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

Guideline on the Management of Blood Cholesterol: Executive Summary

High Blood Cholesterol and ASCVD

Measurements of LDL-C and Non-HDL-C

Recommendations for Measurements of LDL-C and Non-HDL-C		
COR	LOE	Recommendations
I	B-NR	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.
I	B-NR	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.

Measurements of LDL-C and Non-HDL-C

Recommendations for Measurements of LDL-C and Non-HDL-C		
COR	LOE	Recommendations
Ia	C-LD	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.
Ia	C-LD	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.

Patient Management Groups

Table 3. High-, Moderate-, and Low-Intensity Statin Therapy*

	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	Pravastatin 10–20 mg Lovastatin 20 mg Fluvastatin 20–40 mg

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

<u>Major ASCVD Events</u>
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)

Table 4 continued

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)
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

Secondary ASCVD Prevention

Recommendations for Statin Therapy Use in Patients With ASCVD		
COR	LOE	Recommendations
I	A	In patients who are 75 years of age or younger with clinical ASCVD,* high-intensity statin therapy should be initiated or continued with the aim of achieving a 50% or greater reduction in LDL-C levels.
I	A	In patients with clinical ASCVD in whom high-intensity statin therapy is contraindicated or who experience statin-associated side effects, moderate-intensity statin therapy should be initiated or continued with the aim of achieving a 30% to 49% reduction in LDL-C levels.

Secondary ASCVD Prevention

Recommendations for Statin Therapy Use in Patients With ASCVD		
COR	LOE	Recommendations
I	B-NR	In patients with clinical ASCVD who are judged to be very high risk and <i>considered for PCSK9 inhibitor therapy</i> , maximally tolerated LDL-C lowering therapy should include maximally tolerated statin therapy and ezetimibe.
IIa	A ^{SR}	In patients with clinical ASCVD who are judged to be very high risk and who are on maximally tolerated LDL-C lowering therapy with LDL-C 70 mg/dL (≥ 1.8 mmol/L) or higher or a non-HDL-C level of 100 mg/dL (≥ 2.6 mmol/L) or higher, it is reasonable to add a PCSK9 inhibitor following a clinician–patient discussion about the net benefit, safety, and cost.

Secondary ASCVD Prevention

Recommendations for Statin Therapy Use in Patients With ASCVD		
COR	LOE	Recommendations
Ia	B-R	In patients with clinical ASCVD who are on maximally tolerated statin therapy and are judged to be at very high risk and have an LDL-C level of 70 mg/dL (≥ 1.8 mmol/L) or higher, it is reasonable to add ezetimibe therapy.
Value Statement: Low Value (LOE: B-NR)		At mid-2018 list prices, PCSK9 inhibitors have a low cost value ($> \$150,000$ per QALY) compared to good cost value ($< \$50,000$ per QALY) (Section 7 provides a full discussion of the dynamic interaction of different prices and clinical benefit).

