FOCUS ON HDL: AN INTEGRATIVE APPROACH TO DYSLIPIDEMIA
MANAGEMENT AND CARDIAC RISK REDUCTION

By

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A Master’s project submitted in partial fulfillment of
the requirements for the degree of

MASTER OF NURSING

WASHINGTON STATE UNIVERSITY
Department of Nursing

May 2011
To the Faculty of Washington State University:

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Abstract
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Dyslipidemia is a significant risk factor for coronary heart disease (CHD). There are numerous pharmacological therapies targeted at lowering low-density lipoprotein cholesterol (LDL-C), and though this approach does reduce cardiac events, cardiac events related to atherosclerosis still occur in patients who have LDL-C in the desired range. The importance of high-density lipoprotein cholesterol (HDL-C) is becoming more understood in recent years, as is the realization that treating high LDL-C alone may not be enough to sufficiently reduce CHD risk. Low HDL-C is a strong predictor of cardiac risk, and high HDL-C is recognized as being cardio-protective. Emerging research strongly suggests several dietary and lifestyle interventions that notably increase HDL-C, thus reducing cardiac risk. This paper will describe holistic and integrated interventions for dyslipidemia management in concert with current dyslipidemia treatment guidelines for the nurse practitioner.
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Introduction

Nurse practitioners are rapidly becoming the face of primary care. As providers, we bring a different approach to chronic disease management, one that is holistic and emphasizes wellness of the whole person. Thinking outside the box and using a more integrated approach is essential to improving chronic disease management, including dyslipidemia, in primary care.

Dyslipidemia is the presence of elevated LDL-C, elevated triglycerides, or low HDL-C, independently or in combination. Dyslipidemia, along with hypertension and diabetes, is a leading cause of coronary heart disease (CHD)\(^1\). It is well understood that LDL-C is responsible for atherosclerosis, so it seems reasonable that by lowering LDL-C, one would lower their risk of a coronary event. However, coronary events occur in patients who have LDL-C at goal or below, or who are being aggressively treated with a cholesterol lowering medication\(^2\)-(\(^3\)). As a result, the role of HDL-C is becoming more understood, and emerging research is recognizing its importance in reducing cardiac risk.

The most recent guidelines published by the National Cholesterol Education Program, Adult Treatment Panel – III (ATP-III) maintain recommendations to use LDL-C as the primary treatment target for dyslipidemia\(^4\). Though low HDL-C is recognized as a significant independent risk factor of CHD, research does not yet support using HDL-C as a primary treatment target. Dyslipidemia management continues to be driven by reduction of LDL-C, regardless of HDL-C levels. Unfortunately, current dyslipidemia treatment guidelines have not solved the problem of atherosclerotic CHD entirely\(^5\). Emerging research is evaluating HDL-C as a possible primary target for dyslipidemia treatment, and new drugs that target HDL-C...
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production and function are currently being studied\(^6\)(\(^7\)). As the role of HDL-C is becoming more understood, additional interventions to raise HDL-C should be considered in all patients as an adjunct to current treatment guidelines. A holistic approach using integrative treatment interventions that build on current recommended therapies may improve outcomes by reducing cardiac risk.

Literature Review

A review of the literature using CINAHL, Academic Search Complete, Science Direct, Medline and Health Source: Nursing/Academic was completed. The research objective was the importance of HDL-C, and lifestyle and nutritional interventions to raise HDL-C. Search terms used included: “HDL and Cardiac Risk”; “Nurse Practitioner and Dyslipidemia”; “Raising HDL”; “Dietary Interventions for HDL”; “Exercise and HDL”; and “Smoking and HDL”. As a result, a compilation of suggested interventions is presented in this paper, proposing suggestions to nurse practitioners for improved reduction of cardiac risk in patients with dyslipidemia.

Dyslipidemia

Cholesterol is necessary for cell membrane function, vitamin synthesis, and production of hormones and neurotransmitters, and is obtained via dietary consumption and/or produced in the liver from free fatty acids. Cholesterol is transported through the blood stream by low-density lipoproteins (LDL) and high-density lipoproteins (HDL). LDL is referred to as “bad cholesterol” because in excess, it is responsible for atherosclerosis. HDL is referred to as “good cholesterol” due to its role in removing excess cholesterol from the blood stream, reducing the potential for atherosclerosis. Patients are considered to be dyslipidemic if LDL-C is greater than 160mg/dL in
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healthy individuals, or if total cholesterol is greater than 200mg/dL in all individuals (4). The treatment guidelines below will discuss other LDL-C parameters for patients with comorbid CHD risk factors.

