LIPIDS

Over the past several years, recommendations around managing lipids have become more patient-centered. The American Heart Association (AHA) and American College of Cardiology (ACC) 2018 Guidelines on the Management of Blood Cholesterol continue to emphasize many of the key elements that were part of their recommendations in 2013, including the importance of: 1) tailoring care to each individual based on their risk, and 2) working with them to explore their best options and overcome barriers to treatment.[1-3] There is a consistently strong focus on medications, which have strong data supporting their use. Lifestyle changes are also emphasized, recognizing that self-care is an important aspect of lipid management. This clinical tool explores how a Whole Health perspective can broaden our approach to addressing lipids as key cardiac risk factor.

THE LATEST PROFESSIONAL CARE RECOMMENDATIONS

As noted in the "Heart Health" Whole Health overview, many factors contribute to heart disease risk. These all should be factored in as clinicians tailor care to an individual, and they are best considered within the even larger picture of a person's overall health. Most expert panels focus on the Professional Care aspect of the Circle of Health; screening, preventive care, and medications receive significant attention. The majority of guidelines outline which medications should be considered and when, based on a person's age, 10-year risk, and personal preferences. Medical management begins with statin drugs and expands from there.

The latest AHA guidelines mention 10 "Take Home Messages to Reduce Risk of Atherosclerotic Cardiovascular Disease (ASCVD) through Cholesterol Management." These include the following:

1. For everyone, focus on a heart-healthy lifestyle throughout their life course. (This ties in nicely with the Whole Health approach.)
2. In people with ASCXVD, reduce low-density lipoprotein cholesterol (LDL-C) with high-intensity statin drugs, or the strongest intensity they can tolerate.
3. Consider non-statin medications if people are very high risk, and keep LDL-C below 70.
4. Start high-intensity statin therapy in people with an LDL-C $\geq$190 even without calculating their 10-year risk. Add ezetimibe as needed, and consider other medications to keep levels under 100.
5. Start moderate-intensity statins in people 40-75 years old with diabetes if their LDL is $\geq$70.
6. Clinicians should have a "risk discussion" prior to starting statins for primary prevention (i.e., for people without known heart disease). All major risk factors should be reviewed (smoking, blood pressure, A1c, lipids, etc.), and a discussion of 10-year risk should occur. Risks and benefits of therapies should also be addressed. (This recommendation could tie in nicely with creating a Personal Health Plan.)

7. In people aged 40-75 without diabetes, who have a 10-year risk over 7.5%, start a moderate-intensity statin if a discussion of options with the patient favors that. Consider checking coronary artery calcium (CAC) to get additional information.
8. Consider statins in people 40-75 without diabetes, if their 10-year risk is 5%-19.9%. Also consider statins if they have risk-enhancing factors, such as a family history of early ASCVD, LDL-C readings persistently ≥160 mg/dL, metabolic syndrome, chronic kidney disease, chronic inflammatory disease, triglycerides that stay >175, mg/dL, an abnormal ankle brachial index, and/or elevated lipoprotein(a) levels.
9. Consider a CAC in people 40-75 who have no diabetes who have levels of LDL from 70-189, if they have a 10-year risk of 7.5%-19.9%. Proceed with medications based on CAC results.
10. Follow up with labs, success with lifestyle changes, and adherence with medications. Consider additional medications as needed.

To calculate cardiac risk, there are many tools. The authors of the above recommendations suggest two.

1. For clinicians: CV Risk Calculator
2. For patients: Check. Change. Control. Calculator.

These recommendations are evidence-based and have the potential to markedly decrease ASCVD risk. Respecting that the medications are highly researched and highly favored, a Whole Health approach to lipid management can perhaps take care even farther. The power of self-care deserves even greater emphasis, and it must be asked: How might care weave in other potentially beneficial approaches as well? Can eating specific foods help? What is the latest research on various dietary supplements? Where might other aspects of self-care fit in? And how do we support people who prefer not to—or cannot—take medications, for various reasons?

ME AT THE CENTER

Certainly, the emphasis (item #6 on the above list) on a "risk discussion" can be expanded nicely into mapping to a person's MAP (Mission, Aspiration, Purpose). Considering heart disease risk within the broader context of someone's life will increase the chances that a Personal Health Plan (PHP) can be created which will lead to both engagement and adherence on the part of each individual. What are their perspectives on their risk of heart disease (and other chronic diseases)? How would having avoiding a heart attack or other vascular complication affect their ability to live in keeping with what really matters to them?

Costs associated with statin therapy have dropped considerably in recent years, and some recent studies have indicated that people may be able to tolerate them better than was originally thought. For example, a review of 11 trials with over 18,000 older adults found that relative to placebo, statins did not increase risk of muscle-related symptoms, serious adverse events, or total adverse events.[5] Of course, it is always important to discuss tolerability on an individual basis. Proponents of statin therapy point out that even though

adverse effects are possible, they are not, in and of themselves, life-threatening, as opposed to the disease process statins are meant to help prevent. Some research indicates that statin therapy is associated with a strong "nocebo" effect, and that the large majority of people can actually tolerate statin therapy better than they might expect.[6] That said, not everyone does, and even if a person is taking a statin, they should be encouraged to go farther than merely relying on medications to decrease their risk.

