventions. Fortified foods (e.g., Promise Activ and Benecol spreads) typically have 0.5 to 1 g of sterol or stanol per serving.<sup>3</sup> The approximate cost for the recommended 2 g of stanols or sterols from fortified foods is \$0.60 to \$1.20 per day.

Two marine-derived omega-3 fatty acids, eicosapentaenoic acid and docosahexaenoic acid, lower triglyceride levels in a dose-dependent fashion.<sup>16</sup> However, their effects on cardiovascular mortality probably result more from their antiarrhythmic, anti-inflammatory, and other effects than from their effects on lipid levels.<sup>17</sup> A systematic review showed that plant-derived alpha-linolenic acid has no effect on lipid levels.<sup>18</sup>

Extracts of Chinese red yeast rice (a traditional dietary seasoning of *Monascus purpureus*) have several active ingredients, including naturally occurring lovastatin (as monacolin K, 5 mg to 10 mg per typical daily dose). A meta-analysis of 93 trials concluded that red yeast rice lowers total cholesterol, LDL cholesterol, and triglyceride levels.<sup>19</sup> The magnitude of this effect is similar to that of statin medications. Safety and effectiveness are potential concerns because some preparations have been found to contain toxic byproducts of fermentation, and available products are not standardized.<sup>20</sup> Red yeast rice is an option for patients who cannot tolerate statins because of muscle aches.<sup>21</sup>

**Replacing *trans* fats with polyunsaturated fats is the most effective measure for improving blood lipid profiles.**

#### DIETARY APPROACHES

Both low-fat and low-carbohydrate diets affect lipid levels. In a meta-analysis of RCTs comparing these approaches, low-fat diets had the most favorable effects on total cholesterol and LDL cholesterol levels, whereas low-carbohydrate diets had the most favorable effects on triglyceride and HDL cholesterol levels.<sup>22</sup> An RCT showed that the total-to-HDL cholesterol ratio was reduced by 20 percent in participants following a low-carbohydrate diet, compared with a 12 percent reduction in those following a low-fat diet; this was a statistically significant difference.<sup>23</sup> The reduction in the total-to-HDL cholesterol ratio is similar to the reduction in LDL cholesterol levels, and the total cholesterol level is reduced primarily by changes in the LDL cholesterol levels. Meta-analyses of trials of low-glycemic index versus high-glycemic index diets have concluded that low-glycemic index diets have a weak effect on total cholesterol levels,

## Diet and Exercise in Hyperlipidemia

but no effect on LDL and HDL cholesterol or triglyceride levels.<sup>24,25</sup>

The Mediterranean diet is characterized by a high consumption of monounsaturated fats (primarily from olive oil) and low consumption of saturated fats.<sup>2</sup> Other characteristics include limited consumption of red meat, dairy products, eggs, and poultry; increased consumption of fish, tree nuts, vegetables, and whole grains; and moderate consumption of wine. When two versions of a Mediterranean diet were compared with a low-fat diet, the Mediterranean diets lowered the total-to-HDL cholesterol ratio more than the low-fat diet.<sup>26</sup>

The Portfolio Diet is a plant-based TLC diet that is a composite of four additional LDL cholesterol-lowering components: soluble fiber, soy and other vegetable proteins, plant sterols, and almonds<sup>27</sup> (Table 1).<sup>28</sup> In controlled settings, the Portfolio Diet has been shown to reduce LDL cholesterol levels by 29 to 35 percent, comparable to a combination of a diet low in saturated fats and cholesterol plus 20 mg of lovastatin (Mevacor) daily.<sup>2</sup> Among persons eating self-selected Portfolio Diet foods, 32 percent achieved LDL cholesterol reductions of more than 20 percent after one year.<sup>28</sup>

