

Cholesterol Guideline Update

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The Lipid Panel

Triglycerides
High Density Lipoprotein
Low Density Lipoprotein
Apolipoproteins



Objectives

- The participant will be able to discuss the evolution of recommendations for the treatment of dyslipidemia
- The participant will be able to describe the anticipated lipid patterns of those patients with diabetes, and discuss treatment recommendations



Evolution of Treatment Guidelines

A blue arrow pointing to the right, representing the evolution of treatment guidelines. The arrow is divided into five segments, each representing a different set of guidelines:

- 2002 AHA/B Guidelines
- 2013 ACC/AHA Guidelines
- 2014 ADA Guidelines
- 2016 ACC/AHA Guidelines
- 2018 ACC/AHA Guidelines

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New Guidelines – 2018 American Heart Association

- Contrast of differences between 2013 guidelines
 - More personalized
 - More detailed risk assessments
 - New cholesterol lowering guidelines for population at highest risk for CVD

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Personalized Care

- New guidelines consider
 - Family history
 - Ethnicity
 - Coronary Artery Calcium Scores
 - Presence of
 - Metabolic syndrome
 - CKD
 - Chronic inflammatory conditions***
 - Premature Menopause

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More Detailed Risk Assessments

- Elective cholesterol screening in children as young as two years old
 - Healthy lifestyle
 - Awareness of risk
 - Obtain treatment as appropriate



More Detailed Risk Assessments

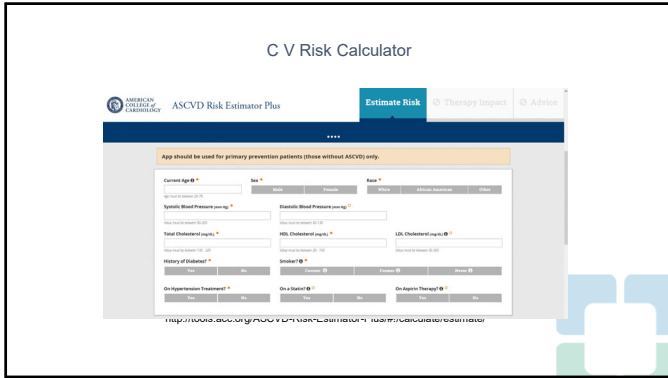
- New category of risk defined
"very high risk of ASCVD"

These are patients who have not obtained LDL of less than 70 mg/dl on maximum statin therapy

- Recommend addition of non statin drugs
 - Ezetimibe
 - PCSK9 inhibitors







C V Risk Calculator

- Low risk = < 5% over 10 years
- Borderline risk = 5% to 7.4%
- Intermediate risk = 7.5% - 19.9%
- High risk = 20% or higher

Monitoring

- Start screening adults ≥ 20 years of age
 - At least every 5 years
- When starting therapy:
 - Initial fasting lipid panel
 - Second fasting lipid panel 4 to 12 weeks after initiating therapy
 - Assess every 3 to 12 months or as clinically indicated thereafter to evaluate adherence/response to therapy

Lloyd-Jones DM, et al. J Am Coll Cardiol 2017;70:1785-822.
 Lloyd-Jones DM, et al. J Am Coll Cardiol 2017;70:1785-822.

Comorbid Disease State Effects

- Diabetes
 - -Elevated triglycerides
- Hypothyroidism
 - -Elevated triglycerides and LDL-C
- Obesity
 - -Elevated triglycerides and LDL-C
- Chronic kidney disease
 - -Elevated triglycerides and LDL-C
- HIV infection
 - -Elevated triglycerides and LDL-C
- Cardiac Events
 - -Falsely low lipids up to 12 weeks post event

