2018 Guideline on the Management of Blood Cholesterol

GUIDELINES MADE SIMPLE

A Selection of Tables and Figures

ACC.org/GMSCholesterol

AMERICAN COLLEGE *of* CARDIOLOGY

©2018, American College of Cardiology B18242

2018 Guideline on the Management of Blood Cholesterol

GUIDELINES MADE SIMPLE

A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

Writing Committee:

Scott M. Grundy, MD, PhD, FAHA, Chair
Neil J. Stone, MD, FACC, FAHA, Vice Chair

Alison L. Bailey, MD, FACC, FAACVPR
Craig Beam, CRE
Kim K. Birtcher, MS, PharmD, AACC, FNLA
Roger S. Blumenthal, MD, FACC, FAHA, FNLA
Lynne T. Braun, PhD, CNP, FAHA, FPCNA, FNLA
Sarah de Ferranti, MD, MPH
Joseph Faiella-Tommasino, PhD, PA-C
Daniel E. Forman, MD, FAHA
Ronald Goldberg, MD
Paul A. Heidenreich, MD, MS, FACC, FAHA
Mark A. Hlatky, MD, FACC, FAHA
Daniel W. Jones, MD, FAHA
Donald Lloyd-Jones, MD, SCM, FACC, FAHA
Nuria Lopez-Pajares, MD, MPH
Chiadi E. Ndumele, MD, PhD, FAHA
Carl E. Orringer, MD, FACC, FNLA
Carmen A. Peralta, MD, MAS
Joseph J. Saseen, PharmD, FNLA, FAHA
Sidney C. Smith, Jr, MD, MACC, FAHA
Laurence Sperling, MD, FACC, FAHA, FASPC
Salim S. Virani, MD, PhD, FACC, FAHA
Joseph Yeboah, MD, MS, FACC, FAHA

The purpose of the present guideline is to address the practical management of patients with high blood cholesterol and related disorders. The 2018 Cholesterol Guideline is a full revision of the *2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol* to Reduce Atherosclerotic Cardiovascular Risk in Adults.

The following resource contains tables and figures from the 2018 Guideline for the Management of Blood Cholesterol. The resource is only an excerpt from the Guideline and the full publication should be reviewed for more tables and figures as well as important context.

CITATION: J Am Coll Cardiol. Nov 2018; DOI: 10.1016/j.jacc.2018.11.003

2018 Guideline on the Management of Blood Cholesterol

GUIDELINES MADE SIMPLE

Selected Table or Figure **Page**

Top Ten Messages to Reduce Risk of ASCVD 4-6

ACC JACC Central Illustration: Overview of Primary and Secondary ASCVD Prevention 7

Four Statin Benefit Groups:

1. *Secondary ASCVD Prevention*

- Clinical ASCVD: Figure 1 8
- Criteria for Very High Risk ASCVD 9

2. *Severe Hypercholesterolemia (LDL-C ≥190)*

- Recommendations for Primary Severe Hypercholesterolemia [LDL-C ≥190 mg/dL (≥4.9 mmol/L)] 10

3. *Diabetes Mellitus in Adults 40-75 Years of Age With LDL- C 70-189 mg/dL*

- Risk Enhancers That Are Independent of Other Risk Factors in Diabetes 11

4. *Primary Prevention Over the Life Span*

- Primary Prevention: Figure 2 12
- Risk-enhancing Factors for Clinician-Patient Risk Discussion 13
- Checklist for Clinician-Patient Shared Decision Making for Initiating Therapy 14
- Selected Examples of Candidates for Coronary Artery Calcium Who Might Benefit from Knowing CAC=0 (In Selected patients if Risk Decision Uncertain) 15

Treatment Considerations:

- High-, Moderate-, and Low-Intensity Statin Therapy 16
- Statin Associated Side Effects (SASS) 17-18

Special Populations:

- Normal and Abnormal Lipid Values in Childhood 19
- Ethnicity Issues in Evaluation, Risk Decisions, and Treatment of ASCVD Risk 20-22

Top 10 Take-Home Messages to Reduce Risk of Atherosclerotic Cardiovascular Disease (ASCVD) through Cholesterol Management

(1 of 3)

1 *In all individuals, emphasize 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 #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%.

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.

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.

"Top Ten Messages" is continued in the next page.

Top 10 Take-Home Messages to Reduce Risk of Atherosclerotic Cardiovascular Disease (ASCVD) through Cholesterol Management

(2 of 3)

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 #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 #8). If risk status is uncertain, consider using coronary artery calcium (CAC) to improve specificity (see #9). If statins are indicated, reduce LDL-C levels by ≥30%, and if 10-year risk is ≥20%, reduce LDL-C levels by ≥50%.