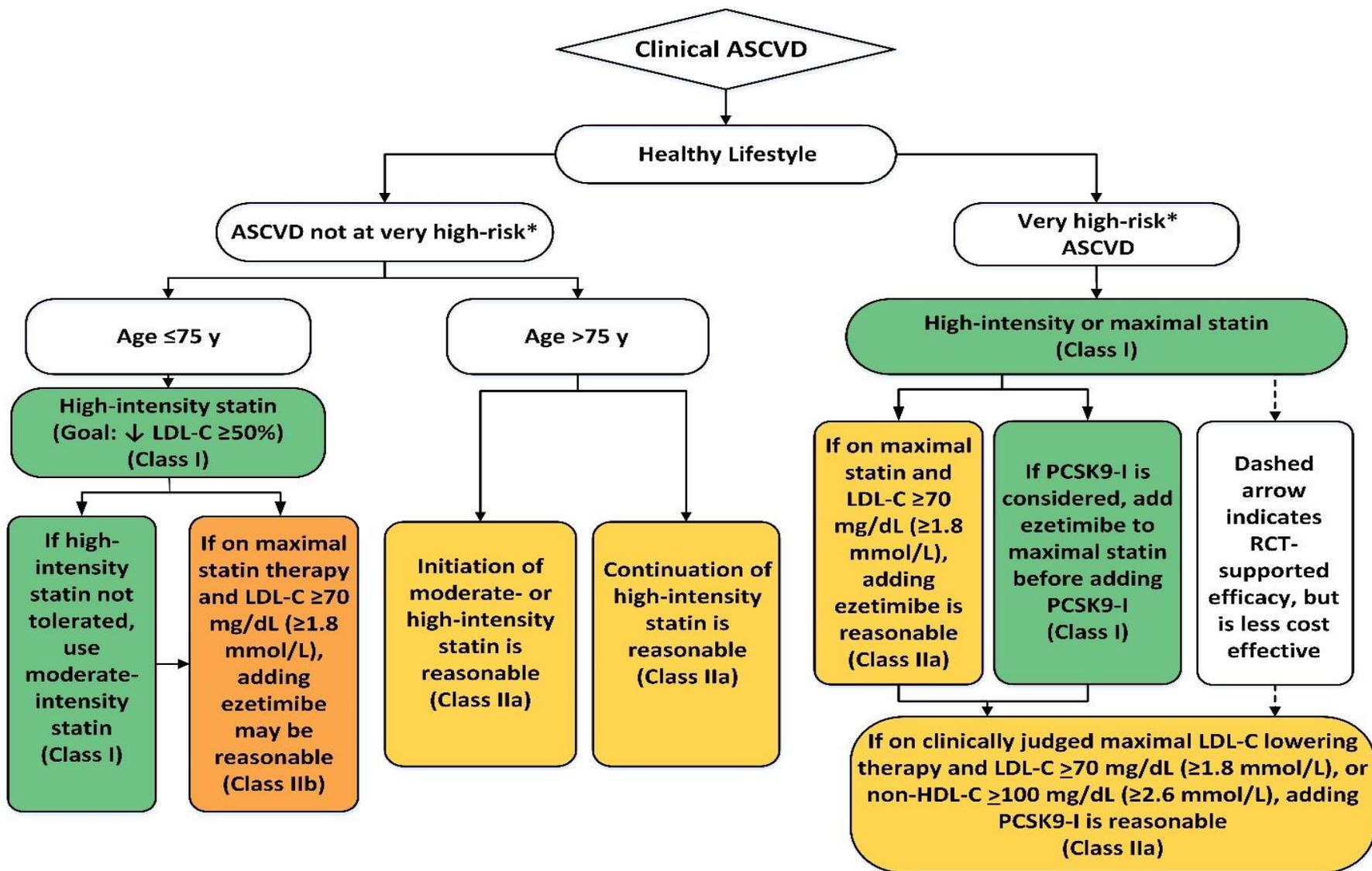
Secondary ASCVD Prevention

Recommendations for Statin Therapy Use in Patients With ASCVD		
COR	LOE	Recommendations
IIa	B-R	In patients older than 75 years of age with clinical ASCVD, it is reasonable to initiate moderate- or high-intensity statin therapy after evaluation of the potential for ASCVD risk reduction, adverse effects, and drug–drug interactions, as well as patient frailty and patient preferences.
IIa	C-LD	In patients older than 75 years of age who are tolerating high-intensity statin therapy, it is reasonable to continue high-intensity statin therapy after evaluation of the potential for ASCVD risk reduction, adverse effects, and drug–drug interactions, as well as patient frailty and patient preferences.

Secondary ASCVD Prevention

Recommendations for Statin Therapy Use in Patients With ASCVD		
COR	LOE	Recommendations
IIb	B-R	In patients with clinical ASCVD who are receiving maximally tolerated statin therapy and whose LDL-C level remains 70 mg/dL (≥ 1.8 mmol/L) or higher, it may be reasonable to add ezetimibe.
IIb	B-R	In patients with heart failure (HF) with reduced ejection fraction attributable to ischemic heart disease who have a reasonable life expectancy (3 to 5 years) and are not already on a statin because of ASCVD, clinicians may consider initiation of moderate-intensity statin therapy to reduce the occurrence of ASCVD events.

Secondary Prevention



Severe Hypercholesterolemia (LDL-C \geq 190 mg/dL [\geq 4.9 mmol/L])

Recommendations for Primary Severe Hypercholesterolemia (LDL-C \geq190 mg/dL [\geq4.9 mmol/L])		
COR	LOE	Recommendations
I	B-R	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.
Ia	B-R	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.

