“The 2013 ACC/AHA Cholesterol Guidelines: What Do They Mean and How Should They Affect Practice?”

Endocrine Grand Rounds
Carl T. Hayden VA Medical Center
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Speaker Disclosures

Dr. Brinton has received:

• **Research** funding: Amarin, Health Diagnostic Laboratory, Merck, Roche; Aurora Foundation; NIH

• Honoraria as **consultant/advisor**: Aegerion, Amarin, Arisaph, AstraZeneca, Atherotech, Daiichi-Sankyo, Essentialis, Genzyme, Janssen, Kowa, Merck, Novartis, Regeneron, Sanofi-Aventis, Takeda

• Honoraria as **speaker**: Amarin, Daiichi-Sankyo, Janssen, Kowa, Merck, Takeda
Learning Objectives

Listeners should be able to:

1. Appreciate the scientific basis of the 2013 ACC/AHA Cholesterol Guidelines (AACG)- including both strengths and limitations
2. Learn the major elements of the AACG approach to cholesterol treatment
3. Discuss the pros and cons of LDL-C and Non-HDL-C targets or goals
4. Understand how a hybrid between the AACG and other past and present guidelines might be beneficial and how to implement
What the 2013 ACC/AHA Cholesterol Guidelines ARE
2013 ACC/AHA Cholesterol Guidelines: Summary

1) Heart healthy lifestyle habits are the foundation to CVD prevention

2) Assess 10-year CVD risk every 4-6 years in adults 40-75 y/o and w/o CVD, DM, not yet on lipid therapy and w/ LDL 70-189 mg/dl

3) Recommend high-intensity statin in those with CVD and age ≤75 years (*statin categ 1*)

4) Recommend high-intensity statin in those with LDL-C $\geq 190$ mg/dl (*statin categ 2*)

5) Recommend moderate- or high-intensity statin for DM-1 or DM-2 aged 40-75 (*statin categ 3*)

6) Recommend moderate- to high-intensity statin for 40-75 y/o with $\geq 7.5\%$ 10-year CVD risk (*statin categ 4*)

2013 ACC/AHA Cholesterol Guidelines: Main Algorithm (part 1)

ASCVD Statin Benefit Groups
Heart healthy lifestyle habits are the foundation of ASCVD prevention. In individuals not receiving cholesterol-lowering drug therapy, recalculate estimated 10-y ASCVD risk every 4-6 y in individuals aged 40-75 y without clinical ASCVD or diabetes and with LDL-C 70-189 mg/dL.

1. Adults age ≥21 y and a candidate for statin therapy
   - Yes: Clinical ASCVD
     - Yes: Age ≤75 y
       - High-intensity statin
         - Moderate-intensity statin if not candidate for high-intensity statin
     - Age >75 y OR if not candidate for high-intensity statin
       - Moderate-intensity statin
   - No: LDL-C ≥190 mg/dL
     - Yes: High-intensity statin
       - Moderate-intensity statin if not candidate for high-intensity statin
     - No: LDL-C <190 mg/dL

2. Definitions of High- and Moderate-Intensity Statin Therapy (See Table 5)
   - High: Daily dose lowers LDL-C by approx. ≥50%
   - Moderate: Daily dose lowers LDL-C by approx. 30% to <50%

2013 ACC/AHA Cholesterol Guidelines: Main Algorithm (part 2)


Dieties
Type 1 or 2
Age 40-75 y

Yes

Moderate-intensity statin

High-Intensity statin

Estimate 10-y ASCVD Risk with Pooled Cohort Equations

≥7.5% estimated 10-y ASCVD risk and age 40-75 y

Yes

Moderate-to-high intensity statin

No

ASCVD prevention benefit of statin therapy may be less clear in other groups

In selected individuals, consider additional factors influencing ASCVD risk and potential ASCVD risk benefits and adverse effects, drug-drug interactions, and patient preferences for statin treatment.
# Approximate Dose-Equivalency of Statin LDL-C Efficacy

<table>
<thead>
<tr>
<th>Rosuva*</th>
<th>Atorva*</th>
<th>Simva</th>
<th>Pitava</th>
<th>Lova</th>
<th>Prava</th>
<th>Fluva</th>
<th>Approx ↓LDL-C</th>
</tr>
</thead>
<tbody>
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<td>5</td>
<td>10**</td>
<td>20**</td>
<td>2**</td>
<td>40**</td>
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<tr>
<td>40</td>
<td>80</td>
<td></td>
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<td></td>
<td></td>
<td>51-55%</td>
</tr>
</tbody>
</table>

*Atorva and rosuva may be *more* effective (½ and 1 doubling respectively).

**Most commonly used dose in US.


Rosuvastatin PI, Pitavastatin PI.
## Approximate Dose-Equivalency of Statin LDL-C Efficacy

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<th>Prava</th>
<th>Fluva</th>
<th>Approx ↓LDL-C</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Moderate-intensity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td>39-47%</td>
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<tr>
<td><strong>High-intensity</strong></td>
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</tbody>
</table>

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**Most commonly used dose in US.