Statins may offer benefits beyond lowering cholesterol levels, but many of those benefits also might be attained through comprehensive diet and lifestyle changes, as noted in Figure 1, below. Fortunately, almost everyone supports the use of prudent diet and lifestyle modifications prior to or alongside pharmaceutical management. Abundant evidence shows that lifestyle modifications including nutrition, physical activity, and not smoking have a significantly positive effect on reducing cardiovascular risk.[7-9] Positive self-care measures have myriad other health benefits as well. And there continues to be controversy around the relationship between levels of various lipid measures and their effects on cardiovascular disease risk, making the case for a big-picture perspective especially important.[10]

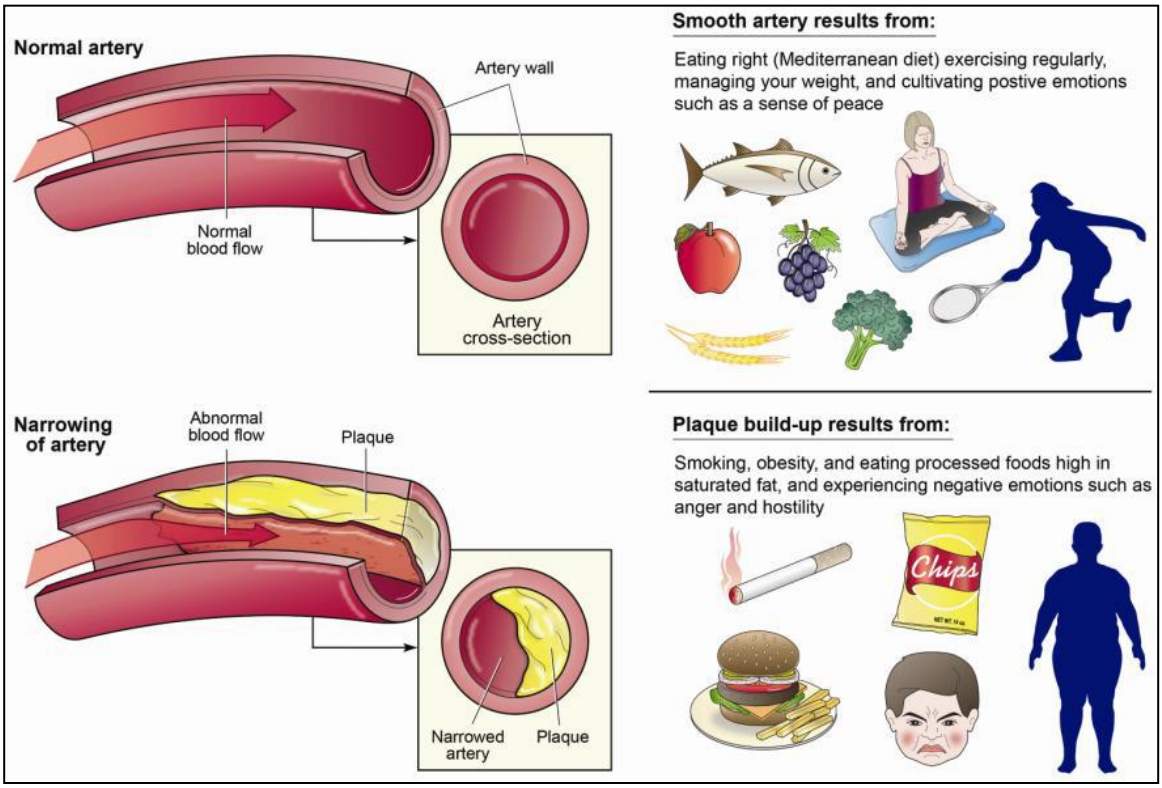

Figure 1. Non-Pharmaceutical Therapy for Lowering Cholesterol.[4]

MINDFUL AWARENESS

While mindful awareness may not have favorable effects on lipids to the same extent as physical activity, it does seem that various formal approaches can have some benefit.[11] For example, transcendental meditation has been found to be associated with

improvements not only related to blood pressure and smoking cessation, but also for cholesterol levels.[12] Of course, mindful awareness approaches – formal and informal – have multiple other benefits as well, as noted in the "Mindful Awareness" Whole Health overview.

FOOD & DRINK

Eating patterns affect lipid levels in a number of ways. Some examples of recent study findings include the following:[13]

- A 1% reduction in saturated or trans- fat intake, with replacement with polyunsaturated fats can reduce LDL-C by about 2 mg/dL. Replacing those calories with "average-quality" carbohydrates could lower LDL by an average of 8.2 mg/dL but increase fasting triglycerides (TGs) by 15 mg/dL.
- Substituting low-glycemic carbohydrates for high-glycemic carbohydrates will lower TGs by 15%-25%. (Find more information in the "Glycemic Index" Whole Health tool.)
- 3.5 gm daily of fish oil (a high dose) will reduce TGs by about 40 mg/dL, on average.
- 3.5-7 gm daily of soluble fiber will lower LDL-C by roughly 8-21 mg/dL.

