Management of Hyperlipidemia

Clinical Practice Guideline
MedStar Health

"These guidelines are provided to assist physicians and other clinicians in making decisions regarding the care of their patients. They are not a substitute for individual judgment brought to each clinical situation by the patient's primary care provider in collaboration with the patient. As with all clinical reference resources, they reflect the best understanding of the science of medicine at the time of publication but should be used with the clear understanding that continued research may result in new knowledge and recommendations."

The following MedStar guideline is based on the Guideline published by American College of Cardiology/American Heart Association in 2018. Statins have been shown to reduce fatal and non-fatal ASCVD events (except in those w/ NYHA class II-IV heart failure or chronic dialysis patients) in studies of both primary prevention and secondary prevention. Many studies also demonstrate a reduction in all-cause mortality. The 2013 guideline abandoned a "treat to target" paradigm and embraced a method of using the maximum tolerated statin intensity in the groups known to benefit. Prior proposed approaches to statin treatment lack supporting randomized controlled trial (RCT) data. Both the 2013 and the present guideline use the pooled cohort equations to estimate 10-year ASCVD (first occurrence nonfatal and fatal MI and fatal stroke) risk in non-Hispanic white and Black patients without clinical ASCVD and identify those most likely to benefit from statins for primary prevention. The current guidelines continue to recommend a heart-healthy diet, regular exercise, avoidance of tobacco products, and maintenance of a healthy weight and stress that all these interventions were included as background therapy of RCTs of pharmacological cholesterol therapy. In addition, the guideline makes clearer that the decision to start a statin medication should only occur after a frank discussion with the patient and shared decision-making.

The current guideline is more detailed than prior guidelines and contains numerous recommendations. While we will attempt to highlight them here, we suggest a review of the full report for additional detail. Additionally, while the guideline contains recommendations for patients of all ages, we will restrict comments here to patients 18 and older.

Guideline Summary

As a summary, we reprint ten "Take-Home Messages" from the report: "Top 10 Take-Home Messages to Reduce Risk of Atherosclerotic Cardiovascular Disease Through Cholesterol Management."

1. In all individuals, emphasize a heart-healthy lifestyle across the life course. A healthy lifestyle reduces atherosclerotic cardiovascular disease (ASCVD) risk at all ages. In younger individuals, healthy lifestyle can reduce development of risk factors and is the foundation of ASCVD risk reduction. In young adults 20 to 39 years of age, an assessment of lifetime risk facilitates the clinician–patient risk discussion (see No. 6) and emphasizes intensive lifestyle efforts. In all age groups, lifestyle therapy is the primary intervention for metabolic syndrome.
2. In patients with clinical ASCVD, reduce low-density lipoprotein cholesterol (LDL-C) with high-intensity statin therapy or maximally tolerated statin therapy. The more LDL-C is reduced on statin therapy, the greater will be subsequent risk reduction. Use a maximally tolerated statin to lower LDL-C levels by ≥50%.

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3. In very high-risk ASCVD, use an LDL-C threshold of 70 mg/dL (1.8 mmol/L) to consider addition of non-statins to statin therapy. Very high-risk includes a history of multiple major ASCVD events or 1 major ASCVD event and multiple high-risk conditions. In very high-risk ASCVD patients, it is reasonable to add ezetimibe to maximally tolerated statin therapy when the LDL-C level remains ≥70 mg/dL (≥1.8 mmol/L). In patients at very high risk whose LDL-C level remains ≥70 mg/dL (≥1.8 mmol/L) on maximally tolerated statin and ezetimibe therapy, adding a PCSK9 inhibitor is reasonable, although the long-term safety (>3 years) is uncertain and cost effectiveness is low at mid-2018 list prices.
4. In patients with severe primary hypercholesterolemia (LDL-C level ≥190 mg/dL [≥4.9 mmol/L]), without calculating 10-year ASCVD risk, begin high-intensity statin therapy without calculating 10- year ASCVD risk. If the LDL-C level remains ≥100 mg/dL (≥2.6 mmol/L), adding ezetimibe is reasonable. If the LDL-C level on statin plus ezetimibe remains ≥100 mg/dL (≥2.6 mmol/L) and the patient has multiple factors that increase subsequent risk of ASCVD events, a PCSK9 inhibitor may be considered, although the long-term safety (>3 years) is uncertain and economic value is low at mid- 2018 list prices.
5. In patients 40 to 75 years of age with diabetes mellitus and LDL-C ≥70 mg/dL (≥1.8 mmol/L), start moderate-intensity statin therapy without calculating 10-year ASCVD risk. In patients with diabetes mellitus at higher risk, especially those with multiple risk factors or those 50 to 75 years of age, it is reasonable to use a high-intensity statin to reduce the LDL-C level by ≥50%.
6. In adults 40 to 75 years of age evaluated for primary ASCVD prevention, have a clinician–patient risk discussion before starting statin therapy. Risk discussion should include a review of major risk factors (e.g., cigarette smoking, elevated blood pressure, LDL-C, hemoglobin A1C [if indicated], and calculated 10-year risk of ASCVD); the presence of risk-enhancing factors (see No. 8); the potential benefits of lifestyle and statin therapies; the potential for adverse effects and drug–drug interactions; consideration of costs of statin therapy; and patient preferences and values in shared decision-making.
7. In adults 40 to 75 years of age without diabetes mellitus and with LDL-C levels ≥70 mg/dL (≥1.8 mmol/L), at a 10-year ASCVD risk of ≥7.5%, start a moderate-intensity statin if a discussion of treatment options favors statin therapy. Risk-enhancing factors favor statin therapy (see No. 8). If risk status is uncertain, consider using coronary artery calcium (CAC) to improve specificity (see No. 9). If statins are indicated, reduce LDL-C levels by ≥30%, and if 10-year risk is ≥20%, reduce LDL-C levels by ≥50%.
8. In adults 40 to 75 years of age without diabetes mellitus and 10-year risk of 7.5% to 19.9% (intermediate risk), risk-enhancing factors favor initiation of statin therapy (see No. 7). Risk- enhancing factors include family history of premature ASCVD; persistently elevated LDL-C levels ≥160 mg/dL (≥4.1 mmol/L); metabolic syndrome; chronic kidney disease; history of preeclampsia or premature menopause (age <40 years); chronic inflammatory disorders (e.g., rheumatoid arthritis, psoriasis, or chronic HIV); high-risk ethnic groups (e.g., South Asian); persistent elevations of triglycerides ≥175 mg/dL (≥1.97 mmol/L); and, if measured in selected individuals, apolipoprotein B ≥130 mg/dL, high-sensitivity C-reactive protein ≥2.0 mg/L, ankle-brachial index <0.9 and lipoprotein (a) ≥50 mg/dL or 125 nmol/L, especially at higher values of lipoprotein (a). Risk-enhancing factors may favor statin therapy in patients at 10-year risk of 5-7.5% (borderline risk).
9. In adults 40 to 75 years of age without diabetes mellitus and with LDL-C levels ≥70 mg/dL- 189 mg/dL (≥1.8-4.9 mmol/L), at a 10-year ASCVD risk of ≥7.5% to 19.9%, if a decision about statin therapy is uncertain, consider measuring CAC. If CAC is zero, treatment with statin therapy may be withheld or delayed, except in cigarette smokers, those with diabetes mellitus, and those with a strong family history of premature ASCVD. A CAC score of 1 to 99 favors statin therapy, especially in those ≥55 years of age. For any patient, if the CAC score is ≥100 Agatston units or ≥75th percentile, statin therapy is indicated unless otherwise deferred by the outcome of clinician–patient risk discussion.