### Exercise

The effects of exercise on serum lipid levels have been studied extensively. Published data have been subjected to meta-analysis, demonstrating that one positive effect of regular aerobic exercise is to raise HDL cholesterol levels by an average of 1.9 to 2.5 mg per dL (0.05 to 0.06 mmol per L).<sup>29,30</sup> Other effects include decreases in total cholesterol, LDL cholesterol, and triglyceride levels by an average of 3.9, 3.9, and 7.1 mg per dL (0.10, 0.10, and 0.08 mmol per L), respectively.<sup>29</sup> The minimal amount of exercise needed to increase HDL cholesterol levels is 900 kcal of energy expenditure per week, or about 120 minutes of typical aerobic exercise.<sup>30</sup> In patients with cardiovascular disease who exercise aerobically, HDL cholesterol levels increase by an average of 9 percent (3.7 mg per dL [0.10 mmol per L]), and triglyceride levels decrease by 11 percent (19.3 mg per dL [0.22 mmol per L]), suggesting greater benefits in this high-risk group.<sup>31</sup> However, in a small study of younger men, those with initially lower HDL cholesterol levels (less than 40 mg per dL [1.04 mmol per L]) responded less to exercise than those with higher levels (increase of 1.9 mg per dL versus 5.1 mg per

dL [0.05 versus 0.13 mmol per L]), possibly because of differences in triglyceride metabolism.<sup>32</sup> There is a great deal of variability in HDL cholesterol responses to exercise, ranging in one study from decreases of 9.3 percent in the least responsive quartile to increases of 18 percent in the most responsive quartile.<sup>33</sup> Improvements in HDL cholesterol levels seem to be related more to the amount of activity than to the intensity of exercise or improvement in fitness.<sup>34</sup> Physical inactivity has profound negative effects on lipid metabolism, including increases in LDL cholesterol levels, but this can be prevented by modest regular exercise.<sup>35</sup>

### Combined Changes in Diet and Exercise

Because dietary approaches tend to lower total cholesterol, LDL cholesterol, and triglyceride levels, and exercise tends to raise HDL cholesterol levels and lower triglyceride levels, it seems logical to combine these approaches. Combinations of dietary interventions and exercise have been studied, and the resulting data have been critically reviewed.<sup>36</sup> The two reviewed approaches were (1) exercise combined with a diet low in saturated fats, and (2) exercise combined with nutritional supplements (fish oil, oat bran, plant sterols). Exercise plus a low-saturated fat diet reduced LDL cholesterol levels by 7 to 15 percent and triglyceride levels by 4 to 18 percent, while increasing HDL cholesterol levels by 5 to 14 percent. Exercise plus nutritional supplements reduced LDL cholesterol levels by 8 to 30 percent and triglyceride levels by 12 to

**Table 1. The Portfolio Diet for Lowering LDL Cholesterol Levels**

Component	Recommended amount
Almonds	23 g whole almonds per 1,000 kcal consumed
Plant sterols	1 g plant sterols (e.g., from an enriched spread) per 1,000 kcal consumed
Soluble fiber	10 g viscous fibers (e.g., from oats, barley, psyllium, okra, eggplant) per 1,000 kcal consumed
Soy protein	22.5 g soy protein (e.g., soy milk, soy meat analogues) per 1,000 kcal consumed
Other	Consume additional sources of plant protein and fiber in the form of dried legumes; eat 5 to 10 daily servings of fruit and vegetables; try to consume a vegetarian diet without dairy foods, eggs, or meat; if egg products are used, they should be egg substitutes or egg whites; if meat or dairy products are consumed, amounts should be restricted, and foods low in saturated fat should be selected

LDL = low-density lipoprotein.

Information from reference 28.

39 percent, while increasing HDL cholesterol levels by 2 to 8 percent. Therefore, combining diet and exercise interventions seems additive, or at least synergistic.

