

## *Non-Pharmaceutical Therapy for Lowering Cholesterol*

### **The Power of Nutrition**

In the Lyon Diet Heart Study, eating a Mediterranean diet compared to a low fat diet resulted in a 70% (12 % reduction vs. a 4%) reduction of heart events in those with documented heart disease.<sup>1</sup> This is three times more effective than statin drugs in preventing a secondary cardiac event.<sup>2</sup> A logical reason why nutrition trumps drug therapy for reducing cardiac events is that it provides the body many more benefits than simply blocking an enzyme, which the liver uses to make cholesterol. The vegetables, fruits, fiber and essential fatty acids help not only reduce cholesterol but also reduce inflammation, cancer risk, the development of arthritis and Alzheimer's disease. Nutrition enhances health of the whole body that includes, but is not limited to, the heart.

**NOTE:** A recent meta-analysis has questioned the use of lipid-lowering agents in the treatment of high risk individuals without coronary artery disease (CAD).<sup>3</sup> Currently guidelines with the highest level of evidence recommend treating with a statin those patients with a 10 year CVD risk greater than 20%, the presence of CAD, or the presence of diabetes.

**To determine risk,** access the [10-Year CVD Risk Calculator](http://hp2010.nhlbi.nih.net/atp/iii/calculator.asp?usertype=prof) (or enter the following URL into your browser: <http://hp2010.nhlbi.nih.net/atp/iii/calculator.asp?usertype=prof>).<sup>4</sup>

For those at low risk (<20%), 239 people would need to be treated with a statin for one life to be saved; 216 would have to be treated to prevent one heart attack, and 291 would have to be treated to prevent one stroke.<sup>5</sup>

There is substantial evidence that lifestyle modifications including diet, exercise, and abstaining from smoking have a significant positive effect on reducing cardiovascular risk.<sup>6-8</sup> These lifestyle modifications should be implemented prior to or alongside the pharmaceutical treatments in all cases.

For an easy to follow food pyramid that defines key ingredients of the Mediterranean diet, see the website at the University of Michigan Integrative Medicine Program at <http://www.med.umich.edu/umim/food-pyramid/about.htm>

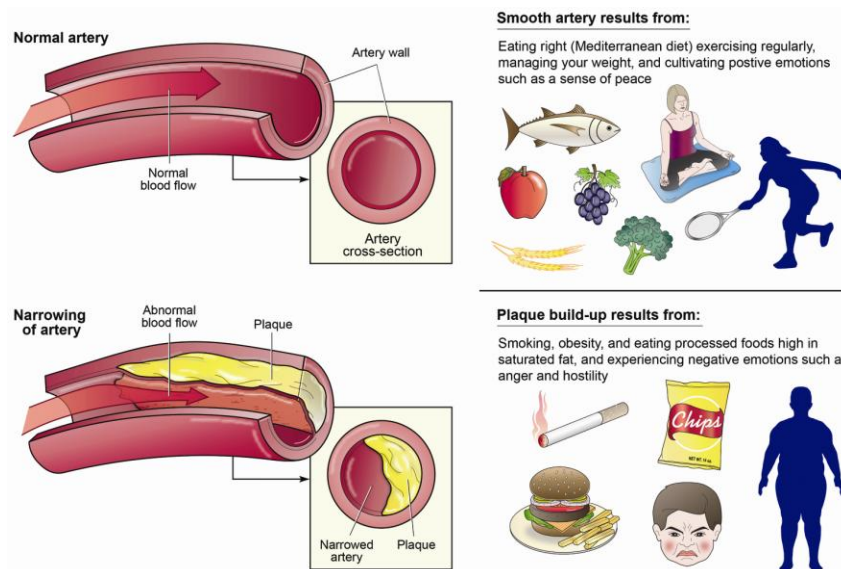
### **Mediterranean Diet:**

- Majority of calories and protein come from plant-based foods (fruits, vegetables, whole grains, legumes, and nuts).
- Moderate fat intake from olive and canola based oils, and nuts.
- If individual eats animal protein, obtain from fish and poultry. Limit red meat.

