

2018 Clinical Practice Guidelines on the Management of Blood Cholesterol

*2018 AHA/ ACC/ AACVPR/ AAPA/ ABC/ ACPM/
ADA/ AGS/ APhA/ ASPC/ NLA/ PCNA Guideline*

Measurements of LDL-C and Non-HDL-C

Recommendations for Measurements of LDL-C and Non-HDL-C

Referenced studies that support recommendations are summarized in [Online Data Supplement 1](#).

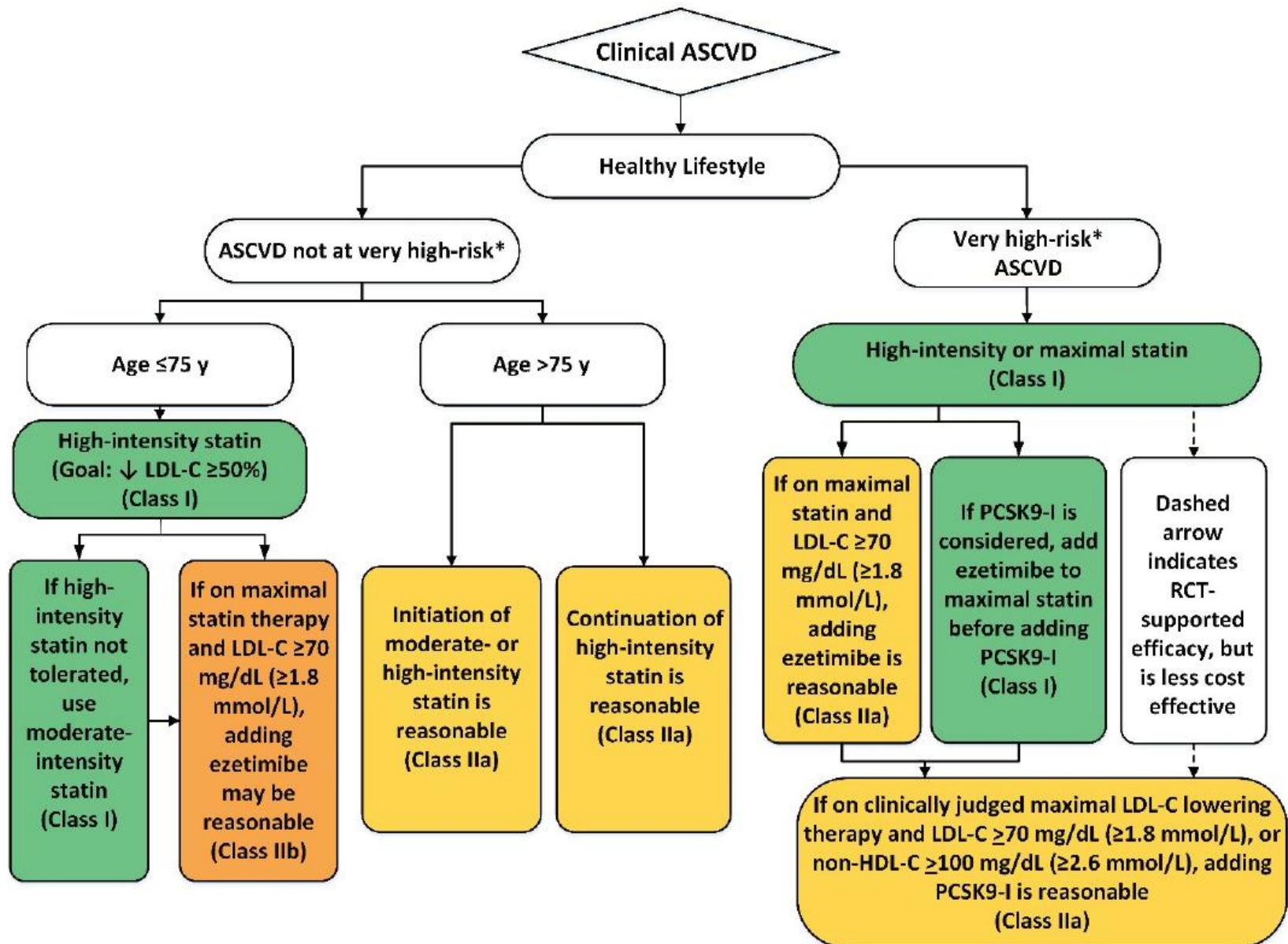
COR	LOE	Recommendations
I	B-NR	1. In adults who are 20 years of age or older and not on lipid-lowering therapy, measurement of either a fasting or a nonfasting plasma lipid profile is effective in estimating ASCVD risk and documenting baseline LDL-C (S2.1-1–S2.1-6).
I	B-NR	2. In adults who are 20 years of age or older and in whom an initial nonfasting lipid profile reveals a triglycerides level of 400 mg/dL (≥ 4.5 mmol/L) or higher, a repeat lipid profile in the fasting state should be performed for assessment of fasting triglyceride levels and baseline LDL-C (S2.1-1–S2.1-4).
IIa	C-LD	3. For patients with an LDL-C level less than 70 mg/dL (< 1.8 mmol/L), measurement of direct LDL-C or modified LDL-C estimate is reasonable to improve accuracy over the Friedewald formula (S2.1-7–S2.1-9).
IIa	C-LD	4. In adults who are 20 years of age or older and without a personal history of ASCVD but with a family history of premature ASCVD or genetic hyperlipidemia, measurement of a fasting plasma lipid profile is reasonable as part of an initial evaluation to aid in the understanding and identification of familial lipid disorders.

