Blue Cross Blue Shield of Rhode Island

2015 PRACTICE GUIDELINES
HYPERLIPIDEMIA

PURPOSE:
Recommendations for treatment of Blood Cholesterol to reduce Atherosclerotic Cardiovascular Disease (ASCVD) risk in adults. Focus is placed on the appropriate intensity of statin therapy with a move away from specific LDL target values. Emphasis is placed on heart healthy lifestyle and dietary habits as the foundation for reducing ASCVD risk.

OVERVIEW:
This guideline describes assessment of risk factors, screening for hyperlipidemia, and treatment of hyperlipidemia for adult risk groups, based on latest guidance (2013) developed by the American College of Cardiologists and American Heart Association

PRACTICE GUIDELINE:
The practice guideline is based on the 2013 guidance Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Disease in Adults released by the American College of Cardiologists (ACC) and American Heart Association(AHA) developed in conjunction with the National Heart Lung, and Blood Institute.

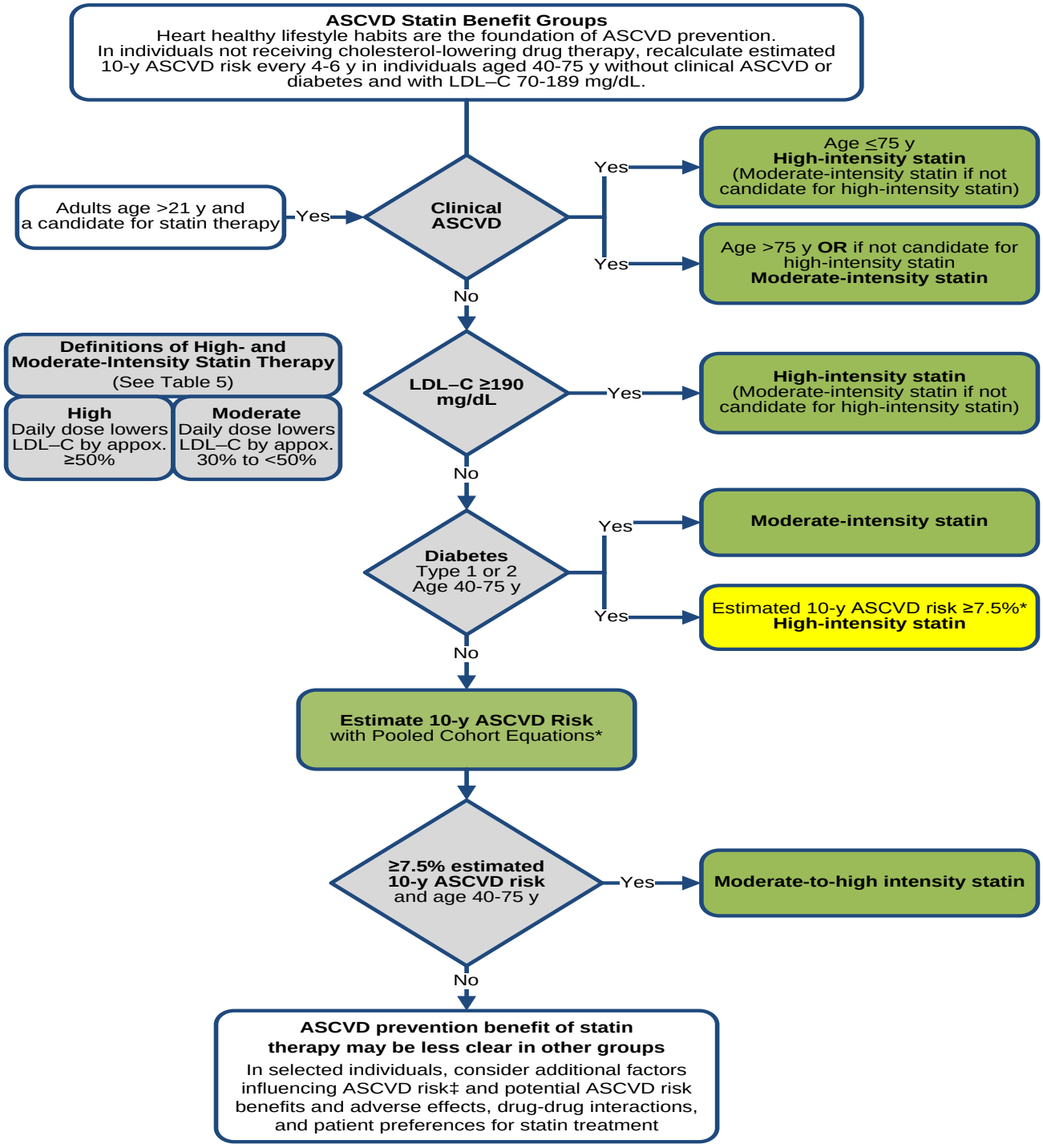
Major Recommendations:

A. Guideline is based on a comprehensive set of data from randomized control trials(RCT's) from which 4 statin benefit groups were identified that focus efforts to reduce ASCVD events in secondary and primary prevention. Focus is on Atherosclerotic Cardiovascular Disease (ASCVD Risk) Reduction: 4 Statin Benefit Groups

    1. Identification of 4 Statin Benefit Groups- in which the potential for an ASCVD risk reduction benefit clearly exceeds the potential for adverse effects in adults with:

        a. Individuals with clinical ASCVD
        b. Individuals with primary elevations of LDL-C greater than or equal to 190 mg/dL.
        c. Individuals 40 – 75 years of age with diabetes with LDL-C of 70 – 189mg/dL.
        d. Individuals without clinical ASCVD or diabetes who are 40 to 75 years of age with LDL-C70-189md/dL and an estimated 10 year ASCVD risk of 7.5% or higher.

B. Guideline identifies high intensity and moderate intensity statin therapy for use in secondary and primary prevention.



Colors correspond to the class of recommendations in the ACC/AHA Table 1. This flow diagram is intended to serve as an easy reference guide summarizing recommendations for ASCVD risk assessment and treatment. Assessment of the potential for benefit and risk from statin therapy for ASCVD prevention provides the *framework* for clinical decision making incorporating patient preferences.

AHA/ACC. Table 5. High- Moderate- and Low-Intensity Statin Therapy Used in the Randomized Control Trial's (RCTs)reviewed by the Expert Panel)*

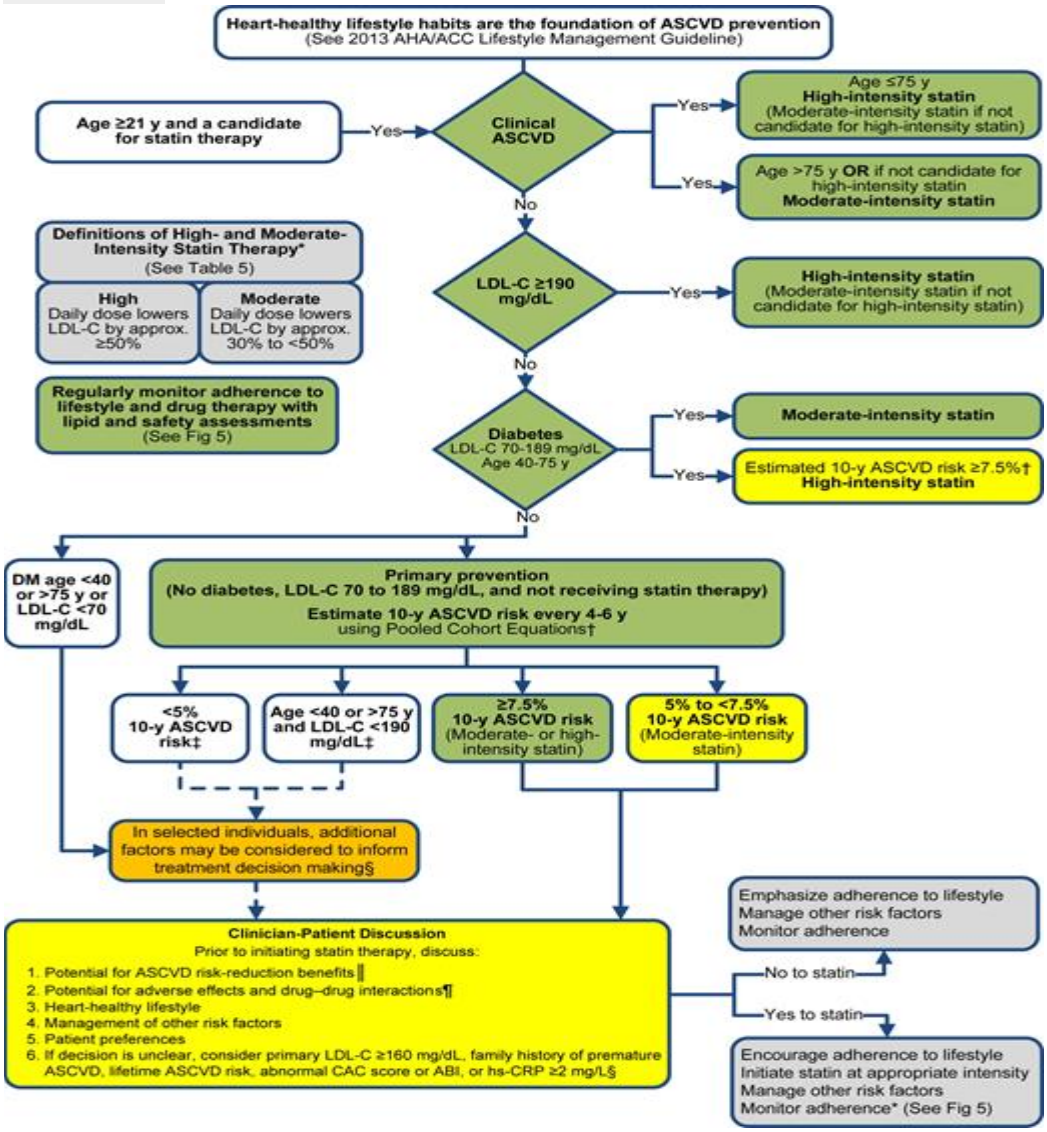
High-Intensity Statin Therapy	Moderate-Intensity Statin Therapy	Low-Intensity Statin Therapy
Daily dose lowers LDL–C by approximately ≥50%	Daily dose lowers LDL–C by approximately 30% to <50%	Daily dose lowers LDL–C by <30%
Atorvastatin (40†)–80 mg **Rosuvastatin 20** *(40)* **mg**	**Atorvastatin 10** *(20)* **mg** **Rosuvastatin** (*5*) **10 mg** **Simvastatin 20–40 mg‡** **Pravastatin 40** *(80)* **mg** **Lovastatin 40 mg** *Fluvastatin XL 80 mg* **Fluvastatin 40 mg bid** *Pitavastatin 2–4 mg*	*Simvastatin 10 mg* **Pravastatin 10–20 mg** **Lovastatin 20 mg** *Fluvastatin 20–40 mg* *Pitavastatin 1 mg*