Screening for dyslipidemia should be done in all healthy adult patients every 5 years, and the National Cholesterol Education Program (NCEP) recommends either a fasting lipid panel, or a non-fasting total cholesterol and HDL (4). More frequent screening is necessary for patients with dyslipidemia or other CHD risk factors such as hypertension or diabetes.

HDL-C

The Framingham Heart Study recognized low HDL-C as an independent risk factor for CHD in 1988 (8). Research over the last several years has uncovered the importance of HDL-C and its role in risk reduction of a coronary event. HDL-C is a key player in reverse cholesterol transport (RCT), a process that removes excess LDL-C from tissues, returning it to the liver for excretion (7; 9). By doing so, HDL-C helps prevent excess LDL-C from causing atherosclerosis.

It is now recognized that every reduction in HDL-C of 1mg/dL results in a 2-3% increase in cardiac risk (6; 10). Ideally, HDL-C should be at 50 or above for women, and 40 or above for men, especially if comorbidities such as diabetes are present (4). Persons with HDL-C below these targets have increased risk of cardiac events regardless of whether or not their LDL-C is within the goal range. Even if LDL is below 125mg/dL, patients with HDL less than the desired range have more than twice the risk of experiencing a cardiac event than if HDL were above goal (3). The example in Box 1 will illustrate the impact of HDL-C on cardiac risk, using Framingham Risk Scores (11).
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In addition to being anti-atherogenic, HDL-C has been shown to enhance the function of endothelial tissue, and has significant antioxidant properties\(^5\). This antioxidant property of HDL-C makes it more difficult for LDL-C to cause damage to arterial walls. As a result, we are seeing an increased focus on HDL-C in the literature, which could lead to future changes in how we manage dyslipidemia.

**Impact of Current Pharmacotherapies on HDL-C**

The NCEP Adult Treatment Panel III (ATP-III) recommends the use of statins as first line treatment for dyslipidemia\(^4\). Statins should be started if LDL-C is greater than 160mg/dL or total cholesterol is greater than 200mg/dL in patients without compelling indications or comorbid illnesses. Patients with diabetes or known heart disease should be on a statin if LDL-C is above 130mg/dL, with a treatment target of less than 70mg/dL. Treatment goals for LDL-C are summarized in Table 1. Statins have a marked effect on lowering LDL-C, and have been proven to reduce cardiac risk significantly, but have a marginal impact on increasing HDL-C. On average, statins have been shown to raise HDL-C levels over the course of a year by 5-10%\(^{10; 12; 13}\).

Fenofibrate, gemfibrozil, and other fibrates increase HDL-C as much as 10-20%\(^{10; 12; 13}\). The major drawback with fibrates is their high cost. Additionally, they elicit unpleasant side effects, such as abdominal pain and diarrhea, and cannot be used in patients with severe renal or hepatic disease. Because they have a marginal effect on LDL-C, they are not considered a first-line treatment for dyslipidemia.
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Niacin is by far the most effective drug for raising HDL-C levels, and should definitely be considered as part of a dyslipidemia treatment plan for anyone with low HDL-C\(^{(13)}\). On average, Niacin will raise HDL-C by 15-35% when taken as directed\(^{(10;12)}\). Patients often complain of intolerable side effects such as flushing or gastrointestinal upset. Flushing is less severe with the extended release niacin, and taking aspirin thirty minutes prior further reduces this side effect, making niacin more tolerable for patients. Niacin should not be used in poorly controlled diabetics, as it can cause hyperglycemia. It also cannot be used in patients with liver disease. As a result, Niacin may not be a good choice for many of our patients. Again, its effect on LDL-C is marginal, and it is not a recommended first line treatment of dyslipidemia.

Integrative Modalities that Increase HDL-C

Therapeutic lifestyle changes are also part of the ATP-III recommendations\(^{(4)}\). However, these guideline recommendations for therapeutic lifestyle changes focus on reduction of LDL-C. Research has shown a moderate effect on HDL-C with changes in diet and exercise. Here, we look at lifestyle interventions that specifically impact HDL-C.

