ICSI Institute for Clinical Systems Improvement

Health Care Guideline

Lipid Management in Adults

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Health Care Guideline:
Lipid Management in Adults

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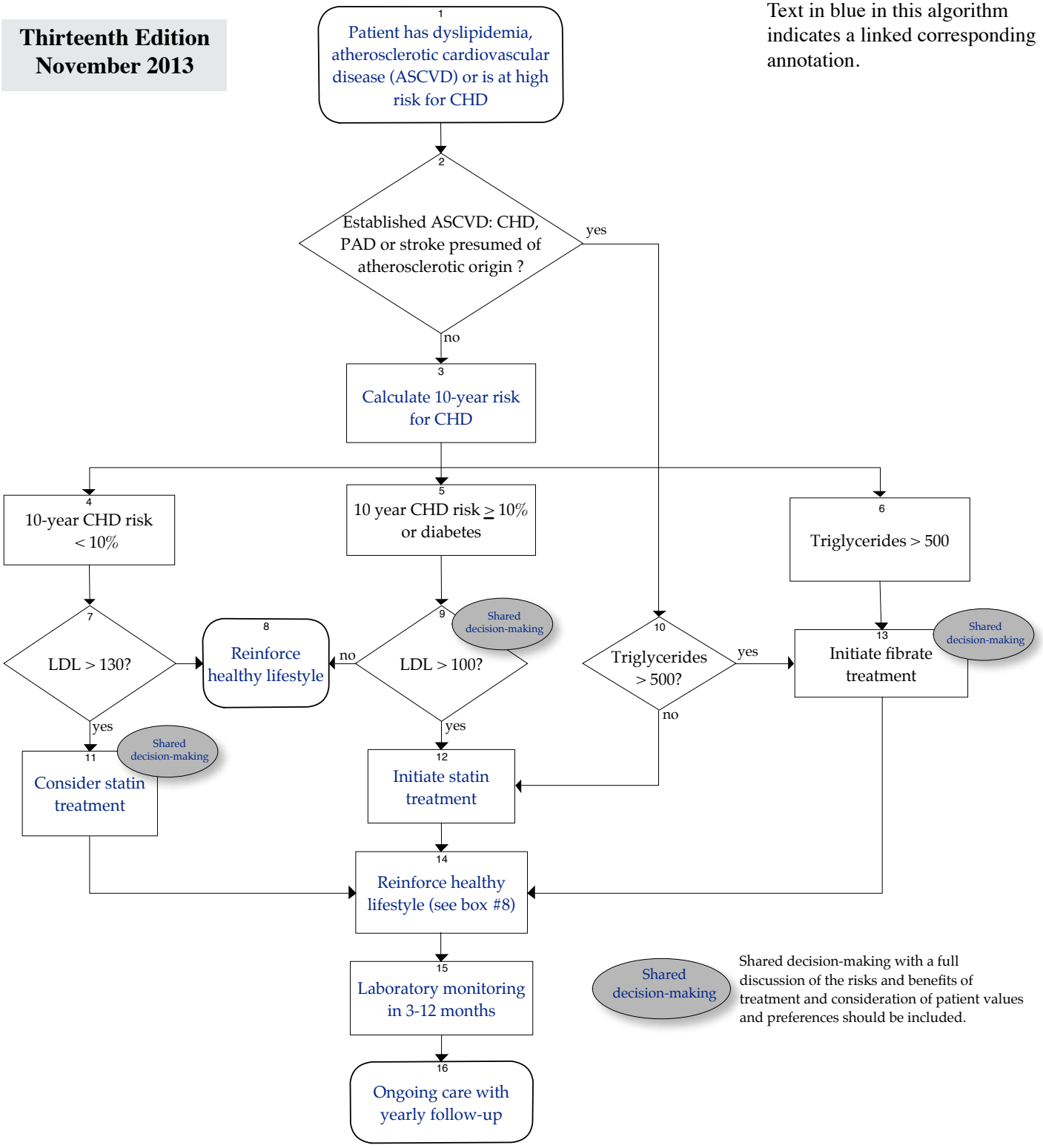

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Evidence Grading

A consistent and defined process is used for literature search and review for the development and revision of ICSI guidelines. The literature search for this guideline consisted of systematic reviews (tier I), randomized control trials and meta-analysis (tier II). Literature search terms for this current revision of this document include lipids, hypercholeserolemia, LDL, HDL, statin therapy and risk assessment from April 2011 through July 2013. Limitations were human data only and English language publications.

In 2011, ICSI began its transition to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system as a method of assessing the quality of evidence and writing recommendations.

GRADE has many advantages over other systems including:

- development by a widely representative group of international guideline developers;
- explicit and comprehensive criteria for downgrading and upgrading quality of evidence ratings;
- clear separation between quality of evidence and strength of recommendations that includes a transparent process of moving from evidence evaluation to recommendations;
- clear, pragmatic interpretations of strong versus weak recommendations for clinicians, patients, and policy makers;
- explicit acknowledgement of values and preferences; and
- explicit evaluation of the importance of outcomes of alternative management strategies.

In the GRADE process, evidence is gathered related to a specific question. Systematic reviews are utilized first and further literature is incorporated with randomized control trials, observational studies or work group submission. The evidence addresses the same population, intervention, comparisons and outcomes. The overall body of evidence for each topic is then given a quality rating.

Once the quality of the evidence has been determined, recommendations are formulated to reflect their strength. The strength of a recommendation is either strong or weak. Low quality evidence rarely has a strong recommendation. Only outcomes that are critical are considered the primary factors influencing a recommendation and are used to determine the overall strength of this recommendation. Each recommendation answers a focused health care question.

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Category	Quality Definitions	Strong Recommendation	Weak Recommendation
High Quality Evidence	Further research is very unlikely to change our confidence in the estimate of effect.	The work group is confident that the desirable effects of adhering to this recommendation outweigh the undesirable effects. This is a strong recommendation for or against. This applies to most patients.	The work group recognizes that the evidence, though of high quality, shows a balance between estimates of harms and benefits. The best action will depend on local circumstances, patient values or preferences.
Moderate Quality Evidence	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.	The work group is confident that the benefits outweigh the risks but recognizes that the evidence has limitations. Further evidence may impact this recommendation. This is a recommendation that likely applies to most patients.	The work group recognizes that there is a balance between harms and benefits, based on moderate quality evidence, or that there is uncertainty about the estimates of the harms and benefits of the proposed intervention that may be affected by new evidence. Alternative approaches will likely be better for some patients under some circumstances.
Low Quality Evidence	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change. The estimate or any estimate of effect is very uncertain.	The work group feels that the evidence consistently indicates the benefit of this action outweighs the harms. This recommendation might change when higher quality evidence becomes available.	The work group recognizes that there is significant uncertainty about the best estimates of benefits and harms.

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Recommendations Table

The following table is a list of evidence-based recommendations for the Lipid Management in Adults guideline.

Note: Other recommendation language may appear throughout the document as a result of work group consensus but is not included in this evidence-based recommendations table.

Topic	Quality of Evidence	Recommendations	Strength of Recommendation	Annotation Number	Relevant Resources
10-Year CHD Risk	Low	Clinicians should use a quantitative estimate of cardiovascular risk to guide lipid management decision-making for the adult population.	Strong	3	*Yusuf, 2004; National Cholesterol Education Program ATP III, 2001; Stamler, 1986*
Statin Use	High	Clinicians should initiate statin therapy regardless of LDL in patients with established ASCVD.	Strong	12	*Cannon, 2004; Heart Protection Study Collaborative Group, 2002; Shepherd 2002; LaRosa, 1999; LIPID Study Group, 1998; Goldberg, 1998; Scandinavian Simvastatin Survival Study Group, 1994*
	High	Clinicians should initiate statin therapy in patients whose LDL is greater than 100 and have a 10-year CHD risk $\geq$ 10% or diabetes.	Strong		*Huffman, 2013; Cholesterol Treatment Trialists, 2012; Sever, 2003; Shepherd, 2002; Heart Protection Study, 2002; Pignone, 2000; Downs, 1998; Frick, 1997; Shepherd, 1995; Lipids Research Clinics Program, 1984*
	Moderate	Combination therapy should be initiated only on an individual basis as no studies have shown a benefit of use at this time, and some studies have shown an increased risk of harm over statin monotherapy.	Strong		*HPS2-THRIVE Collaborative, 2013; Sharma, 2009*

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Topic	Quality of Evidence	Recommendations	Strength of Recommendation	Annotation Number	Relevant Resources
Reinforce Healthy Lifestyle	High	Clinicians should advise patients who are overweight to reduce their caloric intake to achieve weight loss.	Strong	8, 14	*National Cholesterol Education Program, 2002; Stefanick, 1998; Schuler, 1992; Ornish, 1990*
	High	Clinicians should advise a patient to follow a dietary pattern that emphasizes fruits, vegetables, plantoids, fish, nuts and legumes.	Strong		*Stefanick, 1998; Schuler, 1992; Ornish, 1990*
	Moderate	Clinicians should advise a patient to follow a diet low in saturated and trans fats, and added sugars; and high in soluble fiber, with consideration given to adding 2 grams of plant sterol/stanol.	Strong		*Grundy, 2005; Gylling, 1997; Miettinen, 1995; Gylling, 1994; Vanhanen, 1993*

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Foreword

Scope and Target Population

This guideline describes the treatment of adults age 20 and older who are dyslipidemic.

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Aims

1. Increase the percentage of patients with:
   (a) established ASCVD: CHD, PAD or stroke presumed of atherosclerotic origin, or
   (b) a 10-year risk for CHD ≥ 10%, or
   (c) diabetes who are on a statin **OR** have LDL < 100 ml/dL within a 12-month period. *(Annotations #3, 12)*
2. Increase the percentage of patients with established ASCVD or 10-year CHD risk ≥ 10% or diabetes and on lipid-lowering medication who receive regular follow-up care for lipid disorder. *(Annotations #3, 16)*
3. Increase the percentage of patients established ASCVD or 10-year CHD risk ≥ 10% or diabetes and on lipid-lowering therapy who remain on the medication therapy. *(Annotations #3, 12, 16)*

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Clinical Highlights

- Initiate a statin with patients who have established ASCVD. *(Annotations #3, 12)*
- Establish lipid goals based on risk level. *(Annotation #3)*
- Instruct patients on healthy lifestyle and adjunctive measures. *(Annotations #8, 14)*
- Patient adherence with recommended therapy should be reinforced during scheduled follow-up. *(Annotation #16)*

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Implementation Recommendation Highlights

Effective implementation strategies are required for improving the uptake and the use of clinical practice guidelines. The complexities associated with guideline implementation and adherences are vast. Opportunities for implementation partnership exist on the patient level, the care team level, the organization level and/or the market/policy level.

Implementation research can be described as the scientific study of methods to promote the systematic uptake of proven clinical treatments, practices, organizational and management interventions into practice work flows aimed at improving health. In this context, implementation science includes the study of influences on patient, health care, clinician, care teams and organizational behavior in either health care or population settings.

Using available research to work toward an implementation approach for the ICSI Lipid Management in Adults guideline, the following taxonomy compiled by the guideline work group is a framework to engage partnerships in the implementation of the guideline within your current organizational infrastructure *(Mazza, 2013; Rycroft-Malone, 2013; Cook, 2012; Tricco, 2012)*.

Implementation Taxonomy Strategies

1. Audit and Feedback
2. Education
3. Technology
4. Affordability
5. Care Coordination
6. Leadership

The literature recognizes that there is individuality that exists among the users of guidelines (clinician, patient, care teams, health systems, community/policy), and it supports that there are common implementation action themes present among all users. The work group wanted to recognize the individuality of the guideline user while presenting a consistent method to implement the guideline within the context of each organization's infrastructure. The actionable taxonomy provided the crosswalk for users, and the implementation taxonomy categories provide a framework for implementing the guideline. Each category offers strategies specific to the guideline algorithm, aims and measures for use within your organization's current infrastructure. Through the use of the implementation taxonomy strategies, the work group offers a tactical approach to implementing the guideline. The guideline user selects (or customizes) the number of implementation strategies to be used based on what best meets your organization's infrastructure. The implementation matrix tool provided is offered to help systems of care work toward effective and consistent implementation strategies of the ICSI Lipid Management in Adults guideline.