Severe Hypercholesterolemia (LDL-C \geq 190 mg/dL [\geq 4.9 mmol/L])

Recommendations for Primary Severe Hypercholesterolemia (LDL-C \geq 190 mg/dL [\geq 4.9 mmol/L])		
COR	LOE	Recommendations
IIb	B-R	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.
IIb	B-R	In patients 30 to 75 years of age with heterozygous FH and with an LDL-C level of 100 mg/dL (\geq 2.6 mmol/L) or higher while taking maximally tolerated statin and ezetimibe therapy, the addition of a PCSK9 inhibitor may be considered.

Severe Hypercholesterolemia (LDL-C \geq 190 mg/dL [\geq 4.9 mmol/L])

Recommendations for Primary Severe Hypercholesterolemia (LDL-C \geq 190 mg/dL [\geq 4.9 mmol/L])		
COR	LOE	Recommendations
IIb	C-LD	In patients 40 to 75 years of age with a baseline LDL-C level of 220 mg/dL (\geq 5.7 mmol/L) or higher and who achieve an on-treatment LDL-C level of 130 mg/dL (\geq 3.4 mmol/L) or higher while receiving maximally tolerated statin and ezetimibe therapy, the addition of a PCSK9 inhibitor may be considered.
Value Statement: Uncertain Value (B-NR)		Among patients with FH without evidence of clinical ASCVD taking maximally tolerated statin and ezetimibe therapy, PCSK9 inhibitors provide uncertain value at 2018 U.S. list prices.

Diabetes Mellitus in Adults

Recommendations for Patients With Diabetes Mellitus		
COR	LOE	Recommendations
I	A	In adults 40 to 75 years of age with diabetes mellitus, regardless of estimated 10-year ASCVD risk, moderate-intensity statin therapy is indicated.
Ia	B-NR	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.

Diabetes Mellitus in Adults

Recommendations for Patients With Diabetes Mellitus		
COR	LOE	Recommendations
Ila	B-R	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.
Ila	B-NR	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.
Iib	C-LD	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.

Diabetes Mellitus in Adults

Recommendations for Patients With Diabetes Mellitus		
COR	LOE	Recommendations
IIb	C-LD	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.
IIb	C-LD	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 m², retinopathy, neuropathy, or ankle-brachial index (ABI; < 0.9), it may be reasonable to initiate statin therapy.

Table 5. Diabetes-Specific Risk Enhancers That Are Independent of Other Risk Factors in Diabetes Mellitus

Risk Enhancers

- Long duration (≥ 10 years for type 2 diabetes mellitus (S.4.3-20) or ≥ 20 years for type 1 diabetes mellitus)
- Albuminuria ≥ 30 mcg of albumin/mg creatinine
- eGFR < 60 mL/min/1.73 m²
- Retinopathy
- Neuropathy
- ABI < 0.9

Age

This calculator only applies to individuals 40-75 years of age.

Norm: 20 - 79

years

Diabetes

No

Yes

Sex

Female

Male

Smoker

No

Yes

Total cholesterol

Norm: 150 - 200

mg/dL ↔

HDL cholesterol

Norm: 0 - 60

mg/dL ↔

Systolic blood pressure

Norm: 100 - 120

mm Hg

Treatment for hypertension

No

Yes

Race

Race may/may not provide better estimates of
CV risk; optional

White

African American

Other

**Primary Prevention:
Assess ASCVD Risk in Each Age Group
Emphasize Adherence to Healthy Lifestyle**

Age 0-19 y
Lifestyle to prevent or reduce ASCVD risk
Diagnosis of Familial Hypercholesterolemia → statin

Age 20-39 y
Estimate lifetime risk to encourage lifestyle to reduce ASCVD risk
Consider statin if family history premature ASCVD and LDL-C ≥ 160 mg/dL (≥ 4.1 mmol/L)

Age 40-75 y and LDL-C ≥ 70 - <190 mg/dL (≥ 1.8 - <4.9 mmol/L) without diabetes mellitus
10-year ASCVD risk percent begins risk discussion

LDL-C ≥ 190 mg/dL (≥ 4.9 mmol/L)
No risk assessment; High-intensity statin (Class I)

Diabetes mellitus and age 40-75 y
Moderate-intensity statin (Class I)

Diabetes mellitus and age 40-75 y
Risk assessment to consider high-intensity statin (Class IIa)

Age >75 y
Clinical assessment, Risk discussion

ASCVD Risk Enhancers:

- Family history of premature ASCVD
- Persistently elevated LDL-C ≥ 160 mg/dL (≥ 4.1 mmol/L)
- Chronic kidney disease
- Metabolic syndrome
- Conditions specific to women (e.g., preeclampsia, premature menopause)
- Inflammatory diseases (especially rheumatoid arthritis, psoriasis, HIV)
- Ethnicity (e.g., South Asian ancestry)

Lipid/Biomarkers:

- Persistently elevated triglycerides (≥ 175 mg/dL, (≥ 2.0 mmol/L))

In selected individuals if measured:

- hs-CRP ≥ 2.0 mg/L
- Lp(a) levels >50 mg/dL or >125 nmol/L
- apoB ≥ 130 mg/dL
- Ankle-brachial index (ABI) <0.9

**<5%
"Low Risk"**

**Risk discussion:
Emphasize lifestyle to reduce risk factors (Class I)**

**5% - $<7.5\%$
"Borderline Risk"**

**Risk discussion:
If risk enhancers present then risk discussion regarding moderate-intensity statin therapy (Class IIb)**

**$\geq 7.5\%$ - $<20\%$
"Intermediate Risk"**

**Risk discussion:
If risk estimate + risk enhancers favor statin, initiate moderate-intensity statin to reduce LDL-C by 30% - 49% (Class I)**

**$\geq 20\%$
"High Risk"**

**Risk discussion:
Initiate statin to reduce LDL-C $\geq 50\%$ (Class I)**

**If risk decision is uncertain:
Consider measuring CAC in selected adults:
CAC = zero (lowers risk; consider no statin, unless diabetes, family history of premature CHD, or cigarette smoking are present)
CAC = 1-99 favors statin (especially after age 55)
CAC = 100+ and/or ≥ 75 th percentile, initiate statin therapy**

Table 6. Risk-Enhancing Factors for Clinician–Patient Risk Discussion

Risk-Enhancing Factors
<ul style="list-style-type: none">● 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● 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)

Table 6 continued

Risk-Enhancing Factors

- **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 mg/dL or ≥ 125 nmol/L constitutes a risk-enhancing factor especially at higher levels of Lp(a).
 - **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

Primary Prevention Adults 40 to 75 Years of Age With LDL-C Levels 70 to 189 mg/dL (1.7–4.8 mmol/L)

Primary Prevention Recommendations for Adults 40 to 75 Years of Age With LDL Levels 70 to 189 mg/dL (1.7–4.8 mmol/L)		
COR	LOE	Recommendations
I	A	In adults at intermediate-risk, statin therapy reduces risk of ASCVD, and in the context of a risk discussion, if a decision is made for statin therapy, a moderate-intensity statin should be recommended.
I	A	In intermediate-risk patients, LDL-C levels should be reduced by 30% or more, and for optimal ASCVD risk reduction, especially in high-risk patients, levels should be reduced by 50% or more.

Primary Prevention Adults 40 to 75 Years of Age With LDL-C Levels 70 to 189 mg/dL (1.7–4.8 mmol/L)

Primary Prevention Recommendations for Adults 40 to 75 Years of Age With LDL Levels 70 to 189 mg/dL (1.7–4.8 mmol/L)		
COR	LOE	Recommendations
I	B-NR	For the primary prevention of clinical ASCVD* in adults 40 to 75 years of age without diabetes mellitus and with an LDL-C level of 70 to 189 mg/dL (1.7 to 4.8 mmol/L), the 10-year ASCVD risk of a first “hard” ASCVD event (fatal and nonfatal MI or stroke) should be estimated by using the race- and sex-specific PCE, and adults should be categorized as being at low risk (<5%), borderline risk (5% to <7.5%), intermediate-risk (≥7.5% to <20%), and high-risk (≥20%).
I	B-NR	Clinicians and patients should engage in a risk discussion that considers risk factors, adherence to healthy lifestyle, the potential for ASCVD risk-reduction benefits, and the potential for adverse effects and drug–drug interactions, as well as patient preferences, for an individualized treatment decision.

Primary Prevention Adults 40 to 75 Years of Age With LDL-C Levels 70 to 189 mg/dL (1.7–4.8 mmol/L)

Primary Prevention Recommendations for Adults 40 to 75 Years of Age With LDL Levels 70 to 189 mg/dL (1.7–4.8 mmol/L)		
COR	LOE	Recommendations
Ia	B-R	In intermediate-risk adults, risk-enhancing factors favor initiation or intensification of statin therapy.
Ia	B-NR	In intermediate-risk or selected borderline-risk adults, if the decision about statin use remains uncertain, it is reasonable to use a CAC score in the decision to withhold, postpone or initiate statin therapy.