"Top Ten Messages" is continued in the next page.

Top 10 Take-Home Messages to Reduce Risk of Atherosclerotic Cardiovascular Disease (ASCVD) through Cholesterol Management

(3 of 3)

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 #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.

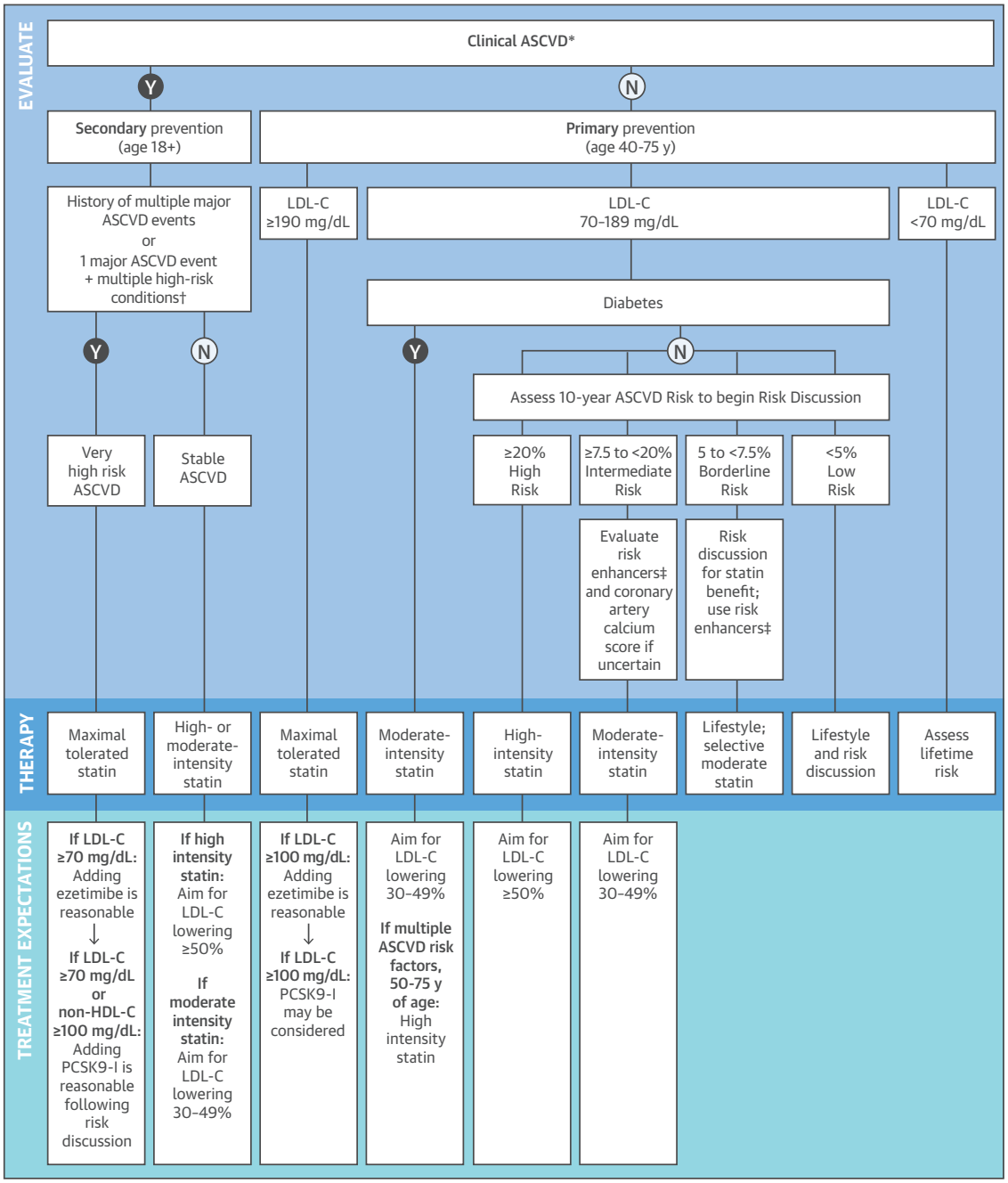
10

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 #3).

Overview of Primary and Secondary ASCVD Prevention

This tool provides a broad overview of the 2018 Cholesterol Guideline.
Please refer to the full guideline document for specific recommendations.



* **Clinical ASCVD** consists of acute coronary syndromes, those with history of myocardial infarction, stable or unstable angina or coronary other arterial revascularization, stroke, TIA, or peripheral artery disease including aortic aneurysm, all of atherosclerotic origin.

