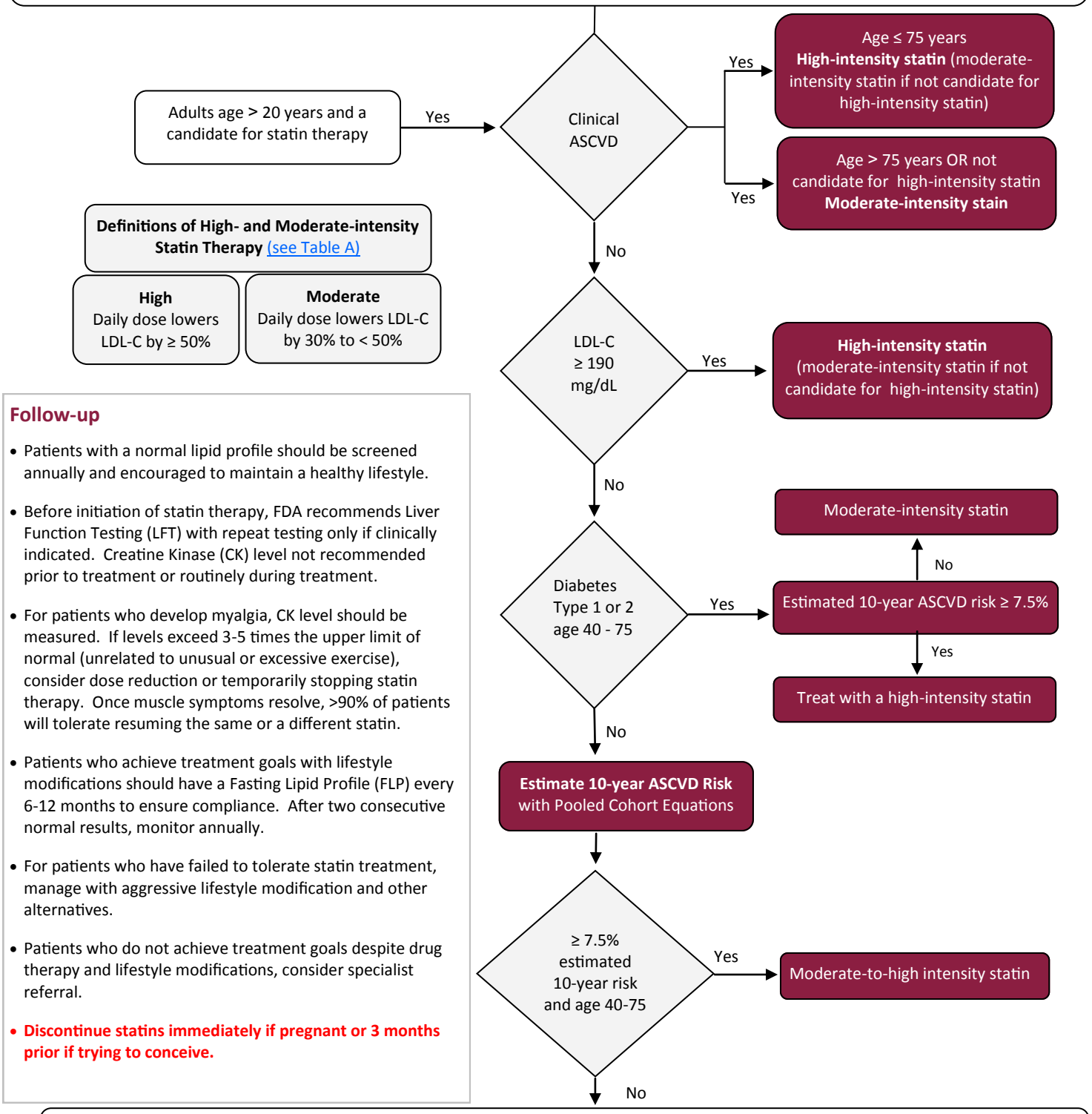
MOUNT CARMEL Health Partners

Hyperlipidemia Clinical Guideline

Definition: Hyperlipidemia is the condition of abnormally elevated levels of any or all lipids and/or lipoproteins in the blood.