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Related ICSI Scientific Documents

Guidelines

- Diagnosis and Treatment Management of Type 2 Diabetes Mellitus
- Diagnosis and Treatment of Chest Pain and Acute Coronary Syndrome (ACS)
- Healthy Lifestyles
- Heart Failure in Adults
- Hypertension Diagnosis and Treatment
- Preventive Services for Adults
- Stable Coronary Artery Disease

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Definition

Clinician – All health care professionals whose practice is based on interaction with and/or treatment of a patient.

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Algorithm Annotations

1. Patient Has Dyslipidemia, Atherosclerotic Cardiovascular Disease (ASCVD) or Is at High Risk for CHD

- Secondary causes of abnormal lipid levels should be considered and treated when appropriate.
- Patients with established ASCVD: coronary heart disease (CHD), peripheral arterial disease (PAD) or stroke presumed of atherosclerotic origin or diabetes.

See Appendix A, "Identified Secondary Causes and Conditions Associated with Hyperlipidemia."

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3. Calculate 10-Year Risk for CHD

Recommendation:

- Clinicians should use a quantitative estimate of cardiovascular risk to guide lipid management decision-making for the adult population *(Strong Recommendation, Low Quality Evidence) (Yusuf, 2004; National Cholesterol Education Program ATPIII, 2001; Stamler, 1986)*.

The National Cholesterol Education Program Adult Treatment Panel III (ATP III) defines high risk as a net of two or more CHD risk factors, which leads to more vigorous intervention *(National Cholesterol Education Program, 2001)*. Identified risk factors are:

- Age 45 years or older for men; age 55 years or older for women. CHD rates are higher in the elderly than in the young, and in men more than in women of the same age.
- A family history of premature CHD, defined as definite myocardial infarction (MI) or sudden death before age 55 in the father or a male primary relative, or before age 65 in the mother or a female primary relative.
- Currently smoking.
- Hypertension, defined as blood pressure greater than 140/90 mmHg (confirmed by measurement on several occasions) or current use of any antihypertensive medication.
- Low HDL-cholesterol level (less than 40 mg/dL).

A **cardiac risk calculator** based on the Framingham study can be accessed through the following Web site: http://cvdrisk.nhlbi.nih.gov/calculator.asp.

Obesity and physical inactivity are not listed as risk factors but should be considered as targets for intervention. Obesity operates through other risk factors (hypertension, hyperlipidemia, decreased HDL-cholesterol and diabetes mellitus).

If HDL-cholesterol is 60 mg/dL or higher, one risk factor may be subtracted because high HDL-cholesterol levels decrease CHD risk. (For example, if a patient has three risk factors but his or her HDL-cholesterol level is 60 mg/dL or higher, one risk factor is subtracted, leaving a total of two risk factors.)

High-sensitivity C-reactive protein (CRP) may have an independent value as a predictor of cardiovascular disease risk and independent value in identifying patients with normal lipids who could benefit from treatment *(Ridker, 2008; Albert, 2002)*.

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8. Reinforce Healthy Lifestyle

Recommendations:

- Clinicians should advise patients who are overweight to reduce their caloric intake to achieve weight loss *(Strong Recommendation, High Quality Evidence) (National Cholesterol Education Program, 2002; Stefanick, 1998; Schuler, 1992; Ornish, 1990)*.
- Clinicians should advise a patient to follow a dietary pattern that emphasizes fruits, vegetables, plantoids, fish, nuts and legumes *(Strong Recommendation, High Quality Evidence) (Stefanick, 1998; Schuler, 1992; Ornish, 1990)*.
- Clinicians should advise a patient to follow a diet low in saturated and trans fats, and added sugars; and high in soluble fiber, with consideration given to adding 2 grams of plant sterol/stanol *(Strong Recommendation, Moderate Quality Evidence) (Grundy, 2005; Gylling, 1997; Miettinen, 1995; Gylling, 1994; Vanhanen, 1993)*.

Diet and exercise are the cornerstones of treatment for asymptomatic patients with dyslipidemia *(Stefanick, 1998)*. Patients with an elevated LDL-cholesterol level should begin the Therapeutic Lifestyle Changes program and an individualized program of regular exercise. A diet low in saturated and trans fats, and added sugars; and high in soluble fiber, with consideration given to adding 2 grams of plant sterol/stanol is recommended.

- Patients who are overweight should be advised to reduce their calorie intake to achieve weight loss.
- Patients should follow the diet and exercise program for a reasonable amount of time to determine whether their LDL-cholesterol level is lowered to the target range. For many asymptomatic patients, a diet and exercise program is sufficient.

Lifestyle modifications include diet; aerobic exercise; weight management; smoking cessation; evaluation of alcohol consumption; and a nutritional supplement containing sitostanol ester, a saturated derivative of a plant seed oil (EPA-DHA). The addition of 2 grams of plant sterol/stanol can effectively lower LDL. To avoid unintended toxic effects from vitamins, patients should be cautioned not to exceed recommended doses.

Vitamin E supplements should not be used. Studies have shown no benefit in preventing clinical outcomes, and smaller studies suggest a blunting of the benefit from antidyslipidemic medications on HDL-C and angiographic progression of vascular disease *(Brown, 2001; Cheung, 2001)*.

Additional information can be found in the ICSI Healthy Lifestyles guideline.

Diet

The evidence in the literature and the NCEP Adult Treatment Panel Consensus Position suggest that adults with elevated lipids, CHD or CHD risk equivalent should be following the ATP III Therapeutic Lifestyle Changes (TLC) diet or something more aggressive.

The TLC diet lowers saturated fat to less than 7% of calories – avoiding trans fat, limiting dietary cholesterol to less than 200 mg/day – and adds dietary options such as 2 grams/day of plant stanols/sterols and at least 5-10 grams/day of viscous water-soluble fiber to enhance LDL lowering, and has an increased emphasis on weight management and physical activity *(National Cholesterol Education Program, 2002; LaRosa, 1999; Stefanick, 1998; Schuler, 1992; Blankenhorn, 1990; Ornish, 1990; Arntzenius, 1985)*.

Evidence suggests there is a link between sugar intake and cardiovascular disease. Studies have shown that when used to replace dietary fats, carbohydrates can elevate plasma triglyceride levels and lower levels of high-density lipoprotein cholesterol. The American Heart Association and 2010 USDA Dietary Guidelines recommend minimizing intake of beverages and foods with added sugars. More specifically, the American

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Heart Association recommends most women should not eat or drink more than 100 calories per day from added sugars and men no more than 150 calories *(Fung, 2009; Johnson, 2009; Appel, 2005; Mensink, 2003; Hellerstein, 2002)*.

It is desirable to have the dietary assessment and education for these individuals carried out by a registered dietitian when possible.

Aerobic exercise

Many cross-sectional studies demonstrate a more favorable lipoprotein profile in men and women who are more active and physically fit when compared to those who are sedentary.

The strongest evidence comes from the National Runner's Health Study (NRHS), which included men and women who responded to a questionnaire assessing health habits. Lipid data was obtained from physicians and compared to running distance. Increasing distance correlated with increased beneficial lipid effects, including decreases in LDL-cholesterol and triglycerides, along with an increase in HDL-cholesterol. These effects were also correlated with the "leanness" of the individual *(Stefanick, 1998; Berg, 1994; Pronk, 1993)*.

The evidence from cross-sectional studies in men suggest that aerobic exercise may induce an increase of 5-10% in HDL-cholesterol, primarily the HDL2 subfraction, and decrease the triglycerides. Additionally, some studies found a decrease in LDL-cholesterol and total cholesterol. These changes are dependent on the intensity and frequency of physical activity. Short-term studies show that baseline fitness affects the lipid response to exercise. Changes in lipids induced by a single exercise session persist about 48 hours, which has implications for the timing of lipid testing *(Williams, 1997)*.

Interpretation of the data from some studies of exercise in women is complicated by the lack of control of the hormonal status. In the NRHS study of women runners, HDL-cholesterol increased irrespective of menstrual status. Interestingly, women using oral contraceptives in this study had a blunted increase in HDL-cholesterol induced by exercise. Not only whether an individual is menopausal, but also the timing of the studies relative to the menstrual cycle affects the outcome. Cross-sectional studies continue to show a beneficial effect in HDL-cholesterol; however, interventional studies in pre- and postmenopausal women fail to consistently show a significant change in HDL-cholesterol *(Taylor, 1993)*.

Weight management

Overweight and obesity increase the risk for cardiovascular disease and adversely affect plasma lipids.

Each 1 kg increase in body weight has been observed to increase plasma triglycerides by 1.04% and decrease HDL-cholesterol by 0.83%.

Conversely, decreases in body weight and body fat are associated with favorable changes in cardiovascular risk factors, including increased HDL-cholesterol concentrations and decreased total cholesterol, LDL-cholesterol and triglyceride concentrations. Every 1 kg decrease in body weight has been observed to decrease triglycerides by 0.77-0.87% and increase HDL-cholesterol by about 1%.

Weight management should be considered an important component of interventions intended to maximize lipid management and reduce risk of cardiovascular disease *(Denke, 1999)*.

Smoking cessation

As well as being an independent risk factor for the development of CHD, cigarette smoking is associated with changes in the lipoprotein distribution and other metabolic factors that promote atherogenesis.

Nicotine stimulation of sympathetic nervous system activity results in elevation of plasma free fatty acids and very low density lipoproteins. Smoking also clearly reduces HDL-cholesterol and may reduce HDL-cholesterol antiatherogenic effects by altering its composition.

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Smoking cessation trials have documented a significant rise in HDL-cholesterol after smoking cessation. Cigarette smoking in women is associated with earlier menopause and lower estrogen levels, which contribute to an increased CHD risk *(McBride, 1992; Billimoria, 1975)*.

Evaluation of alcohol consumption

Light to moderate consumption of alcohol has been associated with lower coronary heart disease rates. This is defined as no more than one drink per day for women or two drinks per day for men. One drink is defined as 12 ounces of regular beer, 5 ounces of wine or 1.5 ounce of distilled spirits (80 proof).

Alcohol may help protect against heart disease by raising levels of HDL-cholesterol. Risks for CHD, hypertriglyceridemia, pancreatitis, hypertension and cardiomyopathy may increase in women who consume more than one drink per day and for men who consume more than two drinks per day.

(Rimm, 1996; Jackson, 1993; Criqui, 1990; Klatsky, 1981).

Sterol and stanol ester nutritional supplement

Clinical studies in men and women with Type 2 diabetes mellitus, hyperlipidemia and known CHD have shown that sitostanol ester, a saturated derivative of a plant sterol, can lower total cholesterol and LDL-cholesterol approximately 10%.

It has no significant effect on HDL-cholesterol and triglyceride levels.

The primary mechanism is blockage of cholesterol absorption. One small randomized study of women demonstrated an additive effect of sitostanol in combination with simvastatin. Caution should be exercised in patients on medications because of limited information about drug interactions *(Grundy, 2005; Gylling, 1997; Miettinen, 1995; Gylling, 1994; Vanhanen, 1993)*.

Fish oil (EPA-DHA)

Omega-3 fats are found in some fatty fish and in some plant sources, such as walnuts, canola and soybean oils, and flaxseed. They do not affect LDL levels but may help protect the heart in other ways. In some studies, people who ate fish had a reduced death rate from heart disease. It is possible that this is related to the effects of omega-3 fats, which may help prevent blood clots from forming and inflammation from affecting artery walls. Omega-3 fats also may reduce the risk for heart rhythm problems and, at high doses, reduce triglyceride levels. Studies have suggested that omega-3 fats reduce the risk for heart attack and death from heart disease for those who already have heart disease *(National Cholesterol Education Program, 2001)*.

The recommended daily amount of omega-3 fatty acids in patients with dyslipidemia is 1 gram of EPA/DHA by capsule supplement, or by eating at least two servings per week of fatty fish. Studies show that 1.5 grams of ALA or more per day from plant sources is associated with a 40-65% reduced risk of death from cardiac events. The amounts of omega-3 fatty acids in various foods are found in the following table, "Omega-3 Fatty Acids." Plant-based sources of omega-3 fatty acids would be ground flaxseed, flaxseed oil, walnut oil, canola oil and soybean oil. Fish meals can be difficult for patients to maintain, and there are issues of potential environmental contaminants including mercury, PCBs, dioxin and others. Because of this, capsule supplements may be preferred, although there is no uniformity of EPA/DHA content or purity. Patients should consult their clinicians or nutritionists regarding this issue *(Kris-Etherton, 2002)*.