The following nutritional and lifestyle interventions have been shown in the literature to have a compelling impact on HDL-C levels, and could be introduced to patients as part of a holistic dyslipidemia treatment plan, and are summarized in Table 2.

Cocoa/Dark Chocolate  Cacao beans, used in cocoa powder or in dark chocolate, contain high amounts of polyphenols, chemicals known to have antioxidant properties. In addition, research has shown that daily consumption of either cocoa powder or dark chocolate can increase HDL-C by 13-24\%. In one study, a cup of hot chocolate containing 26g of pure
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cocoa powder daily increased HDL-C by 24% over the course of 12 weeks (14). Another study reported that consuming 75g of dark chocolate daily increased HDL-C by almost 14% in three weeks (15). Each of these studies had small cohorts (25 and 45, respectively), but the results were very compelling. Both studies were well controlled, and participants in each were taking no other medications or supplements for the duration of the study. The contents of both of cocoa powder and the dark chocolate were pure and produced from high quality cacao beans by the study investigators. Also of note, the cohort ingesting cocoa powder was of Japanese descent, the cohort for the dark chocolate study was Finnish; suggesting that the impact of cacao on HDL is independent of race. In each study, both forms of cacao also were shown to reduce the oxidative capabilities of LDL-C, offering potential further protection against atherogenicity. In recommending this intervention to patients, it is important to remember that milk chocolate, or artificially flavored instant cocoa powders do not offer these same benefits, as they do not possess the high phenol content. Instruct patients to use pure cocoa powder or dark chocolate that is at least 70% cacao or higher, as it is the cacao that contains the polyphenol compounds that are beneficial.

Extra Virgin Olive Oil Olive oil has a beneficial effect on HDL-C as a result of the high polyphenol content. Covas, et al demonstrated that olive oil has increased HDL-C by an average of 2.5mg/dL over the course of two weeks, where participants ingested 25ml of high-polyphenol olive oil daily (16). This study had a large cohort (200 men age 20-60), and the results equate to an almost 8% reduction in cardiac risk. In a smaller cohort of 30 participants, Marrugat, et al observed that 25ml of virgin olive oil daily resulted in a 9-10% increase in HDL-C over the course of three weeks (17). Both studies suggest that adding olive oil to a healthy diet will contribute to reduction of cardiac risk. Suggesting to patients that olive oil be substituted for
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other cooking oils, or used in pastas or salad dressings, could be a feasible way of helping patients incorporate this into their daily diet.

**Fish Oil/Omega-3 FA** The benefits of omega-3 fatty acids in fish oil are well understood. Fish oil possesses antioxidant properties, greatly reduces elevated triglycerides, and also moderately increases HDL-C. There are several over-the-counter (OTC) options for fish oil supplements, as well as prescription strength capsules. The American Heart Association (AHA) recommends that all persons with CHD consume a 3.5 ounce serving of cold-water fish such as salmon at least two times per week (18). If regular fish consumption in not feasible, the AHA recommends a supplement of up to 3g/day of fish oil (19). Higher doses are recommended for patients with significantly elevated triglycerides, and are considered prescription strength. Either way, fish oil has numerous benefits for cardiovascular health (19). Several studies in the literature have been reported, looking at both prescription strength and OTC strength fish oil supplements. A study of patients given prescription strength fish oil (4g/day), in addition to a statin, demonstrated an HDL-C increase of 13% when compared to patients being treated with a statin alone (20). Other studies reported HDL-C increases between 2-13% with 4g/day of fish oil alone (21; 22). Loveza, a prescription strength fish oil, has been shown in multiple studies to increase HDL-C by 13% as a sole agent, simultaneously reducing total cholesterol by 20% (22).