Specific statins and doses are noted in bold that were evaluated in RCTs (18-20,24-39) included in CQ1, CQ2 and the CTT 2010 meta-analysis included in CQ3 (21). All of these RCTs demonstrated a reduction in major cardiovascular events. Statins and doses that are approved by the U.S. FDA but were not tested in the RCTs reviewed by the Expert Panel are listed in *italics*. Individual responses to statins might vary in clinical practice.

*Individual responses to statin therapy varied in the RCTs. There might be a biologic basis for a less-than-average response.
†Evidence from 1 RCT only: down-titration if unable to tolerate atorvastatin 80 mg in IDEAL (19).
‡Although simvastatin 80 mg was evaluated in RCTs, initiation of simvastatin 80 mg or titration to 80 mg is not recommended by the FDA due to the increased risk of myopathy, including rhabdomyolysis.

bid indicates twice daily; FDA, Food and Drug Administration; IDEAL, Incremental Decrease through Aggressive Lipid Lowering study; LDL–C, low-density lipoprotein cholesterol; and RCTs, randomized controlled trials.

Summary of Statin Initiation Recommendations for the Treatment of Blood Cholesterol to Reduce ASCVD Risk in Adults



Initiating Statin Therapy in Individuals With Clinical ASCVD

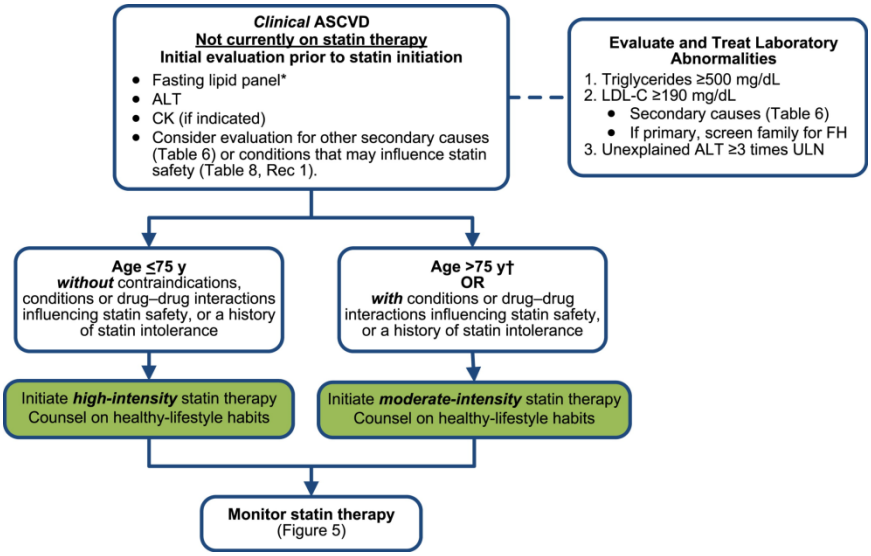


Figure Legend:

Initiating Statin Therapy in Individuals With Clinical ASCVD
Colors correspond to the Classes of Recommendation in Table 1.
***Fasting lipid panel preferred. In a nonfasting individual, a non–HDL-C level ≥220 mg/dL could indicate genetic hypercholesterolemia that requires further evaluation or a secondary etiology. If nonfasting triglycerides are ≥500 mg/dL, a fasting lipid panel is required.**
†It is reasonable to evaluate the potential for ASCVD benefits and for adverse effects, and to consider patient preferences, in initiating or continuing a moderate- or high-intensity statin in individuals with ASCVD who are >75 years of age.
ALT indicates alanine transaminase; ASCVD, atherosclerotic cardiovascular disease; CK, creatine kinase; FH, familial hypercholesterolemia; LDL-C, low-density lipoprotein cholesterol; and ULN, upper limit of normal.

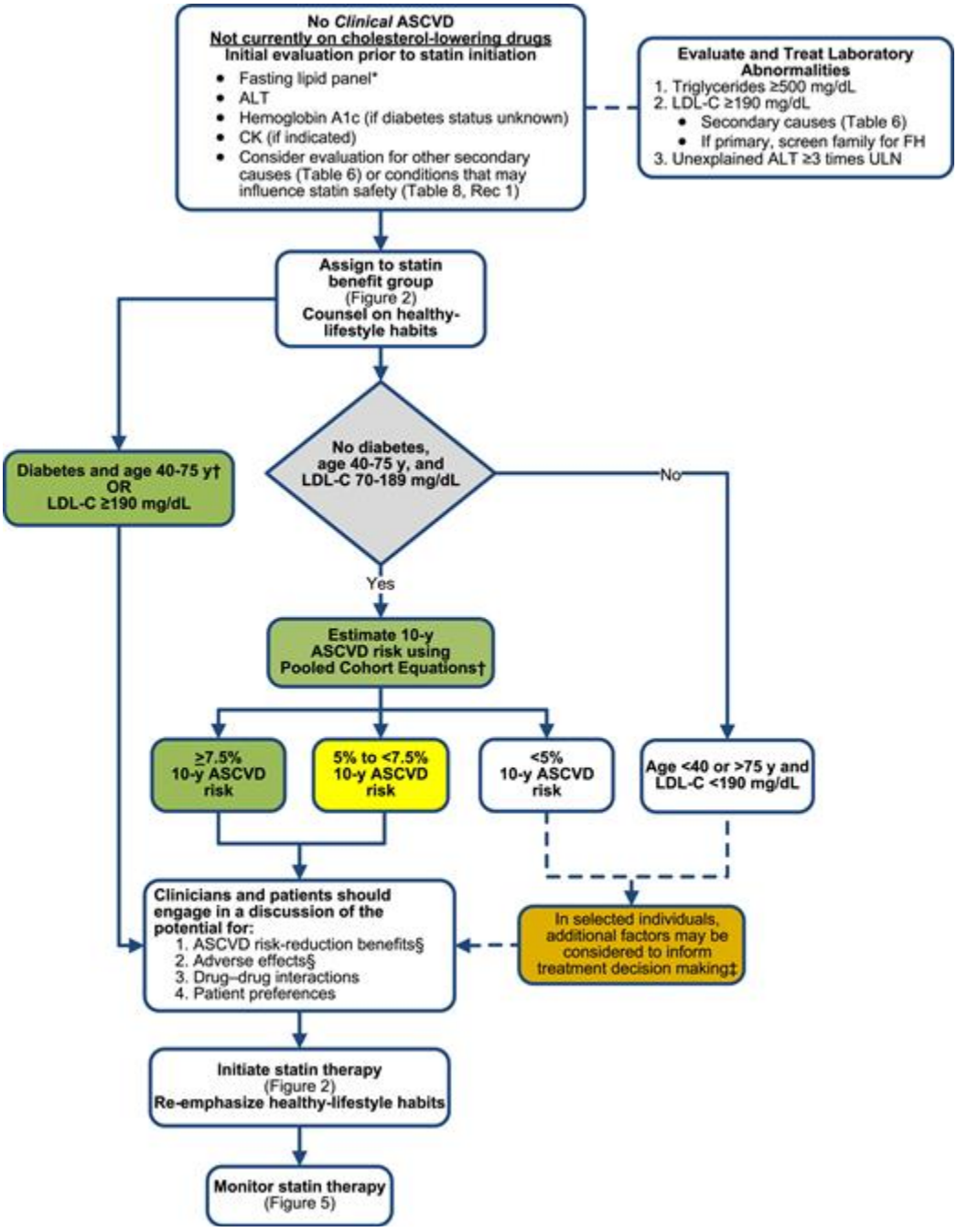
Secondary Causes of Hyperlipidemia Most Commonly Encountered in Clinical Practice