### Effectiveness of Counseling

Physicians have many challenges to address in encouraging lifestyle changes to improve blood lipid profiles and other cardiovascular risks in their patients.<sup>37</sup> These include patients' health beliefs, motivations, and stage of change for new lifestyle behaviors. A Cochrane review showed that patients who received dietary advice had reductions in total cholesterol levels of 6.2 mg per dL (0.16 mmol per L), and in LDL cholesterol of 7.0 mg per dL (0.18 mmol per L), with no significant change in HDL cholesterol levels.<sup>38</sup> An older systematic review of 19 RCTs showed that dietary advice can result in reductions in total cholesterol of only 3 to 6 percent, mainly because dietary targets were not achieved by participants.<sup>39</sup> A Cochrane review of dietitian advice compared with physician advice or self-help material found that dietitians were more successful than physicians in the short to medium term (total cholesterol reduced an additional 9.7 mg per dL [0.25 mmol per L] compared with physician results), but not better than self-help resources.<sup>40</sup>

Counseling to promote increased physical activity also seems to be minimally effective.<sup>41</sup> Evidence reviewed by the U.S. Preventive Services Task Force indicates that the more intensive the counseling, the more change in behavior can be expected.<sup>42</sup> Physicians tend to counsel briefly, though they may also refer patients to dietitians and other educators for in-depth counseling. Low-intensity counseling by physicians produces the greatest effects when patients are already interested in and planning changes in their behaviors.

### Final Comment

The effectiveness of dietary changes and exercise on hyperlipidemia has been clearly demonstrated. However, many counseled patients will not make lasting changes, and responses to lifestyle changes vary among individual patients. It makes sense to help motivated patients learn which lifestyle changes are most likely to improve their lipid-related cardiovascular risk, and then measure the effects that occur as they make changes. Decreased intake of saturated and *trans* fats, increased intake of poly- and monounsaturated fats, moderate alcohol intake, supplementation with plant sterols or stanols, and isocalorically increased consumption of tree nuts are likely to produce the most beneficial changes in lipid levels. The Portfolio Diet and Mediterranean Diet are worth recommending as alternatives to an unenhanced TLC diet. Aerobic

exercise confers additional benefits if done on a regular basis. Physicians should tailor advice to patients in the context of other health conditions and risks.

### The Author

ROBERT B. KELLY, MD, MS, is a faculty member at the Fairview Hospital/Cleveland Clinic Family Medicine Residency Program, Cleveland, Ohio, and the medical director of the Westown Physicians Center in Cleveland. He also is an associate professor at Case Western Reserve University School of Medicine, Cleveland.

Address correspondence to Robert B. Kelly, MD, MS, Fairview Hospital/Cleveland Clinic Family Medicine Residency Program, 18200 Lorain Ave., Cleveland, OH 44111 (e-mail: Robert.Kelly@fairviewhospital.org). Reprints are not available from the author.

Author disclosure: Nothing to disclose.

### REFERENCES

- Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA*. 2001;285(19):2486-2497.
- Katcher HI, Hill AM, Lanford JL, Yoo JS, Kris-Etherton PM. Lifestyle approaches and dietary strategies to lower LDL-cholesterol and triglycerides and raise HDL-cholesterol. *Endocrinol Metab Clin North Am*. 2009;38(1):45-78.
- Van Horn L, McCoin M, Kris-Etherton PM, et al. The evidence for dietary prevention and treatment of cardiovascular disease. *J Am Diet Assoc*. 2008;108(2):287-331.
- Howell WH, McNamara DJ, Tosca MA, Smith BT, Gaines JA. Plasma lipid and lipoprotein responses to dietary fat and cholesterol: a meta-analysis. *Am J Clin Nutr*. 1997;65(6):1747-1764.
- Mensink RP, Zock PL, Kester AD, Katan MB. Effects of dietary fatty acids and carbohydrates on the ratio of serum total to HDL cholesterol and on serum lipids and apolipoproteins: a meta-analysis of 60 controlled trials. *Am J Clin Nutr*. 2003;77(5):1146-1155.
- Brown L, Rosner B, Willett WW, Sacks FM. Cholesterol-lowering effects of dietary fiber: a meta-analysis. *Am J Clin Nutr*. 1999;69(1):30-42.
- Cox C, Mann J, Sutherland W, Ball M. Individual variation in plasma cholesterol response to dietary saturated fat. *BMJ*. 1995;311(7015):1260-1264.
- Wallace AJ, Mann JI, Sutherland WH, et al. Variants in the cholesterol ester transfer protein and lipoprotein lipase genes are predictors of plasma cholesterol response to dietary change. *Atherosclerosis*. 2000;152(2):327-336.
- Lefevre M, Champagne CM, Tulley RT, Rood JC, Most MM. Individual variability in cardiovascular disease risk factor responses to low-fat and low-saturated-fat diets in men: body mass index, adiposity, and insulin resistance predict changes in LDL cholesterol. *Am J Clin Nutr*. 2005;82(5):957-963.
- Griel AE, Kris-Etherton PM. Tree nuts and the lipid profile: a review of clinical studies. *Br J Nutr*. 2006;96(suppl 2):S68-S78.
- Mukuddem-Petersen J, Oosthuizen W, Jerling JC. A systematic review of the effects of nuts on blood lipid profiles in humans. *J Nutr*. 2005;135(9):2082-2089.
- Reynolds K, Chin A, Lees KA, Nguyen A, Bujnowski D, He J. A meta-analysis of the effect of soy protein supplementation on serum lipids. *Am J Cardiol*. 2006;98(5):633-640.
- Ellison RC, Zhang Y, Qureshi MM, Knox S, Arnett DK, Province MA; Investigators of the NHLBI Family Heart Study. Lifestyle determinants