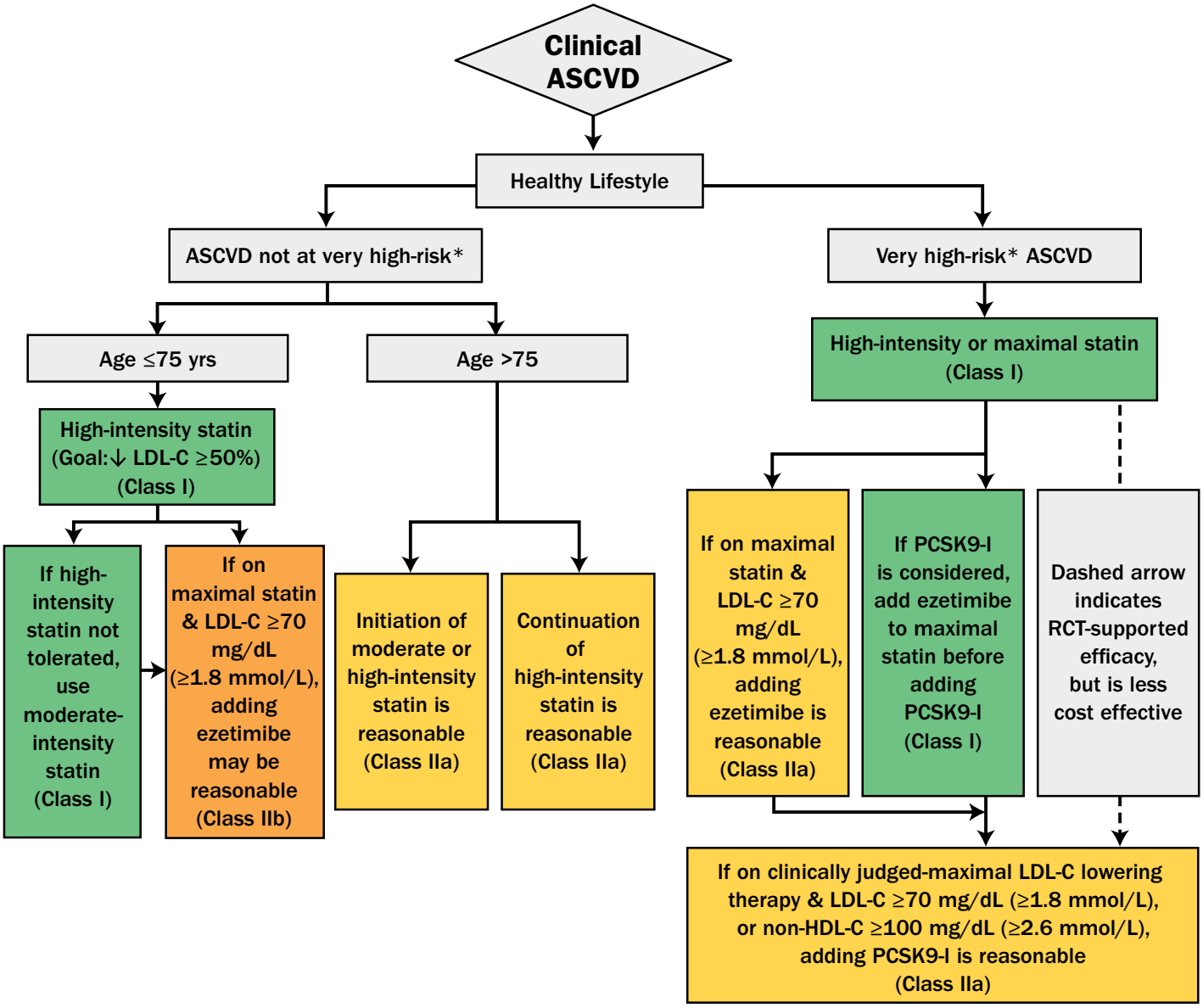
† **Major ASCVD events:** Recent ACS, history of MI, history of Ischemic stroke, symptomatic PAD; **High-Risk Conditions:** ≥65 y of age, heterozygous FH, hx of HF, prior CABG or PCI, DM, HTN, CKD, current smoking, persistently elevated LDL-C≥100 mg/dL.

‡ **Risk Enhancers:** Family history of premature ASCVD, persistently elevated LDL-C ≥160 mg/dl, chronic kidney disease, metabolic syndrome, conditions specific to women (e.g. pre-eclampsia, premature menopause), inflammatory disease (especially psoriasis, RA, or HIV), ethnicity (e.g. South Asian ancestry), Lipid/biomarkers; persistently elevated triglycerides (≥175 mg/dL), if measured: hs-CRP ≥2.0 mg/L, Lp(a) levels ≥50 mg/dL or ≥125 nmol/l, apoB ≥130 mg/dL especially at higher levels of Lp(a), ABI <0.9.