Primary Prevention Adults 40 to 75 Years of Age With LDL-C Levels 70 to 189 mg/dL (1.7–4.8 mmol/L)

Primary Prevention Recommendations for Adults 40 to 75 Years of Age With LDL Levels 70 to 189 mg/dL (1.7–4.8 mmol/L)		
COR	LOE	Recommendations
IIa	B-NR	<p>In intermediate-risk adults or selected borderline-risk adults in whom a CAC score is measured for the purpose of making a treatment decision, AND</p> <ul style="list-style-type: none">• If the coronary calcium score is zero, it is reasonable to withhold statin therapy and reassess in 5 to 10 years, as long as higher risk conditions are absent (diabetes mellitus, family history of premature CHD, cigarette smoking);• If CAC score is 1 to 99, it is reasonable to initiate statin therapy for patients ≥ 55 years of age;• If CAC score is 100 or higher or in the 75th percentile or higher, it is reasonable to initiate statin therapy.

Primary Prevention Adults 40 to 75 Years of Age With LDL-C Levels 70 to 189 mg/dL (1.7–4.8 mmol/L)

Primary Prevention Recommendations for Adults 40 to 75 Years of Age With LDL Levels 70 to 189 mg/dL (1.7–4.8 mmol/L)		
COR	LOE	Recommendations
IIb	B-R	In intermediate-risk adults who would benefit from more aggressive LDL-C lowering and in whom high-intensity statins are advisable but not acceptable or tolerated, it may be reasonable to add a nonstatin drug (ezetimibe or bile acid sequestrant) to a moderate-intensity statin.
IIb	B-R	In patients at borderline risk, in risk discussion, the presence of risk-enhancing factors may justify initiation of moderate-intensity statin therapy.

Monitoring in Response to LDL-C–Lowering Therapy

Recommendation for Monitoring		
COR	LOE	Recommendation
I	A	Adherence to changes in lifestyle and effects of LDL-C–lowering medication should be assessed by measurement of fasting lipids and appropriate safety indicators 4 to 12 weeks after statin initiation or dose adjustment and every 3 to 12 months thereafter based on need to assess adherence or safety.

Primary Prevention in Other Age Groups (Older Adults)

Recommendations for Older Adults		
COR	LOE	Recommendations
IIb	B-R	In adults 75 years of age or older with an LDL-C level of 70 to 189 mg/dL (1.7 to 4.8 mmol/L), initiating a moderate-intensity statin may be reasonable.
IIb	B-R	In adults 75 years of age or older, it may be reasonable to stop statin therapy when functional decline (physical or cognitive), multimorbidity, frailty, or reduced life-expectancy limits the potential benefits of statin therapy.
IIb	B-R	In adults 76 to 80 years of age with an LDL-C level of 70 to 189 mg/dL (1.7 to 4.8 mmol/L), it may be reasonable to measure CAC to reclassify those with a CAC score of zero to avoid statin therapy.

Primary Prevention in Other Age Groups (Children and Adolescents)

Recommendations for Children and Adolescents		
COR	LOE	Recommendations
I	A	In children and adolescents with lipid disorders related to obesity, it is recommended to intensify lifestyle therapy, including moderate caloric restriction and regular aerobic physical activity.
I	B-NR	In children and adolescents with lipid abnormalities, lifestyle counseling is beneficial for lowering LDL-C.

Primary Prevention in Other Age Groups (Children and Adolescents)

Recommendations for Children and Adolescents		
COR	LOE	Recommendations
Ia	B-R	In children and adolescents 10 years of age or older with an LDL-C level persistently 190 mg/dL (≥ 4.9 mmol/L) or higher or 160 mg/dL (4.1 mmol/L) or higher with a clinical presentation consistent with FH (see Section 4.2.) and who do not respond adequately with 3 to 6 months of lifestyle therapy, it is reasonable to initiate statin therapy.
Ia	B-NR	In children and adolescents with a family history of either early CVD* or significant hypercholesterolemia, [†] it is reasonable to measure a fasting or nonfasting lipoprotein profile as early as age 2 years to detect FH or rare forms of hypercholesterolemia.