Nutrition, regular exercise and weight management are the most important influences on lowering cholesterol and preventing heart disease.



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### Key Nutritional Factors for Lowering Cholesterol

- **Water soluble or viscous fiber**

Fiber that absorbs water does three things well in promoting health: 1) reduces the absorption of cholesterol, 2) reduces the speed of absorption of carbohydrates or sugars (lowers glycemic index) [see our handout on [Glycemic Index & Glycemic Load](#)] and 3) if taken before meals, promotes weight loss by absorbing water and giving the sense of being full (satiety).

#### **Good sources of water-soluble fiber**

- **Pectin** is a fiber that binds to bile acids and to cholesterol preventing its absorption. It is found in fruits, vegetables and seeds. Carrots, apples and the white substance on the inner rinds of citrus fruits are excellent sources of pectin. A Scottish study found that eating two carrots a day decreased cholesterol by about 10%.<sup>9</sup>
- **Oat bran** is also a water-soluble fiber that binds cholesterol and prevents absorption. A British study showed a 5% reduction in cholesterol with daily ingestion of oat bran cereal.<sup>10</sup>
- **Ground flaxseed** also has the benefit of being rich in omega-3 fatty acids. The best and most cost-effective way to take flax seed is to buy the seed in bulk and grind up a week's worth in a coffee grinder. Once the seed is ground, it spoils quickly, so direct your patients to store it in the refrigerator. Amount: 1-2 Tbsps. daily over salads, with cereal (oat bran), in smoothies or with water/juice.
- **Barley** contains water-soluble fiber including Beta-Glucan. This type of fiber can also be derived from many other sources including wheat, fungi, and yeast. Barley has been shown to lower LDL cholesterol by about 10 points.<sup>11</sup> The barley in this study came from flakes, barley flour, and pearled barley instead of rice and wheat.



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For lowering cholesterol, 3 grams of barley oil extract or 30 grams of barley bran flour or 0.4 to 6 grams of soluble fiber from barley has been used.<sup>12</sup> Pearled barley, barley flour, flakes, or powder in doses of 3-12 grams daily have also been used.<sup>12</sup>

### **Nutritional fiber supplements**

These can be taken at a dose of 1 Tbsp. in 8-10 oz of water daily or 1 tsp. in 6-8 oz of water before each meal.

- **Psyllium** (Metamucil and others)
- **Methyl cellulose** (Citrucel)
- **Guar gum** (NOW Foods guar gum powder) Less gritty and more palatable than psyllium.
- **Ground flax seed**

**NOTE:** Fiber can inhibit the absorption of pharmaceutical medications as well as some vitamins such as calcium, iron, zinc, and vitamin B<sub>12</sub>. Advise your patients not to take a fiber supplement within an hour of taking vitamins or pharmaceuticals.

### ● **Soy protein**

Diets with a higher amount of protein have been shown to reduce blood pressure and atherogenic cholesterol compared to diets high in carbohydrates. Soy protein has a greater effect on reducing LDL cholesterol than milk derived protein.<sup>13</sup> Soy contains lignan rich fiber, plant sterols (phytosterols) and isoflavones (genistein and daidzien), which have a positive effect on cholesterol through inhibiting absorption and increasing LDL cholesterol receptors for clearing and reducing oxidation of LDL cholesterol. Recent studies have shown a reduction of LDL cholesterol by 10.9% with partially hydrolyzed soy protein as compared to 5.9% reduction with total milk protein.<sup>13</sup>

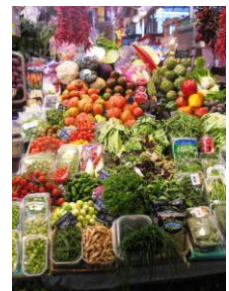
The daily dose of soy protein for lowering cholesterol is between 20-50 gms.