Dietary and non-dietary intake of n-3 polyunsaturated fatty acids may reduce overall mortality and sudden death in patients with stable CAD *(Bucher, 2002)*.

Omega-3 fatty acids

Omega-3 fatty acids are found in fish oil and in some vegetable oils, nuts, seeds and soy. You can get omega-3 fatty acids from some foods or from over-the-counter and prescription supplements. Fish oil contains two

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important omega-3 fatty acids: EPA (eicosapentanoic acid) and DHA (docosahexanoic acid). Plant sources provide ALA (alpha-linolenic acid). Studies of EPA and DHA, suggest that:

- doses of up to 1 gram per day reduce risk of heart attacks in high-risk patients, and
- doses of up to 3 grams per day lower serum triglyceride levels.

Tips for getting more omega-3 fatty acids

- Use vegetable oils that are high in omega-3 fatty acids. Examples are canola oil, soybean oil, flaxseed oil and walnut oil.
- Select fish from the following table and eat at least 7 ounces per week. Prepare fish by grilling, baking, broiling or poaching.
- Add walnuts or ground flaxseed to cereals, yogurt and salads. Whole flaxseeds will not work as well – they simply pass through the body undigested.
- Substitute ground flaxseed for fat (butter or oil) in baked products. Try using 3 tablespoons of ground flaxseed instead of 1 tablespoon of oil.
- Snack on edamame (steamed soybeans, sold fresh or frozen).
- Omega-3 fatty acid supplements should be refrigerated and eaten with food. This will reduce the possibility of a mild fishy aftertaste.

Fish Sources of Omega-3 Fatty Acids
Serving Size: 3.5 ounces, cooked

Safety Note: Pregnant and nursing women and young children should avoid shark, swordfish, king mackerel and tilefish. These contain high levels of mercury. Albacore tuna has more mercury than canned light tuna. Albacore tuna should be limited to no more than 6 ounces per week.

Fish	EPA + DHA content (g/Serving)	Calories/Serving
Farmed salmon	2.15	206
Atlantic herring	2.01	203
Wild salmon	1.84	182
Sardines, canned in tomato sauce	1.35	186
Atlantic mackerel	1.20	262
Farmed rainbow trout	1.15	169
Wild rainbow trout	0.980	150
White tuna, canned in water	0.860	128
Halibut	0.470	140
Shrimp	0.320	99
Fresh yellowfin tuna	0.280	139
Light tuna, canned in water	0.270	116
Atlantic cod	0.160	105

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Plant Sources of Omega-3 Fatty Acids

Food	Amount	Omega-3 fatty acids (g/serving)	Fiber (g/serving)	Calories/Serving
Flaxseed oil	1 tablespoon	7.249	n/a	120
Ground flaxseed	1 tablespoon	1.597	1.9	37
English walnuts	1 tablespoon (7 halves)	1.290	0.9	93
Soy oil	1 tablespoon	0.940	n/a	120
Canola oil	1 tablespoon	0.862	n/a	120
Tofu, raw, firm	1/2 cup	0.733	2.9	183
Green soybeans, cooked	1/2 cup	0.319	3.8	127
Navy beans, cooked	1 cup	0.213	19.1	255
Wheat germ	1/4 cup	0.208	3.8	104
Avocado, raw	1 cup sliced	0.182	9.8	234
Black walnuts	1 tablespoon (7 halves)	0.155	0.5	48
Kidney beans, canned	1 cup	0.125	19.1	210
Baked beans, canned	1 cup	0.104	10.4	239

2006 American Dietetic Association Disorders of Lipid Metabolism Tool Kit.
Sources: www.nal.usda.gov/fnic/foodcomp/search, www.nutritiondata.com, U.S. Food and Drug Administration. *What you need to know about mercury in fish and shellfish*. FDA/CFSAN Consumer Advisory EPA-823-R-04-005. March 2004.
http://www.fda.gov/downloads/Food/ResourcesForYou/Consumers/UCM182158.pdf

See the ICSI Stable Coronary Artery Disease guideline for more information.

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11. Consider Statin Treatment

The use of statin therapy may be considered based on the patient's risk factors. The severity of the dyslipidemia increases the benefit of prescribing a statin. Shared decision-making and a full discussion of the risks and benefits of medication and patient preferences should be included before starting any medications.

Additional information on the ICSI Shared Decision-Making Model can be found on the ICSI Web site.

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12. Initiate Statin Treatment

Recommendations:

- Clinicians should initiate statin therapy regardless of LDL, in patients with established ASCVD *(Strong Recommendation, High Quality Evidence) (Cannon, 2004; Heart Protection Study Collaborative Group, 2002; Shepard, 2002; La Rosa, 1999; LIPID Study Group, 1998; Goldberg, 1998; Scandinavian Simvastatin Survival Study Group, 1994)*.
- Clinicians should initiate statin therapy in patients whose LDL is greater than 100 and have a 10-year CHD risk ≥ 10% or diabetes *(Strong Recommendation, High Quality*

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Evidence) (Huffman, 2013; Cholesterol Treatment Trialists, 2012; Sever, 2003; Shepherd, 2002; Heart Protection Study, 2002; Pignone 2000; Downs, 1998; Frick, 1997; Shepherd, 1995; Lipids Research Clinics Program, 1984).

- Combination therapy should be initiated only on an individual basis, as no studies have shown a benefit to use at this time, and some studies have shown an increased risk of harm over statin monotherapy *(Strong Recommendation, Moderate Quality Evidence) (HPS2-THRIVE Collaborative 2013; Sharma, 2009).*

The decision to begin drug therapy must be based on a clinical discussion with the patient in which the evidence-based outcome data, possible side effects and cost are weighed.

Additional information on the ICSI Shared Decision-Making Model can be found on the ICSI Web site.

No primary prevention studies have addressed pharmacologic lipid treatment in persons at low risk for CHD, and there is no evidence to support drug treatment in this population. In particular, the incidence of CHD in men under 40 and premenopausal women is very low, and drug treatment in these groups is discouraged.

The LDL threshold for drug therapy is consistent with ATP-III. However, in particular cases, drug therapy may be considered at LDL thresholds 30 mg/dL lower than noted in Annotation boxes #4-5.

Table 7: Absolute Risk Reduction and Number Needed to Treat (NNT) with Pharmacologic Lipid Lowering

10-year* risk for CHD	Events prevented/1,000 patients treated	NNT to prevent one event over five years
35%	105	9.5
30%	90	11
25%	75	13
20%	60	17
15%	45	19
10%	30	33
5%	15	67
2.5%	7.5	133

The NNT can be presented to the patient as the number of people who would have to take medication for five years to prevent a non-fatal heart attack. (The major primary prevention studies have been four- to six-year studies.) For example, if the NNT is 13, then 1 of 13 patients would benefit from treatment, and 12 of 13 would not.

* Assumes 30% risk reduction

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Table 8: Primary Prevention for CHD

Therapy	Population	NNT over 5 years	Trial
Statin	Men > 45	40	WOSCOPS
Statin	Men > 45 and HTN	24	WOSCOPS
Statin	Men > 45 and FHx	23	WOSCOPS
Statin	Men > 45/Women > 55 with HDL-cholesterol < 50, LDL-cholesterol > 130	50	AFCAPS

(Ridker, 2008; Downs, 1998; West of Scotland Coronary Prevention Group, 1998; Shepherd, 1995; Levy, 1993; Physicians' Health Study, 1989; Frick, 1987; Lipid Research Clinics Program, 1984)

Statin Therapy Management

Patients with risk factors for coronary heart disease but no history of disease who receive lipid-lowering therapy are likely to experience a decreased risk of coronary heart disease *(Sever, 2003; ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group, The, 2002; Heart Protection Study Collaborative Group, 2002; Shepherd, 2002; Pignone, 2000; Downs, 1998; Shepherd, 1995; Frick, 1987; Lipid Research Clinics Program, 1984)*.

Patients with a history of coronary disease (including unstable angina and acute myocardial infarction) often benefit from treatment with a statin. Studies have consistently shown a decrease in risk of death from coronary heart disease *(Cannon, 2004; Nissen, 2004; Heart Protection Collaborative Study, 2002; Shepherd, 2002; LaRosa, 1999; Goldberg, 1998; LIPID Study Group, 1998; Scandinavian Simvastatin Survival Study Group, 1994)*.

Thus, for care of patients with established ASCVD, or whose 10-year CHD risk ≥ 10% or who have diabetes, the use of statin therapy is recommended.

- For shorter half-life drugs, bedtime or evening dose of statin is more effective (fluvastatin, lovastatin, pravastatin, simivastatin) for higher cholesterol synthesis.
- Dosage adjustments should not be made more often than every four weeks after a fasting lipid panel.
- Please consult manufacturer's product label insert, PDR, etc., for full prescribing information.

Monotherapy

Reducing LDL-cholesterol (LDL-C) levels is the primary approach to lowering risk of CHD in both primary and secondary prevention. In some patients, triglycerides may be elevated along with LDL-C, so reducing triglycerides and increasing HDL-cholesterol (HDL-C) may also be desirable. Selection of drug therapy is dependent on several factors including lipoprotein levels and percent reduction needed to attain goal; concurrent drug therapies that could increase the risk of side effects occurring with specific lipid-lowering drugs; and presence of other medical disorders that may affect drug metabolism, increase risk of side effects or be adversely affected by a specific lipid-lowering drug.

Statins are the drugs of choice for lowering LDL-cholesterol, and aggressive treatment with statins should be pursued. Seven statins are available: atorvastatin, fluvastatin, lovastatin, pravastatin, rosuvastatin, simvastatin, pitavastatin.

Statins also have a modest effect on reducing triglycerides and increasing HDL-cholesterol. Several studies with clinical endpoints support use of statins in primary and secondary prevention.

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If a patient is intolerant to a statin, clinicians are encouraged to have the patient try the other statins before ruling them all out. This is especially important in secondary prevention. In the Heart Protection Study, there was no significant difference between the simvastatin 40 mg and placebo groups, in the number of patients with elevations of serum transaminases or unexplained muscle aches or weakness.

The secondary-prevention VA-HIT trial – utilizing gemfibrozil 600 mg twice daily in patients with normal LDL-cholesterol, low HDL-cholesterol and triglycerides less than or equal to 300 mg/dL – showed a 22% reduction in the combined incidence of CHD death and non-fatal MI. Almost 50% of this study population had evidence of metabolic syndrome or diabetes, and they showed the greatest benefit. Fibric acids have a variable effect on LDL-cholesterol. Fenofibrate may be more effective at lowering LDL-cholesterol than gemfibrozil. They are usually reserved for hypertriglyceridemia or for an isolated low HDL-cholesterol.

In the Coronary Drug Project, a large-scale secondary prevention trial, niacin 3 grams/day reduced mortality 11% over placebo. Niacin has a favorable effect on LDL-cholesterol, triglycerides and HDL-cholesterol and is good for mixed hyperlipidemia. Niacin has a greater effect on HDL-cholesterol than other currently available lipid medications. To improve tolerability and compliance, doses of niacin need to be titrated.

Ezetimibe mainly reduces LDL-cholesterol, with minimal effect on triglycerides or HDL-cholesterol. No clinical outcome studies are currently available, but ezetimibe appears useful for reducing LDL-cholesterol in patients who cannot take a statin and in combination with other LDL-reducing medications.

In the Lipid Research Clinics Coronary Primary Prevention Trial (LRC-CPPT), participants were to take cholestyramine 12 gm twice daily, but compliance varied. A linear relationship was seen with reduction in CHD risk corresponding to cholestyramine dose and reduction in LDL-cholesterol. A 19% reduction in risk of fatal and non-fatal MI was seen in patients taking cholestyramine 24 gm/day. The bile-acid sequestrants reduce LDL-cholesterol, but they can increase triglycerides, so should only be used as monotherapy in patients with baseline triglycerides less than or equal to 200 mg/dL in patients who cannot tolerate other agents.

