ACC/AHA Dyslipidemia Guidelines

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Disclosures

- **Todd Anderson**
  - Clinical Trials: Amgen, Merck, Pfizer, Dalcor
  - Speakers Bureau: Sanofi, Amgen,

Objectives

- To understand the new ACC/AHA lipid guidelines
- To compare and contrast with CCS dyslipidemia guidelines
- To understand implications for care delivery

Approach to Risk Management

Who, how when to screen

How to evaluate risk

When to initiate what treatment

Monitoring and surveillance

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Who to Screen

WHO TO SCREEN

Men ≥40 years of age; women ≥40 years of age (or postmenopausal)

Consider earlier in ethnic groups at increased risk such as South Asian or First Nations individuals

All patients with the following conditions regardless of age:

- Clinical evidence of atherosclerosis
- Abdominal aortic aneurysm
- Diabetes
- Arterial hypertension
- Current cigarette smoking
- Stigmata of dyslipidemia (arcus cornea, xanthelasma or xanthoma)
- Family history of premature CVD*
- Family history of dyslipidemia
- Chronic kidney disease
- Obesity (BMI ≥30 kg/m²)
- Inflammatory bowel disease
- HIV infection
- Erectile dysfuntion
- Chronic obstructive pulmonary disease
- Hypertensive diseases of pregnancy

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How to Screen

HOW TO SCREEN

For all:
- History and physical examination
- Standard lipid panel (TC, LDL-C, HDL-C, TG)
- Non-HDL-C (will be calculated from profile)
- Glucose
- eGFR

Optional:
- ApoB
- Urine albumin:creatinine ratio
  (if eGFR <60 mL/min/1.73m^2, hypertension or diabetes)

NON-FASTING LIPID TESTING IS ACCEPTABLE

Recommendations

- We recommend non-fasting lipid and lipoprotein testing which can be performed in adults in whom screening is indicated as part of a comprehensive risk assessment to reduce CVD events.
Strong Recommendation, High Quality Evidence

- We suggest that for individuals with a history of triglyceride levels > 4.5 mmol/L that lipid and lipoprotein levels be measured fasting
Conditional Recommendation, Low Quality Evidence

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Measurements of LDL-C and Non-HDL-C

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

Risk assessment

1. We recommend that **a cardiovascular risk assessment** using the "10 Year Risk" provided by the **Framingham** model be completed every 5 years for men age 40 to 75, and women age 50 to 75. This should be modified (percent risk doubled) when **family history** of premature CVD is positive (i.e. 1^0 relative <55 years for men; <65 years for women). A risk assessment may also be completed whenever a patient's expected risk status changes. Younger individuals with $\geq$1 risk factor for premature CVD may also benefit from a risk assessment to motivate them to improve their lifestyle.
(Strong Recommendation, Moderate-quality Evidence)

Risk assessment

Risk Assessment Tool	Variables included	Outcomes predicted	Derivation sample	Features
Pooled Cohort Equation http://tools.acc.org/ascvd-risk	Age,sex,race TC, HDL-C, SBP Anti-HT Rx DM Smoking	Hard ASCVD (CHD death, non-fatal MI, stroke)	5 community based cohorts of white and black participants	Sex and race specific equation for 4 groups
Framingham Total CVD risk profile https://reference.Medscape.com/calculator/framingham	Age,sex TC, HDL-C SBP Anti-HT Rx DM Smoking	Total CVD (CHD death, non-fatal MI, stroke, ACS, claudication, heart failure)	Single community based on 2 generations	Sex specific equation for Whites Validated in Canada

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

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.

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

Top 10 Take Home messages

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.

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

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

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 I
- 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)

When to Consider Pharmacological Treatment in Risk Management – Primary prevent

Recommendations

- **Primary prevention:**
a) We recommend management that does not include statin therapy for individuals at low risk (modified FRS < 10 %) to lower the risk of CVD events. *Strong Recommendation, High Quality Evidence*

b) We recommend management that includes statin therapy for individuals at high risk (modified FRS ≥ 20%) to lower the risk of CVD events. *Strong Recommendation, High Quality Evidence*

c) We recommend management that includes statin therapy for individuals at intermediate risk (modified FRS 10-19%) with LDL-C ≥ 3.5 mmol/L to lower the risk of CVD events. Statin therapy should also be considered for intermediate risk persons with LDL-C <3.5 mmol/L but with apo B ≥ 1.2 g/L or non-HDL-C ≥ 4.3 mmol/L or in men ≥ 50 and women ≥ 60 years of age with ≥ 1 CV risk factor. *Strong Recommendation, High Quality Evidence*

Top 10 Take Home messages

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.