Statin Therapy

- Among lipid-lowering drugs, statins are the cornerstone of therapy, in addition to healthy lifestyle interventions
- The intensity of statin therapy is divided into 3 categories: high-intensity, moderate-intensity, and low-intensity

	High Intensity	Moderate Intensity	Low Intensity
LDL-C lowering†	≥50%	30%–49%	<30%
Statins	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 40 mg (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

Secondary Prevention in Patients With Clinical ASCVD



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)

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 m²)
- 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

Severe Hypercholesterolemia (LDL-C $\geq$ 190 mg/dL

COR	LOE	Recommendations
I	B-R	1. In patients 20 to 75 years of age with an LDL-C level of 190 mg/dL ($\geq$ 4.9 mmol/L) or higher, maximally tolerated statin therapy is recommended (S4.2-1–S4.2-7).
IIa	B-R	2. In patients 20 to 75 years of age with an LDL-C level of 190 mg/dL ($\geq$ 4.9 mmol/L) or higher who achieve less than a 50% reduction in LDL-C while receiving maximally tolerated statin therapy and/or have an LDL-C level of 100 mg/dL ($\geq$ 2.6 mmol/L) or higher, ezetimibe therapy is reasonable (S4.2-8–S4.2-10).
IIb	B-R	3. In patients 20 to 75 years of age with a baseline LDL-C level $\geq$ 190 mg/dL ($\geq$ 4.9 mmol/L), who achieve less than a 50% reduction in LDL-C levels and have fasting triglycerides $\leq$ 300 mg/dL ($\leq$ 3.4 mmol/L). while taking maximally tolerated statin and ezetimibe therapy, the addition of a bile acid sequestrant may be considered (S4.2-11, S4.2-12).

Severe Hypercholesterolemia (LDL-C ≥ 190 mg/dL)

IIb	B-R	4. In patients 30 to 75 years of age with heterozygous FH and with an LDL-C level of 100 mg/dL (≥ 2.6 mmol/L) or higher while taking maximally tolerated statin and ezetimibe therapy, the addition of a PCSK9 inhibitor may be considered (S4.2-9, S4.2-13–S4.2-15).
IIb	C-LD	5. In patients 40 to 75 years of age with a baseline LDL-C level of 220 mg/dL (≥ 5.7 mmol/L) or higher and who achieve an on-treatment LDL-C level of 130 mg/dL (≥ 3.4 mmol/L) or higher while receiving maximally tolerated statin and ezetimibe therapy, the addition of a PCSK9 inhibitor may be considered (S4.2-13–S4.2-17).
Value Statement: Uncertain Value (B-NR)		6. Among patients with FH without evidence of clinical ASCVD taking maximally tolerated statin and ezetimibe therapy, PCSK9 inhibitors provide uncertain value at mid-2018 U.S. list prices.