Safety Considerations in Prescribing Statins in Primary Care Settings

DO

- ☐ Check baseline renal function prior to initiating statin therapy.
- ☐ Check ALT or AST levels prior to prescribing a statin and as clinically indicated after initiation.
- ☐ Consider the potential for drug-drug interactions when prescribing statins.
- ☐ Be alert for patient characteristics that may increase the risk for myopathy during statin therapy, such as advanced age (particularly elderly women), renal or liver impairment, diabetes with evidence of hepatic fatty changes, hypothyroidism, drugs of abuse (amphetamines, phencyclidine, heroin, cocaine), surgery, trauma, ischemia-reperfusion, debilitated status, excessive alcohol intake and heavy exercise.
- ☐ Provide patient education regarding recognition and reporting of symptoms of myopathy during statin therapy.
- ☐ Counsel patients to discontinue statin therapy during a short course of a macrolide or ketolide antibiotic (e.g., azithromycin, clarithromycin, erythromycin or telithromycin).
- ☐ Suspect myopathy when a statin-treated patient complains of unexplained, generalized muscle pain, tenderness or weakness. Joint pain, nocturnal leg cramps or localized pain are not symptoms of myopathy.
- ☐ Check CK levels when a patient reports symptoms of myopathy.
- ☐ If CK levels are abnormal and less than five times upper limit of normal, repeat measurement in one week.

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- ☐ If CK levels are elevated to five times upper limit of normal or greater, discontinue statin therapy and monitor serum CK levels.
- ☐ Assess for signs of dehydration or renal compromise in patients with myopathy.
- ☐ Consider the differences in pharmacokinetic profiles among statins, particularly in patients requiring long-term therapy with drugs that are CYP3A4 substrates, inhibitors or both.

DON'T

- ☐ Prescribe statin-fibrate combination therapy in patients with the following conditions: impaired liver or renal function (creatinine level greater than 2.0 mg/dL), cyclosporine or tacrolimus therapy, long-term macrolide antibiotic therapy or azole antifungal therapy, advanced age (greater than 70 years), skeletal muscle conditions.

Statin Treatment in Chronic Kidney Disease

Patients with chronic kidney disease not on dialysis

Patients with chronic kidney disease or end-stage renal disease are at an increased risk for cardiovascular events. For this reason it has been suggested that patients with chronic kidney disease be considered candidates for preventive treatment even in the absence of other risk factors.

The SHARP trial as well as two meta-analyses looking at patients with stage III and IV chronic kidney disease included in statin trials suggest relative risk reduction of cardiovascular end point similar to patients without kidney disease with statin therapy. Primary prevention with statin therapy can be considered in patients with chronic kidney disease not on dialysis in the absence of other risk factors. There may be a higher incidence of myopathy, and it may be preferable to use doses similar to the 20 mg of simvastatin used in the SHARP trial in this population *(Palmer, 2012; Upadhyay, 2012; Baigent, 2011)*.

Patients on hemodialysis

Patients with end-stage renal disease are at increased risk for cardiovascular events. However, several clinical trials and meta-analyses of available studies have shown disappointing benefit of statin therapy in patients on hemodialysis. Although there were significant benefits in the lipid profile, 4-D, AURORA and SHARP trials found no definite clinical benefit with statin therapy in hemodialysis patients. Post hoc subgroup analyses have suggested benefit in diabetic patients and those with pretreatment LDL elevations.

Overall these rather disappointing results suggest that statin therapy should not be routinely prescribed for all patients on dialysis. These studies do not adequately address the issue of discontinuing statin therapy in patients starting dialysis, and also do not address the issues of benefit in dialysis patients who already have established coronary artery disease *(Marz, 2011; Holdaas, 2011; Fellstrom, 2009)*.

(Ballantyne, 2003; Heart Protection Study Collaborative Group, 2002)

Statin Safety and the Muscle

Myalgia

Myalgia is defined as pain or soreness and/or weakness in skeletal muscles in the absence of serum creatinine elevation. Symptoms of myalgia are quite variable and include cramping, pain, aches, tenderness, soreness, stiffness, heaviness, and weakness either at rest or only during physical exertion. Muscle cramping at night only is not likely statin related.

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Myopathy

Myopathy is defined as complaints of myalgia, plus elevation in serum CK (creatinine kinase) greater than 10 times the upper limit of normal (ULN).

The FDA has updated the recommendations for prescribing statins to limit the risk of myopathy.

- Simvastatin 80 mg dose is limited to patients who have been taking an 80 mg dose for greater than 12 consecutive months without evidence of myopathy.
- Some drugs are metabolized through the same pathways that statins follow and when taken concurrently with statins, can increase both the amount of statin in the blood and the risk of myopathy. The manufacturer's product labeling insert should be consulted for specific dosing guidelines.

Rhabdomyolysis

Rhabdomyolysis is defined as CK elevation > 10,000 U/L, in accord with the definition currently used by the FDA, regardless of whether the patient has experienced a change in renal function, because such a CK level places the patient at high risk for acute renal failure. A second component is CK > 10X the ULN with worsening renal function and/or a requirement for medical intervention with intravenous hydration therapy, along with myalgia.

Incidence

Incidence of muscle symptoms or signs (CK = creatinine kinase elevations) is the most prevalent and important adverse effect of statin therapy. The occurrence of serious muscle toxicity with currently marketed statins is rare.

Myopathy occurs in five patients per 100,000 person-years (in clinical trials, the rate is 1.5-3.0%, most often without CK elevation and at an equivalent rate in patients given placebo). In the practice setting, the range is 0.3-33%. The higher rate may occur partly because statin-intolerant patients and high-risk patients are likely to be excluded from clinical trials. In most patients this occurs in the first six months; however, it could be years before myopathy appears.

Rhabdomyolysis occurs in 1.6 patients per 100,000 person-years.

Recommendations regarding statin safety and muscle symptoms

1. Muscle symptoms or increased CK due to statin therapy is rare. Rule out other causes including increased physical activity, trauma, falls, accidents, seizure, shaking chills, hypothyroidism, infections, carbon monoxide poisoning, polymyositis, dematomyositis, polymyalgia rheumatica alcohol abuse and drug abuse (cocaine, amphetamines, heroin or PCP).
2. Baseline pretreatment CK levels are not necessary; however, they can be considered in high-risk patients. Risk factors for muscle toxicity include advanced age and frailty, small body frame, deteriorating renal function, infection, untreated hypothyroidism, interacting drugs, perioperative patients and alcohol abuse.
3. It is not necessary to measure CK levels in asymptomatic patients during treatment. Marked increases are rare and usually related to physical exertion or other causes.
4. Patient education regarding the muscle symptoms to watch for and report is essential for all patients taking statins.
5. Measure CK levels in symptomatic patients to help decide whether to continue therapy or alter dose.

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6. Discontinue statin in patients with intolerable muscle symptoms with or without CK elevation when other etiologies are ruled out.

   Once asymptomatic, resume the same or different statin at the same or lower dose. Recurrence of symptoms with multiple statins and doses requires initiation of other lipid-altering therapy.

   Patient counseling regarding intensification of therapeutic lifestyle changes (reduced intake of trans fat, saturated fats and cholesterol, increased physical activity, and weight control) should be an integral part of management in all patients with statin-associated intolerable muscle symptoms.

7. If patient is asymptomatic or has tolerable muscle complaints but CK less than 10x the ULN, continue statin at same or lower dose while monitoring symptoms.

8. If patient develops rhabdomyolysis (CK greater than 10,000 IU/L or CK greater than 10x the ULN with elevation in serum creatinine, OR requiring IV hydration therapy), stop statin. Hospitalization may be required. Once recovered, the risk vs. benefit of therapy should be carefully reconsidered.

(Jacobson, 2008; McKenney, 2006)

Patients Unable to Use Statin Therapy

Myalgias are common in patients with statins; however, the cause and effect relationship is unclear. We recommend trying other statins or lowering the dose. Consider a 10- to 14-day vacation from statins and see if the myaligia symptoms abate as a diagnostic maneuver. The evidence is inconclusive at this time for treating myalgia with vitamin D and coenzyme Q.

If patients are intolerant to a statin, clinicians are encouraged to have the patient try the other statins in reduced doses before ruling out all statins.

If patients are unable to take a statin, then bile-acid sequestrants, niacin, fibric acid derivatives or fibrates, and ezetimibe are available. In the Lipid Research Clinics Coronary Primary Prevention Trial (LRC-CPPT), cholestyramine 24 grams/day showed a 10% reduction in risk of fatal and non-fatal MI. Adherence in this study varied, but a linear relationship was seen with reduction in CHD risk corresponding to cholestyramine dose and reduction in LDL-cholesterol *(Lipid Research Clinics Program, 1984)*.

In the Coronary Drug Project, niacin 3 grams/day reduced mortality 11% over placebo. There are also studies with angiographic endpoints that showed benefits of bile-acid sequestrants alone and in combination with niacin *(Coronary Drug Project Research Group, The, 1975)*.

The VA-HIT trial, utilizing gemfibrozil 600 mg twice daily, showed a 22% reduction in the combined incidence of CHD death and non-fatal MI.

The ENHANCE study evaluated simvastatin with and without ezetimibe on carotid intima-media thickness in patients with familial hypercholesterolemia and did not find a significant difference after 24 months in this surrogate endpoint, though the LDL was significantly lower with combination therapy *(Kastelein, 2008)*.

The SEAS study, while not showing a difference in aortic stenosis progression with combination therapy, did show a significant reduction in the secondary endpoint of non-fatal ischemic events in the simvastatin/ezetimibe-treated group compared to placebo after 52 months *(Rossebø, 2008)*.

Other Medications

Niacin

Niacin should not be used in combination therapy with a statin, as two major trials have shown increased side effects without any reduction in cardiovascular outcomes. Niacin may be considered as monotherapy in patients who can't tolerate a statin or fibrate.

Niacin (vitamin B3) has been used for many years to lower blood cholesterol levels. In the 1960s niacin was shown in a large clinical trial to reduce myocardial infarction by 26% in men with coronary artery disease as compared to placebo. Niacin lowers LDL cholesterol, triglycerides and lipoprotein(a) and raises HDL cholesterol. Niacin is available in crystalline (immediate-release) and SR (sustained-release) preparations, and is available over the counter. The ER (extended-release) preparation niacin is a prescription drug.

Efficacy

Monotherapy – in the Coronary Drug Project, a large-scale secondary prevention trial, crystalline niacin 3 grams/day reduced mortality 11% over placebo *(Canner, 1986)*.

- It exerts favorable effects on all lipids and lipoproteins, good for mixed hyperlipidemia.
- Crystalline niacin reduces triglycerides 20-40%, increases HDL-cholesterol 15-35% and decreases LDL-cholesterol 6-25%.
- Extended-release niacin reduces triglycerides 11-35%, increases HDL-cholesterol 15-26% and decreases LDL-cholesterol 9-17%.
- Sustained-release niacin reduces triglycerides 10-40%, increases HDL-cholesterol 5-15% and decreases LDL-cholesterol 6-50% (but this latter effect may be due to hepatic toxicity).

Safety

- Flushing and pruritis of face and upper trunk are common and may be alleviated with pre-treatment of aspirin. Tolerance usually develops and patients are more accepting if they know what to expect. With crystalline niacin, flush and pruritis usually occur within 30 minutes and are gone in about that time. Flushing is reduced with SR niacin, but it still occurs.
- Liver toxicity may be associated with niacin. Risk appears greater with SR niacin, and appears dose related (most occurring with doses of 2 grams/day or higher). Hepatoxicity has occurred when patients switched from crystalline niacin to a SR form without a decrease in dose. Patients who are asymptomatic with only elevations in transaminases (to three times the upper limit of normal) may respond to dose reduction. If transaminases exceed three times the upper limit of normal or patients are symptomatic (e.g., nausea, vomiting, diarrhea, anorexia, fatigue and/or jaundice), niacin should be discontinued. With discontinuation, symptoms decline within two weeks and lab abnormalities should resolve within one to four months. In a long-term (59 weeks) study of niacin in an extended-release, median dose of 2 grams/day, less than 1% of participants with normal serum transaminases at baseline had elevations greater than three times the upper limit of normal.
- GI complaints (nausea and abdominal pain) are more common with SR niacin; this can be minimized by taking with meals. Activation of peptic ulcer has occurred, so history of peptic ulcer is a relative contraindication.
- Uric acid may be slightly increased. Rarely, this may lead to acute gouty arthritis.
- Serum glucose concentrations may be increased with higher doses (greater than 3 grams/day), especially in patients with type II diabetes or glucose intolerance. Glucose monitoring is critical for use of niacin in these patients. Some adjustment in their hypoglycemic therapy may be needed. However, data from the Arterial Disease Multiple Intervention Trial (ADMIT) indicate that niacin can usually be safely used in patients with diabetes. Niacin use in patients with diabetes resulted in a small but significant change in HbA1c levels of 0.3% versus placebo.
- Combination with a statin may increase risk of myopathy.