A logical reason why nutrition likely supersedes drug therapy for reducing cardiac events is that it offers the body many more benefits than simply blocking one of the enzymes that the liver uses to make cholesterol. Vegetables, fruits, fiber, and essential fatty acids help not only to reduce cholesterol but also to decrease inflammation, cancer risk, the development of arthritis, and Alzheimer's disease. Nutrition enhances health of the whole body, not just the heart.

THE MEDITERRANEAN DIET

The PREDIMED study[14,15] enrolled over 7,000 Spanish study participants aged 55-80 years at high risk for cardiovascular disease (CVD) but not diagnosed with it. Participants were randomly assigned to one of three diets: 1) A Mediterranean diet rich in nuts, 2) A Mediterranean diet rich in extra virgin olive oil, or 3) a diet promoting a prudent reduction in dietary fat (or the active control group).

The trial was stopped after a median follow-up of 4.8 years because of early evidence of intervention benefit. The primary endpoint, a combination of stroke, heart attack, and cardiovascular deaths, was reduced in the intervention group compared to controls by 30% in the group randomized to a Mediterranean diet plus extra virgin olive oil, and by 28% in those adhering to a Mediterranean diet with nuts. An especially noteworthy benefit was a reduction in the incidence of stroke. PREDIMED also found a marked risk reduction for developing peripheral artery disease in both the Mediterranean diets supplemented with nuts (50%) and olive oil (34%).[16] A 2014 comparison trial showed that following a Mediterranean diet was more protective against sudden cardiac death in women than even the DASH diet.[17]

A 2019 Cochrane review of 30 trials with over 12,400 participants (along with 7 ongoing trials) concluded there was little benefit of the PREDIMED intervention relative to a low-fat diet intervention, when it comes to primary or secondary prevention of cardiovascular disease and related mortality.[18] The study noted that there was low or very-low-quality evidence showing the Medi Diet had minimal effects on LDL-C, high density lipoprotein cholesterol (HDL-C), or TGs.

Those important findings notwithstanding, the Mediterranean diet remains a mainstay for overall heart-healthy eating and decreasing inflammation. The "Food and Drink" Whole Health overview and related tools offer additional information. For an easy-to-follow food pyramid that defines key ingredients of the Mediterranean diet, visit the Oldways .

THE PORTFOLIO DIET

The Portfolio Diet is a Mediterranean-style eating plan that incorporates a number of the beneficial foods and nutrients described below. It has been found to reduce LDL-C by about 30% (similar to 20 mg of the statin drug, lovastatin), when study participants are given the foods for the diet, and by 13% when they receive dietary recommendations alone.[19] However, the diet can be difficult to follow. [19-21]

A 2018 study found that when the Portfolio pattern was used in addition to the National Cholesterol Education Program Step II diet, the combination led to a 17% decrease in LDL-C, as well as to drops in apolipoprotein B, TC, TGs, blood pressure, C-reactive protein, and overall 10—year CVD risk.[22]

The following are elements of a 2,000 calorie/day Portfolio Diet:

- 30 gm of almonds. This is about 23 almonds (1 oz). Walnuts, cashews, Brazil nuts, and macadamia nuts are also beneficial. (The original studies were sponsored by almond growers.)
- 20 gm of viscous fiber from foods such as oats, barley, psyllium, and certain fruits and vegetables. (Less than 1 oz.)
- 50 gm of soy protein from foods such as tofu, soy meat alternatives, and soymilk.
- 2 gm (0.064 ounces) of plant sterols from foods such as specially formulated spreads (refer below for more on whether or not this is a good approach). Other sources include avocado, soybeans, olive oil, and green leafy vegetables.
- Increased consumption of peas, beans, lentils, and peanuts (legumes).

WATER-SOLUBLE (VISCOUS) FIBER

Fiber that absorbs water does three things well in promoting health:

1. It reduces the absorption of cholesterol.
2. It reduces the speed of absorption of carbohydrates or sugars (i.e., it lowers glycemic index). More information is available in the "Glycemic Index" Whole Health tool.