Primary Prevention in Other Age Groups (Children and Adolescents)

Recommendations for Children and Adolescents		
COR	LOE	Recommendations
Ia	B-NR	In children and adolescents found to have moderate or severe hypercholesterolemia, it is reasonable to carry out reverse-cascade screening of family members, which includes cholesterol testing for first-, second-, and when possible, third-degree biological relatives, for detection of familial forms of hypercholesterolemia.
Ia	C-LD	In children and adolescents with obesity or other metabolic risk factors, it is reasonable to measure a fasting lipid profile to detect lipid disorders as components of the metabolic syndrome.

Primary Prevention in Other Age Groups (Children and Adolescents)

Recommendations for Children and Adolescents		
COR	LOE	Recommendations
IIb	B-NR	In children and adolescents without cardiovascular risk factors or family history of early CVD, it may be reasonable to measure a fasting lipid profile or nonfasting non HDL-C once between the ages of 9 and 11 years, and again between the ages of 17 and 21 years, to detect moderate to severe lipid abnormalities.

Table 9. Normal and Abnormal Lipid Values in Childhood*†

	Acceptable, mg/dL	Borderline, mg/dL	Abnormal, mg/dL
TC	<170 (<4.3 mmol)	170-199 (4.3-5.1 mmol)	≥200 (≥5.1 mmol)
Triglycerides (0-9 y)	<75 (<0.8 mmol)	75-99 (0.8-1.1 mmol)	≥100 (≥1.1 mmol)
Triglycerides (10-19 y)	<90 (<1.0 mmol)	90-129 (1.0-1.5 mmol)	≥130 (≥1.4 mmol)
HDL-C	>45 (>1.2 mmol)	40-45 (1.0-1.2 mmol)	<40 (<1.0 mmol)
LDL-C	<110 (<2.8 mmol)	110-129 (2.8-3.3 mmol)	≥130 (≥3.4 mmol)
Non-HDL-C	<120 (<3.1 mmol)	120-144 (3.1-3.7 mmol)	≥145 (≥3.7 mmol)

Hypertriglyceridemia

Recommendations for Hypertriglyceridemia		
COR	LOE	Recommendations
I	B-NR	In adults 20 years of age or older with moderate hypertriglyceridemia (fasting or nonfasting triglycerides 175 to 499 mg/dL [1.9 to 5.6 mmol/L]), clinicians should address and treat lifestyle factors (obesity and metabolic syndrome), secondary factors (diabetes mellitus, chronic liver or kidney disease and/or nephrotic syndrome, hypothyroidism), and medications that increase triglycerides.
IIa	B-R	In adults 40 to 75 years of age with moderate or severe hypertriglyceridemia and ASCVD risk of 7.5% or higher, it is reasonable to reevaluate ASCVD risk after lifestyle and secondary factors are addressed and to consider a persistently elevated triglyceride level as a factor favoring initiation or intensification of statin therapy (see Section 4.4.2.).

Hypertriglyceridemia

Recommendations for Hypertriglyceridemia		
COR	LOE	Recommendations
IIa	B-R	In adults 40 to 75 years of age with severe hypertriglyceridemia (fasting triglycerides ≥ 500 mg/dL [≥ 5.6 mmol/L]) and ASCVD risk of 7.5% or higher, it is reasonable to address reversible causes of high triglyceride and to initiate statin therapy.
IIa	B-NR	In adults with severe hypertriglyceridemia (fasting triglycerides ≥ 500 mg/dL [≥ 5.7 mmol/L]), and especially fasting triglycerides ≥ 1000 mg/dL (11.3 mmol/L)), it is reasonable to identify and address other causes of hypertriglyceridemia), and if triglycerides are persistently elevated or increasing, to further reduce triglycerides by implementation of a very low-fat diet, avoidance of refined carbohydrates and alcohol, consumption of omega-3 fatty acids, and, if necessary to prevent acute pancreatitis, fibrate therapy.