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Dosing

Please consult drug reference for full prescribing information.

- Slow dosage titration allows patient to develop tolerance to flushing and pruritis.
- Crystalline niacin can be taken twice a day. Avoiding hot beverages and alcohol at time of dosing is recommended. A single brand should be used to prevent the inadvertent switch to an SR form.
- SR niacin should also be titrated. Further increase should be based on response and tolerance. A single brand should be used because of significant variability in bioavailability.
- Extended-release niacin should be taken at bedtime with a low-fat snack. Further titration should be based on patient response and tolerance. Women may respond at lower doses.

Gemfibrozil, Fenofibrate and Fenofibrate Micronized

Efficacy

- Prior to initiating a fibric acid, lifestyle therapies should be intensified for moderately elevated triglycerides. These include reduction of liquid sugar, all refined starches and saturated fat; increased moderate-intensity exercise; and weight reduction.
- With fibric acids, triglycerides are reduced 30-50% and HDL-cholesterol increases 10-20%. Total cholesterol is only modestly reduced (5-20%) in patients without elevated triglycerides. Effect on LDL-cholesterol is variable: fenofibrate may lower LDL-cholesterol more than gemfibrozil, but it is less effective than statins (dependent on baseline triglyceride level).
- Good for severe hypertrigylceridemia (triglycerides > 500 mg/dL) in patients at risk for pancreatitis and for prevention of CHD (not proven for fenofibrate) when patient has an abnormal lipid triad of depressed HDL-cholesterol, elevated LDL-cholesterol and elevated triglycerides. May be particularly useful in diabetics with mixed hyperlipidemia and for patients with dysbetalipoproteinemia. The combination of simvastatin and fenofibrates did not reduce fatal or non-fatal cardiovascular events as compared to simvastatin alone in patients with type 2 diabetes in the ACCORD lipid trial.
- The VA-HIT trial utilizing gemfibrozil showed a 22% reduction in CHD death and non-fatal MI in patients with documented CHD and low HDL-cholesterol as their primary lipid abnormality.

Safety

- Myositis has occurred rarely in patients on monotherapy with fibric acids. Risk of myopathy and possibly rhabdomyolysis appears increased when taken with statins, particularly with gemfibrozil in combination with statins.

  There may be a potential difference in risk of myopathy between gemfibrozil and fenofibrate when combined with statins. Gemfibrozil is contraindicated in coordination with simvastatin. Combination therapy with lovastatin and rosuvastatin should be avoided. Fenofibrate had no effect on plasma levels of rosuvastatin. Generally, fenofibrate may be used in combination with statins if the benefits outweigh the risk.
- Cholelithiasis and cholecystitis can occur (0.3-1% incidence) due to increased cholesterol excreted in the bile. Fibric acids are contraindicated in patients with pre-existing gallbladder disease.
- Use with caution in patients with a history of liver disease. Fibric acids are contraindicated in patients with hepatic impairment, including primary biliary cirrhosis, or in severe renal impairment.
- Hematologic adverse reactions are rare.

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- Warfarin's anticoagulant effect may be potentiated; INR should be monitored closely and the initiation of a fibric acid, with dose changes, and with discontinuing a fibric acid.

Dosing

Please consult manufacturer's product labeling insert for specific dosing.

Ezetimibe

Efficacy

- Long-term effects on cardiovascular morbidity and mortality are unknown.
- LDL-cholesterol lowered about 18%.
- Additive LDL-cholesterol reduction when used in combination with statins.
- FDA approved Ezetimibe with fenofibrate.

Safety

- Short-term tolerability is similar to placebo. Long-term safety is unknown.
- Not recommended for use in patients with moderate to severe hepatic impairment based on Child-Pugh score. The AUC (area under the curve) of ezetimibe increased fourfold in patients with moderate hepatic impairment (Child-Pugh score 7 to 9).
- Co-administration with cyclosporine increased ezetimibe blood level 12-fold in one renal transplant patient. Patients on cyclosporine and ezetimibe should be monitored carefully.
- Cholestyramine co-administration decreased the mean AUC (area under the curve) of total ezetimibe by 55%. Ezetimibe should be given two hours before or four hours after bile-acid sequestrants.

Dosing

Please consult manufacturer's product labeling insert.

(Dujovne, 2002; Gagne, 2002; McKenney, 2002)

Bile-Acid Sequestrants

Efficacy

- In the Lipid Research Clinics Coronary Primary Prevention Trial (LRD-CPPT), a 19% reduction in risk of fatal and non-fatal MI was seen in patients taking cholestyramine 24 g/day. In those patients who didn't take 24 g/day, a linear relationship was seen with reduction in CH risk corresponding to cholestyramine dose and reduction in LDL-cholesterol *(Lipid Research Clinics Program, 1984)*.
- LDL-cholesterol lowered 15-30% (dose dependent).
- Triglycerides may increase 15% – should not be used as sole therapy if triglycerides are greater than 200 mg/dL and should not be used at all if triglycerides are greater than 400 mg/dL.
- Effects apparent within one week and maximum at two to three weeks.
- Useful for patients with moderately elevated LDL-cholesterol.
- Good for combination therapy.

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- LDL-cholesterol reductions enhanced with low doses.
- Most potent with statin.

Safety

- Not systemically absorbed – side effects limited to GI tract.
- Patients who have phenylketonuria (PKU) should know that Questran® Lite, Prevalite®, and flavored colestipol powder contain aspartame. Regular Questran® and unflavored colestipol powder and tablets do not.
- Drug interactions are minimized by taking other medications one hour before the sequestrant or four hours after.
- The net effect of combination warfarin is unpredictable. Cholestyramine decreases the absorption of warfarin and may reduce warfarin's half-life by interfering with enterohepatic circulation. Vitamin K absorption may also be reduced; thus, the net effect on coagulation is hard to predict. Colestipol and colesevelam have been reported not to interact with warfarin, and thus may be safer agents. Separating these agents by at least four hours from warfarin and close monitoring of INR is recommended.
- While not contraindicated in pregnancy and lactation, consideration must be given to potential adverse effects on the baby because of impaired maternal absorption of nutrients and vitamins.

Please consult manufacturer's product labeling insert, or PDR for full prescribing information.

(McKenney, 2001; National Cholesterol Education Program, 2001; Lipid Research Clinics Program, 1984)

Combination Therapy

Studies of combination therapy have failed to show any benefit beyond statin monotherapy. Combination therapy should only be considered on an individual basis; attention to the additional cost, complexity and risk for side effects argue against routine use until further studies indicate what groups of patients might benefit *(HPS2-THRIVE, 2013; Sharma, 2009)*.

As national lipid guidelines have focused on specific LDL goals, it has become common practice to adjust medication therapy, including using combinations of medications, to achieve these goals. Common combinations include statin-fibrate, statin-niacin and statin-ezetimibe.

A systematic review of combination therapy for dyslipidemia concluded that the limited evidence available suggests that combinations of lipid-lowering agents do not improve clinical outcomes more than statin monotherapy.

Statin-Fibrate

Historically, fibrates (gemfibrozil or fenofibrate) have been used with statins, resulting in enhanced LDL lowering as well as a higher incidence of myopathy. Only one randomized controlled trial to date has evaluated the clinical benefit of this combination on vascular events.

In the lipid arm of the ACCORD study, people with type 2 diabetics were randomized to simvastatin plus fenofibrate versus simvastatin alone. No benefit in the combined vascular outcome or individual clinical outcome was seen.

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Statin-Niacin

Although low HDL-cholesterol is associated with a significant increase in the risk of cardiovascular events in population studies, recent clinical trials have not demonstrated improved outcomes by increasing HDL-cholesterol with niacin among individuals with CVD and optimally controlled LDL-cholesterol on statins.

- Several randomized controlled trials (ARBITER-2, ARBITER-3, HATS) tested the efficacy of adding niacin to statin therapy in individuals with coronary artery disease or CAD equivalents. The statin-niacin treated patients in all three trials had reduced carotid intima-media thickness progression, and the HATS trial showed reduced CVD primary endpoints when antioxidants were not used. No published clinical trial to date has evaluated the clinical benefit of this combination on vascular events.
- The AIM-HIGH trial, demonstrated no additional benefit from the addition of niacin to statin therapy over a three-year follow-up period among 3,414 patients with atherosclerotic vascular disease and low baseline LDL-cholesterol levels (70 mg/dl), although there was significant improvement in LDL-cholesterol, HDL-cholesterol and triglycerides in the niacin plus statin group compared to the statin alone group. The trial was stopped prematurely because of no differences in primary endpoints between groups.
- The HPS-2-THRIVE study found that the addition of ER (extended-release) niacin, plus a new anti-flush drug, to statin therapy demonstrated no additional benefit compared to a statin alone in myocardial infarction or stroke incidence in over 25,000 high risk men and women with CVD over a four-year period. In addition, niacin caused a significant number of expected and unexpected side effects. Previous side effects included hot flashes, flushing, gastrointestinal symptoms, increased uric acid, increased glucose and increased risk of developing diabetes. The trial identified infection and bleeding (gastrointestinal and intracranial) as side effects not demonstrated in earlier studies. Serious adverse effects included new onset diabetes, infection, bleeding and a trend toward increased heart failure. The trial was stopped prematurely for not meeting its primary endpoints.

Statin-Ezetimibe

The addition of ezetimibe to a statin significantly improves LDL-cholesterol over either agent alone. To date no large clinical trials have been completed evaluating the effect of this combination versus statin alone on clinical vascular endpoints.

Two recent trials cast doubt on the cardiovascular benefit of ezetimibe. In ENHANCE, the combination of ezetimibe-simvastatin versus simvastatin alone failed to show any benefit in carotid intima-media thickness (CIMT) despite greater LDL lowering. In ARBITER-6 ezetimibe was inferior to niacin in reducing CIMT, causing the trial to be halted after 14 months. Neither study reported data on vascular events *(Taylor, 2009)*.

Cholesterylester transfer protein (CETP) inhibitors

There are negative trials of CETP inhibitors and statins in combination on both CIMT and clinical endpoints. This drug class is not currently clinically available *(Cannon, 2010; Barter, 2007)*.

Bile acid or fish oils

No randomized control trials looking at clinical vascular endpoints are available for other agents such as fish oils or bile acid sequestrants used in combination therapy. Clinical trials of fish oil as a monotherapy have not shown benefits regarding cardiovascular endpoints.

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13. Initiate Fibrate Treatment

Management of Elevated Triglycerides and/or Low HDL

The link between triglycerides and CHD is complex and may be explained by the association of high triglycerides, low HDL-cholesterol and unusually atherogenic LDL-cholesterol. Elevated triglycerides also often reflect an increase in triglyceride-rich remnant lipoproteins that have atherogenic potential.

Patients with primarily triglyceride elevation and normal or moderately elevated cholesterol are candidates for treatment if there is evidence of cholesterol-rich VLDL and IDL (intermediate density lipoprotein) particles, typically found in patients with triglyceride levels between 200 and 499 mg/dL and occasionally between 500 and 1,000 mg/dL. If triglycerides are greater than 500, fibrates become first-line therapy. The clinician may wish to consider the use of statin therapy. This is especially true if there is a strong family history of CHD and dyslipidemia, such as familial combined hyperlipidemia, or if the patient has evidence of atherosclerotic disease. Treatment can also be supported in diabetics with or without low HDL-cholesterol. Shared decision-making and a full discussion of the risks and benefits of medication and patient preferences should be included before starting any medications.

Additional information on the ICSI Shared Decision-Making Model can be found on the ICSI Web site.

Patients with very high triglycerides (greater than 1,000 mg/dL) are at increased risk of hepatomegaly, splenomegaly, hepatic steatosis and pancreatitis, and are candidates for dietary and drug therapy. Patients with fasting triglycerides less than 1,000 mg/dL are at less immediate risk of pancreatitis. After ruling out or controlling for secondary causes (e.g., diabetes mellitus, hypothyroidism, chronic renal failure, alcohol abuse, hormone replacement therapy and/or oral contraceptives), the National Institutes of Health recommend dietary measures for initial management of borderline and high triglycerides (please see Appendix A, "Identified Secondary Causes and Conditions Associated with Hyperlipidemia," for additional secondary causes). If dietary and lifestyle modification (weight reduction if needed, decrease in alcohol, increase physical activity, smoking cessation) does not lower triglycerides to desired level, then drug therapy is indicated.