3. If taken before meals, it promotes weight loss by absorbing water and giving one a sense of being full (satiety).

Good food sources of water-soluble fiber include the following:

- **Pectin.** Pectin is a fiber that binds to bile acids and to cholesterol, preventing their 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%.[23]
- **Oat bran**. 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.[24]
- **Ground flaxseed.** Flaxseed also has the benefit of being rich in omega-3 fatty acids. The best and most cost-effective way to take flaxseed is to buy the seed in bulk and grind up a week's worth in a coffee grinder. (Wipe the inside of the grinder after each use to prevent collection of rancid remnants). Once flaxseed is ground, it spoils quickly, so it should be refrigerated. Patients should aim for 1-2 tbsp daily sprinkled over salads, with cereal (oat bran), in smoothies, or with water/juice.
- **Barley.** Barley contains water-soluble fiber including beta-glucan. This type of fiber comes from other sources as well, including wheat, fungi, and yeast. Barley has been shown to lower LDL-C by about 10 points.[25] The barley in this study came from flakes, barley flour, and pearled barley. For lowering cholesterol, 3 gm of barley oil extract, 30 gm of barley bran flour, or 0.4-6 gm of soluble fiber from barley were used.[26] Pearled barley, barley flour, flakes, or powder in doses of 3-12 gm daily have also been used to lower cholesterol.[26]

There a number of fiber supplements that can also be used. 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. (For a list of good-quality supplemental fiber products, visit ConsumerLab website). Consider one (or more, as needed) of the following:

- **Psyllium.** A review of 28 trials found that an average dose of around 10 gm of psyllium significantly reduced LDL-C and non-HDL cholesterol, as well as apolipoprotein B.[27]
- **Methyl cellulose**
- **Guar gum**
- **Ground flaxseed.** Flax must be ground, as noted above, for full benefit.

Note: Fiber can inhibit the absorption of pharmaceuticals as well as some vitamins and minerals such as calcium, iron, zinc, and vitamin B12. Advise patients *not* to take a fiber supplement within an hour of taking pharmaceuticals or supplements.

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.[28] Soy protein has a greater effect on reducing LDL-C than milk-derived protein.[29] Soy contains lignan rich fiber, plant sterols (phytosterols), and isoflavones (genistein and daidzein), all of which have a positive effect on cholesterol through inhibiting absorption in the gut and increasing LDL-C receptors for clearing LDL-C and reducing its oxidation. Studies have shown a reduction of LDL cholesterol by an average of 4.76 mg/dL in people consuming 25 gm of soy protein for 6 weeks.[30] Total cholesterol (TC) dropped an average of 6.41. Soy protein does not seem to have a major effect on HDL-C or TGs.[31]

The daily dose of soy protein for lowering cholesterol is between 20-50 gm. Approximately 10 gm of soy can be obtained from 1 to 2 cups of soymilk, 4 oz of tofu, 1 oz of soy flour, or 1/2 cup of textured soy protein. As is so often the case, eating the whole food is more beneficial than taking a supplement. Soy supplements contain isoflavones (such as genistein and daidzein) but tend not to include fiber or plant sterols, which are needed to optimize soy's effectiveness in lowering cholesterol.

PLANT STEROLS AND STANOLS

Sterols and stanols are fats found in plants, including fruits, vegetables, nuts, seeds, cereals, legumes, and vegetable oils (particularly soybean oil). They inhibit cholesterol absorption through the gut by approximately 50%.[32,33] Most studies indicate they lower LDL-C by an average of 8%-10%, regardless of a person's age, ethnicity, body weight, or sex.[34]

Eating a Mediterranean diet rich in plant-based foods provides a good amount of these potentially beneficial compounds. Functional food products containing plants sterols/stanols have been used to lower cholesterol. These include specially formulated spreads, yogurts, and fortified orange juice. However, recent research questions how effective plant sterols and stanols are, noting that different people respond differently to these compounds; those with higher de novo cholesterol synthesis may not respond as well or may even experience some adverse effects.[35]

For those who respond to it, the beneficial dose of plant sterols/stanols in supplements plateaus around 2 gm daily.[36] A tablespoon of a fortified spread contains 0.85-1 gm of sterols/stanols. Taking 2-3 tbsp of these spreads may lead to excessive calorie consumption, making weight loss difficult.

NUTS

Nuts are an excellent source of omega-3 polyunsaturated fats, fiber, plant sterols, and flavonoids. These compounds are all beneficial for cholesterol and heart health, as noted in a 2019 review of 7 meta-analyses. Nut consumption decreases CVD mortality by 19%-25%, stroke mortality by 17%-18%, and LDL-C by 0.6-10.1 mg/dL, depending on the study.[37] TC is also reduced. Nuts are also high in calories, so it is best to limit consumption to no more than ¼ cup (1 oz), or about a handful, daily.[38] Increasing nut consumption works best if the nuts are consumed in place of saturated fats in the diet. Cashew consumption might reduce systolic blood pressure but has no effects on lipid profile, according to current evidence.[39]

LEGUMES

Legumes are pod-contained fruits. They 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, four servings of legumes per week reduced inflammatory markers, cholesterol, and blood pressure.[40]

SPICES

A number of spices affect cholesterol absorption in the small intestine.[41] For example, ginger and black pepper down-regulate acetyl-CoA acetyltransferase 2. They also, along with garlic, inhibit microsomal triacylglycerol transport protein. Turmeric also has anti-absorptive effects. These spices also have effects on various enzymes that metabolize cholesterol in the liver and influence macrophage activity. These spices are ideally consumed in the diet, but they can also be taken as supplements.