Jacobson T, et al. J Clin Lipidol. 2014; 8:473-88



Risk-Enhancing Factors

- Family history of premature ASCVD
 - Males, age <55y; Females, age <65y
- Primary hypercholesterolemia
 - -LDL-C 160-189 mg/dL, non-HDL-C 190-219mg/dL
- Metabolic syndrome
 - -Increased waist circumference, TG >175mg/dL, elevated BP, elevated BG, HDL-C <40mg/dL (men) or <50mg/dL (women)
- Chronic kidney disease
 - -eGFR 15-59 mL/min/1.73m²with or without albuminuria, not with dialysis or kidney transplant
- Chronic inflammatory conditions
- **History of premature menopause or pregnancy conditions that raise risk of ASCVD**
- High-risk race/ethnicities
- Lipid/biomarkers associated with increased ASCVD risk



Evidence

- Statin therapy reduces cardiovascular events in patients with or at risk for ASCVD
- Meta-analysis of 27 randomized trials, with 174,000 participants
 - -For every ~40mg/dLLDL-C reduction with statins, relative risk of major adverse cardiovascular events is reduced by ~20-25%
 - -Relative risk reductions similar in primary vs secondary prevention, lower vs. higher risk

Lancet 2012 Aug 11;380(9841):581-90. doi: 10.1016/S0140-6736(12)60367-4.



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

- In patients 20 to 75y
 - -No risk assessment necessary –high intensity statin indicated
 - -If <50% reduction in LDL-C or LDL-C ≥ 100mg/dL on max tolerated statin, ezetimibe is reasonable
 - Consider bile acid sequestrant if < 50% reduction in LDL-C and fasting TG ≤ 300 mg/dL with max tolerated statin and ezetimibe
- In patients 30 to 75y with heterozygous FH and LDL-C ≥ 100mg/dL on max tolerated statin and ezetimibe, consider PCSK9 inhibitor
- In patients 40 to 75y with LDL-C ≥ 220mg/dL at baseline with LDL-C ≥ 130mg/dL on max tolerated statin and ezetimibe, consider PCSK9 inhibitor

Patients with Diabetes Mellitus (DM)

- Adults 40-75y, moderate intensity statin is indicated regardless of ASCVD risk
 - -If LDL-C 70-189mg/dL, assess 10y ASCVD risk with race and gender specific PCE
 - -If 10y ASCVD risk is ≥ 20%, consider adding ezetimibe to max tolerated statin to reduce LDL-C by ≥ 50%
- If multiple ASCVD risk factors present, consider high intensity statin
- Adults >75y already on statin, reasonable to continue
 - -May also be reasonable to initiate statin tx
- Adults 20-39y with long duration DM, albuminuria, eGFR <60mL/min/1.73m², retinopathy, neuropathy, or ABI <0.9
 - -Reasonable to initiate statin therapy

PCE = Pooled Cohort Equation
ABI = ankle brachial index
eGFR = estimated glomerular filtration rate

Candidates for CAC Measurement

- Patients reluctant to start statin therapy
- Patients concerned for statin re-challenge following history of statin intolerance
- Older patients with low risk factors
- Men 55-80y; Women 60-80y
- Patients age 40-55y with 10yr ASCVD risk 5 to <7.5% with factors that increase ASCVD risk

Grunley SM, et al. J Am Coll Cardiol. 2018; doi:10.1016/j.jacc.2018.11.003

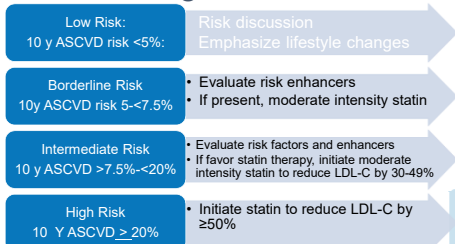
Coronary Artery Calcium (CAC)

- Marker of the extent of coronary atherosclerosis
- CAC score and coronary plaque burden:
 - -0 = No identifiable disease
 - Lowers risk; no statin treatment unless DM, family hx of premature CHD, or current smoker
 - -1 to 99 = Mild disease
 - Favors statin, especially after age 55
 - >100 = Moderate to severe disease
 - Initiate statin therapy