Selected Examples of Candidates for CAC Measurement Who Might Benefit From Knowing Their CAC Score Is Zero

CAC Measurement Candidates Who Might Benefit from Knowing Their CAC Score Is Zero
• Patients reluctant to initiate statin therapy who wish to understand their risk and potential for benefit more precisely • Patients concerned about need to reinstitute statin therapy after discontinuation for statin-associated symptoms • Older patients (men, 55-80 y of age; women, 60-80 y of age) with low burden of risk factors who question whether they would benefit from statin therapy • Middle-aged adults (40-55 y of age) with PCE-calculated 10-year risk of ASCVD 5% to <7.5% with factors that increase their ASCVD risk, although they are in a borderline risk group

Coronary calcium score - Prognosis

MESA – 6722 subjects
162 events

HR 7.08 for major
Coronary event
With CAC >100

B

Coronary-artery calcium score
— >300
— 101–300
— 1–100
— 0

Cumulative Incidence of Coronary Events (%)

Years to Event

Detrano NEJM 2008;356:1336
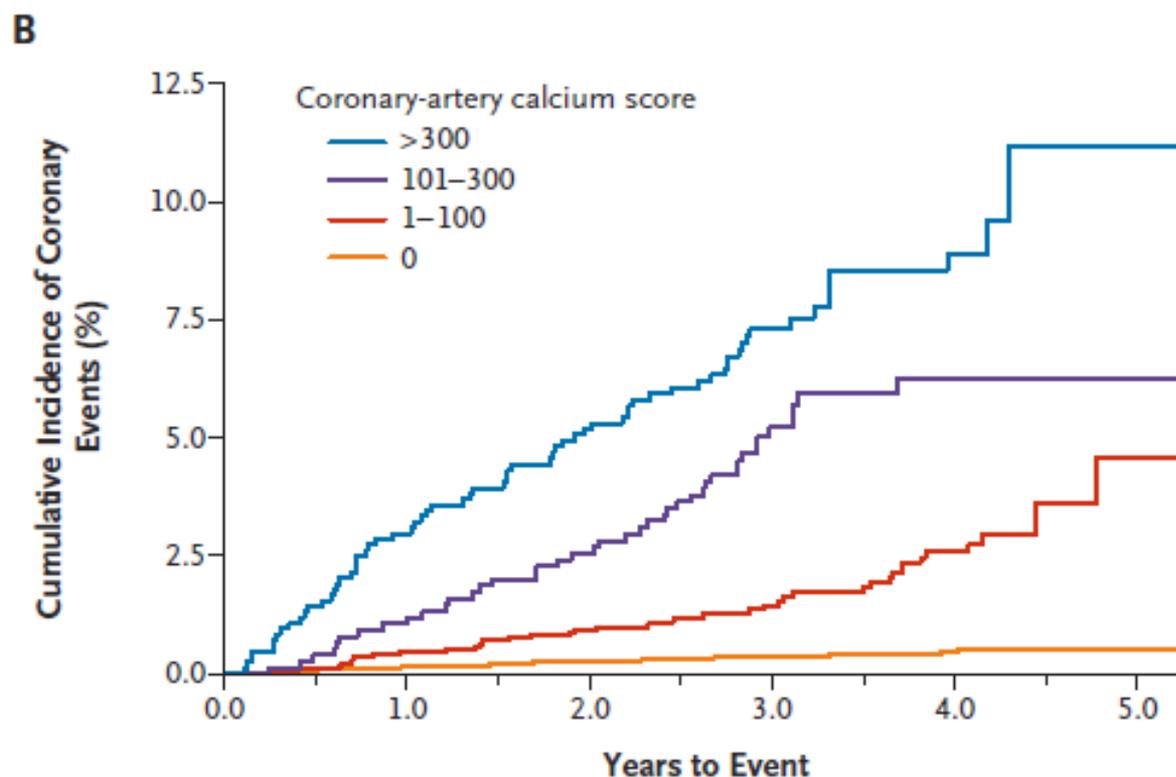
Top 10 Take Home messages

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.