Uncontrolled glucose levels in patients with diabetes mellitus contribute to hypertriglyceridemia. Glucose levels in patients with diabetes should be under control to bring triglyceride levels under control.

When triglycerides are over 400 mg/dL, the LDL-cholesterol cannot be calculated and a direct measure of LDL, where available, is preferred. Although the LDL-cholesterol can be calculated when the triglycerides are moderately elevated (200-400 mg/dL), keep in mind that the LDL-cholesterol may be underestimated due to the Friedenwald equation.

LDL-cholesterol = Total cholesterol minus HDL-cholesterol minus (triglyceride divided by 5).

Non-HDL-cholesterol becomes a secondary target when triglycerides are 200-499. The non-HDL target is 30 mg/dL higher than the LDL target.

Non-HDL-cholesterol = total-cholesterol minus HDL-cholesterol.

(McKenney, 2001; National Cholesterol Education Program, 2001; Grundy, 1998)

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14. Reinforce Healthy Lifestyle

See Annotation #8.

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15. Laboratory Monitoring in 3-12 Months

Obtain a fasting lipid panel or lipid panel with direct LDL and transaminase as indicated (or see drug insert or drug companion) *(McKenney, 2001)*.

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16. Ongoing Care with Yearly Follow-Up

Adherence and Lifestyle Modifications

Poor adherence can limit the effectiveness of therapies. In asymptomatic conditions such as hyperlipidemia, this can be especially problematic. Long-term adherence to drug therapy for chronic conditions is estimated to be only about 50%. Adherence in clinical trials is often much higher, due to multiple factors including patient selection, close monitoring and educational efforts of medical staff.

Some factors associated with poor adherence are number of drugs, complexity and frequency of drug administration, adverse side effects, asymptomatic conditions, cost and psychosocial problems.

The first step is to identify potential non-adherence. Some signs of non-adherence include missed visits, inability to reach by phone, medication refill history, rescheduling of appointments, complaints about office visits, impatience during visits, failure to achieve therapeutic goals, and change in clinicians.

Suggested ways to improve adherence include asking about compliance in a non-threatening way at each visit; simplification of the drug regimen (frequency and complexity); reminder systems; drug-count devices; pill minders; involvement of family or friends; a health care team approach including nurses, dietitians, pharmacists and educators, in addition to physicians; written instructions; and educating the patient about the medications, including potential adverse effects, importance of therapy, realistic goals, necessity of lifelong treatment, and importance of continued attention to non-pharmacologic therapy (i.e., diet, exercise).

Additionally, the doctor-patient relationship can play a key role in improving compliance, in part through the physician's efforts to understand the patient's perspective on compliance.

Assess the patient's knowledge of his/her medication and medical condition:

> "Can you explain why you are taking this medication?"
>
> "How do you take your medication (with food or on an empty stomach; in the morning or the evening)?"

Assess the patient's medication administration process:

> "Many patients have difficulty remembering to take their medication. From what you recall, have you ever had trouble remembering to take your medications?"
>
> "How do you remember to take your medication each day? Do you use a reminder device such as a pillbox or alarm?"

Assess the patient's barriers to adherence:

> "What is the most difficult task for you in reaching your cholesterol goal?"
>
> "Are you comfortable with your ability to follow the treatment plan that we have designed for you?"
>
> "Are you experiencing any unusual symptoms that you fear may be due to your medication?"
>
> "Is the cost of your medications interfering with your treatment?"

For more information on adherence please refer to Appendix B, "NCEP Recommendations on Strategies to Improve Adherence."

(Riesen, 2004; Nichols-English, 2000; Insull, 1997)

Laboratory Monitoring

Coronary risk status and a lipid profile should be obtained at least annually *(McKenney, 2001; National Cholesterol Education Program, 2001)*.

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The Aims and Measures section is intended to provide protocol users with a menu of measures for multiple purposes that may include the following:

- population health improvement measures,
- quality improvement measures for delivery systems,
- measures from regulatory organizations such as Joint Commission,
- measures that are currently required for public reporting,
- measures that are part of Center for Medicare Services Physician Quality Reporting initiative, and
- other measures from local and national organizations aimed at measuring population health and improvement of care delivery.

This section provides resources, strategies and measurement for use in closing the gap between current clinical practice and the recommendations set forth in the guideline.

The subdivisions of this section are:

- Aims and Measures
- Implementation Recommendations
- Implementation Tools and Resources
- Implementation Tools and Resources Table

Aims and Measures

1. Increase the percentage of patients with:

   (a) established ASCVD: CHD, PAD or stroke presumed of atherosclerotic origin, or

   (b) a 10-year risk for CHD ≥ 10%, or

   (c) diabetes who are on a statin **OR** have LDL < 100 ml/dL within a 12-month period. *(Annotations #3, 12)*

   Measure for accomplishing this aim:

   Outcome measure

   a. Percentage of patients with:

      - established ASCVD: CHD, PAD or stroke presumed of atherosclerotic origin, or
      - whose 10-year risk for CHD ≥ 10%, or
      - diabetes who are on a statin **OR** have LDL < 100 ml/dL within a 12-month period. *(Annotations #3, 12)*

2. Increase the percentage of patients with established ASCVD or 10-year CHD risk ≥ 10% or diabetes and on lipid-lowering therapy who remain on the medication therapy. *(Annotations #3, 12, 16)*

   Measure for accomplishing this aim:

   a. Percentage of patients with established ASCVD, or 10-year CHD risk ≥ 10%, or diabetes and on lipid-lowering medication who has a fasting lipid panel within 24 months of medicaion prescription.

   b. Percentage of patints with (a) established ASCVD, or (b) with 10-year CHD risk ≥ 10%, or (c) diabetes, (d) on lipid-lowering medication, and (e) most recent LDL > 100 mg/dL, who are prescribed a maximal recommended dose of a potent statin (such as simvastatin, pitavistatin, rosuvastatin or atorvastatin).

3. Increase the percentage of patients with established ASCVD or 10-year CHD risk ≥ 10%, or diabetes, and on lipid-lowering therapy who remain on the medication therapy. *(Annotations #3, 12, 16)*

   Measure for accomplishing this aim:

   a. Percentage of patients with established ASCVD, or 10-year CHD risk ≥ 10%, or diabetes (diabetes, peripheral arterial disease, occlusive carotid disease, abdominal aortic aneurysm) and on lipid-lowering therapy who remain on lipid-lowering therapy 12 months after therapy was prescribed.

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Measurement Specifications

Measurement #1a

Percentage of patients with:

(a) established ASCVD: CHD, PAD or stroke presumed of atherosclerotic origin, or

(b) a 10-year risk for CHD ≥ 10%, or

(c) diabetes, who are on a statin **OR** have LDL < 70 ml/dL within a 12-month period.

Population Definition

Patients with (a) established ASCVD, (b) 10-year risk for CHD ≥ 10%, or (c) diabetes.

Data of Interest

$$\frac{\text{\# of patients on a statin therapy OR have LDL < 100 mg/dL}}{\text{\# of patients as specified in the population definition}}$$

Numerator/Denominator Definitions

Numerator: Patients who are on a statin therapy **OR** have LDL < 100 mg/dL.

Denominator: Patients with (a) established ASCVD, (b) 10-year risk for CHD ≥ 10%, or (c) diabetes.

Method/Source of Data Collection

Query EMR for patients in the clinic's panel and who fit the denominator criteria. Of those patients who fit denominator criteria, find the number of patients who are on a statin therapy **OR** have LDL < 100 mg/dL within a 12-month period.

Time Frame Pertaining to Data Collection

Semi-annually.

Notes

This is an outcome measure, and improvement is associated with a higher score.

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Measurement #2a

Percentage of patients established ASCVD, or 10-year CHD risk ≥ 10%, or diabetes and on lipid-lowering medication who have a fasting lipid panel within 24 months of medication prescription.

Population Definition

Patients with (a) established ASCVD, (b) 10-year CHD risk ≥ 10%, or (c) diabetes.

Data of Interest

$$\frac{\text{\# of patients on who have a fasting lipid panel within 24 months}}{\text{\# of patients as specified in the population definition}}$$

Numerator/Denominator Definitions

Numerator: Patients who have a fasting lipid panel within 24 months of prescription for lipid-lowering medication.

Denominator: Patients with (a) established ASCVD, (b) 10-year CHD risk ≥ 10%, or (c) diabetes.

Method/Source of Data Collection

Query EMR for patients seen in the clinic in the last 24 months and who fit denominator criteria. Then of those patients who fit denominator criteria, find the number of patients who had fasting lipid panel within 24 months of prescription for lipid lowering medication.

Time Frame Pertaining to Data Collection

Monthly.

Notes

This is a process measure, and improvement is associated with a higher score.

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Measurement #2b

Percentage of patients with:

(a) established ASCVD, or

(b) a 10-year CHD risk ≥ 10% or,

(c) diabetes

(d) on lipid-lowering medication, and

(d) most recent LDL > 100 mg/dL, who are prescribed a maximal recommended dose of a potent statin (such as simvastatin, pitavistatin, rosuvastatin or atorvastatin).

Population Definition

Patients with (a) established ASCVD, or (b) 10-year CHD risk ≥ 10%, or (c) diabetes, most recent LDL > 100 mg/dL and are prescribed lipid-lowering medication.

Data of Interest

$$\frac{\text{\# of patients on a maximal recommended dose of a potent statin}}{\text{\# of patients as specified in the population definition}}$$

Numerator/Denominator Definitions

Numerator: Patients with LDL > 100 who are prescribed a maximal recommended dose of a potent statin.

Denominator: Patients with (a) established ASCVD, or (b) 10-year CHD risk ≥ 10%, or (c) diabetes and most recent LDL > 100 mg/dL and are prescribed lipid-lowering medication.

Method/Source of Data Collection

Query EMR for patients seen in the clinic in the last 12 months and who fit denominator criteria. Then of those patients who fit denominator criteria, find the number of patients who were prescribed a maximal dose of a potent statin (such as simvastatin, pitavistatin, rosuvastatin, or atorvastatin).

Time Frame Pertaining to Data Collection

Annually.

Notes

This is a process measure, and improvement is associated with a higher score.

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Measurement #3a

Percentage of patients with established ASCVD, or 10-year CHD risk ≥ 10%, or diabetes and on lipid-lowering therapy who remain on lipid-lowering pharmacotherapy 12 months after therapy was prescribed.

Population Definition

Patients with (a) established ASCVD, or (b) 10-year CHD risk ≥ 10%, or (c) diabetes, and are prescribed lipid-lowering pharmacotherapy.

Data of Interest

$$\frac{\text{\# of patients who remain on pharmacotherapy 12 months after therapy was prescribed}}{\text{\# of patients as specified in the Population Definition}}$$

Numerator/Denominator Definitions

Numerator: Patients who remain on pharmacotherapy 12 months after therapy was prescribed.

Denominator: Patients with (a) established ASCVD, (b) 10-year CHD risk ≥ 10%, or (c) diabetes, and are prescribed lipid-lowering medication.

Method/Source of Data Collection

Query EMR for patients seen in the clinic in the last 12 months and who fit denominator criteria. Then of those patients who fit denominator criteria, find the number of patients who remained on pharmacotherapy 12 months after therapy was prescribed.

Time Frame Pertaining to Data Collection

Annually.

Notes

This is a process measure, and improvement is associated with a higher score.

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The subdivisions of this section are:

- References
- Appendices

References

Links are provided for those new references added to this edition (author name is highlighted in blue).