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10. Assess adherence and percentage response to LDL-C–lowering medications and lifestyle changes with repeat lipid measurement 4 to 12 weeks after statin initiation or dose adjustment, repeated every 3 to 12 months as needed. Define responses to lifestyle and statin therapy by percentage reductions in LDL-C levels compared with baseline. In ASCVD patients at very high-risk, triggers for adding non-statin drug therapy are defined by threshold LDL-C levels ≥70 mg/dL (≥1.8 mmol/L) on maximal statin therapy (see No. 3)."

Recent update in INFECTIOUS DISEASES (September 2023); and UpToDate: For persons ≥40 years of age with HIV and a low-density lipoprotein cholesterol ≥190 and/or a 10-year ASCVD score ≥5 percent, we recommend a statin (Grade 1B). For those with lower risk, to discuss statin use, but the absolute benefit is smaller.

HIV infection is associated with an excess risk of cardiovascular disease. A randomized trial evaluated the efficacy of lipid-lowering therapy with pitavastatin for primary prevention in over 7700 persons with HIV ≥40 years of age receiving antiretroviral therapy who had a 10-year atherosclerotic cardiovascular disease (ASCVD) risk score <15 percent. Pitavastatin reduced the relative risk of major cardiovascular events (e.g., myocardial infarction, stroke) by 35 percent compared with placebo; the trial was stopped early for this apparent benefit. Based on these data, statins recommended in all persons ≥40 years of age with an ASCVD score ≥5 percent, particularly if the score is ≥7.5 percent; for those with lower baseline risk, to discuss statin use, although the absolute benefit is smaller. For persons younger than 40 years and older than 75years of age, the recommended approach is the same as in persons without HIV.[17, 18, 19.]

Who to Screen?

The US Preventive Services task force (USPSTF) concludes with moderate certainty that statin use for the prevention of CVD events and all-cause mortality in adults aged 40 to 75 years with no history of CVD and who have one or more CVD risk factors (i.e. dyslipidemia, diabetes, hypertension, or smoking) and an estimated 10-year CVD event risk of 10% or greater has at least a moderate net benefit. (B recommendation).

The USPTF concludes with moderate certainty that statin use for the prevention of CVD events and all-cause mortality in adults aged 40 to 75 years with no history of CVD and who have one or more CVD risk factors (i.e., dyslipidemia, diabetes, hypertension, or smoking) and an estimated 10-year CVD event risk of 7.5% to less than 10% has at least a small net benefit. The decision to initiate therapy should depend on individual patient preference for a potential small benefit relative to the potential harms and inconvenience of taking a daily medication. (C Recommendation).

The USPTF concludes that the evidence is insufficient to determine the balance of benefits and harms of statin use for the primary prevention of CVD events and mortality in adults 76 years or older with no history of CVD.[16] This recommendation replaces the 2016 USPSTF recommendation on statin use for primary prevention of CVD.

The 2018 and 2019 AHA/ACC guidelines define cardiovascular risk categories as high (10-year risk of cardiovascular events ≥ 20%), intermediate (10-year risk of cardiovascular events ≥7.5% to 20%, and borderline (10-year risk of cardiovascular events 5% to < 7.5%).[2, 3.]

The guidelines recommend initiation of statin therapy in persons at intermediate or high risk and a risk.

discussion for persons at borderline risk and recommend consideration of risk enhancers to refine risk assessments based on the Pooled Cohort Equations and inform decision-making for persons at intermediate and borderline risk. These risk enhancers include family h/o premature ASCVD (first-degree male relative with onset < 55 yo or female < 65 yo), LDL-C ≥160 mg/dL, persistently elevated triglyceride > 175, presence of chronic kidney disease, metabolic syndrome, preeclampsia, premature menopause, inflammatory diseases, hs-CRP ≥2 mg/dL, HIV, and South Asian ancestry.[2,3] ethnicity, ABI < 0.9.

The guideline recommends consideration of lifetime risk in patients 20-39 and treatment of those with a family history and LDL ≥160. The main argument provided is to allow risk reduction strategies to take place (e.g., diet and exercise). They further recommend screening non-pregnant adults 40-75 with risk re-evaluated every 4-6 yrs.

The guideline clearly states that a fasting lipid panel is NOT REQUIRED. Studies indicate that a less than 10 percent improvement in levels occur with fasting (Sidhu Arch Int Med 2012; Nov 12:1).

Risk Calculation

An integral first step in the guideline is calculation of the ASCVD pooled risk. There are several ASCVD risk calculators available to capture population-specific risk profiles. Available in MedConnect Calculators:
ASCVD Risk Estimator:

- Using MedConnect
  - Calculators Tab > Cardiology > ACC/AHA 2013 Cardiovascular Risk Assessment
    -- Allows copying and pasting into note.
  - ASCVD Risk Estimator > a component that can be added to the appropriate specialty clinic Workflow. Has a link to the ACC Guideline, Risk enhancing factors, and a "Risk Educator" section where inputs can be varied to help the patient understand the impact of interventions.
  - **ASCVD Risk Estimator Plus (2018)** — The ASCVD Risk Estimator Plus incorporates the 2013 ACC/AHA pooled cohort equation (calculator 1), the 2016 Million Hearts Longitudinal ASCVD Risk Assessment Tool, and ACC/AHA guideline recommendations. The ASCVD Risk Estimator Plus provides estimates of the potential benefit of specific risk-lowering interventions (statins, antihypertensive medication, aspirin, smoking cessation), and enables updating and tracking of changes in risk over time based on a patient's actual response to interventions.
- Phone: ACC ASCVD Risk Estimator Plus
  - iOS App: https://itunes.apple.com/us/app/ascvd-risk-estimator/id808875968?mt=8
  - Android App: https://play.google.com/store/apps/details?id=org.acc.cvrisk&hl=en
- Web: http://tools.acc.org/ASCVD-Risk-Estimator/

PREVENT calculator: The 2023 AHA PREVENT calculator was developed, in part, because the 2013 pooled cohort equation overestimate the risk of incident ASCVD in some contemporary populations. The PREVENT calculator was derived and validated with more contemporary data from over 6.6 million patients.[22,23, 24.]

- Risk factors – The PREVENT base model includes age, sex, total and HDL cholesterol, systolic blood pressure, body mass index, estimated glomerular filtration rate (eGFR), diabetes, current

smoking, antihypertensive therapy, statin therapy and optional factors (urinary albumin-creatinine ratio, HbA1c, and zip code for estimating social deprivation index).

- The PREVENT calculator estimates risks of incident ASCVD (MI, fatal CHD, and stroke), HF, and CVD (defined as ASCVD and/or HF). Ten-year risks for these endpoints are estimated for adults aged 30 to 79; 30-year risks are estimated for adults aged 30 to 59.