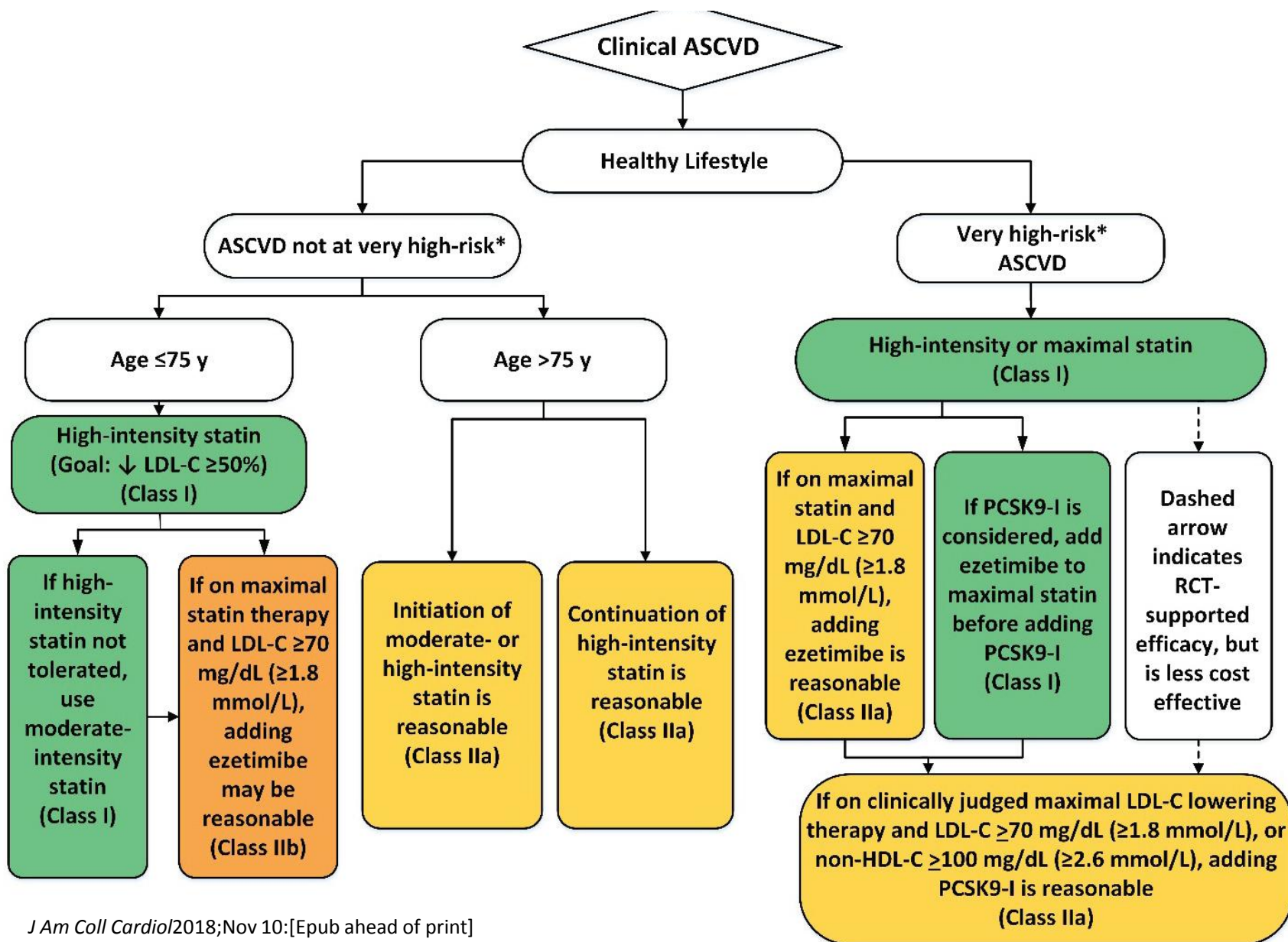
Diabetes Mellitus in Adults

COR	LOE	Recommendations
I	A	1. In adults 40 to 75 years of age with diabetes mellitus, regardless of estimated 10-year ASCVD risk, moderate-intensity statin therapy is indicated (S4.3-1–S4.3-9).
Ila	B-NR	2. In adults 40 to 75 years of age with diabetes mellitus and an LDL-C level of 70 to 189 mg/dL (1.7 to 4.8 mmol/L), it is reasonable to assess the 10-year risk of a first ASCVD event by using the race and sex-specific PCE to help stratify ASCVD risk (S4.3-10, S4.3-11).
Ila	B-R	3. In adults with diabetes mellitus who have multiple ASCVD risk factors, it is reasonable to prescribe high-intensity statin therapy with the aim to reduce LDL-C levels by 50% or more (S4.3-12, S4.3-13).
Ila	B-NR	4. In adults older than 75 years of age with diabetes mellitus and who are already on statin therapy, it is reasonable to continue statin therapy (S4.3-5, S4.3-8, S4.3-13).