Rosuvastatin PI, Pitavastatin PI.
<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Units</th>
<th>Value</th>
<th>Acceptable range of values</th>
<th>Optimal values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>M (for males) or F (for females)</td>
<td>m</td>
<td>M or F</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>years</td>
<td>53</td>
<td>20-79</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td>AA (for African Americans) or WH (for whites or others)</td>
<td>wh</td>
<td>AA or WH</td>
<td></td>
</tr>
<tr>
<td>Total Cholesterol</td>
<td>mg/dL</td>
<td>192</td>
<td>130-320</td>
<td>170</td>
</tr>
<tr>
<td>HDL-Cholesterol</td>
<td>mg/dL</td>
<td>45</td>
<td>20-100</td>
<td>50</td>
</tr>
<tr>
<td>Systolic Blood Pressure</td>
<td>mm Hg</td>
<td>118</td>
<td>90-200</td>
<td>110</td>
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<tr>
<td>BP Rx (if SBP ≥120)</td>
<td>Y (for yes) or N (for no)</td>
<td>n</td>
<td>Y or N</td>
<td>N</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Y (for yes) or N (for no)</td>
<td>n</td>
<td>Y or N</td>
<td>N</td>
</tr>
<tr>
<td>Smoker</td>
<td>Y (for yes) or N (for no)</td>
<td>n</td>
<td>Y or N</td>
<td>N</td>
</tr>
</tbody>
</table>

**Your 10-Year ASCVD Risk (%)**

4.2

10-Year ASCVD Risk (%) for Someone Your Age with Optimal Risk Factor Levels (shown above in column E)

2.9

**Your Lifetime ASCVD Risk* (%)**

36.0

Lifetime ASCVD Risk (%) for Someone at Age 50 with Optimal Risk Factor Levels (shown above in column E)

5.0

10-Year and Lifetime ASCVD Risks

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at age 50 years with your risk factor levels. In rare cases, 10-year risks may exceed lifetime risks given that the estimates come from different approaches.
2013 ACC/AHA Risk Calculator

• **Pros**
  - Adds stroke to outcomes
  - Adds African descent as racial choice
  - Adds lifetime risk
  - Adds comparison to optimal risk
  - Consolidates “major risk factors” (diabetes, smoking) with risk calculator
  - Otherwise similar to Framingham Score

• **Cons**
  - No lifetime risk after 60 yrs old
  - No family history
  - No other races (e.g. Hispanic and Asian)
  - No inflammatory disorders, CRF, etc.
  - No prior validation, restricted to sources

https://my.americanheart.org/professional/StatementsGuidelines/PreventionGuidelines/Prevention-Guidelines_UCM_457698_SubHomePage.jsp
2013 ACC/AHA Guideline on Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk

✓ Focus *solely* on cholesterol-lowering
✓ *Only* looked at highest-quality RCTs & metaanalyses
✓ Statins clearly reduce atherosclerotic CVD (ASCVD)
✓ Patients to receive statins*
  - Clinical ASCVD
  - LDL-C ≥190 mg/dL
  - Diabetes (type 1 or 2) and 40–75 y/o
  - ≥7.5% estimated 10-y ASCVD risk and 40–75 y/o

* ASCVD risk reduction clearly outweighs the risk of adverse events (including excess cases of new onset diabetes, and rare cases of myopathy and hemorrhagic stroke).

ACC=American College of Cardiology; AHA=American Heart Association; CVD=cardiovascular disease; LDL-C=low-density lipoprotein cholesterol; RCT=randomized controlled trial.

What the 2013 ACC/AHA Cholesterol Guidelines Are NOT
Lipid Management Guidelines and Recommendations: Summary

2002: NCEP ATP III
Identifies TG as a primary target for lipid-lowering therapy when TG ≥500 mg/dL; secondary target of LDL-C

2008: ADA/ACCF
Recommends assessment of global risk to determine goal lipoprotein levels (including non-HDL-C and Apo B)

2012: AACE Dyslipidemia
Recommends global risk assessment; classifying elevated TG to help guide treatment; identifies goal lipoprotein levels (including non-HDL-C and Apo B)

2012: Endocrine Society
Provides recommendations for lifestyle modification and/or TG-lowering therapy based on level of hypertriglyceridemia

2014: IAS
Defines LDL-C and non–HDL-C as atherogenic, with optimal levels for these parameters by patient risk, and notes the importance of their assessment

2011: AHA
Recommends the use of marine-derived omega-3 PUFAs for patients who need to lower TG levels

2013: AHA/ACC
Identifies atherosclerotic CVD patient groups benefiting from statin use; not a comprehensive approach to treating lipid disorders

2013: EAS
Identifies TG as a primary target (with LDL-C and non–HDL-C as secondary targets) when TG >885 mg/dL

ACCF=American College of Cardiology Foundation; NCEP ATP III=National Cholesterol Education Program Adult Treatment Panel III; PUFAs=polyunsaturated fatty acids.