Guideline Summary based on Four Statin Benefit Groups

As with the 2013 guideline, in the 2018 guideline there are four groups of age ≥ 21 yo men and non-pregnant/non-nursing women for whom atherosclerotic cardiovascular disease benefit from statins clearly exceeds adverse event risk (w/o NYHA II-IV HF and/or on hemodialysis). The guidelines recommend which intensity statin should be initiated in these cases, with some caveats:

- **Individuals with clinical ASCVD** (ACS, h/o MI, stable or unstable angina, coronary or arterial revascularization, CVA, TIA or PAD presumed atherosclerotic): High-Intensity statin preferred.
- **Individuals with LDL-C >= 190 mg/dL**: High-Intensity statin preferred
- **Individuals 40-75 years of age *with diabetes and* LDL-C 70-189 mg/dL**: Moderate intensity statin is recommended for these patients. If diabetes risk-enhancing factors are present (p 31 Table 5) such as long duration, albuminuria, low GFR, retinopathy, neuropathy, or a low ABI, a high-intensity statin is recommended. If >20% risk, then statin+ ezetimibe is recommended.
- **Individuals 40-75 years of age *without* diabetes *or* clinical ASCVD *and* with LDL 70-189 mg/dL *and* an estimated 10-year ASCVD risk of 7.5% or higher** àModerate to High-Intensity Statin.

Shared Decision-Making

While present in the 2013 guideline, the 2018 version makes it much more explicit that a shared decision-making decision needs to occur before starting a statin medication. They imply that patients should not be started on medication if the outcome of the discussion is not favorable. Detailed advice on conducting this risk discussion is provided via a checklist (Table 7)

Table 7. Checklist for Clinician–Patient Shared Decision-Making for Initiating Therapy

Checklist Item	Recommendation

ASCVD risk assessment	• Assign to statin treatment group; use ASCVD Risk Estimator Plus.*
	  ○ In lower-risk primary-prevention adults 40-75 y of age with LDL-C ≥70 mg/dL (≥1.8 mmol/L).
	  ○ Not needed in secondary prevention, in those with LDL-C ≥190 mg/dL (≥4.9 mmol/L), or in those 40-75 y of age with diabetes mellitus.
	• Assess other patient characteristics that influence risk. See Risk-Enhancing Factors (Section 4.4.1.3. and Table 6)
	• Assess CAC (Section 4.4.1.4.) if risk decision is uncertain and additional information is needed to clarify ASCVD risk.
	  ○ Use decision tools to explain risk (e.g., ASCVD Risk Estimator Plus,* Mayo Clinic Statin Choice Decision Aid).

Lifestyle modifications	• Review lifestyle habits (e.g., diet, physical activity, weight or body mass index, and tobacco use). • Endorse a healthy lifestyle and provide relevant advice, materials, or referrals. (e.g., CardioSmart, AHA Life's Simple 7, NLA Patient Tear Sheets, PCNA Clinicians' Lifestyle Modification Toolbox, cardiac rehabilitation, dietitian, smoking cessation program).
Potential net clinical benefit of pharmacotherapy	• Recommend statins as first-line therapy. • Consider the combination of statin and nonstatin therapy in selected patients. • Discuss potential risk reduction from lipid-lowering therapy. • Discuss the potential for adverse effects or drug–drug interactions.
Cost considerations	• Discuss potential out of pocket cost of therapy to the patient (e.g., insurance plan coverage, tier level, copayment).
Shared decision-making	• Encourage the patient to verbalize what was heard (e.g., patient's personal ASCVD risk, available options, and risks/benefits). • Invite the patient to ask questions, express values and preferences, and state ability to adhere to lifestyle changes and medications. • Refer patients to trustworthy materials to aid in their understanding of issues regarding risk decisions. • Collaborate with the patient to determine therapy and follow-up plan.

Care Algorithm for Primary Prevention

Based on age, co-morbid diseases, and risk, the algorithm guides you through a decision on whether to start a statin medication. (see Table 5 for USPSTF recommendations).

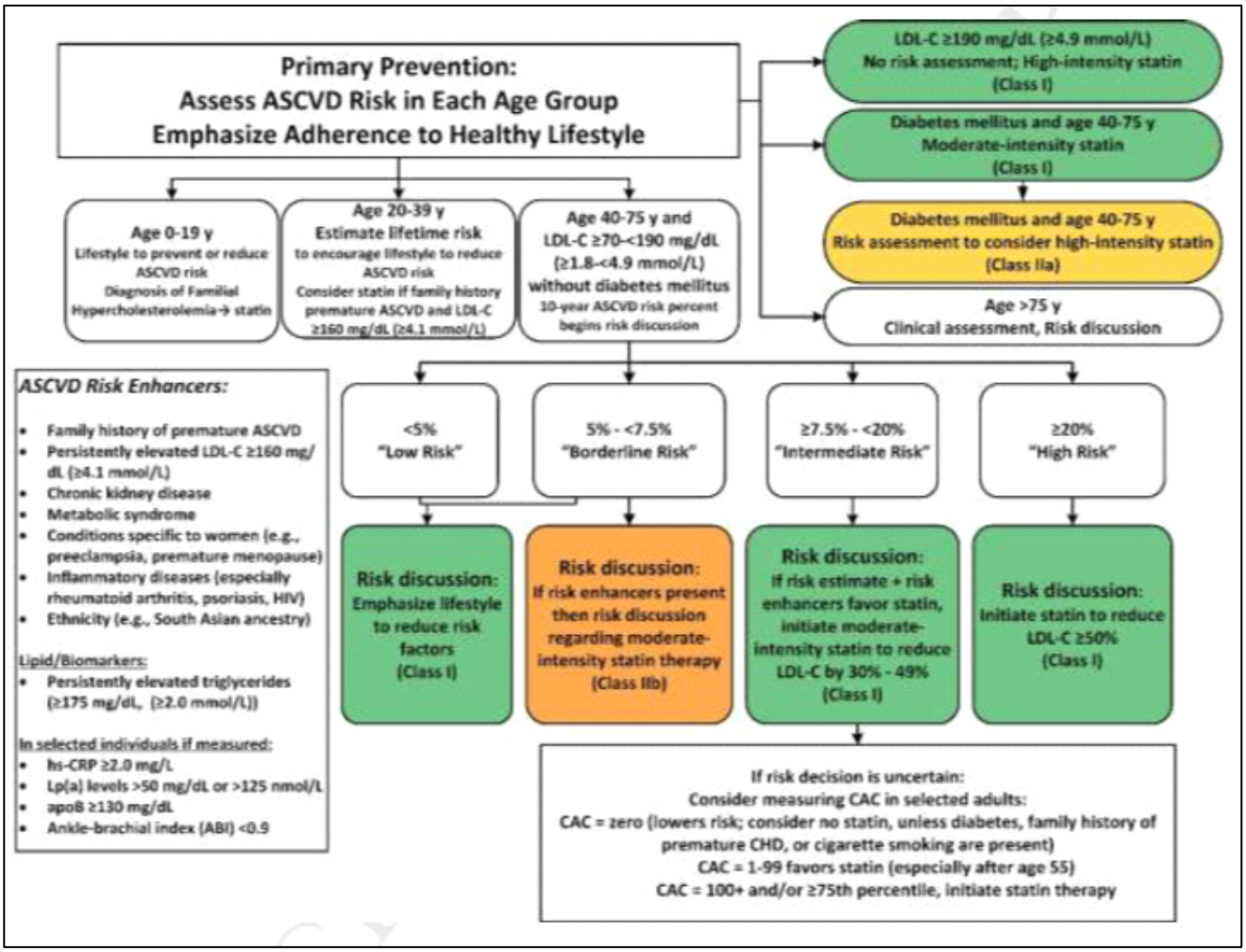

Figure 3: 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: Executive Summary
Circulation. 2019;140: e563–e595. DOI: 10.1161/CIR.0000000000000677

Ongoing lifestyle modification is recommended for all patients. All patients should have a risk discussion as noted above before starting a statin.