Diabetes Mellitus in Adults

COR	LOE	Recommendations
IIb	C-LD	5. In adults with diabetes mellitus and 10-year ASCVD risk of 20% or higher, it may be reasonable to add ezetimibe to maximally tolerated statin therapy to reduce LDL-C levels by 50% or more (S4.3-14, S4.3-15).
IIb	C-LD	6. In adults older than 75 years with diabetes mellitus, it may be reasonable to initiate statin therapy after a clinician–patient discussion of potential benefits and risks (S4.3-5, S4.3-8, S4.3-13).
IIb	C-LD	7. In adults 20 to 39 years of age with diabetes mellitus that is either of long duration (≥ 10 years of type 2 diabetes mellitus, ≥ 20 years of type 1 diabetes mellitus), albuminuria (≥ 30 mcg of albumin/mg creatinine), estimated glomerular filtration rate (eGFR) less than 60 mL/min/1.73 m ² , retinopathy, neuropathy, or ABI (< 0.9), it may be reasonable to initiate statin therapy (S4.3-5, S4.3-6, S4.3-8, S4.3-16–S4.3-25).

Secondary Prevention in Patients With Clinical ASCVD



Risk-Enhancing Factors for Clinician–Patient Risk Discussion

- Family history of premature ASCVD (males, age <55 y; females, age <65 y)
- Primary hypercholesterolemia (LDL-C, 160–189 mg/dL [4.1–4.8 mmol/L]; non-HDL-C 190–219 mg/dL [4.9– 5.6 mmol/L])*
- Metabolic syndrome (increased waist circumference, elevated triglycerides [>175 mg/dL], elevated blood pressure, elevated glucose, and low HDL-C [<40 mg/dL in men; <50 in women mg/dL] are factors; tally of 3 makes the diagnosis)
- Chronic kidney disease (eGFR 15–59 mL/min/1.73 m² with or without albuminuria; not treated with dialysis or kidney transplantation)
- Chronic inflammatory conditions such as psoriasis, RA, or HIV/AIDS

Risk-Enhancing Factors for Clinician–Patient Risk Discussion

- History of premature menopause (before age 40 y) and history of pregnancy-associated conditions that increase later ASCVD risk such as preeclampsia
- High-risk race/ethnicities (e.g., South Asian ancestry)
- Lipid/biomarkers: Associated with increased ASCVD risk
 - Persistently* elevated, primary hypertriglyceridemia (≥ 175 mg/dL);
 - If measured:
 - Elevated high-sensitivity C-reactive protein (≥ 2.0 mg/L)
 - Elevated Lp(a): A relative indication for its measurement is family history of premature ASCVD. An Lp(a) ≥ 50
- Elevated apoB ≥ 130 mg/dL: A relative indication for its measurement would be triglyceride ≥ 200 mg/dL. A level ≥ 130 mg/dL corresponds to an LDL-C > 160 mg/dL and constitutes a risk-enhancing factor
- ABI < 0.9

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).

Checklist for Clinician–Patient Shared Decision-Making for Initiating Therapy

Checklist Item	Recommendation
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.

Top 10 Messages to Reduce Risk of Atherosclerotic CVD through Cholesterol Management is as follows:

- In all individuals, emphasize a heart-healthy lifestyle across the life course.
- In patients with clinical ASCVD, reduce low-density lipoprotein cholesterol (LDL-C) with high intensity statin therapy or maximally tolerated statin therapy.
- In very high-risk ASCVD, use a LDL-C threshold of 70 mg/dL (1.8 mmol/L) to consider addition of nonstatins 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 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.
- 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

Top 10 Messages to Reduce Risk of Atherosclerotic CVD through Cholesterol Management is as follows:

- In adults 40 to 75 years of age evaluated for primary ASCVD prevention, have a clinician–patient risk discussion before starting statin therapy.
- 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 $\geq 7.5\%$, start a moderate-intensity statin if a discussion of treatment options favors statin therapy
- 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
- In adults 40 to 75 years of age without diabetes mellitus and with LDL-C levels ≥ 70 mg/dL to 189 mg/dL (≥ 1.8 – 4.9 mmol/L), at a 10-year ASCVD risk of $\geq 7.5\%$ to 19.9%, if a decision about statin therapy is uncertain, consider measuring CAC.
- 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.