## Diet and Exercise in Hyperlipidemia

- of high-density lipoprotein cholesterol: the National Heart, Lung, and Blood Institute Family Heart Study. *Am Heart J*. 2004;147(3):529-535.
14. Baer DJ, Judd JT, Clevidence BA, et al. Moderate alcohol consumption lowers risk factors for cardiovascular disease in postmenopausal women fed a controlled diet. *Am J Clin Nutr*. 2002;75(3):593-599.
  15. Katan MB, Grundy SM, Jones P, Law M, Miettinen T, Paoletti R; Stresa Workshop Participants. Efficacy and safety of plant stanols and sterols in the management of blood cholesterol levels. *Mayo Clin Proc*. 2003;78(8):965-978.
  16. von Schacky C, Harris WS. Cardiovascular benefits of omega-3 fatty acids. *Cardiovasc Res*. 2007;73(2):310-315.
  17. Breslow JL. n-3 fatty acids and cardiovascular disease. *Am J Clin Nutr*. 2006;83(6 suppl):1477S-1482S.
  18. Wendland E, Farmer A, Glasziou P, Neil A. Effect of alpha linolenic acid on cardiovascular risk markers: a systematic review. *Heart*. 2006;92(2):166-169.
  19. Liu JP, Zhang J, Shi Y, Grimsgaard S, Alraek T, Fønnebo V. Chinese red yeast rice (*Monascus purpureus*) for primary hyperlipidemia: a meta-analysis of randomized controlled trials. *Chin Med*. 2006;1:4.
  20. Ong HT, Cheah JS. Statin alternatives or just placebo: an objective review of omega-3, red yeast rice and garlic in cardiovascular therapeutics. *Chin Med J (Engl)*. 2008;121(16):1588-1594.
  21. Becker DJ, Gordon RY, Halbert SC, French B, Morris PB, Rader DJ. Red yeast rice for dyslipidemia in statin-intolerant patients: a randomized trial. *Ann Intern Med*. 2009;150(12):830-839.
  22. Nordmann AJ, Nordmann A, Briel M, et al. Effects of low-carbohydrate vs low-fat diets on weight loss and cardiovascular risk factors: a meta-analysis of randomized controlled trials [published correction appears in *Arch Intern Med*. 2006;166(8):932]. *Arch Intern Med*. 2006;166(3):285-293.
  23. Shai I, Schwarzfuchs D, Henkin Y, et al.; Dietary Intervention Randomized Controlled Trial (DIRECT) Group. Weight loss with a low-carbohydrate, Mediterranean, or low-fat diet [published correction appears in *N Engl J Med*. 2009;361(27):2681]. *N Engl J Med*. 2008;359(3):229-241.
  24. Kelly S, Frost G, Whittaker V, Summerbell CD. Low glycaemic index diets for coronary heart disease. *Cochrane Database Syst Rev*. 2004;(4):CD004467.
  25. Opperman AM, Venter CS, Oosthuizen W, Thompson RL, Vorster HH. Meta-analysis of the health effects of using the glycaemic index in meal-planning. *Br J Nutr*. 2004;92(3):367-381.
  26. Estruch R, Martínez-González MA, Corella D, et al.; PREDIMED Study Investigators. Effects of a Mediterranean-style diet on cardiovascular risk factors: a randomized trial. *Ann Intern Med*. 2006;145(1):1-11.
  27. Kendall CW, Jenkins DJ. A dietary portfolio: maximal reduction of low-density lipoprotein cholesterol with diet. *Curr Atheroscler Rep*. 2004;6(6):492-498.