Garlic. A 2012 meta-analysis of 26 studies found that garlic significantly reduced TC triglyceride levels but did not significantly affect HDL-C or LDL-C levels. Compared with the placebo groups, serum TC and triglyceride levels in the garlic group were reduced by a minimal amount.[42] The benefits of garlic were greater for individuals who used it long-term and who had higher baseline TC levels. Garlic powder and aged garlic extract were more effective in reducing serum TC levels, while garlic oil was more effective in lowering serum TG levels. One meta-analysis concluded that taking garlic for >2 months reduced TC by an average of 17 mg/dL and LDL by 9 mg/dL.[43]

Ginger. A dose of 3 gm daily of ginger for 45 days reduced TC by 27, TGs by 36, and LDL-C by 17 mg/dL.[44]

Turmeric. 2,000 mg/day of curcumin, an active compound in turmeric, when taken for 8 weeks, was found to reduce TC by 20, LDL by 23, and TGs by 17% in people with nonalcoholic fatty liver disease.[45] However, 4 gm daily did not affect lipids in elderly people with cognitive dysfunction.[46] Turmeric does have favorable effects in people with metabolic syndrome, including when taken with black pepper.[47]

FATS

Different fats affect cholesterol in different ways. Historically, people have been encouraged to limit sources of saturated fat from the diet, including meat, eggs, butter, whole milk, fried foods, and tropical oils such as palm and coconut oils. A reduction in TC, TGs, and inflammation results from replacing saturated fats with monounsaturated fatty acids (MUFAs) and polyunsaturated fatty acids (PUFAs). However, keep in mind that experts have recently called into question the influence of dietary fats on CVD risk, stating that the real culprit is likely the plethora of highly processed, manufactured foods on store shelves, including processed meats.[48,49]

A 2020 review in the Journal of the American College of Cardiology noted that limiting saturated fatty acid intake may not be particularly helpful, as doing so has not been found to specifically decrease CVD mortality. Saturated fats increase LDL-C, but not the small, dense particles that tend to correlate to increased CVD risk. The review notes that "whole-fat dairy, unprocessed meat, eggs, and dark chocolate are ...not associated with increased risk of CVD."[50]

MONOUNSATURATED FATTY ACIDS

MUFAs (e.g., olive and canola oils, avocados, and nuts) lower LDL-C and may raise HDL-C. Olive oil is particularly useful because it contains squalenes that may help prevent colon, lung, and skin cancer.

POLYUNSATURATED FATTY ACIDS

Compared to monounsaturated fats, PUFAs are more effective at lowering TGs and overall cardiovascular risk.[23,51] The GISSI study of over 11,000 men with heart disease found that 850 mg of omega-3 fatty acids reduced the risk of sudden cardiac death by 45%.[52] Polyunsaturated fats include omega-3 fatty acids and omega-6 fatty acids. The ratio of omega-6 to omega-3 fatty acid intake is important, and the ideal ratio is considered around 4:1. With the use of partially hydrogenated oils in cooking (these oils are also rich in trans-fatty acids), this ratio has increased to greater than 25:1.[53] For the body to benefit from the anti-inflammatory effects of the omega-3 fatty acids, this ratio must improve. Advise patients to consume more omega-3 fatty acids and fewer omega-6 fatty acids.[54] Both types of PUFA, in the right ratios, are necessary for optimal health.

- Omega-3 fatty acids are found in cold-water fish, nuts, vegetables, flaxseed, soy, and hemp.
- Omega-6 fatty acids are present in partially hydrogenated vegetable oils used in foods with a long shelf life, such as chips, crackers, and cookies. Red meat and dairy are sources of both saturated fat and omega-6 fatty acids.

FISH OIL VERSUS FLAXSEED OIL

Fish oil contains the omega-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). In contrast, flaxseed needs to be metabolized to EPA and DHA, so it is not as efficient a source of DHA and EPA. For lowering TGs, supplemental doses of 3-4 gm of total

EPA and DHA (form fish oil) are needed. Supplements with DHA and EPA derived from algae are also available. Ground flaxseed, while not an optimal omega-3 source, is a good source of fiber, which also has potential benefits, as noted above. It is often taken at a dose of 1 tbsp daily.

There is an inverse relationship between heart attack risk and the amount of EPA and DHA one consumes. The recommended daily dose of total EPA and DHA is 1,000 mg for cardioprevention and up to 4,000 mg daily for lowering triglycerides.[55] When dosing for therapeutic benefit, it is important to look at the total amount of EPA and DHA in each capsule. This ratio is generally about 3:2 EPA to DHA. If 1 gm of fish oil capsule has 300 gm of EPA and 200 mg of DHA (a total of 500 mg EPA + DHA), a person will need to take 2 capsules to get 1 gm of omega-3 fatty acids.

FDA-approved fish oil capsules (available by prescription) contain 465 mg EPA and 375 mg DHA. For hypertriglyceridemia, a standard dose is 2 gm twice daily. Cost may be high; 120 tablets can cost around $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 reduce this side effect.