If a risk decision is "uncertain," the guideline now gives the option to measure coronary artery calcium (CAC). If the score is 0, consideration may be given to avoiding statin use except in smokers, diabetics, and those with a positive family history. A score of 1-99 favors statin therapy, and if ≥100 the guideline recommends statin therapy.

Care Algorithm for Secondary Prevention/Clinical ASCVD

Statin medications are recommended for most patients with ASCVD. A risk calculation is generally not needed.

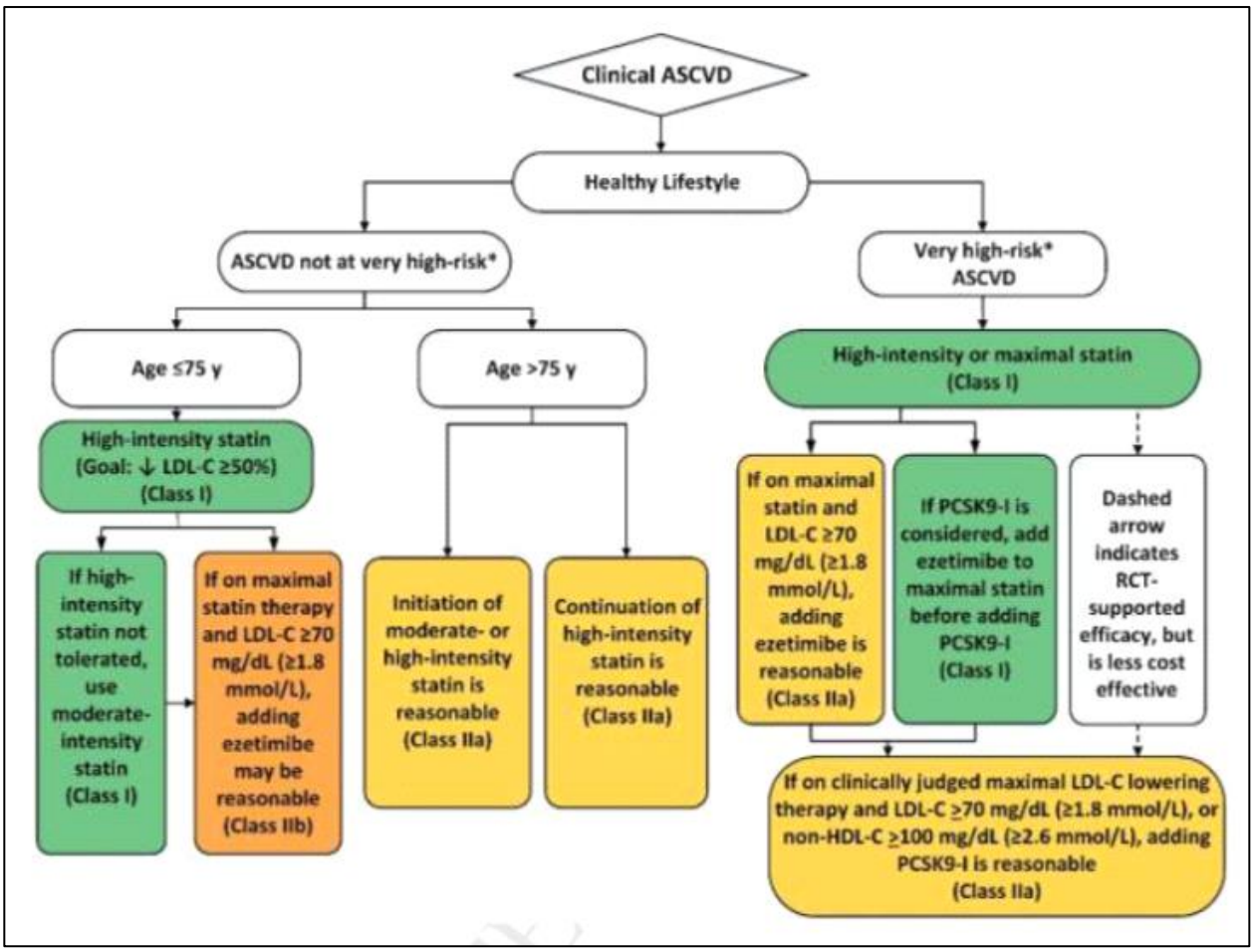

Figure 1. Secondary prevention in patients with clinical ASCVD
Circulation. 2019;139: e1046–e1081. DOI: 10.1161/CIR.0000000000000624

The algorithm is divided into two branches based on whether the patient has "very high-risk ASCVD" or not, meaning the risk for future ASCVD events. The guideline suggests a "history of multiple major ASCVD events or 1 major ASCVD event and multiple high-risk conditions" as defining very high risk. See below for Table 4, criteria for very high risk).

For patients ≤75 yrs. or at very high risk, if a suggested goal of <70 LDL is not reached on maximal statin levels, it is suggested to add ezetimibe.

In order to consider a PCSK9 inhibitor, the patient should be very high risk, already on maximal statin therapy and ezetimibe, and not have reached LDL <70.

Table 4. Very High-Risk* of Future ASCVD Events

Major ASCVD Events
Recent ACS (within the past 12 mo)
History of MI (other than recent ACS event listed above)
History of ischemic stroke
Symptomatic peripheral arterial disease (history of claudication with ABI <0.85, or previous revascularization or amputation (S4.1-39))
High-Risk Conditions
Age ≥65 y
Heterozygous familial hypercholesterolemia
History of prior coronary artery bypass surgery or percutaneous coronary intervention outside of the major ASCVD event(s)
Diabetes mellitus
Hypertension
CKD (eGFR 15-59 mL/min/1.73 m^2) (S4.1-15, S4.1-17)
Current smoking
Persistently elevated LDL-C (LDL-C ≥100 mg/dL [≥2.6 mmol/L]) despite maximally tolerated statin therapy and ezetimibe
History of congestive HF

*Very high risk includes a history of multiple major ASCVD events or 1 major ASCVD event and multiple high-risk conditions.

ABI indicates ankle-brachial index; ACS, acute coronary syndrome; ASCVD, atherosclerotic cardiovascular disease; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; HF, heart failure; LDL, low-density lipoprotein cholesterol; and MI, myocardial infarction.