- Approximately 10 gms of soy can be obtained from 1 to 2 cups of soy milk, 4 oz of tofu, 1 oz of soy flour, or 1/2 cup of textured soy protein.
- Eating the whole food is more beneficial than taking a soy supplement unless it consists of whole soy protein. Soy supplements often only include isoflavones (such as genistein and daidzien) and do not include the fiber or the plant sterols, which limit their effectiveness in lowering cholesterol.

### ● **Plant sterols and stanols**

Sterols and stanols are types of cholesterol found in plants such as fruits, vegetables, nuts, seeds, cereals, legumes, vegetable oils (particularly soybean oil). They inhibit cholesterol absorption through the gut by approximately 50%.<sup>14,15</sup>

Eating a Mediterranean diet that is rich in plants provides a rich source of plant sterols and stanols and is the best way to lower cholesterol. If a change in diet is difficult, the following products can be used to lower cholesterol.





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### Functional foods containing plant sterols/stanols:

- Spreads: Take Control® and Benecol®
- Fortified Orange Juice: Minute Maid Premium Heart Wise®

**NOTE:** The beneficial dose of plant sterols/stanols in supplement form is 2-3 gms/day. One Tbsp. of a fortified spread = 0.85-1gm. Two to three Tbsps. of these spreads is a high amount and may lead to excessive calorie consumption making weight loss difficult.

### Plant sterol derived nutritional supplements

- **Beta-sitosterol.** Doses can range from 100-1000 mg of beta-sitosterol based on the product available. The most effective dose is 700 mg to 1 gm 30 minutes before each meal.
- **Nuts**

Nuts are an excellent source of omega-3 polyunsaturated fat, fiber, plant sterols and flavonoids. These are all beneficial for cholesterol and heart health. Nuts are also high in calories so the dose should remain less than ¼ cup or about a handful a day (1 oz) unless weight gain is needed.<sup>16</sup> “Eat a handful, not a can full!” Increasing nut consumption works best at lowering cholesterol if they are consumed in place of saturated fat in the diet. After combining the results from 4 major epidemiological trials on nutrition and the risk of heart disease, regular nut consumption reduced the risk by an average of 37%.<sup>17</sup>
- **Legumes**

Legumes are pod contained fruits and include peas, beans, lentils, soy, and peanuts. A 2011 study found that along with a low calorie diet, and in some cases independent of the diet, 4 servings of legumes per week reduced the inflammatory markers, cholesterol, and blood pressure.<sup>18</sup>



### Summary: The Portfolio Diet<sup>19-21</sup>

The portfolio diet is a Mediterranean eating plan that incorporates the nutritional ingredients described above. It has been found to reduce LDL cholesterol by about 30% (similar to 20 mg of the statin lovastatin), when the foods were provided and by 13% when only the dietary recommendations were provided.<sup>21</sup>

### The Portfolio Diet (daily amounts for 2000 cal/ day diet)

- 30 grams of almonds – about 23 almonds (one ounce). Walnuts, cashews, Brazil nuts and macadamia nuts are also beneficial.
- 20 grams of viscous fiber from foods such as oats, barley, psyllium, and certain fruits and vegetables. (< 1 ounce)
- 50 grams of soy protein from foods such as tofu, soy meat alternatives and soy milk. 10 grams of soy can be obtained from 1 to 2 cups of soy milk, 4 oz of tofu, 2 oz of soy flour, or 1/2 cup of textured soy protein
- 2 grams (.064 ounces) of plant sterols from foods such as Benecol® or Take Control® spreads (one Tbsp. = 1gm). Other food sources include: avocado, soybeans, olive oil and green leafy vegetables.
- Increased consumption of peas, beans, lentils, and peanuts (legumes).