Atherosclerotic Cardiovascular Disease (ASCVD) Statin Benefit Groups

Heart-healthy lifestyle habits are the foundation of ASCVD prevention. In individuals not receiving cholesterol-lowering drug therapy, recalculate estimated 10-year ASCVD risk every 4 - 6 years in those ages 40 - 75 years without clinical ASCVD or diabetes and with LDL-C 70 - 189 mg/dL.



Definitions of High- and Moderate-intensity Statin Therapy (see Table A)

High	Moderate
Daily dose lowers LDL-C by ≥ 50%	Daily dose lowers LDL-C by 30% to < 50%

Follow-up

- Patients with a normal lipid profile should be screened annually and encouraged to maintain a healthy lifestyle.
- Before initiation of statin therapy, FDA recommends Liver Function Testing (LFT) with repeat testing only if clinically indicated. Creatine Kinase (CK) level not recommended prior to treatment or routinely during treatment.
- For patients who develop myalgia, CK level should be measured. If levels exceed 3-5 times the upper limit of normal (unrelated to unusual or excessive exercise), consider dose reduction or temporarily stopping statin therapy. Once muscle symptoms resolve, >90% of patients will tolerate resuming the same or a different statin.
- Patients who achieve treatment goals with lifestyle modifications should have a Fasting Lipid Profile (FLP) every 6-12 months to ensure compliance. After two consecutive normal results, monitor annually.
- For patients who have failed to tolerate statin treatment, manage with aggressive lifestyle modification and other alternatives.
- Patients who do not achieve treatment goals despite drug therapy and lifestyle modifications, consider specialist referral.
- **Discontinue statins immediately if pregnant or 3 months prior if trying to conceive.**

ASCVD prevention benefit of statin therapy may be less clear in other groups. In selected individuals, consider additional factors influencing ASCVD risk ‡ and potential ASCVD risk benefits and adverse effects, drug-drug interactions, and patient preferences for statin treatment.

Hyperlipidemia is the condition of abnormally elevated levels of any or all lipids and/or lipoproteins in the blood. Lipids are transported in a protein capsule, a lipoprotein, the size of which determines its density (high or low).

Treatment should begin by making therapeutic lifestyle changes including weight reduction, diet modification (reduce animal products and increase plant products), reduction in alcohol consumption, cessation of tobacco use, and increase in physical activity levels.

Diagnosis

Cholesterol Screening: Perform fasting (9- to 12-hour) lipoprotein profile for adults age 20 and older once every five years, or more frequently if clinical determines the patient to be at increased risk for atherosclerotic disease.

These guidelines introduces the American College of Cardiology (ACC)/American Heart Association (AHA) Pooled Cohort Risk Equation (available at http://my.americanheart.org/cvriskcalculator or as a smartphone app) for an estimation of ten-year cardiovascular disease risk. The calculator can be used to determine if a high, moderate, or low dose statin is appropriate for primary prevention. This calculator tends to overestimate patients' risk, particularly in contemporary "real-world" population into clinician-patient decision-making.

The 2013 guidelines do not recommend titrating the statin dose to achieve a specific LDL target as it is thought that treating to a given target may result in under-treatment or overtreatment if an evidence-based statin dose is not used. The addition of a non-statin therapy has not been proven to further reduce cardiovascular risk and, therefore, non-statins are no longer routinely recommended.

Dyslipidemia is typically asymptomatic, but is common and an important predictor of coronary heart disease which is the leading cause of mortality in industrialized countries. Coronary heart disease causes about half of all deaths in the United States. Mortality from cardiovascular events has decreased substantially over the last 50 years. The rates, however, of events themselves (e.g., acute myocardial infarction and stroke) have declined more slowly suggesting an increased importance of preventing events. Identifying those at risk for coronary heart disease and starting appropriate therapies to reduce CHD risk are thus the primary goals of screening for dyslipidemia.

Treatment

For patients **without** atherosclerotic cardiovascular disease, assess additional risk factors, i.e., lipids, blood pressure, diabetes, smoking ,and family history of premature coronary heart disease (CHD) every 4 to 6 years in patients 20 to 79 years of age.