When combined with vitamin E, omega-3s have been found to significantly reduce very low-density lipoprotein (VLDL) levels[56], but care should be taken, given that certain forms of vitamin E supplements may increase risk of certain complications, particularly in smokers.[57]

MEAT

A review of 36 studies concluded that "substituting red meat with high-quality plant protein sources, but not with fish or low-quality carbohydrates, leads to more favorable changes in blood lipids and lipoproteins."[58] Consuming oily fish leads to significant improvements in TC and HDL-C levels.[59] Following Mediterranean diet patterns of meat consumption is a reasonable approach.

ARTICHOKE (AND ARTICHOKE LEAF EXTRACT)

Cooked artichoke hearts or artichoke leaf extract (ALE) are both thought to improve lipid profiles. A 2018 review found that 2-3 gm of ALE lowers LDL-C by 8-49 mg/dL, TC by 12-55 mg/dL, and TGs by 11-51 mg/dL. Artichoke extract contains luteolin and chlorogenic acid. Some constituents seem to block HMG-CoA reductase, the same way statin medications do. Other than causing flatulence and the occasional mild allergic reaction, artichoke appears to be safe, with no known drug-herb interactions.[60] Encourage regular consumption of artichokes as a part of the Mediterranean diet.

POLYPHENOLS

Many plants, especially those with blue or purple coloration, contain phenolic compounds, including oligomeric proanthocyanidins (OPCs), flavonols, and polyflavan-3-ols. These compounds do not have a significant influence on cholesterol, but they appear protective against heart disease, particularly in those who eat a diet high in unhealthy fats. One of the phenolic compounds found in grapes (particularly pinot noir wine), is called resveratrol. A study in the journal *Nature* found that rats fed a high saturated fat diet while given high doses of resveratrol significantly outlived those not given resveratrol. The resveratrol group also had improved coordination and stamina.[61,62] For humans to achieve a similar dose of resveratrol, they would have to drink 150-200 bottles of wine a day! Supplements are a better way to go in this case. More research is still needed to determine if resveratrol supplementation has a clinically meaningful benefit for treating dyslipidemia or preventing/treating heart disease.[63]

Other foods rich in polyphenols include olive oil, blueberries, cranberries, bilberries, black currants, peanuts, green and black tea, onions, legumes, and parsley.

GREEN AND BLACK TEA

One study showed a significant reduction in total and LDL-C by 11.3% and 16.4%, respectively, after consumption of theaflavin-enriched tea extract.[64] Another study showed that both green and black tea extracts inhibit HMG-CoA reductase by phosphorylating the enzyme.[65] A 2014 systematic review found a significant moderate effect of green tea on TC and LDL-C levels.[66] A 2013 Cochrane review concluded that green and black tea, analyzed together lowered LDL-C by an average of 18.7 mg/dL. Researchers noted that the overall effects of green and black tea on CVD risk require additional study.[67] Although these studies are promising, there is currently not enough evidence to recommend tea or tea extract specifically for treatment of hypercholesterolemia. However, tea has many other health benefits as well.[68]

ALCOHOL

High alcohol intake is associated with CVD and increased TG levels.[69] Moderate alcohol consumption in the form of wine or beer may have a small but significant benefit in heart disease,[7] likely because of the effects of polyphenols (which spirits do not have). A moderate effect on HDL-C levels may also occur,[70] but exercise, weight loss, and smoking cessation may be more efficacious and less likely to cause harm.[71] Although the incidence of ischemic stroke is reduced with moderate ethanol consumption, an increase in hemorrhagic stroke has been noted.[72] Significant medication interactions can exist with alcohol. Of course, a history of alcohol abuse, addiction, and/or pancreatitis must be considered when suggesting alcohol as an option to raise HDL-C.[73]

PROBIOTICS

A 2019 systematic review concluded that supplementation with probiotics significantly reduced TC, LDL-C, and TGs.[74] It also raised HDL-C. It was recommended that probiotic supplementation be an adjunctive treatment for dyslipidemias. A review of 11 trials found that various probiotic interventions led to average decreases of 6.6 mg/dL for TC and 8.6 mg/dL for LDL-C.[75] They were even more effective if taken for longer than four weeks.

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

- Fruits: apples, citrus fruits, and dark-colored grapes and berries. Blue and purple fruits.
- Vegetables: artichokes, avocados, beans, carrots, garlic, lentils, onions, peas, peanuts, soybeans, and other products made from soy. Blue and purple vegetables.
- Whole grains: barley, oat bran, and wheat
- Oils and spreads: canola, olive, and soybean oils
- Cold-water fish: herring, mackerel, salmon, and sardines
- Beverages: green and black tea, possibly wine
- Other: ground flaxseed, mushrooms, nuts, and probiotics.

MOVING THE BODY

Physical activity has clear benefits when it comes to lipid profiles. There is a dose-response relationship between activity level and improvement of HDL-C levels.[76] It would seem that activity also offsets or prevents increases in LDL-C and TGs. High-intensity aerobic exercise seems to be more effective than standard physical activity when it comes to clearing plasma LDL-C and TGs.[77] With resistance training, more movement (more repetitions at lower weights) seems to have a greater impact than increasing intensity (more weight, fewer repetitions). Mixing aerobic and resistance training may augment the benefits of exercise on lipids over aerobic exercise alone.