Secondary ASCVD Prevention

First Statin Benefit Group

Figure 1: Secondary Prevention in Patients with Clinical ASCVD



*Very high-risk includes a history of multiple major ASCVD events or 1 major ASCVD event and multiple high-risk conditions (**Table 4** on following page).

Figure 1

AMERICAN COLLEGE of CARDIOLOGY

Secondary ASCVD Prevention

First Statin Benefit Group

Very High-Risk for Future ASCVD Events*

Table 4

Major ASCVD Events
Recent acute coronary syndrome (within the past 12 months)
History of myocardial infarction (other than recent acute coronary syndrome event listed above)
History of ischemic stroke
Symptomatic peripheral arterial disease (history of claudication with ankle brachial index <0.85, or previous revascularization or amputation)
High-Risk Conditions
Age ≥65 years
Heterozygous familial hypercholesterolemia
History of prior coronary artery bypass surgery or PCI outside of the major ASCVD event(s)
Diabetes Mellitus
Hypertension
Chronic kidney disease (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 heart failure

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

Severe Hypercholesterolemia

Second Statin Benefit Group

Recommendations for Primary Severe Hypercholesterolemia [LDL-C ≥190 mg/dL (≥4.9 mmol/L)]

COR	LOE	Recommendations
I	B-R	1. In patients 20 to 75 years of age with an LDL-C level of 190 mg/dL (≥4.9 mmol/L) or higher, maximally tolerated statin therapy is recommended.
IIa	B-R	2. In patients 20 to 75 years of age with an LDL-C level of 190 mg/dL (≥4.9 mmol/L) or higher who achieve less than 50% reduction in LDL-C while receiving maximally tolerated statin therapy and/or have an LDL-C level of 100 mg/dL (≥2.6 mmol/L) or higher, ezetimibe therapy is reasonable.
IIb	B-R	3. In patients 20 to 75 years of age with a baseline LDL-C ≥190 mg/dL (≥4.9 mmol/L), who achieve less than a 50% reduction in LDL-C levels and have fasting triglycerides ≤300 mg/dL (≤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	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.
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 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.
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 US list prices.

Diabetes Mellitus in Adults

Third Statin Benefit Group

Diabetes-specific Risk Enhancers That Are Independent of Other Risk Factors in Diabetes

Table 5

- Long duration (≥10 years for type 2 diabetes or ≥ 20 years for type 1 diabetes)
- Albuminuria ≥30 mcg albumin/mg creatinine
- eGFR <60 ml/min/1.73 m^2
- Retinopathy
- Neuropathy
- ABI <0.9