Circulation. 2019;139: e1046–e1081. DOI: 10.1161/CIR.0000000000000624

Table 5 Clinician Summary: Statin use for Primary Prevention of Cardiovascular Disease in Adults

What does the USPSTF recommend?	**For adults aged 40 to 75 years who have 1 or more cardiovascular risk factors (ie, dyslipidemia, diabetes, hypertension, or smoking) and an estimated 10-year cardiovascular disease (CVD) risk of 10% or greater:** Initiate a statin. **Grade: B** **For adults aged 40 to 75 years who have 1 or more cardiovascular risk factors (ie, dyslipidemia, diabetes, hypertension, or smoking) and an estimated 10-year CVD risk of 7.5% to less than 10%:** Selectively offer a statin. **Grade: C** **For adults 76 years or older:** The evidence is insufficient to recommend for or against starting a statin. **I statement**
To whom does this recommendation apply?	These recommendations apply to adults 40 years or older who do not already have CVD or signs or symptoms of CVD. They do not apply to adults with a low-density lipoprotein cholesterol level greater than 190 mg/dL (4.92 mmol/L) or known familial hypercholesterolemia. These populations are at very high risk for CVD and considerations on the use of statins in these populations can be found in other organizations' guidelines on management of hypercholesterolemia.
What's new?	This recommendation is consistent with the 2016 USPSTF recommendation.
How to implement this recommendation?	Consider the patient's age. • **For adults aged 40 to 75 years:** ◦ Determine whether the patient has a cardiovascular risk factor (ie, dyslipidemia, diabetes, hypertension, or smoking). ◦ Estimate CVD risk using a CVD risk estimator. ◦ In patients who have a cardiovascular risk factor and an estimated 10-year CVD risk of 10% or greater, initiate a moderate-intensity statin after discussing the rationale and provided the patient agrees. ◦ In patients who have a cardiovascular risk factor and an estimated 10-year CVD risk of 7.5% to less than 10%, the benefit of starting a statin is smaller, so clinicians should selectively offer a statin, taking patient values and preferences into account. • **For adults 76 years or older:** The evidence is insufficient to recommend for or against starting a statin.
What additional information should clinicians know about this recommendation?	• Age is one of the strongest risk factors for CVD. • Men have a higher prevalence of CVD than females, although women experience higher mortality from certain cardiovascular events. On average, men experience CVD events earlier in life compared with women. • Among both sexes, Black persons have the highest prevalence of CVD. • To achieve the full benefits of statin use, it is essential to equitably improve statin use in both women and men of all races and ethnicities, and especially among Black and Hispanic adults, who have the highest prevalence of CVD and the lowest utilization of statins, respectively.
Why is this recommendation and topic important?	CVD is the leading cause of mortality in the US, accounting for more than 1 in 4 deaths. In 2019, there were an estimated 558 000 deaths caused by coronary heart disease and 109 000 deaths caused by ischemic stroke.
What are additional tools and resources?	• The Million Hearts initiative provides information on statins at https://millionhearts.hhs.gov/learn-prevent/scoop-on-statins.html • The Centers for Disease Control and Prevention has information about cholesterol-lowering medications, including statins, at https://www.cdc.gov/cholesterol/treating_cholesterol.htm, and resources for clinicians at https://www.cdc.gov/cholesterol/educational_materials.htm
Where to read the full recommendation statement?	Visit the USPSTF website (https://www.uspreventiveservicestaskforce.org/uspstf/) or the *JAMA* website (https://jamanetwork.com/collections/44068/united-states-preventive-services-task-force) to read the full recommendation statement. This includes more details on the rationale of the recommendation, including benefits and harms; supporting evidence; and recommendations of others.

The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decision-making to the specific patient or situation.

JAMA. 2002;328(8):746-753. Doi:10.1001/jama.2002.13044

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Statin Choice

Choose medication and dose to achieve the desired LDL-C reduction. From Table 3

High Intensity	**Moderate Intensity**	**Low Intensity**
Lowers LDL-C ≥50%	*Lowers LDL-C 30-49%*	*Lowers LDL-C ≤30%*
Atorvastatin (40 mg‡) 80 mg Rosuvastatin 20 mg (40 mg)	Atorvastatin 10 mg (20 mg) Rosuvastatin (5 mg) 10 mg Simvastatin 20-40 mg**	Simvastatin 10 mg*
	Pravastatin 40mg (80 mg) Lovastatin 40 mg (80 mg) Fluvastatin XL 80 mg Fluvastatin 40 mg BID Pitavastatin 1-4 mg	Pravastatin 10-20 mg Lovastatin 20 mg Fluvastatin 20-40 mg

**-FDA does not recommend use of simvastatin 80 mg due to increased risk of myopathy

Modification of Statin Choice

Since the following patient characteristics predispose to adverse statin effects, a moderate-intensity statin should be used:

- Multiple or serious co-morbidities, including impaired renal/ hepatic function.
- H/o previous statin intolerance or muscle disorder
- Unexplained elevation of ALT > 3 x upper limit of normal
- Patient characteristics or concomitant use of medicines affecting statin metabolism.
- Age >= 75 yo: Fewer people > 75 were included in the reviewed RCTs but evidence supports continuing tolerated statins. The small amount of available data does not clearly support starting high-intensity statins for secondary prevention; a larger amount of data does support the use of moderate-intensity statins. Few data in this group indicate a primary prevention benefit, so one must consider risk and benefits; Pooled Cohort Equations can be used in ages 79. Older individuals: PREVENT and ASCVD Risk Estimator Plus estimate risk for adults up to age 79. If a patient older than 79 years of age without known ASCVD is interested in a more precise estimate of risk, the clinician can use one of these calculators and enter an age of 79 to provide a rough estimate of 10-year ASCVD risk and thereby inform risk discussions. Decisions regarding the discontinuation of periodic risk assessment should be made in collaboration with each individual patient based on the patient's overall functional status, life expectancy, and values and preferences for risk factor modification.
- A lower intensity than recommended statin may be considered for other compelling indications including a history of hemorrhagic stroke or Asian ancestry.

Initial Evaluation for those not currently on statin
Clinical ASCVD:

- lipid panel, ALT
- CK should not routinely be measured during statin therapy.

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- Baseline measurement of CK may be reasonable if there is concern for risk based on personal or family history of statin intolerance or muscle disease, clinical presentation, or concomitant drug treatment that may increase myopathy risk.
- During statin treatment, it is reasonable to measure CK in individuals with muscle symptoms (pain, tenderness, stiffness, cramping, weakness, generalized fatigue)
- Routine monitoring of transaminases during statin therapy is no longer recommended. It is reasonable, however, to re-measure ALT in the setting of unusual fatigue, weakness, appetite loss, abdominal pain, dark urine, jaundice/icterus. For elevations in ALT > 3 times upper limit of normal, further investigation and either reducing statin dose, change to a different statin or stopping the medication are warranted.

No Clinical ASCVD: as above and screen for diabetes with HgbA1c or fasting glucose if diabetes status unknown

Evaluate for secondary causes as appropriate, particularly if Triglycerides are ≥ 500 mg/dL or LDL-C ≥190 mg/dL.

Common Secondary Causes of Hyperlipidemia Seen in Clinical Practice

Secondary Cause	Elevated LDL-C	Elevated Triglyceride
Diet	Saturated or trans-fat, weight gain, anorexia	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, most beta blockers (carvedilol – most favorable) effect on lipid profile), thiazides, clozapine, olanzapine)
Diseases	Biliary obstructions, nephrotic syndrome	Nephrotic syndrome, chronic renal failure, lipodystrophies
Disorders, altered metabolism	Hypothyroidism, obesity, pregnancy	Diabetes (poorly controlled), hypothyroidism, obesity, pregnancy

Monitoring Therapy

- Lipid lowering agents should be taken indefinitely or as long as treating hypercholesterolemia remains consistent with the patient's health and treatment goals. Lipid levels return to baseline once medication is stopped. Guidance is included in the guideline for patients over 75years old.
- Lipid panel 4-12 weeks after starting statin to determine adherence and then every 3-12 months as

clinically indicated.