### **Other Helpful Foods for Lowering Cholesterol**

- **Essential fatty acids**

There is a difference in the type of fats we eat and their effects on cholesterol. In general, we want to limit the total saturated fat content of the diet. This includes foods such as meat, eggs, butter, whole milk, fried foods and tropical oils such as palm and coconut. A reduction in cholesterol, triglycerides and inflammation results from replacing saturated fats with monounsaturated fatty acids (MUF) and polyunsaturated fatty acids (PUF).

- **Monounsaturated Fatty Acids (MUF).** Monounsaturated fats (olive and canola oils, avocados and nuts) lower LDL and may even raise HDL. Olive oil is particularly useful because it contains squalenes that may also help prevent colon, lung and skin cancer.
- **Polyunsaturated Fatty Acids (PUF).** Compared to monounsaturated fats, PUF have more of an effect on lowering triglycerides and a greater overall reduction in cardiovascular risk.<sup>9</sup> The GISSI study of over 11,000 men with heart disease showed that 850 mg of omega-3 fatty acids reduces the risk of sudden cardiac death by 45%.<sup>22</sup> Polyunsaturated fats consist of omega-3 fatty acids and omega-6 fatty acids. The ratio of omega-6 to omega-3 fatty acids is important, and the ideal ratio is thought to be around 4:1. With the use of partially hydrogenated oils in cooking (also rich in trans-fatty acids) this ratio has increased to greater than 25:1.<sup>23</sup> In order for the body to benefit from the anti-inflammatory effects of the omega-3 fatty acids, this ratio needs to improve by consuming more omega-3 fatty acids and fewer omega-6 fatty acids.<sup>24</sup>

↑ **Omega-3 Fatty Acids:** Cold water fish, nuts, vegetables, flax seed, soy, hemp.

↓ **Omega-6 Fatty Acids:** Partially hydrogenated vegetable oils found in foods with a long shelf life such as chips, crackers and cookies. Sources of both saturated fat and omega-6 fatty acids also include red meat and dairy.

- **Reducing triglycerides and decreasing the risk of fatal heart attack with fish oil.** When comparing fish oil to flax seed oil for lowering cholesterol, fish oil already consists of the two active ingredients Eicosapentaenoic Acid (EPA) and docosahexaenoic acid (DHA) (two types of omega-3 fatty acids) whereas flax seed needs to be metabolized to EPA and DHA. For lowering triglycerides, supplemental doses of 3-4 gms of EPA + DHA are needed in the form of fish oil. Ground flax seed has fiber, which is also beneficial and can be used in conjunction with the fish oil at a dose of one Tbsp daily.

There is an inverse dose response to the amount of EPA + DHA consumed and the rate of having a fatal heart attack, but don't overdo it. The recommended dose of EPA + DHA is 1000 mg daily for prevention and up to 4000 mg daily for lowering triglycerides.<sup>25</sup>





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**Dosing fish oil:** Fish oil capsules will often come in a total oil dose of 500-1000 mg. When dosing for therapeutic benefit, it is important to look at the amount of EPA + DHA in each capsule. This ratio is generally about 3:2 EPA to DHA. If 1 gm of fish oil capsule has 300 mg of EPA and 200 mg of DHA (total of 500 mg EPA + DHA), you would need to prescribe 2 capsules to = 1 gm of therapeutic omega-3 essential fatty acids.

- Sample brands of fish oil (over-the-counter): Nordic Naturals, Kirkland (Costco), Swanson, Trader Joe's, Solgar, New Chapter, and CVS. For example, Kirkland Signature Enteric Fish Oil has 410 mg EPA + 274 mg DHA = 684 mg Omega 3s per capsule, so two pills daily would generally be enough for cardiovascular disease prevention and it would take about six pills to reduce triglycerides. This Kirkland product is one of the lowest priced products at about \$0.01 per 100mg of EPA + DHA. \$16.99 for 180 capsules.
- FDA approved fish oil (prescriptions only): lovaza 1 capsule = 465 mg EPA and 375 mg DHA. For hypertriglyceridemia, prescribe 2 gms twice/day. Cost: 120 tablets~\$170. The benefits of this formulation compared to over-the-counter fish oil are the higher concentration of EPA/DHA and the FDA monitoring of quality.