  28. Jenkins DJ, Kendall CW, Faulkner DA, et al. Assessment of the longer-term effects of a dietary portfolio of cholesterol-lowering foods in hypercholesterolemia. *Am J Clin Nutr*. 2006;83(3):582-591.
  29. Halbert JA, Silagy CA, Finucane P, Withers RT, Hamdorf PA. Exercise training and blood lipids in hyperlipidemic and normolipidemic adults: a meta-analysis of randomized, controlled trials. *Eur J Clin Nutr*. 1999;53(7):514-522.
  30. Kodama S, Tanaka S, Saito K, et al. Effect of aerobic exercise training on serum levels of high-density lipoprotein cholesterol: a meta-analysis. *Arch Intern Med*. 2007;167(10):999-1008.
  31. Kelley GA, Kelley KS, Franklin B. Aerobic exercise and lipids and lipoproteins in patients with cardiovascular disease: a meta-analysis of randomized controlled trials. *J Cardiopulm Rehabil*. 2006;26(3):131-139.
  32. Zmuda JM, Yurgalevitch SM, Flynn MM, et al. Exercise training has little effect on HDL levels and metabolism in men with initially low HDL cholesterol. *Atherosclerosis*. 1998;137(1):215-221.
  33. Leon AS, Gaskell SE, Rice T, et al. Variability in the response of HDL cholesterol to exercise training in the HERITAGE Family Study. *Int J Sports Med*. 2002;23(1):1-9.
  34. Kraus WE, Houmard JA, Duscha BD, et al. Effects of the amount and intensity of exercise on plasma lipoproteins. *N Engl J Med*. 2002;347(19):1483-1492.
  35. Slentz CA, Houmard JA, Johnson JL, et al. Inactivity, exercise training and detraining, and plasma lipoproteins. STRRIDE: a randomized, controlled study of exercise intensity and amount. *J Appl Physiol*. 2007;103(2):432-442.
  36. Varady KA, Jones PJ. Combination diet and exercise interventions for the treatment of dyslipidemia: an effective preliminary strategy to lower cholesterol levels? *J Nutr*. 2005;135(8):1829-1835.
  37. Olendzki B, Speed C, Domino FJ. Nutritional assessment and counseling for prevention and treatment of cardiovascular disease. *Am Fam Physician*. 2006;73(2):257-264.
  38. Brunner EJ, Rees K, Ward K, Burke M, Thorogood M. Dietary advice for reducing cardiovascular risk. *Cochrane Database Syst Rev*. 2007;(4):CD002128.
  39. Tang JL, Armitage JM, Lancaster T, Silagy CA, Fowler GH, Neil HA. Systematic review of dietary intervention trials to lower blood total cholesterol in free-living subjects. *BMJ*. 1998;316(7139):1213-1220.
  40. Thompson RL, Summerbell CD, Hooper L, et al. Dietary advice given by a dietitian versus other health professional or self-help resources to reduce blood cholesterol. *Cochrane Database Syst Rev*. 2003;(3):CD001366.
  41. Hudon C, Fortin M, Soubhi H. Single risk factor interventions to promote physical activity among patients with chronic diseases: systematic review. *Can Fam Physician*. 2008;54(8):1130-1137.
  42. U.S. Preventive Services Task Force. Behavioral counseling in primary care to promote a healthy diet: recommendations and rationale. <http://www.ahrq.gov/clinic/3rduspstf/diet/diettr.htm>. Accessed February 5, 2010.