Patients may complain of the side effects of indigestion, or not tolerate the “fishy” taste of fish oil supplementation. This can be remedied by having patients keep their fish oil capsules in the refrigerator or freezer, which has been shown to reduce the indigestion and fishy taste. Also, there are many over-the-counter (OTC) options available for fish oil, though consumers must be encouraged to read the nutritional labels to assure an effective choice of product. Fish oil is effective as an Omega-3 fatty acid due to the ratio of eicosapentaenoic acid (EHA) and
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docosahexaenoic acid (DHA), and OTC options can contain different ratios of EHA:DHA, which may not yield the desired benefits. The AHA recommends at least 1g/day of omega-3 FA, at 3:2 ratio of EHA:DHA, which may require up to three capsules daily of OTC fish oil (19).

Prescription strength fish oil should be considered in patients with elevated triglycerides, as well as low HDL-C. A cost-benefit analysis is essential here, as prescription strength fish oil will inevitably raise LDL-C by as much as 10% (19).

**Cranberry Juice** Though only one study was found in the literature regarding the effect of cranberry juice on HDL-C, the results are compelling. Cranberries possess high phenol content, with resultant antioxidant properties. A study of thirty obese men (waist circumference >90cm), with a mean age of 51 years who consumed 250ml of cranberry juice cocktail daily for 8 weeks, demonstrated a 8-10% increase in HDL-C (23). Abdominal obesity and elevated BMI are linked to low-HDL and higher cardiac risk (10; 24). Participants were healthy, though with low HDL-C at baseline, non-diabetic, and on no lipid-lowering medications. They were instructed to take no other vitamins or nutritional supplements during the study period. This study exemplifies the significance of the impact of cranberry juice alone on HDL-C. Suggesting an intervention such as consuming one cup of cranberry juice daily may be an effective intervention. The cranberry juice used in this study was Ocean Spray Cranberry Juice Cocktail, which contains no added sugar or sweeteners. Diabetics may or may not be candidates for this intervention depending on their level of glycemic control and other dietary factors.

**Walnuts** Two studies were reported describing the value of daily walnut consumption, showing beneficial increases in HDL-C. Zibaeezehad, et al, in a controlled trial, witnessed a 9% increase in HDL-C over the course of 8 weeks when participants consumed 20g/day of Persian Walnuts (25). Persian Walnuts (also known as English Walnuts) are commonly found in
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grocery stores. A second study examined the lipid profiles of persons who already regularly consume high quantities of walnuts as part of their daily diet\(^{(26)}\). 793 participants aged 18-65 were screened for the quantity of walnut or walnut oil consumption. Those with a high amount of walnut or walnut oil consumption, (those who reported using walnut oil every day and eating walnuts more than twice per week), were found to have high levels of HDL-C, on average, 64.5mg/dL. Limitations of this study include: self report of walnut intake; data based on frequency of consumption, not actual amount consumed; and though other dietary factors, age and gender were noted, these factors were not controlled. Walnuts contain polyunsaturated fatty acids, and walnut oil contains 1.4g/tbsp of omega-3 fatty acids, which are known to have a preventative role in cardiovascular disease\(^{(19)}\). Patients may be receptive to interventions such as adding a half cup of walnuts to their diet daily, especially if the health benefits are better understood.

**Regular Moderate Exercise** Moderate to vigorous exercise, 30-40 minutes daily, 3-5 days per week, has a myriad of cardiovascular benefits, one of which is increasing HDL-C. The AHA recommends 150 minutes per week of moderate to vigorous exercise, or 30 minutes 5 days/week to maintain or improve cardiovascular health\(^{(27)}\). Patients are aware that exercise has benefits, but many do not understand how exercise can improve dyslipidemia. The literature is dense with studies regarding exercise and cardiovascular health. The studies and recommended exercises discussed here focus on raising HDL-C.

Many patients with known CHD have the opportunity to participate in cardiac rehabilitation exercise programs. Studies have reported that over the course of three months to five years, participants engaging in cardiac rehab consisting of moderate exercise (70-85% of maximum heart rate) for 30-40 minutes three days per week achieved an increase in HDL-C of
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up to 20% (28; 29; 30). The moderate exercises consisted of jogging, brisk walking, or stationary cycling. Brochu, et al and Savage, et al, demonstrated significant increases in HDL-C after three months, and Warner, et al, reported sustained increases in HDL-C after five years. All three studies reported that women in cardiac rehabilitation programs experienced a greater increase in HDL-C than men with the same intervention.