Secondary Cause	Elevated LDL-C	Elevated Triglycerides
Diet	Saturated or trans fats, weight gain, anorexia nervosa	Weight gain, very-low-fat diets, high intake of refined carbohydrates, excessive alcohol intake
Drugs	Diuretics, cyclosporine, glucocorticoids, amiodarone	Oral estrogens, glucocorticoids, bile acid sequestrants, protease inhibitors, retinoic acid, anabolic steroids, sirolimus, raloxifene, tamoxifen, beta blockers (not carvedilol), thiazides
Diseases	Biliary obstruction, nephrotic syndrome	Nephrotic syndrome, chronic renal failure, lipodystrophies
Disorders and altered states of metabolism	Hypothyroidism, obesity, pregnancy∗	Diabetes (poorly controlled), hypothyroidism, obesity; pregnancy∗

∗Cholesterol and triglycerides rise progressively throughout pregnancy (80); treatment with statins, niacin, and ezetimibe are contraindicated during pregnancy and lactation.

LDL-C indicates low-density lipoprotein cholesterol

Initiating Statin Therapy in Individuals without *Clinical* ASCVD

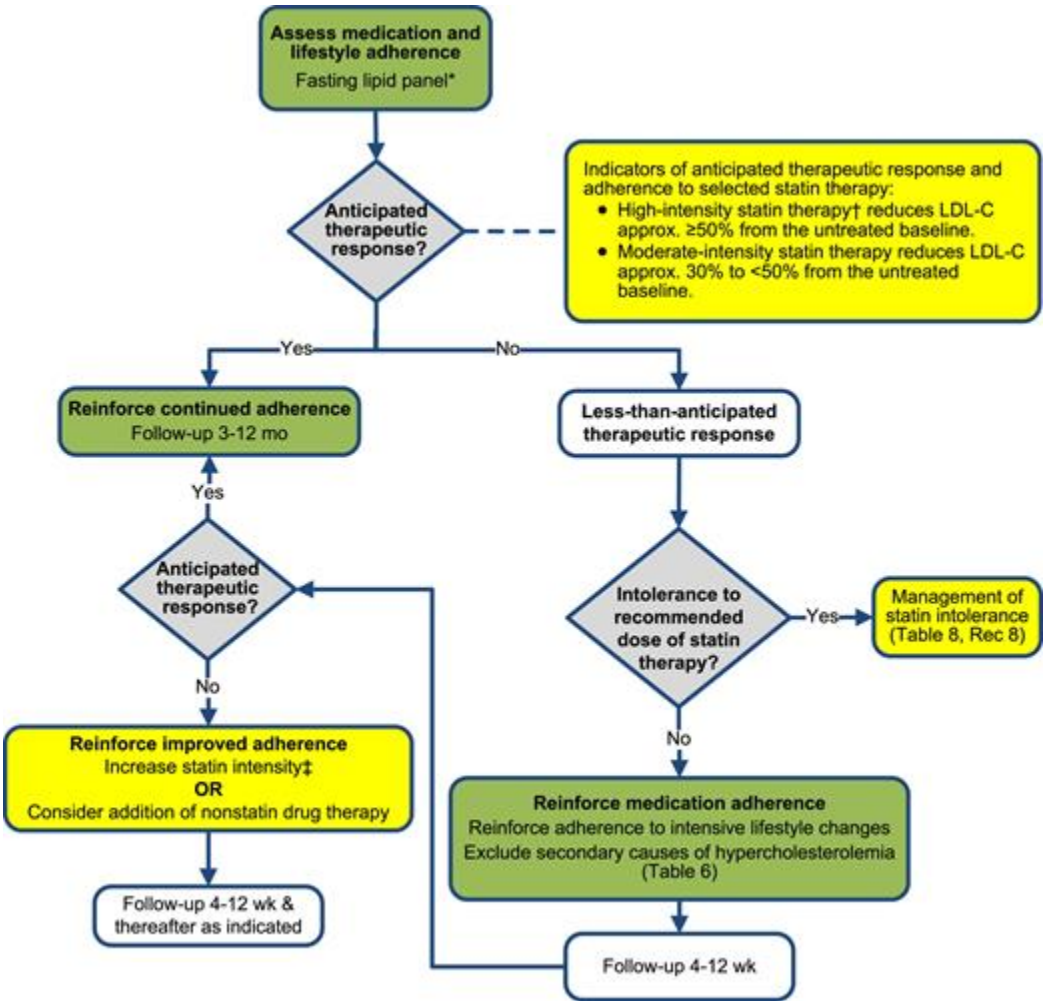


Statin Safety Recommendations:

Patient characteristics that may influence statin safety include but are not limited to: multiple or serious comorbidities, including impaired renal or hepatic function; a history of previous statin intolerance or muscle disorders; concomitant use of drugs affecting statin metabolism; a history of hemorrhagic stroke; and age >75 years. Asian ancestry may also influence the initial choice of statin intensity.

This guideline recommends against routine measurement of creatine kinase in individuals receiving statin therapy. This measurement should be reserved for those with muscle symptoms. However, measurement of a baseline creatine kinase may be useful in those at increased risk of adverse muscle events.
This guideline recommends that baseline measurement of transaminase (alanine transaminase; ALT) levels should be performed before initiation of statin therapy.

Statin Therapy:
Monitoring Therapeutic Response and Adherence



Testing:
The evidence is less clear with regard to the most appropriate tests for determining whether an anticipated therapeutic response to statin therapy has occurred on the maximally tolerated dose. RCT evidence to support the use of specific LDL-C or non–HDL-C targets was not identified. The focus is on the intensity of the statin therapy, but as an aid to monitoring response to therapy and adherence, it is reasonable to use the following as indicators of anticipated therapeutic response to statin therapy:

- High-intensity statin therapy generally results in an average LDL-C reduction of ≥50% from the untreated baseline.

- Moderate-intensity statin therapy generally results in an average LDL-C reduction of 30% to <50% from the untreated baseline.
- LDL-C levels and percent reduction are to be used only to assess response to therapy and adherence. They are not to be used as performance standards.

Lifestyle as the Foundation for ASCVD Risk-Reduction Efforts:
Diet:
Consumption of a dietary pattern that emphasizes intake of vegetables, fruits, and whole grains; includes low-fat dairy products, poultry, fish, legumes, nontropical vegetable oils and nuts; and limits intake of sweets, sugar-sweetened beverages and red meats.

- Adapt this dietary pattern to appropriate calorie requirements, personal and cultural food preferences, and nutrition therapy for other medical conditions (including diabetes mellitus).
- Achieve this pattern by following plans such as the DASH dietary pattern, the USDA Food Pattern, or the AHA diet.
- Aim for a dietary pattern that achieves 5% to 6% of calories from saturated fat.
- Reduce percent of calories from saturated fat.
- Reduce percent of calories from trans fat.

Physical Activity:
In general, encourage patients to engage in aerobic physical activity to reduce LDL–C and non-HDL–C. 3 to 4 sessions a week, lasting on average 40 minutes per session, and involving moderate-to-vigorous intensity physical activity.

IMPLEMENTATION CONSIDERATIONS:
Consultation with a dietician is a covered benefit in most benefit plans.

MONITORING:

REFERENCE/SOURCE:
U.S. Preventive Services Task Force (USPSTF): Guide to Clinical Preventive Services, Third Edition: Periodic Updates; available at: www.ahrq.gov/clinic/uspstfix.htm
2013 AHA/ACC Lifestyle Management Guideline
AHA/ACC Guidelines for Secondary Prevention for Patients with Coronary and Other Atherosclerotic Vascular Disease: 2006 Update Circulation. Vol. 113 No. 19 May 2006

REVIEWS AND APPROVALS:
Medical Peer Review Committee Dates: 3/15/97, 07/07/99, 05/02/01, 04/02/03, 4/6/05; 4/4/07, 4/1/09, 4/20/11, 3/20/2013
Professional Advisory Committee (PAC) 3/18/15