Back to Table of Contents

Primary Prevention Over The Life Span

Fourth Statin Benefit Group

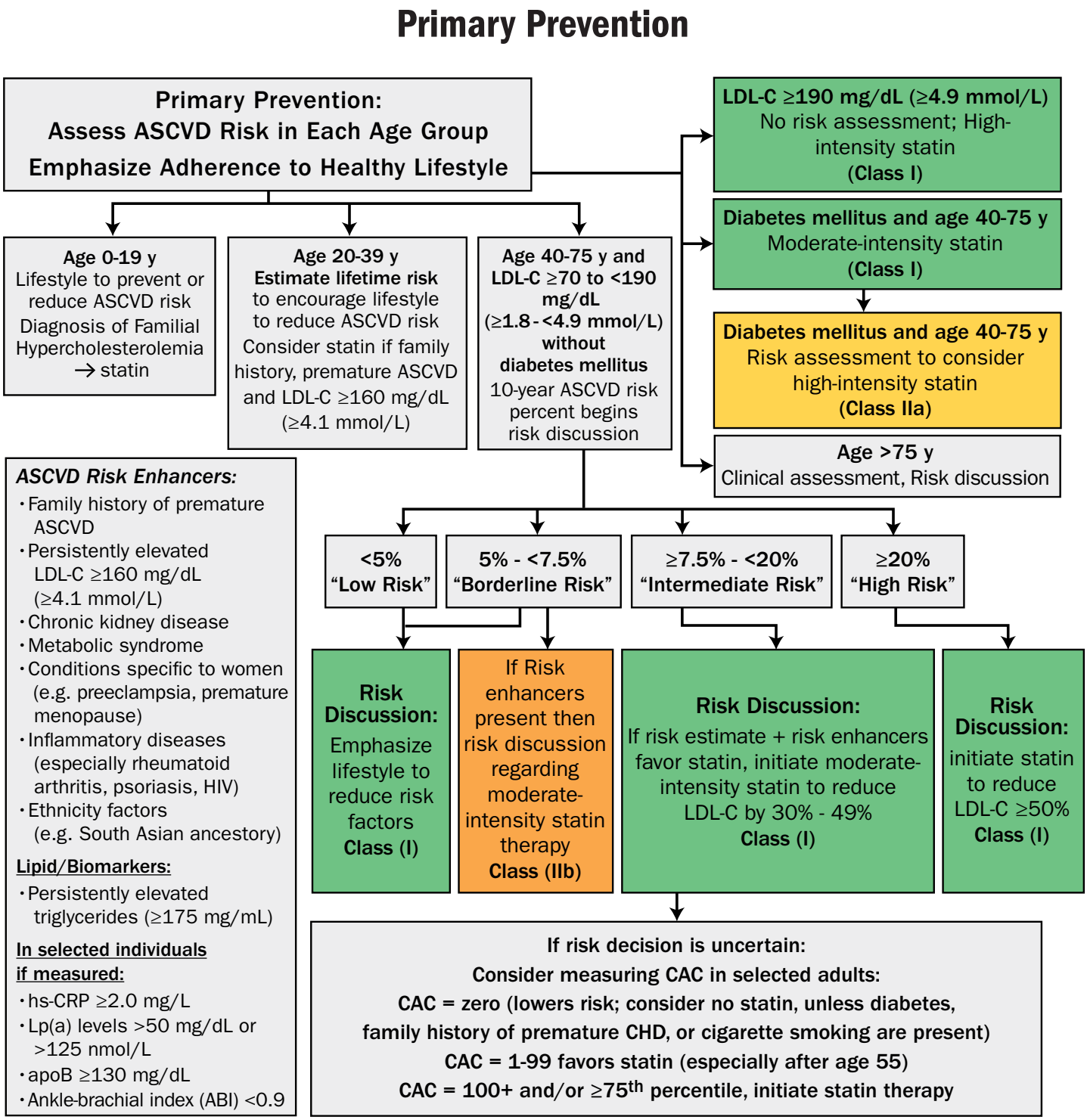


Figure 2

AMERICAN COLLEGE of CARDIOLOGY

Treatment Considerations

Risk-enhancing Factors for Clinician-Patient Risk Discussion

- **Family history of premature ASCVD;** (males <55 years; females <65 years)
- **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 TG (>175 mg/dL, elevated BP, elevated glucose, low HDL-C (<40 mg/dL in men, <50 mg/dL in women) are factors; tally of 3 makes the diagnosis)
- **Chronic kidney disease** (eGFR 15- 59 ml/min per 1.73 m^2 with or without albuminuria; not treated with dialysis or kidney transplantation)
- **Chronic inflammatory conditions** such as psoriasis, rheumatoid arthritis (RA) or human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS)
- **History of premature menopause (before age 40) and history of pregnancy-associated conditions that increase later ASCVD risk such as pre-eclampsia**
- **High-risk ethnicities** (e.g. South Asian ancestry)
- **Lipid/Biomarkers:** Associated with increased ASCVD risk

  -Persistently* elevated, primary hypertriglyceridemia (≥175 mg/dl);

  -If measured:

  - **High-sensitivity C-reactive protein** - (≥2.0 mg/L)
  - **Elevated lipoprotein (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 apo B ≥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**

AIDS indicates acquired immunodeficiency syndrome; ABI, ankle-brachial index; apoB, apolipoprotein B; ASCVD, atherosclerotic cardiovascular disease; eGFR, estimated glomerular filtration rate; HDL-C, high-density lipoprotein cholesterol; HIV, human immunodeficiency virus; LDL-C, low-density lipoprotein cholesterol; Lp(a), lipoprotein (a); and RA, rheumatoid arthritis.

*Optimally, 3 determinations

Primary Prevention Over The Life Span

Fourth Statin Benefit Group

Checklist for Clinician-Patient Shared Decision Making for Initiating Therapy

Table 7

Checklist Item	Recommendation
ASCVD Risk Assessment	• Assign to statin treatment group; use ASCVD risk estimator plus* ○ In lower risk primary prevention adults 40-75 years with LDL-C ≥70 mg/dL (≥1.8 mmol/L). ○ Not needed in secondary prevention, LDL-C ≥190 mg/dL (≥4.9 mmol/L) and those 40-75 years with diabetes. • Assess other patient characteristics which influence risk. See Risk Enhancing Factors *(Section 4.4.1.3 and Table 6)* • Assess coronary artery calcium *(section 4.4.1.4)* if risk decision uncertain and additional information is needed to clarify ASCVD risk ○ Use decision tools to explain risk (ASCVD risk estimator plus- http://tools.acc.org/ASCVD-Risk-Estimator-Plus, Mayo Clinic Statin Choice Decision Aid)
Lifestyle Modifications	• Review lifestyle habits (diet, physical activity, weight/BMI, tobacco use) • Endorse a healthy lifestyle and provide relevant advice/materials/referrals (CardioSmart, AHA Life's Simple 7, NLA Patient Tear Sheets, PCNA Clinicians' Lifestyle Modification Toolbox, cardiac rehab, dietitian, smoking cessation program)
Potential Net-Clinical Benefit of Pharmacotherapy	• Recommend statins as first-line therapy • Consider the combination of statin and non-statin therapy in select patients • Discuss potential risk reduction from lipid-lowering therapy • Discuss the potential for adverse effects/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 patient to verbalize what was heard (personal ASCVD risk, available options and their risk/benefit) • Invite the patient to ask questions, express values/preferences, 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