**NOTE:** Excessive burping of a fishy taste can suggest a spoiled product, which should be replaced. Freezing the capsules and taking them at night can also reduce this side effect.

- **Garlic**

A meta-analysis of 26 studies reported in 2012 found that garlic significantly reduced total cholesterol and triglyceride levels but not HDL and LDL. Compared with the placebo groups, serum total cholesterol and triglyceride levels in the garlic group were reduced by 0.28 (95% CI, - 0.45, - 0.11) mmol L<sup>-1</sup> ( $P = 0.001$ ) and 0.13 (95% CI, - 0.20, - 0.06) mmol L<sup>-1</sup> ( $P < 0.001$ ), respectively.<sup>26</sup> The benefits of garlic were greater for individuals who used it long-term and who had higher baseline total cholesterol levels. Garlic powder and aged garlic extract were more effective in reducing serum total cholesterol levels, and garlic oil was more effective in lowering serum triglyceride levels.

- **Artichoke**

Artichoke extract contains cynaroside and its derivative called luteolin. Both of these constituents seem to block HMG-CoA reductase, similar to statin medications in lowering cholesterol. Encourage regular consumption of the whole food as a part of the Mediterranean diet.

- **Artichoke extract supplement.** There is some preliminary evidence supporting artichokes' ability to lower LDL cholesterol by 23% over a 6-week period.<sup>27</sup> Other than inducing flatulence and the possibility of an allergic reaction, artichoke appears to be safe with no known drug-herb interactions.<sup>28</sup>

Dose: We recommend eating the food. If this is not possible, the dose of Artichoke Extract is 1800 mg in divided doses (600 mg three times/day or 900 mg twice/day).



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- **Grapes**

Grape products contain phenolic compounds including oligomeric proanthocyanidins (OPCs), flavonols, and polyflavan-3-ols. These chemical structures do not have a significant influence on cholesterol but appear to be protective against heart disease, particularly in those who eat a high saturated fat diet. One of the phenolic compounds found in grapes (particularly pinot noir wine), is called resveratrol. A study in the journal *Nature* found that rodents fed a high saturated fat diet while given high doses of resveratrol significantly outlived the rats not given resveratrol and showed improved coordination and stamina.<sup>29-30</sup> For humans to achieve a similar dose of resveratrol, they would have to drink 150-200 bottles of wine a day! The beneficial phenols found in grapes may help explain the “French paradox” where despite a high fat diet, the French have a lower risk of heart disease possibly because of their love of wine.<sup>31</sup>



**Foods rich in polyphenols include:** grapes, wine, blueberries, cranberries, bilberries, black currant, peanuts, green and black tea, onions, legumes and parsley. Any blue, purple or dark colored grape or berry will be rich in these polyphenols.

- **Green and Black Tea**

One study showed a significant reduction in total and LDL cholesterol of 11.3% and 16.4%, respectively, after consumption of theaflavin enriched tea extract.<sup>32</sup> Another study showed that both green and black tea extracts inhibit HMG-CoA reductase by phosphorylating the enzyme.<sup>33</sup> Although these studies are promising, there is currently not enough evidence to recommend tea or tea extract for treatment of hypercholesterolemia; however, green tea has many health benefits that extend beyond the heart.