- first degree male relatives with CHD before age 55;
- first-degree female relative with CHD before age 65.

Lifestyle changes are recommended to reduce cardiovascular risk.

1. Adhere to a heart-healthy diet that includes consumption of vegetables, fruits, whole-grain, low fat dairy, poultry, fish, beans, non-tropical vegetable oils, and nuts, but avoid red meat (e.g., Mediterranean style diet*, DASH [Dietary Approach to Stop Hypertension] diet**).
2. Limit sugary drinks and sweets.
3. Limit saturated and trans-fat to 5% to 6% of calories.
4. Limit sodium intake to 2400 mg daily (about 1 teaspoon table salt); kosher/sea salt have the same sodium content per teaspoon. For adults who would benefit from blood pressure lowering, further sodium reduction is ideal.
5. Exercise regularly; engage in moderate to vigorous aerobic activity for at least 40 minutes (on average) 3 to 4 times each week.
6. Avoid tobacco.
7. Maintain a healthy weight.

Evaluation

Perform a complete history and physical.

Assess risk factors, comorbidities and identifiable causes of hyperlipidemia:

- Diabetes
- Hypothyroidism
- Obstructive liver disease
- Chronic kidney disease (CKD)
- Medications that increase LDL and lower HDL cholesterol (e.g., progestins, anabolic steroids, and corticosteroids)
- Obesity

Patient Diet Resources Websites:

*http://www.mayoclinic.org/healthy-lifestyle/nutrition-and-healthy-eating/in-depth/mediterranean-diet/art-20047801

**https://www.nhlbi.nih.gov/health/health-topics/topics/dash

Five Statin Benefit Groups

1. Individuals with a clinical atherosclerotic cardiovascular disease (ASCVD) --- acute coronary syndromes or a history of myocardial infarction, stable or unstable angina, coronary or other arterial revascularization, stroke, TIA, or peripheral arterial disease presumed to be of atherosclerotic origin --- without New York Heart Association (NYHA) class II-IV heart failure or receiving hemodialysis.
    - Patients should be treated with a high-intensity statin (may consider moderate-intensity statin if patient is not a candidate for a high-intensity statin).
2. Individuals with primary elevations of low-density lipoprotein cholesterol (LDL-C) greater than 190 mg/dL.
    - Patients should be treated with a high-intensity statin (may consider moderate-intensity statin if patient is not a candidate for a high-intensity statin).
3. Individuals 40 - 75 years of age with diabetes and LDL-C 70-189 mg/dL without clinical ASCVD.
    - If ASCVD risk is greater than 7.5%, patients should be treated with a high-intensity statin.
    - If ASCVD risk is less than 7.5%, patients should be treated with a moderate-intensity statin.
4. Individuals without clinical ASCVD or diabetes who are 40 - 75 years of age with LDL-C 70-189 mg/dL and have an estimated 10-year ASCVD risk of 7.5% or higher.
    - Patients should be treated with a moderate to high-intensity statin.
5. Individuals 40-75 years of age with LDL-C less than 70 mg/dL, should have no treatment.

If a patient does not fit into one of the five statin benefit groups (e.g., LDL 70 to 189 mg/dL [1.8 to 4.9 mmol/L.] with a 10-year risk 5% to 7.5%), but there is clinical suspicion that the patient may benefit from a statin, additional factors can be taken into consideration:

- LDL 160 mg/dL or higher or other evidence of genetic hyperlipidemia.
- Cardiovascular disease onset in a first degree male relative before age 55, or in a first-degree female relative before age 65.
- High-sensitivity C-reactive protein 2 mg/dL or higher.
- Ankle-brachial index less than 0.9.
- Elevated lifetime risk of atherosclerotic cardiovascular disease.
- Coronary artery calcium (CAC) score 300 Agatston units or higher, or 75th percentile or higher for age, gender, and ethnicity.