*ASCVD Risk Predictor Plus is available at: http://tools.acc.org/ASCVD-Risk-Estimator-Plus/#!/calculate/estimate/

AHA indicates American Heart Association; ASCVD, atherosclerotic cardiovascular disease; CAC, coronary artery calcium; CKD, chronic kidney disease; HIV, human immunodeficiency virus; LDL-C, low-density lipoprotein cholesterol; and NLA, National Lipid Association.

Primary Prevention Over the Life span

Fourth Statin Benefit Groups

Selected Examples of Candidates for Coronary Artery Calcium Measurement Who Might Benefit from Knowing CAC Score is Zero

Table 8

1. Patients reluctant to initiate statin who wish to understand their risk and potential for benefit more precisely
2. Patients concerned about need to re-institute statin therapy after discontinuation for statin associated symptoms
3. Older patients (men 55 to 80; women 60-80 years old) with low burden of risk factors who question whether they would benefit from statin therapy
4. Middle-aged adults (40-55 years old) with PCE calculated 10-year risk for ASCVD 5 to <7.5% with factors that increase their ASCVD risk, even though they are in a borderline risk group

ASCVD indicates atherosclerotic cardiovascular disease; CAC, coronary artery calcium; LDL-C, low-density lipoprotein cholesterol; and PCE, pooled cohort equations.

Caveats: If patient is intermediate risk and if a risk decision is uncertain and a CAC score is performed, it is reasonable to withhold statin therapy unless higher risk conditions such as cigarette smoking, family history of premature ASCVD, or diabetes are present, and to reassess CAC score in 5-10 years. Moreover, if CAC is recommended, it should be performed in facilities that have current technology that delivers the lowest radiation possible.

Treatment Considerations

High-, Moderate-, and Low-Intensity Statin Therapy*

Table 3

	High-Intensity	Moderate-Intensity	Low-Intensity
LDL-C Lowering†	≥50%	30% to 49%	<30%
Statins	**Atorvastatin (40 mg‡) 80 mg** **Rosuvastatin 20 (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

BID indicates twice daily; FDA, U.S. Food and Drug Administration; LDL-C, low-density lipoprotein cholesterol; RCT, randomized controlled trial; VOYAGER, an indiVidual patient data meta-analysis Of statin therapY in At risk Groups: Effects of Rosuvastatin, atorvastatin and simvastatin; and XL, extended release.

Percent LDL-C reductions with the primary statin medications used in clinical practice (atorvastatin, rosuvastatin, simvastatin) were estimated using the median reduction in LDL-C from the VOYAGER database (13). Reductions in LDL-C for other statin medications (fluvastatin, lovastatin, pitavastatin, pravastatin) were identified according to FDA-approved product labeling in adults with hyperlipidemia, primary hypercholesterolemia, and mixed dyslipidemia.

Boldface type indicates specific statins and doses that were evaluated in RCTs, and the Cholesterol Treatment Trialists'2010 meta-analysis. All these RCTs demonstrated a reduction in major cardiovascular events.

Italic type indicates statins and doses that have been approved by the FDA but were not tested in the RCTs reviewed.

*Percent reductions are estimates from data across large populations. Individual responses to statin therapy varied in the RCTs and should be expected to vary in clinical practice.

†LDL-C lowering that should occur with the dosage listed below each intensity.

‡Evidence from 1 RCT only: downtitration if unable to tolerate atorvastatin 80 mg in the IDEAL (Incremental Decrease through Aggressive Lipid Lowering) study.

§Although simvastatin 80 mg was evaluated in RCTs, initiation of simvastatin 80 mg or titration to 80 mg is not recommended by the FDA because of the increased risk of myopathy, including rhabdomyolysis.