A 2018 review noted that, while more research is needed, tai chi seems to have at least a small positive effect on HDL-C, LDL-C, and TC.[78] Yoga shows some preliminary evidence of having benefit, as well.[79]

POWER OF THE MIND

Stress reduction has any number of benefits, and a 2018 study recently concluded that over 9-10 years, persistently high levels of psychological well-being, as measured using data from the Midlife in the US (MIDUS) cohort of over 1,000 people, predicted healthier overall HDL-C and TG levels[80], after controlling for a large number of variables. This was especially true for people with high levels of self-acceptance and environmental mastery. LDL-C levels were not affected, but they have been in other studies.

DIETARY SUPPLEMENTS

Note: Please refer to the *Passport to Whole Health*, Chapter 15 on Dietary Supplements for more information about how to determine whether or not a specific supplement is appropriate for a given individual. Supplements are not regulated with the same degree of oversight as medications, and it is important that clinicians keep this in mind. Products vary greatly in terms of accuracy of labeling, presence of adulterants, and the legitimacy of claims made by the manufacturer.

Several reviews have rated the level of evidence for dozens of different supplements[81-83], when it comes to lipid management. Many of the most-effective supplements are derived from foods, so they are featured in the Food and Drink section, above. Note that only in the case of a specific bran of red yeast rice extract has there been a trial specifically finding a benefit of a supplement for reducing cardiovascular events; most studies focus on how supplements affect LDL-C levels; it is assumed (but not confirmed) that if LDL-C goes down, there will be a cardiac risk benefit.[84,85]

A 2018 update concluded that the most-commonly used lipid-lowering nutraceuticals are safe overall, with any side effects being likely to be "mild and reversible."[86] Caution is recommended when using these supplements in the elderly, children, people with liver or renal failure, or people taking numerous other drugs (particularly anticoagulants, when it comes to supplements, for example, like fish oil, ginger, and garlic).

Some of the strongest recommendations are for the following:

- Berberine. Dose 300 mg/day. It upregulates the LDL-C receptor, stabilizes LDL receptor mRNA, and favorably affects gut absorption and bile acid excretion.[85]
- Omega-3s. 1-5 gm daily.
- Red yeast rice. 1,200-4,800 mg daily. More details below.

Some supplements, for which reviews note evidence as less clear but are labeled as "may be considered," include the following:

- Artichoke extract, 1,800-2,700 mg daily.
- Bergamot. 1,300 mg/day. The first clinical study of this supplement was completed in 2015.[87]
- Fiber supplements. Wide range of doses, ranging in studies from 3 to 200 gm.
- Garlic supplements. 5-6 gm daily.
- Green tea extract. 1-5 gm a day is used in studies.
- Lupin. 25 gm/day. Lupin is a legume in the same family as peanuts.
- Spirulina. 1-10 gm a day. Spirulina is a type of algae often described as a functional food. A 2015 meta-analysis found that it significantly and favorable affects TC, LDL-C, and TGs, as well as HDL-C.[88]
- Other spices, like ginger and turmeric, also show promise, as noted previously. A 2018 review and meta-analysis found that ginger supplementation significantly

affects TGs and LDL-C, particularly at lower doses (<2 gm daily).[89] Turmeric supplementation, and supplementation of its constituent compound, curcumin, were described in a 2017 meta-analysis to be both beneficial and potentially useful as an adjunct to conventional drug therapy.[90]

A few other supplements, while not being featured in recent reviews cited above, have also shown some promise:

- Cinnamon supplements reduce TGs (24 mg/dL) and TC (14 mg/dL), but do not improve HDL-C or LDL-C.[91]
- Conjugated linoleic acid supplements have been found to lower LDL-C.[92]
- Cumin (black seed) was found, in a 2018 meta-analysis, to lower TC an average of nearly 11 mg/dL and LDL-C by around 7 mg/dL.[93] Another 2018 review and meta-analysis also concluded it improved TGs and TC, but not find significant effects on LDL-C or HDL-C.[94]
- Gamma-oryzanol, a compound from purified rice bran oil, lowered LDL-C and also reduced platelet aggregation and endothelial adhesion.[95]
- Inositol has shown potential benefits, but more studies are needed.[96]
- Melatonin, typically used to benefit sleep, has also shown promise. It was found in a 2018 meta-analysis of 8 trials to reduce TGs by an average of about 31 mg/dL and TC by about 18.5 mg/dL.[97] No affect was found for LDL-C levels. Higher doses and longer duration of use resulted in greater improvements. A 2019 trial reported similar findings.[98]
- *Panax ginseng* may reduce TC and LDL-C levels by a small amount.[99]
- Purslane seems to improve TGs (and fasting glucose), but not any other lipid parameters.[100]
- Vitamin C does not seem to help with lipid levels overall, but it may help in those with dyslipidemia or those who have low vitamin C status at baseline.[101]

Several studies now recommend against the use of supplements or synthesized foods that contain plant sterols or stanols.[77] Niacin, once a go-to for lipid management, has not been found as clinically effective as originally hoped. Selenium supplementation has minimal benefit.[102] Neither does supplementation with folate.[103]

RED YEAST RICE

Red yeast rice (RYR) extract 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, a statin-like compound that is also found in the drug lovastatin. These acids inhibit HMG-CoA reductase and reduce cholesterol production by the liver. In addition, RYR 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 are likely due to the combined effects of these compounds.