- High-intensity statin therapy generally results in ≥50% decrease from untreated baseline (if baseline is unknown, LDL-C < 100 has generally been observed)
- Moderate-intensity statin therapy generally results in 30-49% reduction.
- Percent reduction may be used to indicate adherence (but can also indicate biologic variability); attention should be paid to adherence and lifestyle therapy, evaluation, and treatment for secondary causes; clinical judgment should be used to decide if any therapy should be increased.
- Ongoing monitoring of LFTs is NOT recommended by the FDA given that there is a low risk of clinically significant increase in LFTs.
- A decrease in statin dose may be considered when 2 consecutive LDL-C values are < 40 mg/dL.
- It may be harmful to initiate or increase a simvastatin dose to 80 mg/dL due to the risk of rhabdomyolysis; lovastatin should be avoided in the setting of several medicines and dose limitations exist for other medicines; make sure to check labeling.
- Current diabetes screening guidelines should be maintained for those on statins.
- A review of manufacturer's prescribing information may be useful prior to initiation of any cholesterol lowering drug.
- To evaluate and treat muscle symptoms:
    - Obtain a history of baseline symptoms prior to starting therapy.
    - For unexplained severe symptoms, discontinue statin and evaluate CK, Cr, UA
    - For mild-moderate symptoms
        - Discontinue statin until symptoms can be evaluated.
        - Evaluate for conditions that might increase risk (hypothyroidism, reduced renal or hepatic function, rheumatologic disorder like polymyalgia rheumatica, steroid myopathy, vitamin D deficiency, primary muscle disease)
        - If symptoms resolve and there is no contraindication, give the same statin at an original or lower dose and observe for symptoms.
        - If causal relationship exists, discontinue original statin and when symptoms resolve, use a low dose of different statin. Pravastatin and fluvastatin are the statins with the least intrinsic muscle toxicity.
        - Once that dose is tolerated, it can be gradually increased.
        - If symptoms do not resolve after 2 months without statin, or CK does not return to normal, consider other causes.
        - If the statin is determined to not be the cause, or if the predisposing condition has been treated, the original statin at the original dose can be resumed.
    - For presentation with a confusional state or memory impairment, it may be reasonable to evaluate for non-statin causes (e.g., exposure to other drugs, systemic, or neuropsychiatric causes) in addition to possible statin adverse effects.
    - Statins used in combination with other cholesterol-lowering drug therapies may require more intensive monitoring.
    - Even lower-intensity statin therapy can reduce ASCVD events, so maximum intensity that does not cause adverse events should be used.
    - Adverse events involving statins should be reported to the FDA MedWatch program.

Non-statin Therapy

Non-statin therapy can be considered in high-risk patients (including those with clinical ASCVD less than 75 years old those with LDL-C > 190 or diabetes) who have a less-than-anticipated response to statins or are unable to tolerate the recommended statin intensity; clinicians should preferentially prescribe drugs w/ RCT proof of ASCVD risk reduction that exceeds risk of adverse effects.

- **Cholesterol-Absorption Inhibitor (Ezetimibe)**
  - Most common "add-on" medication in those not meeting goal with statin only.
  - Lowers LDL-C levels by 13-20%
  - Reasonable to obtain transaminases at baseline; when co-administered with statin, monitor LFTs as clinically indicated and stop if ALT > 3x ULN.
- **Bempedoic acid:**
  - may be used in statin-intolerant patients who require modest lipid lowering; reduces LDL by 20 to 25 percent and recently has been shown to reduce cardiovascular events. Need for measuring serum uric acid and stabilizing patients with active gout. Approved for patients with heterozygous familial hypercholesterolemia or established ASCVD who require additional lowering of LDL-C.
- **Bile Acid Sequestrants (Colesevelam)**
  - Not absorbed and not associated with systemic side effects.
  - Lowers LDL-C levels by 15-30%
  - Do not use if baseline fasting trig > 300 mg/dL or type III hyperlipoproteinemia; fasting lipids should be obtained at baseline, at 3 months and then Q6-12 months.
  - May be used with caution if baseline trig is 250-299 with fasting lipids at 6 weeks; discontinue if triglycerides exceed 400 mg/dL.
- **PCSK9 Inhibitors**
  - Evolocumab (Repatha, Repatha SureClick) and Alirocumab (Praluent)
  - Reduce LDL_C by as much as 60% in patients on statins; Evolocumab has been shown to reduce cardiovascular events but not mortality.
  - The current guideline recommends that patients be on high-intensity or maximal tolerated dose of a statin and ezetimibe before considering.
  - Indications
    - **Homozygous familial hypercholesterolemia:** Adjunct to diet and other LDL-lowering therapies (e.g., statins, ezetimibe, LDL apheresis) for the treatment of patients with homozygous familial hypercholesterolemia (HoFH) who require additional lowering of LDL-C. (evolocumab only)
    - **Hyperlipidemia, primary:** Adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease (CVD), who require additional lowering of low-density lipoprotein cholesterol (LDL-C). (evolocumab and alirocumab)
  - Administered subcutaneously: monthly evolocumab (Repatha) or every 2 weeks alirocumab.

  - (Praluent). Evolocumab does have an alternate q 2week regimen for primary hyperlipidemia)

  - Repatha (140 mg) $337 per dose every 2 weeks; Sureclick $337, Pushtronex $209 /420 mg dose once monthly
  - Praluent (75 mg – 150 mg) $304 per dose; Repatha –utilizing monthly dosing regimen $1853.

- **Small Interfering RNA (Inclisiran)**
  - adjunct to diet and maximally tolerated statin therapy for treatment of heterozygous familial hypercholesterolemia or atherosclerotic cardiovascular disease that requires further LDL-C lowering in allergic responses to both evolucumab and alirocumab or persons who have difficulty using a pen injector due to arthritis and/or weakness of the hands.
  - subcutaneous injection administered every three months for two doses, then every six months thereafter.
- **ANGPTL3:** Monoclonal antibody against Angiopoietin-like proteins.
  Angiotensin like proteins are regulators of lipoprotein metabolism which is a hormone produced by the liver that inhibits lipoprotein lipase, an enzyme that breaks down plasma triglycerides. In addition, it lowers LDL-C using a low-density lipoprotein-independent mechanism. Evinacumab in patients with refractory hypercholesterolemia or familial hypercholesterolemia. Evinacumab is a fully human monoclonal antibody against ANGPTL3, and it has been shown to significantly decrease LDL-C when given either subcutaneously or intravenously. A 2020 phase 2 trial randomly assigned 272 patients with refractory hypercholesterolemia and either heterozygous familial hypercholesterolemia (FH) or non-heterozygous FH with clinical atherosclerotic cardiovascular disease to various doses of evinacumab or placebo All patients were treated with a PCSK9 inhibitor and a statin at a maximum-tolerated dose, with or without ezetimibe. At week 16, evinacumab significantly reduced LDL-C by 50 percent with intravenous (IV) administration (15 mg/kg IV every four weeks) and 56 percent with subcutaneous administration (450 mg subcutaneously every week). Through its effects on endothelial lipase, evinacumab reduces hepatic very-low-density lipoprotein cholesterol production and secretion and, consequently, LDL-C [20, 21]
- **Fibrates**
  - Primarily used for hypertriglyceridemia
  - Gemfibrozil should not be initiated in patients on statin therapy due to increased risk of muscle symptoms and rhabdomyolysis.
  - Fenofibrate –concurrent use with statin therapy is no longer recommended. FDA has deemed that benefits of combined therapy do not outweigh risks.
- **Omega-3 Fatty Acids**
  - Primarily used for hypertriglyceridemia
  - If EPA and/or DHA are used for trig > 500 mg/dL, evaluate in setting of GI disturbance, skin changes, bleeding.