Issues Specific to Women

Recommendations for Issues Specific to Women		
COR	LOE	Recommendations
I	B-NR	Clinicians should consider conditions specific to women, such as premature menopause (age <40 years) and history of pregnancy-associated disorders (hypertension, preeclampsia, gestational diabetes mellitus, small-for-gestational-age infants, preterm deliveries), when discussing lifestyle intervention and the potential for benefit of statin therapy.
I	C-LD	Women of childbearing age who are treated with statin therapy and are sexually active should be counseled to use a reliable form of contraception.
I	C-LD	Women of childbearing age with hypercholesterolemia who plan to become pregnant should stop the statin 1 to 2 months before pregnancy is attempted, or if they become pregnant while on a statin, should have the statin stopped as soon as the pregnancy is discovered.

Adults With Chronic Kidney Disease

Recommendations for Adults With CKD		
COR	LOE	Recommendations
IIa	B-R	In adults 40 to 75 years of age with LDL-C 70 to 189 mg/dL (1.7 to 4.8 mmol/L) who are at 10-year ASCVD risk of 7.5% or higher, CKD not treated with dialysis or kidney transplantation is a risk-enhancing factor and initiation of a moderate-intensity statin or moderate-intensity statins combined with ezetimibe can be useful.
IIb	C-LD	In adults with advanced kidney disease that requires dialysis treatment who are currently on LDL-lowering therapy with a statin, it may be reasonable to continue the statin.
III: No Benefit	B-R	In adults with advanced kidney disease who require dialysis treatment, initiation of a statin is not recommended.

Adults With Chronic Inflammatory Disorders and HIV

Recommendations for Adults With Chronic Inflammatory Disorders and HIV		
COR	LOE	Recommendations
Ia	B-NR	In adults 40 to 75 years of age with LDL-C 70 to 189 mg/dL (1.7 to 4.8 mmol/L) who have a 10-year ASCVD risk of 7.5% or higher, chronic inflammatory disorders and HIV are risk-enhancing factors and in risk discussion favor moderate-intensity statin therapy or high-intensity statin therapy.
Ia	B-NR	In patients with chronic inflammatory disorders or HIV, a fasting lipid profile and assessment of ASCVD risk factors can be useful as a) a guide to benefit of statin therapy and b) for monitoring or adjusting lipid-lowering drug therapy before and 4 to 12 weeks after starting inflammatory disease-modifying therapy or antiretroviral therapy.
Ia	B-NR	In adults with RA who undergo ASCVD risk assessment with measurement of a lipid profile, it can be useful to recheck lipid values and other major ASCVD risk factors 2 to 4 months after the patient's inflammatory disease has been controlled.

Statin Safety and Statin-Associated Side Effects

Statin Safety and Statin-Associated Side Effects

Recommendations for Statin Safety and Statin-Associated Side Effects		
COR	LOE	Recommendations
I	A	A clinician–patient risk discussion is recommended before initiation of statin therapy to review net clinical benefit, weighing the potential for ASCVD risk reduction against the potential for statin-associated side effects, statin–drug interactions, and safety, while emphasizing that side effects can be addressed successfully.
I	A	In patients with statin-associated muscle symptoms (SAMS), a thorough assessment of symptoms is recommended, in addition to an evaluation for nonstatin causes and predisposing factors.

Statin Safety and Statin-Associated Side Effects

Recommendations for Statin Safety and Statin-Associated Side Effects		
COR	LOE	Recommendations
I	B-R	In patients with indication for statin therapy, identification of potential predisposing factors for statin-associated side effects, including new-onset diabetes mellitus and SAMS, is recommended before initiation of treatment.
I	B-R	In patients with statin-associated side effects that are not severe, it is recommended to reassess and to rechallenge to achieve a maximal LDL-C lowering by modified dosing regimen, an alternate statin or in combination with nonstatin therapy.

Statin Safety and Statin-Associated Side Effects

Recommendations for Statin Safety and Statin-Associated Side Effects		
COR	LOE	Recommendations
I	B-R	In patients with increased diabetes mellitus risk or new-onset diabetes mellitus, it is recommended to continue statin therapy, with added emphasis on adherence, net clinical benefit, and the core principles of regular moderate-intensity physical activity, maintaining a healthy dietary pattern, and sustaining modest weight loss.
I	C-LD	In patients treated with statins, it is recommended to measure creatine kinase levels in individuals with severe statin-associated muscle symptoms, objective muscle weakness, and to measure liver transaminases (aspartate aminotransferase, alanine aminotransferase) as well as total bilirubin and alkaline phosphatase (hepatic panel) if there are symptoms suggesting hepatotoxicity.