Grundy SM, et al. J Am Coll Cardiol. 2018; doi:10.1016/j.jacc.2018.11.003

Clinical Status	Age Range	Statin Intensity	LDL-C % Reduction Goal	LDL-C Level Goal (mg/dL)
Primary Prevention				
LDL > 190	20-75	High	50 or >	<100
Diabetes LDL > 70	40-75	Moderate	30 or >	
High Risk LDL > 70	40-75	High	50 or >	
Intermediate Risk LDL > 70	40-75	Moderate	30 or >	
Secondary Prevention				
Very high risk ASCVD	>18	High	50 or >	<70
All other ASCVD	>18	High	50 or >	

Primary Prevention: Adults 40-75y, LDL-C 70-189mg/dL without DM



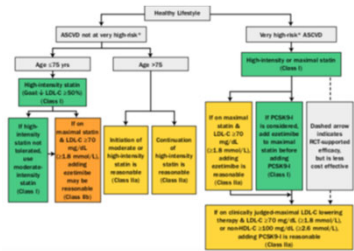
Secondary ASCVD Prevention: Risk Assessment

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 <0.95, or previous revascularization or amputation)
High Risk Conditions
Age ≥65 years
Heterozygous familial hypercholesterolemia
History of prior coronary artery bypass surgery or PCI (subsets 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

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

Grundy SM, et al. J Am Coll Cardiol 2014, doi: 10.1016/j.jacc.2014.11.003

Secondary Prevention



Intensities and LDL-C Lowering

High Intensity	Moderate Intensity	Low Intensity
Daily dosing average LDL-C ↓ ≥ 50%	Daily dosing average LDL-C ↓ 30 to < 50%	Daily dosing average LDL-C ↓ < 30%
Atorvastatin 40 to 80mg Rosuvastatin 20 to 40mg	Atorvastatin 10 to 20mg Rosuvastatin 5 to 10mg Simvastatin 20 to 40mg Pravastatin 40 to 80mg Lovastatin 40mg Fluvastatin XL 80mg Fluvastatin 40mg B/D Pitavastatin 1 to 4mg	Simvastatin 10mg Pravastatin 10 to 20mg Lovastatin 20mg Fluvastatin 20 to 40mg

Key Take Aways

- Emphasize a heart-healthy lifestyle across the life course
- 2. In patients with clinical ASCVD, reduce low-density lipoprotein cholesterol (LDL-C) with high-intensity statins or maximally tolerated statins
- 3. In very high-risk ASCVD, use an LDL-C threshold of 70 mg/dl to consider addition of nonstatins to statins
- 4. In patients with severe primary hypercholesterolemia (LDL-C level ≥ 190 mg/dl, without calculating 10-year ASCVD risk, begin high-intensity statin therapy
- 5. In patients 40 to 75 years of age with diabetes mellitus and an LDL-C level of ≥ 70 mg/dl, start moderate-intensity statins without calculating 10-year ASCVD risk.
- - In patients with DM 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 $\geq 50\%$

Grundy SM, et al. J Am Coll Cardiol. 2018; doi: 10.1016/j.jacc.2018.11.023

Key Take Aways

- In adults 40 to 75 years of age evaluated for primary ASCVD prevention, have a clinician-patient risk discussion before starting statin therapy
- 7. In adults 40 to 75 years of age without DM and with LDL-C levels ≥ 70 mg/dl, at a 10-year ASCVD risk of $\geq 7.5\%$, start a moderate-intensity statin if a discussion of treatment options favors statin therapy
- 8. In adults 40 to 75 years of age without DM and 10-year risk of 5%-19.9%, risk-enhancing factors favor initiation of statin therapy
- 9. In adults 40 to 75 years of age without DM and with LDL-C levels ≥ 70 mg/dl-89 mg/dl, at a 10-year ASCVD risk of $\geq 7.5\%$ -19.9%, if a decision about statin therapy is uncertain, consider measuring CAC
- 10. Assess adherence and percentage response with repeat lipid measurement 4 to 12 weeks after statin initiation or dose adjustment, repeated every 3 to 12 months as needed

Grundy SM, et al. J Am Coll Cardiol. 2018; doi: 10.1016/j.jacc.2018.11.023



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