- **Niacin**
  - **Rarely used as there are more effective and safer medications available.**
  - Obtain transaminases, fasting glucose or A1c and uric acid before initiation, during up- titration to maintenance dose, then every 6 months
  - Niacin should not be used if LFTs are > 2-3 x ULN; there are persistent severe cutaneous symptoms, persistent hyperglycemia, acute gout, unexplained abdominal pain, or GI symptoms, or if new onset atrial fibrillation or weight loss occurs.
  - If an adverse effect occurs, risk: benefit ratio must be considered before restarting.
  - To reduce cutaneous symptoms:
    - Start low dose and titrate over weeks as tolerated.
    - Take w/ food or premedicate w/ 325 mg ASA 30 min prior to dose.
    - If using extended-release preparation: increase from 500 mg to 2000 mg/day over 4-8 weeks, <= weekly
    - If using immediate-release preparation: increase from 100 mg TID and up-titrate to 3g/daily, in 2-3 divided doses.

2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease
A separate Guideline on the Primary Prevention of Cardiovascular Disease was also issued by the AHA/ACC in 2019. The guideline emphasizes the following:

- Maintenance of a healthy weight
- Consuming a diet consisting of vegetables, fruits, nuts, whole grains, lean vegetable or animal protein and fish and avoiding trans fats, red meat (especially processed red meats), refined carbohydrates and sweetened beverages.
- Engaging in at least 150 per week of moderate-intensity physical activity or 75 minutes per week of vigorous intensity physical activity
- Smoking cessation

Patient education:
UpToDate-Patient Education High Cholesterol and Lipid Treatment Options
UpToDate-Patient Education Diet and Health
AHA-Healthy for Good Eat Smart
Dietary Guidelines for Americans 2020-25

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HMG- CoA Reductase Inhibitors (Statins)			
Average LDL-C reduction: Low Intensity <30%, Moderate Intensity 30% to <50%, High Intensity ≥50%			
Drug		**Dose**	**Comments /Safety**
Atorvastatin (Lipitor) ($116-$321)	Moderate Intensity	10 -20 mg daily	(see guideline pages 9-11 for additional recommendations) Baseline measurement of CK is reasonable for individuals believed to be at increased risk for adverse muscle events. During statin therapy, it is reasonable to measure CK in individuals with muscle symptoms, including pain, tenderness, stiffness, cramping, weakness, or generalized fatigue. Baseline measurement of hepatic transaminase levels (AST and ALT) should be performed before initiating statin therapy. During statin therapy, it is reasonable to measure hepatic function if symptoms suggesting hepatotoxicity arise. Individuals receiving statin therapy should be evaluated for new-onset diabetes mellitus. Continue statin therapy if diabetes develops. If unexplained severe muscle symptoms or fatigue develop during statin therapy, promptly discontinue the statin, and address the possibility of rhabdomyolysis by evaluating CK,
	High Intensity	40 - 80 mg daily	
Fluvastatin ($150-$300)	Low Intensity	20-40 mg nightly	
	Moderate Intensity	40 mg twice daily	
Fluvastatin XL (Lescol XL) ($262-$277)	Moderate Intensity	80 mg daily	
Lovastatin ($68-$292) Lovastatin extended release (Altoprev) ($1300 – brand only)	Low Intensity	20 mg nightly *IR form to be taken with*	
	Moderate Intensity	40-80 mg nightly *IR form to be taken with evening meal.*	
Pitavastatin (Livalo) ($384 – brand only) (Zypitamag) ($279 – brand only)	Low Intensity	1 mg daily	
	Moderate Intensity	2-4 mg daily	
Pravastatin ($30-$144)	Low Intensity	10-20 mg daily	
	Moderate Intensity	40-80 mg daily	
Rosuvastatin (Crestor) ($43-$269)	Moderate Intensity	5-10 mg daily, do not crush or chew.	
	High Intensity	20-40 mg daily, do not crush or chew	
Simvastatin	Low Intensity	10 mg nightly	

(Zocor) ($84-$147)	Moderate Intensity	20-40 mg nightly	creatinine, and a urinalysis for myoglobinuria.

Cost per 30 days of generic medication unless otherwise specified.

Significant Statin Drug Interactions	
Atorvastatin	Use with caution in patients in patients taking strong CYP3A4inhibitors. Consider alternate agents. Examples of common medications to avoid with atorvastatin: • Cyclosporine • Gemfibrozil • Tipranavir plus ritonavir • Telaprevir • Itraconazole Use with caution and use with the lowest atorvastatin dose necessary: • Lopinavir + ritonavir • Amiodarone Do not exceed 20 mg daily atorvastatin with the following agents: • Darunavir + ritonavir • Fosamprenavir • Fosamprenavir + ritonavir • Saquinavir + ritonavir Administer 1 hour before or at least 4 hours after cholestyramine or colestipol. Use statins with caution with niacin ≥1000 mg/day. Experts suggest avoiding grapefruit with atorvastatin due to inhibition of the CYP3A4 enzyme
Fluvastatin	Do not exceed Fluvastatin 20 mg twice daily (Fluvastatin may be least likely to interact): Cyclosporine Administer 1 hour before or at least 4 hours after cholestyramine or colestipol. Avoid with Fluvastatin: Gemfibrozil, Fenofibrate Use statins with caution with niacin ≥1000 mg/day

Lovastatin	Use with caution in patients in patients taking strong CYP3A4 inhibitors. Consider alternate agents. Contraindicated with lovastatin: • Itraconazole • Ketoconazole • Posaconazole • Erythromycin • Clarithromycin • Telithromycin • HIV protease inhibitors • Boceprevir • Telaprevir • Nefazodone Avoid with lovastatin: • Cyclosporine • Gemfibrozil Do not exceed 20 mg lovastatin daily with: • Danazol • Diltiazem • Verapamil • Clarithromycin Administer 1 hour before or at least 4 hours after cholestyramine or colestipol. Use statins with caution with niacin ≥1000 mg/day. Limit extended-release niacin to 2000 mg and lovastatin dose to 40mg daily when used in combination.

Pitavastatin	Contraindicated with Pitavastatin: Cyclosporine Limit dose to 1 mg daily with: Erythromycin Limit dose to 2 mg daily with: Rifampin
Pravastatin	Administer 1 hour before or at least 4 hours after cholestyramine or colestipol Avoid use with pravastatin: Gemfibrozil. Do not exceed pravastatin 20 mg daily: Cyclosporine Do not exceed pravastatin 40 mg daily: • Clarithromycin • Azithromycin Use statins with caution with niacin ≥1000 mg/day
Rosuvastatin	Do not exceed rosuvastatin 5 mg: • Cyclosporine Do not exceed rosuvastatin 10 mg daily: • Atazanavir ± ritonavir • Lopinavir + ritonavir Avoid use with rosuvastatin: • Gemfibrozil Administer 1 hr. before or at least 4 hours after cholestyramine or colestipol. Use statins with caution with niacin ≥1000 mg/day
Simvastatin	Contraindicated with simvastatin: • HIV protease inhibitors • Boceprevir • Telaprevir • Itraconazole • Ketoconazole • Posaconazole • Danazol • Clarithromycin • Erythromycin Do not exceed simvastatin 20 mg: • Amiodarone • Amlodipine Administer 1 hour before or at least 4 hours after cholestyramine or colestipol. Use statins with caution with niacin ≥1000 mg/day. Limit extended-release niacin to 2000 mg and simvastatin dose to 40mg daily when used in combination. Experts suggest avoiding grapefruit with simvastatin.