Treatment Considerations

Statin Associated Side Effects (SASE)
(1 of 2)

Table 11

Statin Associated Side Effects	Frequency	Predisposing Factors	Quality of Evidence
Statin Associated Muscle Symptoms (SAMS) • Myalgias (CK normal)	Infrequent (1%–5%) in RCTs/frequent (5%–10%) in observational studies and clinical setting	Age, female, low BMI, high- risk medications (CYP3A4 inhibitors, OATP1B1 inhibitors), comorbidities (HIV, renal, liver, thyroid, pre-existing myopathy), Asian descent, excess alcohol, high levels of physical activity and trauma.	RCTs cohorts/observational
• Myositis/Myopathy (CK >ULN) with concerning symptoms/objective weakness	Rare		RCTs cohorts/observational
• Rhabdomyolysis (CK >10xULN + renal injury)	Rare		RCTs Cohorts/observational
• Statin-associated autoimmune myopathy (SAAM) (HMGCR Ab's, incomplete resolution)	Rare		Case reports
New onset Diabetes Mellitus	Depends on population; more frequent if diabetes mellitus risk factors such as BMI ≥30, fasting blood sugar ≥100 mg/dL; metabolic syndrome or A1c ≥6% are present	Diabetes risk factors/ metabolic syndrome High-intensity statin therapy	RCTs/Meta-analyses

Table 11 *is continued in the next page. For references please see page 18.*

Treatment Considerations

Statin Associated Side Effects (SASE)
(2 of 2)

Table 11 *(continued from previous page)*

Statin Associated Side Effects	Frequency	Predisposing Factors	Quality of Evidence
Liver • Transaminase elevation 3xULN	Infrequent		RCTs/cohorts/observational Case reports
• Hepatic Failure	Rare		
CNS • Memory/Cognition	Rare/Unclear		Case reports; no increase in memory/cognition problems in three large scale RCTs
Cancer	No definite association		RCTs/meta-analyses
Other • Renal Function • Cataracts • Tendon Rupture • Hemorrhagic Stroke • Interstitial Lung Disease • Low Testosterone	 Unclear/unfounded Unclear Unclear/unfounded Unclear Unclear/unfounded Unclear/unfounded		

CK indicates creatine kinase; HIV, human immunodeficiency virus; HMGCR, 3-hydroxy-3-methyl-glutaryl-coenzyme A reductase; SAMS, statin-associated muscle symptoms; SAAM, statin-associated autoimmune myopathy; SASE, statin associated side effects; and ULN, upper limit of normal. "

Special Populations

Normal and Abnormal Lipid Values in Childhood*†

Table 9

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

HDL-C indicates high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; NCEP, National Cholesterol Education Program; SI, Système international d'unités (International System of Units); and TC, total cholesterol.

Values given are in mg/dL. To convert to SI units, divide the results for TC, LDL-C, HDL-C, and non-HDL-C by 38.6; for triglycerides, divide by 88.6.

*Values for plasma lipid and lipoprotein levels are from the NCEP Expert Panel on Cholesterol Levels in Children. Non-HDL-C values from the Bogalusa Heart Study are equivalent to the NCEP Pediatric Panel cutpoints for LDL-C.

†The cutpoints for high and borderline high represent approximately the 95th and 75th percentiles, respectively. Low cutpoints for HDL-C represent approximately the 10th percentile.

Special Populations

Ethnicity Issues in Evaluation, Risk Decisions, and Treatment of ASCVD Risk *(1 of 3)*

Table 10

Ethnic/racial groupings	Asian-Americans*	Hispanic/Latino-Americans†	Blacks	Comments
Evaluation				
ASCVD Issues informed by ethnicity	South Asian and East Asian ASCVD risk varies by country of origin; Individuals from South Asia (see below) have increased ASCVD risk	Race and country of origin together with socioeconomic status and acculturation level may explain risk factor burden more precisely. e.g. ASCVD risk is higher among individuals from Puerto Rico than from Mexico.	ASCVD risk assessment in black women shows increased ASCVD risk compared to their otherwise similar white counter-parts	Heterogeneity in risk according to racial/ethnic groups and within racial/ethnic groups. Native American/Alaskan populations have high rates of risk factors for ASCVD compared to non-hispanic whites.
Lipid issues informed by ethnicity	Lower levels of HDL-C compared to whites Higher prevalence of LDL-C among Asian Indians, Filipinos, Japanese, and Vietnamese compared to whites. An increased prevalence of high TGs was seen in all Asian American subgroups	Hispanic/Latino women have higher prevalence of low HDL-C compared to Hispanic/Latino men	Higher levels of HDL-C and lower levels of triglycerides (TG) than in Non-Hispanic Whites or Mexican-Americans.	All ethnic groups appear to be at greater risk for dyslipidemia, but important to identify those with more sedentary behavior and less favorable diet.
Metabolic issues informed by ethnicity	Increased Metabolic Syndrome (MetS) seen with lower waist circumference than in whites. DM develops at a lower lean body mass and at earlier age (19-21) Majority of risk in South Asians explained by known risk factors, especially those related to insulin resistance	DM disproportionately present compared to whites and blacks. Increased prevalence MetS, DM in Mexican Americans compared to whites & Puerto Ricans.	Increased DM and hypertension	Increased prevalence of DM. Features of MetS vary by ethnicity. Waist circumference, not weight, should be used to determine abdominal adiposity when possible

Table 10 is continued in the next page. For footnotes please refer to pages 21 and 22.