Not only patients with known CHD benefit from exercise interventions. A study of 63 sedentary individuals, who were assigned to either an aerobic or strength training regimen three days per week, for 16 weeks, demonstrated increases in HDL-C of 5% for both regimens (31). Participants agreed to make no other dietary or lifestyle changes during the course of the study. This shows that exercise alone, with no other intervention, can raise HDL-C, thereby reducing cardiac risk, if only moderately so.

Patients reluctant to start an aerobic or vigorous exercise program can still increase HDL-C by less strenuous activities such as yoga. Khatri, et al, reported that patients with known metabolic syndrome benefited from a three month yoga program, reporting an average increase in HDL-C of 7mg/dL (32). This equates to a 20% decrease in overall cardiac risk. Sayeed, et al, found similar results, showing a 6.5mg/dL increase in HDL-C after a one-week intervention of Sudarshan Kriya Yoga, daily for 40 minutes (33). Other studies yielding significant results were noted in a literature review by Monson, where increases in HDL-C of 8-10% were reported after three months of yoga, practiced for 180 minutes per week (34). Limitations of this data center around the different types of yoga practices one can choose to engage in, therefore, it is unclear if all forms of yoga will yield the same results. Also, no study mentioned here evaluated physical exertion (heart rate, vital capacity, etc), so it is difficult to compare a yoga intervention to other forms of moderate or vigorous exercise. Nonetheless, recommending participation in
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activities such as yoga to patients who cannot or choose not to participate in other forms of exercise most likely will benefit their lipid profile.

**Smoking Cessation** The fact that smoking is bad for cardiovascular health is no mystery to most patients or providers. Getting your patients to quit smoking is no easy feat. As providers, we are obligated to encourage our patients to try. Providing patients with more information about how, specifically, cigarette smoking decreases cardiac health may be a worthwhile intervention and a more motivating approach. Even a reduction in the number of cigarettes smoked per day can have a beneficial effect on HDL-C. It is shown in the literature that people who smoke have lower HDL-C. Maeda, et al, reported that cigarette smoking contributes a 5.7% decrease in HDL-C (35). In a meta-analysis, Craig, et al reported a dose-dependent relationship between smoking and HDL-C, with heavy smokers having a 9% decrease in HDL compared to an almost 5% decrease in light smokers (36). Light smokers in this study smoked less than 10 cigarettes per day, whereas heavy smokers used greater than 20 cigarettes per day. Regardless, this phenomenon may encourage patients who are reluctant to quit smoking or who are unsuccessful at quitting to make a stronger effort to cut back. It is also shown in the literature that by quitting smoking, one can improve their HDL-C by up to 20% (35).

**Discussion: Implications for Practice**

As nurse practitioners, we can go beyond the current guidelines for dyslipidemia management by integrating interventions that target raising HDL-C, and helping patients understand the whole picture of cholesterol health. Patients both with and without dyslipidemia should be informed of the importance of HDL-C, and presented with options to decrease their
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Cardiac risk by raising their HDL-C. In patients with dyslipidemia, these nutritional and lifestyle interventions can be initiated in conjunction with lipid-lowering drug therapy.

Several nutritional and lifestyle interventions were reviewed in the literature and presented in this paper. Some results are more compelling than others. Of the most compelling, olive oil and dark chocolate or cocoa powder report the most significant impact on raising HDL-C, and were best supported by the literature. As stated previously, 25ml of olive oil consumption daily can raise HDL-C by as much as 10%. The nurse practitioner can reasonably suggest an intervention of olive oil consumption to all patients, recommending that olive oil be substituted for other oils in cooking. The benefits of cacao consumption, either in dark chocolate or powder form, are well documented in the literature, as discussed above. 75g of dark chocolate (preferably 70% cacao or more) is approximately 2/3 of one regular bar, and could be suggested to patients as a daily intervention to increase HDL-C by as much as 24%. Inform patients that the higher the cacao content, the lower the fat and sugar content, so a higher percentage of cacao affords better nutritional value overall. One cup of cocoa using 26g of pure cocoa powder and low-fat or skim milk, or a non-dairy substitute such as rice milk, offers similar results for raising HDL-C. Suggesting these interventions to dyslipidemic patients, in concert with pharmacological treatments, can improve overall lipid profiles and reduce cardiac risk.