Non-statins		
Clinicians treating high-risk patients who have a less-than-anticipated response to statins, who are unable to tolerate recommended intensity of a statin, or who are completely statin intolerant may consider the addition of a non-statin cholesterol-lowering therapy.		
Drug	**Dose**	**Other**
Selective Cholesterol Absorption Inhibitor		When ezetimibe is co-administered with a statin, monitor transaminase levels as clinically indicated, and discontinue ezetimibe if persistent ALT elevations >3 times ULN occur. Absorption decreased by bile acid sequestrants; administer ezetimibe at least 2hrs before or 4hrs after.
Ezetimibe (Zetia) (339)	10 mg every day	
Bile Acid Sequestrants		BAS should not be used in individuals with baseline fasting triglyceride levels ≥300 mg/dL or type III hyperlipoproteinemia. Use BAS with caution if baseline triglyceride levels are 250 to 299 mg/dL and evaluate a fasting lipid panel in 4 to 6 weeks after initiation. Discontinue the BAS if triglycerides exceed 400 mg/dL. The bile acid sequestrant should be taken 1 hour after or 4 hours before other medications due to binding interactions. Granules must be administered as solution; not to be taken in dry form.
Cholestyramine granules • Cholestyramine $2/4g powder or $5/4g packet • Questran $2/4g powder or $7/4g packet • Cholestyramine Light packets $4/4g or $4/4g powder (brand only) • Prevalite packets $3/4g powder or $5/4g packet	Initial: 4g 1-2 times daily with food Usual: 4g 2-4 times a day with food. Max 24g/day	
Colestipol (Colestid) • Colestipol granules $/5g • Colestipol tablets $76-$605	Tabs: Initial: 2 g 1-2 times daily Usual: 2-16 g/day, may be split into divided doses Granules: Initial: 5g 1-2 times daily Usual: 5-30g/day, may be split into divided doses	
Colesevelam (Welchol) $198-$713	3.75 g (6 tabs) once daily or 1.875g (3 tabs) twice daily with meals	
Fibrates		

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Fenofibrate		
Trilipix and its generics	45-135mg daily	Fenofibrate dose may need to be adjusted based on patient's renal function. Gemfibrozil should not be initiated in patients on statin therapy because of an increased risk for muscle symptoms and rhabdomyolysis.
Antara and its generics (micronized) $108-$325	30-90mg daily or 13-130mg daily or 67-200mg daily depending on generic formulation	
Lipofen and its generics (non-micronized) $98-$196	50-100mg daily	
Fibricor and its generics $355-$709	35-105mg daily	
TriCor and its generics (nanocrystals) $20-$37	48-145mg daily	
Fenoglide and its generics (nonmicronized) $86-$313	40-120 mg once daily or 54-160mg once daily depending on generic formulation	
Gemfibrozil (Lopid) $95	600 mg twice a day 30 minutes before meals	
Antilipemic Agents		
Niacin (Most niacin products are available over the counter) Immediate release *Niacor* ($5-$14) Extended-release *Niaspan* ($2-$5)	Generally, not recommended unless intolerable to other therapies or goals cannot be achieved with other therapies. Immediate release: Initial: 250mg with evening meal Usual: 2-6 g in 3 divided doses Extended release: Initial: 500 mg every evening Usual: 1-2 g every evening	Niacin should not be used if: Hepatic transaminase elevations are higher than 2 to 3 times ULN. Persistent severe cutaneous symptoms, persistent hyperglycemia, acute gout or unexplained abdominal pain or gastrointestinal symptoms occur. New-onset atrial fibrillation or weight loss may occur. Use only if triglyceride goals are not met with other therapies

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Omega-3-acid ethyl esters *(Lovaza) $576* Also available OTC	4g/day as single dose or 2 divided doses	If used for the management of severe hypertriglyceridemia, defined as triglycerides ≥500 mg/dL, it is reasonable to evaluate the patient for gastrointestinal disturbances, skin changes, and bleeding. Do not crush, break, or chew.
Icosapent Ethyl (*Vascepa*) $404	**Hypertriglyceridemia, severe** **CV event risk reduction, adjunct Tx.** 2 g twice daily	Patients in the icosapent ethyl group were more likely to be hospitalized for atrial fibrillation or flutter; this is not a contraindication for its use but is a consideration and should be part of clinician-patient shared decision making.
Combination Products Ezetimibe/Simvastatin	10/40 mg nightly	See individual agents
PCSK9 Inhibitors		
Evolocumab (brand name only) Repatha: $337/140mg Repatha SureClick: $337/140mg Repatha Pushtronex: $209/420mg	**Hyperlipidemia, primary:** SubQ: 140 mg every 2 weeks or 420 mg once monthly **Homozygous familial hypercholesterolemia:** SubQ: 420 mg once monthly; after 12 weeks may increase to 420mg every 2 weeks if needed.	Most common side effect: >10%: Respiratory: Nasopharyngitis (6% to 11%) Influenza 8-9% Hypersensitivity reactions have been reported. Once monthly dose given as SubQ infusion over 9 minutes or as three 140mg injections within a 30- minute period.
Alirocumab (Praluent – brand name only) $304 per 75mg or 150mg injection	**Hyperlipidemia SubQ** Initial 75mg once every 2 weeks or 300mg every 4 weeks Maximum:150 mg every 2 weeks **Homozygous familial hypercholesterolemia:** SubQ: 150mg every 2 weeks	Most common side effect: injection site reaction (7%), Influenza (6%), Diarrhea 5%. Liver enzyme disorder 3% Hypersensitivity reactions have been reported. If giving 300mg dose, administer two 150mg injections in two different injection sites.
Antilipemic Small Interfering Ribonucleic Acid (siRNA) Agent		

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Inclisiran (Leqvio – brand name only) $4048/284mg	**Primary hyperlipidemia, (adjunct Tx)** **Heterozygous familial hypercholesterolemia** Single 284mg injection followed by a second injection at 3 months and then every 6 months	Most common side effects: injection site reaction (8%), arthralgia (5%), and bronchitis (4%)
Angiopoietin-Like Protein 3 Inhibitor		
Evinacumab (Evkeeza – brand name only) $14553/345mg vial	**Homozygous familial hypercholesterolemia** 15mg/kg IV every 4 weeks	May cause nasopharyngitis, dizziness, rhinorrhea, and nausea. Female patients should be advised to use effective contraception during treatment and for at least 5 months after last dose.
Antilipemic Agents		
Bempedoic Acid (Nexletol – brand name only) $490 **Combination Products** Bempedoic Acid/Ezetimibe 180/10 mg daily (Nexlizet- brand name only) $489	**Primary hyperlipidemia** **Heterozygous familial hypercholesterolemia** Dose: 180mg once daily	May cause hyperuricemia, gout, and tendon rupture. See individual agents.
Lomitapide (Juxtapid – brand name only) $68541	**Homozygous familial hypercholesterolemia** Initial: 5mg daily Max: 60 mg daily	Boxed Warning: hepatotoxicity; available through REMS program only. Administer at least 2 hours after evening meal to decrease risk of GI adverse effects. Do not crush or chew. Most common side effects: chest pain (24%), fatigue (17%), GI effects such as diarrhea (up to 79%) and nausea (65%)

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