- **Ethanol**

Moderate versus occasional ethanol consumption has been shown to have a small but significant risk reduction in heart disease.<sup>6</sup> A moderate effect on increasing HDL levels, raising levels 12%, has also been shown.<sup>34,35</sup> Although the incidence of ischemic stroke was reduced with moderate ethanol consumption, an increase in hemorrhagic stroke was also seen.<sup>36</sup> Significant drug interactions exist with alcohol. Of course a history of alcohol abuse, addiction, and/or pancreatitis must be considered when suggesting ethanol as an option to raise HDL.<sup>37</sup>

### Encourage patients to incorporate the following foods into their diets to help lower cholesterol

- **Fruits:** apples, citrus fruits, and dark colored grapes and berries
- **Vegetables:** artichokes, avocados, beans, carrots, garlic, lentils, onions, peas, peanuts, soybeans and other products made from soy
- **Whole grains:** barley, oat bran, wheat
- **Oils and spreads:** canola oil, olive oil, soybean oil, Benecol®, Take Control®,
- **Cold water fish:** herring, mackerel, salmon, sardines
- **Beverages:** Beta-sitosterol fortified orange juice (Minute Maid Premium Heart Wise®), green and black tea, alcohol (especially red wine) no more than 1-2/day
- **Other:** ground flax seed, mushrooms, nuts



### **Other Supplements and Vitamins**

- **Red Yeast Rice (RYR)**

This supplement is made by fermenting white rice with the yeast, *Monascus purpureus*. The fermentation process turns the yeast red and produces mevinic acids. One of these acids is called monacolin K or mevinolin which is also found in the statin drug, lovastatin. These acids inhibit HMG CoA reductase and reduce cholesterol production from the liver. Red yeast also contains sterols, including beta-sitosterol (also found in vegetables), isoflavones (also found in soy), and monounsaturated fatty acids (also found in olive oil). The cholesterol-lowering effects likely are a combination of the statin-like mevinic acids and its other plant-based constituents.

A randomized trial compared 40 mg of simvastatin + educational pamphlet to Red Yeast Rice 1200 mg twice daily, fish oil (~ 3.5 gms daily) and a 12 week program that focused on the importance of a Mediterranean diet, exercise and relaxation. After 12 weeks, there was a 39% reduction of LDL in the simvastatin group and a 42% reduction in the RYR + lifestyle group.<sup>38</sup> Research in China has shown that those patients who had a previous MI who were randomized to RYR had a decreased incidence of cardiac events and death.<sup>39</sup>

**Dose:** 1200 to 1800 mg twice daily. (3.6 gms RYR = 6 mg of lovastatin) Inappropriate fermentation practice can result in the chemical citrinin which is a nephrotoxin.

Products that have been found to be free of citrinin while having high concentrations of active ingredients as tested by a private lab (consumerlab.com) include:

- Cholestene Red Yeast Rice, 600 mg capsules
- Chole-sterin Red Yeast Rice, 600 mg capsules
- NSI Red Yeast Rice, 600 mg capsules
- Doctors Best Red Yeast Rice, 1200 mg capsules.

**NOTE:** Although Red Yeast Rice appears to be associated with less myopathy,<sup>40</sup> it can still cause this side effect as well as rhabdomyolysis and hepatotoxicity. It shares the same side effect profile as other statin medications and liver enzymes should be monitored.

- **Niacin**

Niacin (Vitamin B3) has been shown to decrease total cholesterol, LDL and triglyceride levels while increasing the good (HDL) cholesterol. Its main drawback is the side effects of flushing and stomach upset. The usual dose of Niacin is 1000-1500 mg daily taken in divided doses. Patients need to start low and increase slowly as tolerated. See below for a titration chart.

#### **Immediate release niacin**

Immediate release niacin can be purchased over the counter without a prescription. It is available in 100 mg, 250 mg, 500 mg, and 1000 mg tablets. Advise patients to avoid the “no-flush” niacin (Inositol Hexaniacinate) due to lack of efficacy.

Sample brands of immediate-release niacin are: Twinlabs, NOW, Nature’s Way, Solaray.





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### Sample Dosing Schedule for Immediate-Release Niacin

Day #	Breakfast 100mg	Dinner 100mg	Total Dose per Day
1 - 3	0	1	100 mg
4 - 6	1	1	200 mg
7 - 9	1	2	300 mg
10 - 12	2	2	400 mg
13 - 15	2	3	500 mg
16 - 18	3	3	600 mg
19 - 21	3	4	700 mg
22 - 24	4	4	800 mg **

\*\* Continue the same dose titration gradually until taking 1000 mg to 1500 mg a day total. A repeat blood test should be done at that time.