Less compelling interventions found in this review include cranberry juice and walnuts. Both show promise in the literature, but further research is warranted. Only one study showed a positive correlation between cranberry juice and HDL-C, but the results were significant. Walnuts offer other health benefits as well, such as fiber, protein, and unsaturated fats, and could be a reasonable intervention to suggest for dyslipidemic patients in hopes of raising HDL-C. More controlled studies are needed to confirm a stronger correlation between walnut
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consumption and HDL-C. However, nothing in the literature suggests that any of these nutritional interventions are in any way harmful, so making recommendations based on the available literature would be an appropriate intervention for the nurse practitioner to suggest for dyslipidemic patients.

Exercise and smoking cessation are highly recommended to decrease cardiovascular risk, regardless of lipid status. The literature demonstrates that these recommendations are especially important for patients with dyslipidemia, and the nurse practitioner should include patient education interventions as part of every treatment plan. The effect of exercise and smoking on HDL-C is well documented in the literature, and the other health benefits of these interventions are well understood. Helping patients understand specifically how exercise and smoking cessation will improve their cardiac risk may be a motivating factor to improve compliance.

Conclusion

As the importance of HDL-C is becoming understood, more research is needed to discover interventions that increase HDL-C, thus reducing cardiac risk. Pharmaceutical research is well underway, but data does not yet support changes to the current dyslipidemia guidelines to reflect this new understanding. Some nutritional and lifestyle interventions are well supported in the literature, though more research is needed. Nurse practitioners can devise treatment plans that maintain current treatment guidelines, whilst suggesting holistic interventions that may increase HDL-C and improve cardiac risk.
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References


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Box 1: Two patients who differ only by their HDL-C level, demonstrating the impact of HDL-C on cardiac risk, using Framingham Risk Scores. Numbers in parentheses represent points for each risk factor. Neither patient in this example has diabetes or smokes, yielding a score of (0) points for each of those risk factor categories.
<table>
<thead>
<tr>
<th>LDL</th>
<th>Treatment Recommendations without Compelling Indications*</th>
<th>Treatment Recommendations with Compelling Indications*</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;70mg/dL</td>
<td>None</td>
<td>Therapeutic Lifestyle Changes if Diabetic</td>
</tr>
<tr>
<td>&gt;100mg/dL</td>
<td>None</td>
<td>Therapeutic Lifestyle Changes/Consider Statin if Diabetic</td>
</tr>
<tr>
<td>&gt;130mg/dL</td>
<td>Therapeutic Lifestyle Changes</td>
<td>Begin Statin Therapy</td>
</tr>
<tr>
<td>&gt;160mg/dL</td>
<td>Begin Statin Therapy</td>
<td>Increase Statin or Consider additional drug</td>
</tr>
<tr>
<td>HDL</td>
<td>Consider Niacin or Fibrate Therapy Once LDL Goal is Met</td>
<td>Consider Niacin or Fibrate Therapy Once LDL Goal is Met</td>
</tr>
</tbody>
</table>

Table 1: Summary of dyslipidemia treatment guidelines using LDL-C as target for treatment.
Source: U.S. Department of Health and Human Services, National Cholesterol Education Program, Adult Treatment Panel – III, 2001. *Compelling Indications include diabetes, hypertension, 2+ cardiac risk factors, or >20% 10yr cardiac risk
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<table>
<thead>
<tr>
<th>Integrative Nutritional or Lifestyle Intervention</th>
<th>Effect on HDL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cocoa/Dark Chocolate</td>
<td>13-24% Increase</td>
</tr>
<tr>
<td>Extra Virgin Olive Oil</td>
<td>9-10% Increase</td>
</tr>
<tr>
<td>Fish Oil/Omega-3 FA</td>
<td>2-13% Increase</td>
</tr>
<tr>
<td>Cranberry Juice</td>
<td>8-10% Increase</td>
</tr>
<tr>
<td>Walnuts</td>
<td>9% Increase</td>
</tr>
<tr>
<td>Moderate-Vigorous Regular Exercise</td>
<td>Up to 20% Increase</td>
</tr>
<tr>
<td>Smoking Cessation</td>
<td>Up to 20% Increase</td>
</tr>
</tbody>
</table>

Table 2. Summary of interventions and their resultant effect on HDL-C.