A randomized trial compared three groups:

1) 40 mg of simvastatin plus reading an educational pamphlet
2) Red yeast rice at a dose of 1,200 mg twice daily, plus fish oil (3.5 gm daily)
3) A 12-week program that emphasized the importance of a Mediterranean diet, exercise, and relaxation

After 12 weeks, there was a 39% reduction of LDL-C in the simvastatin group and a 42% reduction in the RYR/lifestyle group.[104] Research in China has shown that people who had a previous myocardial infarction who received RYR had a lower incidence of cardiac events and death.[105] A typical expected change in LDL-C level with RYR would be a drop of 15%-25%.[81] A 2016 review of 10 trials found that RYR and simvastatin had equivalent effects in all the outcomes examined, including effects on various lipid laboratory tests.[106] A 2017 review of 21 trials found comparable benefits between RYR and statin drugs in general.[107]

The recommended dose of RYR is 1,200 to 1,800 mg twice daily; 3.6 gm of RYR contains the equivalent monacolin K to 6 mg of lovastatin. Inappropriate fermentation practice can lead to the creation of the chemical citrinin, which is a nephrotoxin, so it is important to use products from reliable manufacturers. A recent review and meta-analysis found that RYR "seems to be overall tolerable and safe."[108] Some experts strongly argue against using RYR in place of statins, in part due to unclear quality of different products available on the supplement market.[109]

A list of products that have been found to have the amount of active ingredients stated on their labels without containing any of the toxin citrinin are listed on the ConsumerLab website.

Note: Although Red Yeast Rice appears to be associated with fewer cases of myopathy,[110] it can still cause muscle pain, as well as hepatotoxicity. It shares the same side effect profile as other statin medications, and liver enzymes should be monitored the same way they would be for statins.

NIACIN

Based on findings from AIM-HIGH[111,112] and HPS2-THRIVE[113] trials, and given its potential for side effects, niacin now appears *not* to be helpful in the management of hyperlipidemia beyond potential leading to some increase HDL-C.

COENZYME Q10

Coenzyme q10, involved in mitochondrial function, has been used for many years to ameliorate stain-related muscle pain (myopathy), but research findings have been mixed. A 2018 study in the Journal of the AHA did conclude that it does indeed reduce statin-related muscle symptoms.[114] Dosing is 100 mg 2-3 times daily, and it is quite safe.

IN CONCLUSION

As you work with people on managing cardiac risk, lipids are an important risk factor to be aware of, all within the larger picture of a person's Whole Health. Keeping in mind the latest recommendations from expert panels, findings from the ever-expanding body of research on the topic, and what we know about the wide-reaching benefits of various aspects of self-care, can guide effective personal health planning. A plan can be as simple as incorporating a potentially helpful food, or it may be more elaborate, depending on each individual's needs and preferences.

RESOURCES

- The American Heart Association (AHA) and American College of Cardiology (ACC) 2018 Guidelines on the Management of Blood Cholesterol: https://www.ahajournals.org/doi/10.1161/CIR.0000000000000625
- Check. Change. Control. Calculator.: https://ccccalculator.ccctracker.com
- Check. Change. Control. Cholesterol.: https://www.heart.org/-/media/files/health-topics/cholesterol/chlstrmngmntgd_181110.pdf
- ConsumerLab: http://www.consumerlab.com
- CV Risk Calculator: https://static.heart.org/riskcalc/app/index.html#!/baseline-risk
- "Food and Drink": https://www.va.gov/WHOLEHEALTHLIBRARY/self-care/food-and-drink.asp
- "Glycemic Index": https://www.va.gov/WHOLEHEALTHLIBRARY/tools/glycemic-index.asp
- "Heart Health": https://www.va.gov/WHOLEHEALTHLIBRARY/professional-care/heart-health.asp
- "Mindful Awareness": https://www.va.gov/WHOLEHEALTHLIBRARY/self-care/mindful-awareness.asp
- Oldways: https://oldwayspt.org/traditional-diets/mediterranean-diet
- "*Passport to Whole Health*": https://www.va.gov/WHOLEHEALTHLIBRARY/docs/Passport_to_WholeHealth_FY2020_508.pdf
- "Take Home Messages to Reduce Risk of Atherosclerotic Cardiovascular Disease (ASCVD) through Cholesterol Management": https://www.heart.org/-/media/files/health-topics/cholesterol/chlstrmngmntgd_181110.pdf

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