Table A: High, Moderate, and Low-Intensity Statin Therapy

High-Intensity Statin Therapy	Moderate-Intensity Statin Therapy	Low-Intensity Statin Therapy
Daily dose lowers LDL-C, on average, by approximately greater than or equal to 50%	Daily dose lowers LDL-C, on average, by approximately 30% to less than 50%	Daily dose lowers LDL-C, on average, by less than 30%
Atorvastatin (40[1])-80 mg **Rosuvastatin 20 *mg***	**Atorvastatin 10** *(20)* ***mg*** **Rosuvastatin** *(5)* ***10 mg*** **Simvastatin 20-40 mg[2]** **Pravastatin 40** *(80)* ***mg*** **Lovastatin 40 mg** *Fluvastatin XL 80 mg* **Fluvastatin XL 40 mg bid** *Pitavastatin 2-4 mg*	*Simvastatin 10 mg* **Pravastatin 10-20 mg** **Lovastatin 20 mg** *Fluvastatin 20-40 mg* *Pitavastatin 1 mg*

[1] Evidence from 1 RCT only: down-tiration if unable to tolerate atorvastatin 80 mg in IDEAL (47).

[2] 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.

Note: Statins and doses that are approved by the U.S. FDA but were not tested in the RCTs reviewed are listed in *italics.*

Table B: Available Drug Therapy Options

Drug Class	Drug and Dose	Effects	Side Effects	Contraindications
HMG CoA reductase inhibitors (statins)	Lovastatin (20-80 mg) Pravastatin (10-40 mg)* Simvastatin (10-40 mg) Fluvastatin (20-80 mg)* Atorvastatin (10-80 mg) Rosuvastatin (5-40mg; for initial therapy, limit dose to 20 mg) Pitavastatin (1-4 mg)	LDL decreases 18-63% HDL increases 5-15% TG decreases 7-30%	Myopathy, increased liver enzymes	Absolute: Active or chronic liver disease Relative: Concomitant use of certain drugs** Amiodarone, Telithromycin, Erythromycin, Itraconazole, Clarithromycin & other azoles
Bile acid sequestrants	Cholestyramine (4-24 g) Colestipol (10-30 g) Colesevelam (1.5-4.5 g)	LDL decreases 15-30% HDL increases 3-5% TG No change or increases	Gastrointestinal distress, constipation, decreased absorption of other drugs	Absolute: Dysbeta-lipoproteinemia TG greater than 400mg/dL Relative: TG greater than200mg/dL
Fibric acids	Fenofibrate (48-145 mg)	LDL decreases 5-20% HDL increases 10-20% TG decreases 20-50%	Dyspepsia, gallstones, myopathy	Absolute: Severe renal disease Severe hepatic disease
B vitamin***	Niacin (250-2000 mg)	LDL decreases 5-25% HDL increases 15-35% TG decreases 20-35%	Flushing, puritis, nausea, hyperglycemia, hepatotoxicity	Relative: Hepatic impairment, active peptic ulcer disease
Cholesterol absorption inhibitor	Ezetimibe (10 mg)	LDL decreases 18%	Diarrhea, arthralgia, rhabdomyolysis, hepatitis, pancreatitis, thrombocytopenia, Potentiates warfarin	Absolute: Moderate to severe hepatic impairment
PCSK9**** inhibitors	Evolucumab (140 mg subcutaneously every 2 weeks or 420 mg monthly) Alirocumab (75-150 mg subcutaneously)	LDL decreases 31-61%	Respiratory infection, back pain, injection-site reactions, arthralgia, fatigue	None

*Lower myopathy risk

**Cyclosporine, macrolide antibiotics, various antifungal agents, and cytochrome P-450 inhibitors (fibrates and niacin) should be used with appropriate caution.

***Several over-the-counter formulations exist.

****PCSK9 inhibitors haven't been proven to improve CV outcomes or to be safe long-term. These drugs are extremely expensive.

ICD-10 Codes - Hyperlipidemia

ICD 10	Description
I25.10	Atherosclerotic heart disease of native coronary artery without angina pectoris
I25.10	Atherosclerotic heart disease of native coronary artery with angina pectoris
E78.0	Pure hypercholesterolemia
E78.1	Pure hyperglyceridemia
E78.2	Mixed hyperlipidemia
E78.4 E78.5	Other hyperlipidemia Hyperlipidemia, unspecified

* Note: These are the most commonly used ICD codes.

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