Statin Safety and Statin-Associated Side Effects

Recommendations for Statin Safety and Statin-Associated Side Effects		
COR	LOE	Recommendations
I	B-R	In patients at increased ASCVD risk with chronic, stable liver disease (including non-alcoholic fatty liver disease) when appropriately indicated, it is reasonable to use statins after obtaining baseline measurements and determining a schedule of monitoring and safety checks.
Ila	B-R	In patients at increased ASCVD risk with severe statin-associated muscle symptoms or recurrent statin-associated muscle symptoms despite appropriate statin rechallenge, it is reasonable to use RCT proven nonstatin therapy that is likely to provide net clinical benefit.

Statin Safety and Statin-Associated Side Effects

Recommendations for Statin Safety and Statin-Associated Side Effects		
COR	LOE	Recommendations
III: No Benefit	B-R	Coenzyme Q10 is not recommended for routine use in patients treated with statins or for the treatment of SAMS.
III: No Benefit	C-LD	In patients treated with statins, routine measurements of creatine kinase and transaminase levels are not useful.

Table 11. Statin-Associated Side Effects

Statin-Associated Side Effects	Frequency	Predisposing Factors	Quality of Evidence
Statin-associated muscle symptoms (SAMS)			
Myalgias (CK Normal)	Infrequent (1% to 5%) in RCTs; frequent (5% to 10%) in observational studies and clinical setting	Age, female sex, low body mass index, high-risk medications (CYP3A4 inhibitors, OATP1B1 inhibitors), comorbidities (HIV, renal, liver, thyroid, preexisting myopathy), Asian ancestry, excess alcohol, high levels of physical activity, and trauma	RCTs cohorts/observational
Myositis/myopathy (CK > ULN) with concerning symptoms or objective weakness	Rare		RCTs cohorts/observational
Rhabdomyolysis (CK > 10 × ULN + renal injury)	Rare		RCTs cohorts/observational
Statin-associated autoimmune myopathy (HMGCR antibodies, incomplete resolution)	Rare		Case reports
New-onset diabetes mellitus	Depends on population; more frequent if diabetes mellitus risk factors are present, such as body mass index ≥30, fasting blood sugar ≥100 mg/dL; metabolic syndrome, or A1c ≥6%.	Diabetes mellitus risk factors/metabolic syndrome High-intensity statin therapy	RCTs/meta-analyses

Table 11. Statin-Associated Side Effects

Statin-Associated Side Effects	Frequency	Predisposing Factors	Quality of Evidence
Liver			
Transaminase elevation 3 × ULN	Infrequent		RCTs/ cohorts/observational Case reports
Hepatic failure	Rare		
Central nervous system			
Memory/cognition	Rare/unclear		Case reports; no increase in memory/cognition problems in 3 large-scale RCTs
Cancer	No definite association		RCTs/meta-analyses

Table 11. Statin-Associated Side Effects

Statin-Associated Side Effects	Frequency	Predisposing Factors	Quality of Evidence
Other			
Renal function	Unclear/unfounded		
Cataracts	Unclear		
Tendon rupture	Unclear/unfounded		
Hemorrhagic stroke	Unclear		
Interstitial lung disease	Unclear/unfounded		
Low testosterone	Unclear/unfounded		

Top 10 Take-Home Messages

- **2018 Cholesterol Guidelines**

Top 10 Take Home Messages

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.

Top 10 Take Home Messages

- 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 $\geq 50\%$.

- 3. 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 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.

Top 10 Take Home Messages

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) & 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 \geq 70 mg/dL (\geq 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 \geq 50%.

Top 10 Take Home Messages

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;
- the consideration of costs of statin therapy; and
- the patient preferences & values in shared decision-making.

Top 10 Take Home Messages

- 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 $\geq 7.5\%$, 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 $\geq 30\%$, and if 10-year risk is $\geq 20\%$, reduce LDL-C levels by $\geq 50\%$.

Top 10 Take Home Messages

- 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 yrs)
- 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);

Top 10 Take Home Messages

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 $\geq 7.5\%$ 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 ≥ 75 th percentile, statin therapy is indicated unless otherwise deferred by the outcome of clinician–patient risk discussion.

Top 10 Take Home Messages

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 nonstatin drug therapy are defined by threshold LDL-C levels ≥ 70 mg/dL (≥ 1.8 mmol/L) on maximal statin therapy (see No. 3).



Thanks For Your Attention