Albert CM, Ma J, Rifai N, et al. Prospective study of c-reactive protein, homocysteine, and plasma lipid levels as predictors of sudden cardiac death. *Circulation* 2002;105:2595-99. (Reference)

ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group, The. Major outcomes in moderately hypercholesterolemic, hypertensive patients randomized to pravastatin vs usual care: the antihypertensive and lipid-lowering treatment to prevent heart attack trial (ALLHAT-LLT). *JAMA* 2002;288:2998-3007. (Reference)

Appel LJ, Sacks FM, Carey VJ, et al. Effects of protein, monounsaturated fat, and carbohydrate intake on blood pressure and serum lipids: results of the omniheart randomized trial. *JAMA* 2005;294:2455-64. (Reference)

Arntzenius AC, Kromhout D, Barth JD, et al. Diet, lipoproteins, and the progression of coronary atherosclerosis: the Leiden intervention trial. *N Engl J Med* 1985;312:805-11. (Reference)

Baigent C, Landray MJ, Reith C, et al. The effects of lowering LDL cholesterol with simvastatin plus ezetimibe in patients with chronic kidney disease (study of heart and renal protection): a randomised placebo-controlled trial. *Lancet* 2011;377:2181-92. (Reference)

Ballantyne CM, Corsini A, Davidson MH, et al. Risk for myopathy with statin therapy in high-risk patients. *Arch Intern Med* 2003;163:553-64. (Reference)

Barter PJ, Caulfield M, Eriksson M, et al. Effects of torcetrapib in patients at high risk for coronary events. *N Engl J Med* 2007;357:2109-22. (Reference)

Berg A, Frey I, Baumstark MW, et al. Physical activity and lipoprotein lipid disorders. *Sports Med* 1994;17:6-21. (Reference)

Billimoria JD, Pozner H, Metselaar B, et al. Effect of cigarette smoking on lipids, lipoproteins, blood coagulation, fibrinolysis and cellular components of human blood. *Artherosclerosis* 1975;21:61-76. (Reference)

Blankenhorn DH, Johnson RL, Mack WJ, et al. The influence of diet on the appearance of new lesions in human coronary arteries. *JAMA* 1990;263:1646-52. (Reference)

Brown BG, Zhao XQ, Chait A, et al. Simvastatin and niacin, antioxidant vitamins, or the combination for the prevention of coronary disease. *N Engl J Med* 2001;345:1583-92. (Reference)

Bucher HC, Hengstler P, Schindler C, Meier G. N-3 polyunsaturated fatty acids in coronary heart disease: a meta-analysis of randomized controlled trials. *Am J Med* 2002;112:298-304. (Reference)

Canner PL, Berge KG, Wenger NK, et al. Fifteen year mortality in coronary drug project patients: long-term benefit with niacin. *JACC* 1986;8:1245-55. (Reference)

Cannon CP, Braunwald E, McCabe CH, et al. Intensive versus moderate lipid-lowering with statins after acute coronary syndromes. *N Engl J Med* 2004;350:1495-504. (Reference)

Cannon CP, Shah S, Dansky HM, et al. Safety of anacetrapib in patients with or at high risk for coronary heart disease. *N Engl J Med* 2010;363:2406-15. (Reference)

Cheung MC, Zhao XQ, Chait A, et al. Antioxidant supplements block the response of HDL to simvastatin-niacin therapy in patients with coronary artery disease and low HDL. *Arterioscler Thromb Vasc Biol* 2001;21:1320-26. (Reference)

Return to Table of Contents

Cholesterol Treatment Trialists' (CTT) Collaborators, Mihaylova B, Emberson J, et al. The effects of lowering LDL cholesterol with statin therapy in people at low risk of vascular disease: meta-analysis of individual data from 27 randomised trials. *Lancet* 2012;380:581-90. (Meta-analysis)

Cook JM, O'Donnell C, Dinnen S, et al. Measurement of a model of implementation for health care: toward a testable theory. *Implement Sci* 2012;7:59. (Reference)

Coronary Drug Project Research Group, The. Clofibrate and niacin in coronary heart disease. *JAMA* 1975;231:360-81. (Reference)

Criqui MH. The reduction of coronary heart disease with light to moderate alcohol consumption: effect or artifact? *Br J Addict* 1990;85:854-57. (Reference)

Denke MA. Revisiting the effectiveness of the National Cholesterol Education Program's Step I and Step II Diets: cholesterol-lowering diets in a pharmaceutically driven world. *Am J Clin Nutr* 1999;69:581-82. (Reference)

Downs JR, Clearfield M, Weis S, et al. Primary prevention of acute coronary events with lovastatin in men and women with average cholesterol levels: results of AFCAPS/TexCAPS. *JAMA* 1998;279:1615-22. (High Quality Evidence)

Dujovne CA, Ettinger MP, McNeer JF, et al. Efficacy and safety of a potent new selective cholesterol absorption inhibitor, ezetimibe, in patients with primary hypercholesterolemia. *Am J Cardiol* 2002;90:1092-97. (Reference)

Fellström BC, Jardine AG, Schmieder RE, et al. Rosuvastatin and cardiovascular events in patients undergoing hemodialysis. *N Engl J Med* 2009;360:1395-407. (Reference)

Frick MH, Elo O, Haapa K, et al. Helsinki heart study: primary-prevention trial with gemfibrozil in middle-aged men with dyslipidemia. *N Engl J Med* 1987;317:1237-45. (Reference)

Fung TT, Malik V, Rexrode KM, et al. Sweetened beverage consumption and risk of coronary heart disease in women. *Am J Clin Nutr* 2009;89:1037-42. (Reference)

Gagne C, Bays HE, Weiss SR, et al. Efficacy and safety of ezetimibe added to ongoing statin therapy for treatment of patients with primary hypercholesterolemia. *Am J Cardiol* 2002;90:1084-91. (High Quality Evidence)

Goldberg RB, Mellies MJ, Sacks FM, et al. Cardiovascular events and their reduction with pravastatin in diabetic and glucose-intolerant myocardial infarction survivors with average cholesterol levels: subgroup analyses in the Cholesterol and Recurrent Events (CARE) Trial. *Circulation* 1998;98:2513-19. (Moderate Quality Evidence)

Grundy SM. Consensus statement: role of therapy with 'statins' in patients with hypertriglyceridemia. *Am J Cardiol* 1998;81:1B-6B. (Reference)

Grundy SM. Stanol esters as a component of maximal dietary therapy in the national cholesterol education program adult treatment panel III report. *J Cardiol* 2005;96:47D-50D. (Reference)

Gylling H, Miettinen TA. Serum cholesterol and cholesterol and lipoprotein metabolism in hyper cholesterolaemic NIDDM patients before and during sitostanol ester-margarine treatment. *Diabetologia* 1994;37:773-80. (Low Quality Evidence)

Gylling H, Radhakrishan R, Miettinnen TA. Reduction of serum cholesterol in postmenopausal women with previous myocardial infarction and cholesterol malabsorption induced by dietary sitostanol ester margarine. *Circulation* 1997;96:4226-31. (Moderate Quality Evidence)

Heart Protection Study Collaborative Group. MRC/BHF heart protection study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial. *Lancet* 2002;360:7-22. (High Quality Evidence)

Return to Table of Contents

Hellerstein MK. Carbohydrate-induced hypertriglyceridemia: modifying factors and implications for cardiovascular risk. *Curr Opin Lipidol* 2002;13:33-40. (Reference)

Holdaas H, Holme I, Schmieder RE, et al. Rosuvastatin in diabetic hemodialysis patients. *J Am Soc Nephrol* 2011;22:1335-41. (Reference)

HPS2-THRIVE Collaborative Group. HPS2-THRIVE randomized placebo-controlled trial in 25,673 high-risk patients of ER niacin/laropiprant: trial design, pre-specified muscle and liver outcomes, and reasons for stopping study treatment. *Eur Heart J* 2013;34:1279-91. (High Quality Evidence)

Insull W. The problem of compliance to cholesterol altering therapy. *J Intern Med* 1997;241:317-25. (Reference)

Jackson R, Beaglehole R. The relationship between alcohol and coronary heart disease: is there a protective effect? *Curr Opin Lipidol* 1993;4:21-26. (Reference)

Jacobson TA. Toward "pain-free" statin prescribing: clinical algorithm for diagnosis and management of myalgia. *Mayo Clin Proc* 2008;83:687-700. (Reference)

Johnson RK, Appel LJ, Brands M, et al. Dietary sugars intake and cardiovascular health: a scientific statement from the American heart association. *Circulation* 2009;120:1011-20. (Reference)

Kastelein JJP, Akdim F, Stroes ESG, et al. Simvastatin with or without ezetimibe in familial hypercholesterolemia. *N Engl J Med* 2008;358:1431-43. (Reference)

Klatsky AL, Friedman GD, Siegelaub AB. Alcohol and mortality: a 10-year Kaiser-Permanente experience. *Ann Intern Med* 1981;95:139-45. (Reference)

Kris-Etherton PM, Harris WS, Appel LJ. Fish consumption, fish oil, omega-3 fatty acids, and cardiovascular disease. *Circulation* 2002;106:2747-57. (Reference)

LaRosa JC, Jiang H, Vupputuri S. Effect of statins on risk of coronary disease: a meta-analysis of randomized controlled trials. *JAMA* 1999;282:2340-46. (Meta-analysis)

Levy D. A multifactorial approach to coronary disease risk assessment. *Clin Exp Hypertens* 1993;15:1077-86. (Reference)

Lipid Research Clinics Program. The lipid research clinics coronary primary prevention trial results. I. Reduction in incidence of coronary heart disease. *JAMA* 1984;251:351-64. (Reference)

LIPID Study Group, The. Prevention of cardiovascular events and death with pravastatin in patients with coronary heart disease and a broad range of initial cholesterol levels. *New Engl J Med* 1998;339:1349-57. (High Quality Evidence)

März W, Genser B, Drechsler C, et al. Atorvastatin and low-density lipoprotein cholesterol in type 2 diabetes mellitus patients on hemodialysis. *Clin J Am Nephrol* 2011;6:1316-25. (Reference)

Mazza D, Bairstow P, Buchan H, et al. Refining a taxonomy for guideline implementation: results of an exercise in abstract classification. *Implement Sci* 2013;8:32. (Reference)

McBride PE. The health consequences of smoking: cardiovascular diseases. *Med Clin North Am* 1992;76:333-53. (Reference)

McKenney J. Combination therapy for elevated low-density lipoprotein cholesterol: the key to coronary artery disease risk reduction. *Am J Cardiol* 2002;90:8K-20K. (Reference)

McKenney JM, Davidson MH, Jacobson TA, Guyton JR. Final conclusions and recommendations of the national lipid association statin safety assessment task force. *Am J Cardiol* 2006;97:89C-94C. (Reference)

Return to Table of Contents

McKenney JM, Hawkins DW. Management of lipid disorders. *In* Handbook on the Management of Lipid Disorders 2nd Edition. Richmond, VA: National Pharmacy Cholesterol Council, 2001. (Reference)

Mensink RP, Zock PL, Kester ADM, Katan MB. Effects of dietary fatty acids and carbohydrates on the ratio of serum total to HDL cholesterol and on serum lipids and apolipoproteins: a meta-analysis of 60 controlled trials. *Am J Clin Nutr* 2003;77:1146-55. (Reference)

Miettinen TA, Puska H, Gylling H, et al. Reduction of serum cholesterol with sitostanol-ester margarine in a mildly hypercholesterolemic population. *New Engl J Med* 1995;333:1308-12. (Low Quality Evidence)

National Cholesterol Education Program. Detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III) National Institutes of Health. 2001. (Guideline)

National Cholesterol Education Program. Third report of the national cholesterol education program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III) final report. *Circulation* 2002;106:3143-421. (Guideline)

Nichols-English G, Poirier S. Optimizing adherence to pharmaceutical care plans. *J Am Pharm Assoc* 2000;40:475-85. (Reference)

Nissen SE, Tuzcu EM, Schoenhagen P, et al. Effect of intensive compared with moderate lipid-lowering therapy on progression of coronary atherosclerosis: a randomized controlled trial. *JAMA* 2004;291:1071-80. (Reference)

Ornish D, Brown SE, Scherwitz LW, et al. Can lifestyle changes reverse coronary heart disease? *Lancet* 1990;336:129-33. (High Quality Evidence)

Palmer SC, Craig JC, Navaneethan SD, et al. Benefits and harms of statin therapy for persons with chronic kidney disease: a systematic review and meta-analysis. *Ann Intern Med* 2012;157:263-75. (Reference)

Physicians' Health Study Research Group, Steering Committee of the. Final report on the aspirin component of the ongoing physicians' health study. *N Engl J Med* 1989;321:129-35. (Reference)

Pignone M, Phillips C, Mulrow C. Use of lipid-lowering drugs for primary prevention of coronary heart disease: meta-analysis of randomised trials. *BMJ* 2000;321:1-5. (Meta-analysis)

Pronk NP. Short term effects of exercise on plasma lipids and lipoproteins in humans. *Sports Med* 1993;16:431-48. (Reference)

Ridker PM, Danielson E, Fonseca FAH, et al. Rosuvastatin to prevent vascular events in men and women with elevated C-reactive protein. *N Engl J Med* 2008;359:2195-207. (Reference)