Top 10 Take Home messages

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%.

Top 10 Take Home messages

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.

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

Major ASCVD Events
Recent ACS (within the past 12 mo)
History of MI (other than recent ACS event listed above)
History of ischemic stroke
Symptomatic peripheral arterial disease (history of claudication with ABI <0.85, or previous revascularization or amputation)

Top 10 Take Home messages

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%.

When to Consider Pharmacological Treatment in Risk Management – Statin Indicated conditions

CLINICAL ATHEROSCLEROSIS

Myocardial infarction, acute coronary syndromes

Stable angina, documented coronary disease by angiography (>10% stenoses)

Stroke, TIA, documented carotid disease

Peripheral artery disease, claudication and/or ABI < 0.9

ABDOMINAL AORTIC ANEURYSM

Abdominal aorta > 3.0 cm or

Previous aneurysm surgery

DIABETES MELLITUS

$\geq$ 40 years of age or

> 15 years duration and age $\geq$ 30 years or

Microvascular complications

CHRONIC KIDNEY DISEASE

> 3 months duration and

ACR > 3.0 mg/mmol or

eGFR < 60 ml/min/1.73m^2

LDL-C $\geq$ 5.0 MMOL/L

LDL-C $\geq$ 5.0 mmol/L or

Document familial hypercholesterolemia

Excluded 2nd causes

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Category	Consider Initiating pharmaco-therapy if	Target	NNT
Primary prevention	High FRS (≥20%) all	LDL-C < 2.0 mmol/L or > 50% ↓ Or Apo B < 0.8 g/L Or non-HDL-C < 2.6 mmol/L	35
	Intermediate FRS (10-19%) LDL-C ≥ 3.5 mmol/L or Non-HDL ≥ 4.3 mmol/L or Apo B ≥ 1.2 g/L or Men ≥ 50 and women ≥ 60 yrs and one additional CVD RF		40
Statin indicated conditions	Clinical atherosclerosis*		20
	Abdominal aortic aneurysm		
	Diabetes mellitus >40 yrs 15 yrs duration for age >30 yrs (DM 1) Microvascular disease		
	Chronic kidney disease (age ≥ 50 y) eGFR < 60 mL/min/1.73 m^2 or ACR > 3 mg/mmol		
	LDL-C ≥ 5. 0 mmol/L	>50% ↓ in LDL-C	

FRS – modified Framingham Risk Score; ACR – albumin:creatinine ratio; * consider LDL-C < 1.8 mmol/L for subjects with ACS within last 3 mo

Summary

- New ACC/AHA guidelines have many similarities to 2016 CCS version

- Screening can begin at an earlier age

- More emphasis on CAC for undecided patients

- Use of threshold for additive therapy as opposed to targets

- Conservative approach to PCSK9i

- Use or risk enhancers to focus discussion on shared-decision making

Secondary Prevention

Clinical ASCVD
↓
Healthy Lifestyle

ASCVD not at very high-risk*

- Age ≤75 y
  - High-intensity statin (Goal: ↓ LDL-C ≥50%) (Class I)
    - If high-intensity statin not tolerated, use moderate-intensity statin (Class I)
    - If on maximal statin therapy and LDL-C ≥70 mg/dL (≥1.8 mmol/L), adding ezetimibe may be reasonable (Class IIb)
- Age >75 y
  - Initiation of moderate- or high-intensity statin is reasonable (Class IIa)
  - Continuation of high-intensity statin is reasonable (Class IIa)

Very high-risk* ASCVD

- High-intensity or maximal statin (Class I)
  - If on maximal statin and LDL-C ≥70 mg/dL (≥1.8 mmol/L), adding ezetimibe is reasonable (Class IIa)
  - If PCSK9-I is considered, add ezetimibe to maximal statin before adding PCSK9-I (Class I)
  - Dashed arrow indicates RCT-supported efficacy, but is less cost effective
  - If on clinically judged maximal LDL-C lowering therapy and LDL-C ≥70 mg/dL (≥1.8 mmol/L), or non-HDL-C ≥100 mg/dL (≥2.6 mmol/L), adding PCSK9-I is reasonable (Class IIa)