### Extended-release niacin

This formulation is more convenient since it can be dosed once a day at bedtime. It causes less flushing but can also cause more liver toxicity, and liver enzymes should be monitored. Extended-Release Niacin requires a prescription [Niaspan® \(Abbott Laboratories\)](#) 500, 750 and 1000 ER. Start 500 mg at bedtime and increase by 500 mg each week with a maximum dose of 2000 mg at bedtime.

### Reducing side effects

The most common side effect from niacin is flushing of the skin. This reaction is well documented and is mediated by prostaglandin. Flushing of the skin is commonly described as redness or itching and tingling sensations that typically occurs on the face, neck, chest, and back. The flushing sensation can be a nuisance, but not serious. The flushing is usually transient and will go away within 10 to 60 minutes. As the body adjusts to the niacin, the flushing will become milder and eventually resolve.

Following are some tips to minimize the flushing side effect:

- Advise patients not to take niacin with hot beverages, alcohol, or spicy food.
- Titrate up the dosage VERY SLOWLY, every 3 to 7 days.
- Encourage patients to take the niacin with breakfast and dinner to avoid stomach upset and promote more even absorption.
- Patients can take half of a regular adult aspirin or 81 mg twenty minutes before each niacin dose. They may need to take the aspirin for three to four weeks, until the body adjusts.

**NOTE:** If cholesterol remains elevated despite incorporating these lifestyle measures, the cause may be related to an increased production of cholesterol from the liver, and the patient would benefit from a prescription medication (statin) to reduce risk.



**SUMMARY--RAISING HDL**  
**Each 1 point (mg/dl) rise in HDL reduces cardiovascular risk by 2-3%<sup>41</sup>**

- **Avoid smoking:** stopping smoking raises HDL by 4 mg/dl<sup>42</sup>
- **Engage in aerobic exercise:** the more the better. Raises HDL 5-10%.<sup>43</sup>
- **Maintain appropriate weight:** 22 lbs of weight loss (10 kg) raises HDL by 20%.<sup>44</sup>
- **Eat a low carbohydrate diet rich in soy protein, soluble fiber and monounsaturated fats** including olive/canola oils and avocados.<sup>45</sup>
- **Consume foods rich in proanthocyanidins<sup>46</sup>** (e.g., dark grapes, blueberries, cranberries, red wine in moderation).
- **Consider niacin (Nicotinic Acid):** at appropriate doses, raises HDL 15-37%.<sup>47</sup> Other drugs that raise HDL include fibrates, thiazolidinediones and bile acid sequestrants.
- **Consider EtOH:** 1-2 drinks per day can raise cholesterol HDL by 12%. Red wine has the benefit of both alcohol and proanthocyanidins. Moderation is key.<sup>35</sup>

**Summary of Lipid Effects**

	LDL Cholesterol	HDL Cholesterol	Triglycerides
Fiber	↓ 5-26%	–	–
Soy	↓ 10%	–	–
Plant Stanols/Sterols	↓ 5-17%	–	–
Nuts (Walnuts)	↓ 8-16%	–	–
Fish Oil	–	–	↓ 20-50%
Garlic	–	–	↓ 13%
Artichoke Extract	↓ Up to 23%	–	–
Red Yeast Rice	↓ 25-35%	–	–
Niacin	↓ 10-15%	↑ 35%	↓ 20-50%
EtOH ( 1-2 drinks/day)	–	↑ 12%	–

Above chart adapted from Natural Medicines Comprehensive Database. Monograph on Clinical Management of Hyperlipidemia. <http://www.naturaldatabase.com>. Last accessed: 2/16/12.

A corresponding [handout for patients](#) is also available.

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