Riesen WF, Darioli R, Noll G. Lipid-lowering therapy: strategies for improving compliance. *Curr Med Res Opin* 2004;20:165-73. (Reference)

Rimm EB, Klatsky A, Grobbee D, et al. Review of moderate alcohol consumption and reduced risk of coronary heart disease: is the effect due to beer, wine, or spirits? *BMJ* 1996;312:731-36. (Reference)

Rossebø AB, Pedersen TR, Boman K, et al. Intensive lipid lowering with simvastatin and ezetimibe in aortic stenosis. *N Engl J Med* 2008;359:1343-56. (Reference)

Rycroft-Malone J, Seers K, Chandler J, et al. The role of evidence, context, and facilitation in an implementation trial: implications for the development of the PARIHS framework. *Implement Sci* 2013;8:28. (Reference)

Scandinavian Simvastatin Survival Study Group. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). *Lancet* 1994;344:1383-89. (Reference)

Return to Table of Contents

Schuler G, Hambrecht R, Schlierf G, et al. Regular physical exercise and low-fat diet: effects on progression of coronary artery disease. *Circulation* 1992;86:1-11. (High Quality Evidence)

Sever PS, Dahlöf B, Poulter NR, et al. Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower-than-average cholesterol concentrations, in the Anglo-Scandinavian cardiac outcomes trial – lipid lowering arm (ASCOT-LLA): a multicentre randomised controlled trial. *Lancet* 2003;361:1149-58. (High Quality Evidence)

Sharma M, Ansari MT, Abou-Setta AM, et al. Systematic review: comparative effectiveness and harms of combination therapy and monotherapy for dyslipidemia. *Ann Intern Med* 2009;151:622-30. (Systematic Review)

Shepherd J, Blauw GJ, Murphy BM, et al. Pravastatin in elderly individuals at risk of vascular disease (PROSPER): a randomised controlled trial. *Lancet* 2002;360:1623-30. (High Quality Evidence)

Shepherd J, Cobbe SM, Ford I, et al. Prevention of coronary heart disease with pravastatin in men with hypercholesterolemia. *N Engl J Med* 1995;333:1301-07. (High Quality Evidence)

Stalenhoef AFH, de Graaf J, Wittekoek ME, et al. The effect of concentrated n-3 fatty acids versus gemfibrozil on plasma lipoproteins, low density lipoprotein heterogeneity and oxidizability in patients with hypertrigliceridemia. *Artherosclerosis* 2000;153:129-38. (Reference)

Stamler J, Wentworth D, Neaton JD. Is relationship between serum cholesterol and risk of premature death from coronary heart disease continuous and graded? Findings in 356,222 primary screenees of the multiple risk factor intervention trial (MRFIT). *JAMA* 1986;256:2823-28. (Low Quality Evidence)

Stefanick ML, Mackey S, Sheehan M, et al. Effects of diet and exercise in men and postmenopausal women with low levels of HDL-cholesterol and high levels of LDL-cholesterol. *N Engl J Med* 1998;339:12-20. (High Quality Evidence)

Stone NJ. Secondary causes of hyperlipidemia. *Med Clin North Am* 1994;78:117-41. (Reference)

Taylor AJ, Villines TC, Stanek EJ, et al. Extended-release niacin or ezetimibe and carotid intima-media thickness. *N Engl J Med* 2009;361:2113-22. (Reference)

Taylor F, Huffman MD, Macedo AF, et al. Statins for the primary prevention of cardiovascular disease. *Cochrane Database Syst Rev* 2013;1:CD004816. (High Quality Evidence)

Taylor PA, Ward A. Women, high-density lipoprotein cholesterol, and exercise. *Arch Intern Med* 1993;153:1178-84. (Reference)

Tricco AC, Ivers NM, Grimshaw JM, et al. Effectiveness of quality improvement strategies on the management of diabetes: a systematic review and meta-analysis. *Lancet* 2012;379:2252-61. (Reference)

Upadhyay A, Earley A, Lamont JL, et al. Lipid-lowering therapy in persons with chronic kidney disease: a systematic review and meta-analysis. *Ann Intern Med* 2012;157:251-62. (Reference)

Vanhanen HT, Blomqvist S, Enholm C, et al. Serum cholesterol, cholesterol precursors, and plant sterols in hypercholesterolemic subjects with different apoE phenotypes during dietary sitostanol ester treatment. *J Lipid Res* 1993;34:1535-44. (Moderate Quality Evidence)

West of Scotland Coronary Prevention Group. Influence of pravastatin and plasma lipids on clinical events in the West of Scotland Coronary Prevention Study (WOSCOPS). *Circulation* 1998;97:1440-45. (High Quality Evidence)

Williams PT. Relationship of distance run per week to coronary heart disease risk factors in 8,283 male runners. *Arch Intern Med* 1997;157:191-98. (Reference)

Yusuf S, Hawken S, Óunpuu S, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. *Lancet* 2004;364:937-52. (Low Quality Evidence)

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Appendix A – Identified Secondary Causes and Conditions Associated with Hyperlipidemia

	Cholesterol	Triglyceride	HDL-Cholesterol
Drugs			
Antihypertensives:			
Thiazides	Increase	Increase	
Loop diuretic			Decrease
Beta-blockers		Increase	Increase/Decrease
Hormones:			
Glucocorticoids	Increase	Increase	
Anabolic steroids	Increase		Increase
Oral contraceptives	Increase/Decrease	Increase	Increase/Decrease
Estrogens	Decrease	Increase	Increase
Progestins	Increase		Decrease
Growth hormone		Increase	
Others:			
Amiodarone	Increase		
Isotretinoin	Increase	Increase	Decrease
Cyclosporine	Increase		
Diseases/Conditions			
Metabolic/Endocrine:			
Diabetes (esp NIDDM)	Increase	Increase	Decrease
Hypothyroidism	Increase	Increase	
Anorexia nervosa	Increase		
Obesity	Increase	Increase	Decrease
Pregnancy	Increase	Increase	
Acromegaly		Increase	
Hyperuricemia/gout	Increase	Decrease	
Liver Disorders:			
Hepatocellular	Increase	Decrease	
Cholestasis	Increase		Decrease
Renal Diseases:			
Nephrotic syndrome	Increase	Increase	Decrease
Chronic renal failure	Increase/Decrease	Increase/Decrease	Decrease
Others:			
SLE	Increase	Increase	
Rheumatoid arthritis	Decrease	Decrease	Increase
Pancreatitis		Increase	
Dietary Factors			
Alcohol abuse		Increase	Increase
High-fat diet	Increase	Increase	
Low-fat diet	Decrease	Decrease	Decrease
High-cholesterol diet	Increase		
Weight gain		Increase	
Very high-fiber diet	Decrease		

(McKenney, 2001; Stone, 1994)

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Appendix B – NCEP Recommendations on Strategies to Improve Adherence

The ATPIII guideline "Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults," includes recommendations on strategies to improve adherence by patients and clinicians. Adult Treatment Panel III (ATPIII) guideline recommends the use of state-of-the-art multidisciplinary methods that target the patients, clinicians and health delivery systems to achieve maximum adherence to primary and secondary prevention efforts. The following table summarizes the ATPIII recommendations regarding adherence.

Interventions to Improve Adherence

Focus on the Patient

- Simplify medication regimens
- Provide explicit patient instruction and use good counseling techniques to teach the patient how to follow the prescribed treatment
- Encourage the use of prompts to help patients remember treatment regimens
- Use systems to reinforce adherence and maintain contact with the patient
- Encourage the support of family and friends
- Reinforce and reward adherence
- Increase visits for patients unable to achieve treatment goal
- Increase the convenience and access to care
- Involve patients in their care through self-monitoring

Focus on the Physician and Medical Office

- Teach physicians to implement lipid treatment guidelines
- Use reminders to prompt physicians to attend to lipid management
- Identify a patient advocate in the office to help deliver or prompt care
- Use patients to prompt preventive care
- Develop a standardized treatment plan to structure care
- Use feedback from past performance to foster change in future care
- Remind patients of appointments and follow up missed appointments

Focus on the Health Delivery System

- Provide lipid management through a lipid clinic
- Utilize case management by nurses
- Deploy telemedicine
- Utilize the collaborative care of pharmacists
- Execute critical care pathways in hospitals

Source: *(National Cholesterol Education Program, 2001)*

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ICSI has long had a policy of transparency in declaring potential conflicting and competing interests of all individuals who participate in the development, revision and approval of ICSI guidelines and protocols.

In 2010, the ICSI Conflict of Interest Review Committee was established by the Board of Directors to review all disclosures and make recommendations to the board when steps should be taken to mitigate potential conflicts of interest, including recommendations regarding removal of work group members. This committee has adopted the Institute of Medicine Conflict of Interest standards as outlined in the report, Clinical Practice Guidelines We Can Trust (2011).

Where there are work group members with identified potential conflicts, these are disclosed and discussed at the initial work group meeting. These members are expected to recuse themselves from related discussions or authorship of related recommendations, as directed by the Conflict of Interest committee or requested by the work group.

The complete ICSI policy regarding Conflicts of Interest is available at http://bit.ly/ICSICOI.

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ICSI facilitates and coordinates the guideline development and revision process. ICSI, member medical groups and sponsoring health plans review and provide feedback but do not have editorial control over the work group. All recommendations are based on the work group's independent evaluation of the evidence.

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All ICSI documents are available for review during the revision process by member medical groups and sponsors. In addition, all members commit to reviewing specific documents each year. This comprehensive review provides information to the work group for such issues as content update, improving clarity of recommendations, implementation suggestions and more. The specific reviewer comments and the work group responses are available to ICSI members at http://www.LipidMgmt.

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Acknowledgements

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ICSI Document Development and Revision Process

Overview

Since 1993, the Institute for Clinical Systems Improvement (ICSI) has developed more than 60 evidence-based health care documents that support best practices for the prevention, diagnosis, treatment or management of a given symptom, disease or condition for patients.

Audience and Intended Use

The information contained in this ICSI Health Care Guideline is intended primarily for health professionals and other expert audiences.

This ICSI Health Care Guideline should not be construed as medical advice or medical opinion related to any specific facts or circumstances. Patients and families are urged to consult a health care professional regarding their own situation and any specific medical questions they may have. In addition, they should seek assistance from a health care professional in interpreting this ICSI Health Care Guideline and applying it in their individual case.

This ICSI Health Care Guideline is designed to assist clinicians by providing an analytical framework for the evaluation and treatment of patients, and is not intended either to replace a clinician's judgment or to establish a protocol for all patients with a particular condition.

Document Development and Revision Process

The development process is based on a number of long-proven approaches and is continually being revised based on changing community standards. The ICSI staff, in consultation with the work group and a medical librarian, conduct a literature search to identify systematic reviews, randomized clinical trials, meta-analysis, other guidelines, regulatory statements and other pertinent literature. This literature is evaluated based on the GRADE methodology by work group members. When needed, an outside methodologist is consulted.

The work group uses this information to develop or revise clinical flows and algorithms, write recommendations, and identify gaps in the literature. The work group gives consideration to the importance of many issues as they develop the guideline. These considerations include the systems of care in our community and how resources vary, the balance between benefits and harms of interventions, patient and community values, the autonomy of clinicians and patients and more. All decisions made by the work group are done using a consensus process.

ICSI's medical group members and sponsors review each guideline as part of the revision process. They provide comment on the scientific content, recommendations, implementation strategies and barriers to implementation. This feedback is used by and responded to by the work group as part of their revision work. Final review and approval of the guideline is done by ICSI's Committee on Evidence-Based Practice. This committee is made up of practicing clinicians and nurses, drawn from ICSI member medical groups.

Implementation Recommendations and Measures

These are provided to assist medical groups and others to implement the recommendations in the guidelines. Where possible, implementation strategies are included that have been formally evaluated and tested. Measures are included that may be used for quality improvement as well as for outcome reporting. When available, regulatory or publicly reported measures are included.

Document Revision Cycle

Scientific documents are revised every 12-24 months as indicated by changes in clinical practice and literature. ICSI staff monitors major peer-reviewed journals every month for the guidelines for which they are responsible. Work group members are also asked to provide any pertinent literature through check-ins with the work group midcycle and annually to determine if there have been changes in the evidence significant enough to warrant document revision earlier than scheduled. This process complements the exhaustive literature search that is done on the subject prior to development of the first version of a guideline.

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