Special Populations

Ethnicity Issues in Evaluation, Risk Decisions, and Treatment of ASCVD Risk *(2 of 3)*

Table 10 *(continued from previous page)*

Ethnic/racial groupings	Asian-Americans*	Hispanic/Latino-Americans†	Blacks	Comments
Risk Decisions				
Pooled Cohort Equations (PCE)	No separate PCE available; use PCE for whites. PCE may underestimate ASCVD risk in South Asians PCE may overestimate risk in East Asians	No separate PCE available; use PCE for non-Hispanic whites. If African American ancestry also, then use PCE for blacks	Use PCE for blacks	Country specific race/ethnicity, along with socio-economic status, may affect estimation of risk of PCE
Coronary Artery Calcium (CAC) Score	In terms of CAC burden, South Asian men were similar to non-Hispanic white men, but higher CAC when compared to blacks, Latinos and Chinese Americans. South Asian women had similar CAC to whites and other ethnic women, although CAC burden higher in older age	CAC predicts similarly in whites and those who identify as Hispanic/Latino	In MESA, CAC score was highest in whites and Hispanic men, with blacks having significantly lower prevalence and severity of CAC.	Risk factor differences in MESA between ethnicities didn't fully explain variability in CAC However, CAC predicted ASCVD events over and above traditional risk factors in all ethnicities
Treatment *(will continue in the next page)*				
Lifestyle counseling (Utilize principles of Mediterranean & DASH diets)	Utilize lifestyle counseling to recommend a heart healthy diet consistent with racial/ethnic preferences to avoid weight gain, and address BP and lipids	Utilize lifestyle counseling to recommend a heart healthy diet consistent with racial/ethnic preferences to avoid weight gain, address BP and lipids	Utilize lifestyle counseling to recommend a heart healthy diet consistent with racial/ethnic preferences to avoid weight gain, address BP and lipids	Need to disaggregate Asian and Hispanic/Latino groups due to regional differences in lifestyle preferences. Challenge is to avoid increased sodium, sugar and calories as groups acculturate

Table 10 is continued in the next page.

CK, creatine kinase; DASH, Dietary Approaches to Stop Hypertension; DM, type 2 diabetes mellitus; MESA, Multi-Ethnic Study of Atherosclerosis; MetS, metabolic syndrome; and PCE, pooled cohort equations.

Footnotes are continued in the next page.

Special Populations

Ethnicity Issues in Evaluation, Risk Decisions, and Treatment of ASCVD Risk *(3 of 3)*

Table 10 *(continued from previous page)*

Ethnic/racial groupings	Asian-Americans*	Hispanic/Latino-Americans†	Blacks	Comments
Treatment *(continued)*				
Intensity of Statin therapy and Response to LDL-C lowering	Japanese patients may be sensitive to statin dosing. In an open-label, randomized primary prevention trial, Japanese participants had a reduction in CVD events with low-intensity doses of pravastatin as compared to placebo. In a secondary prevention trial, Japanese participants with CAD benefitted from a moderate-intensity doses of pitavastatin.	No sensitivity to statin dosage compared to non-Hispanic white or black individuals	No sensitivity to statin dosage compared to non-Hispanic white individuals	Using a lower statin intensity in Japanese patients may give results similar to those seen with higher intensities in non-Japanese patients
Safety	Higher rosuvastatin plasma levels in Japanese, Chinese, Malay, and Asian-Indians compared to whites. FDA recommends a lower starting dose (5 mg of rosuvastatin in Asians vs. 10 mg in whites). Caution urged as dose uptitrated.	No specific safety issues with statins related to Hispanic/Latino ethnicity	Baseline serum CK values are higher in blacks than in whites. The 95th percentile race/ethnicity specific and sex-specific serum CK normal levels are available for assessing changes in serum CK.	Clinicians should take Asian ethnicity into account when prescribing dose of rosuvastatin (see package insert). In adults of East Asian descent, other statins should be used preferentially over simvastatin.

*The term Asian characterizes a diverse portion of the world's population. Individuals from Bangladesh, India, Nepal, Pakistan, and Sri Lanka make up most of the South Asian group. Individuals from Japan, Korea, and China make up most of the East Asian group.

†The term Hispanics/Latinos in the United States characterizes a diverse population group. This includes white, black, and Native American races. Their ancestry goes from Europe to America, including among these, individuals from the Caribbean, Mexico, Central and South America