ACC/AHA Cholesterol Guideline History

• ~2008 NHLBI convenes expert panel
  – New evidence rule: multiple quality RCTs only (single RCTs, pre-1995, observational, biological, expert opinion excluded—several panelists quit)
  – No NCEP consortium formed
• Mid 2012 writing completed
• Bureaucratic review ~1 yr
• Summer-Fall 2013
  – NHLBI no longer in guideline business
  – NHLBI “to be published as evidence review”, to serve as basis for new guideline consortium effort
  – Panel insists on prompt publication as guidelines
• Fall 2013:
  – AHA/ACC endorse NHLBI work after cursory review
  – Other reviewers/organizations decline to endorse
• November 12, 2013: Guidelines Published
ACC/AHA Guidelines In Perspective

• *Not* NCEP/ATP-IV
• *Not* the “official US guidelines”
• *Not* the most recent ones
• “Orphan” guidelines (not NHLBI, no NCEP consortium, only superficial review from ACC & AHA)
• “Odd man out” re: “no lipid goals” (vs ATP-I to III, ADA, AACE, European, Canadian, International)
## Evidence Levels for Guidelines

<table>
<thead>
<tr>
<th>Evidence Level</th>
<th>2013 ACC/AHA Cholest. Guidelines</th>
<th>All other Lipid Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple HQ RCTs*</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Meta-analyses of RCTs*</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Single HQ RCT**</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Lower-quality (&amp; earlier) RCTs***</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Observational Data***</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Biological MoA (animals, cells, etc)***</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Expert Opinion***</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

**Yes, give stronger emphasis to stronger evidence**

**No, don’t exclude weaker evidence (prepond. of evidence)**

**Yes, use statins first and aggressively**

**No, don’t exclude non-statins**

Certainty of Evidence: *Level A; **Level B, ***Level C.
Lipid Goals: Pro vs Con

Case Against Chol. Goals

• “No longer appropriate” to say “lower is best” (?)
• “No” RCTs have formally tested:
  – Lipid goals vs no goal
  – One goal vs another
• “Unknown” incremental CVD benefit (?)
• AE rates w/ combo Rx “unknown” (?)
• “Nonstatins do not have favorable risk/benefit” (!)
• May lead to statin under-Rx/non-statin over-Rx
• Falling short “may make pts feel bad”
• Goals are arbitrary

Case For Chol. Goals

• Lower IS Better (↑’ing evidence)
• No new data showing goals useless/harmful
• Helps check and maintain pt compliance?
• Builds on 25 years of NCEP—less confusing
• Helps clinicians & payers get oriented
• Can integrate with high vs medium intensity Rx
Incidence of CV events is proportionally related to the LDL-C level.


Statins Reduce CHD and CVD Events

N=90,056

**Major CHD Events**

**Major CVD Events**

Cholesterol Treatment Trialists: Similar %↓ASCVD Independent of Starting LDL-C

MVEs were reduced ~22% (0.76-0.80, p< 0.0001) for every 1.0 mmol/L (39 mg/dL) reduction in LDL-C cholesterol over 5 years of treatment.

MVE reduction was ~independent of baseline LDL-C.

<table>
<thead>
<tr>
<th>Baseline LDL-C</th>
<th>RR per 39 mg/dL reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 78 mg/dL</td>
<td>0.78 (0.61-0.99)</td>
</tr>
<tr>
<td>78-97 mg/dL</td>
<td>0.77 (0.67-0.89)</td>
</tr>
<tr>
<td>98-116 mg/dL</td>
<td>0.77 (0.70-0.85)</td>
</tr>
<tr>
<td>117-136 mg/dL</td>
<td>0.76 (0.70-0.82)</td>
</tr>
<tr>
<td>&gt; 137</td>
<td>0.80 (0.76-0.83)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>0.78 (0.76-0.80)</td>
</tr>
</tbody>
</table>

Lancet 2010; 376: 1670-81
10 Points to Remember on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults

Summary Prepared by Melvyn Rubenfire, MD
Point 1

The 2013 ACC/AHA Expert Panel included all 16 members of the National Heart, Lung, and Blood Institute Adult Treatment Panel (ATP) IV, and the document review included 23 expert reviewers and representatives of federal agencies. The expert panel recommendations arose from careful consideration of an extensive body of higher quality evidence derived from randomized controlled trials (RCTs), and systematic reviews and meta-analyses of RCTs.
Point 1

The 2013 ACC/AHA Expert Panel included all 16 members of the National Heart, Lung, and Blood Institute Adult Treatment Panel (ATP) IV, and the document review included 23 expert reviewers and representatives of federal agencies. The expert panel recommendations arose from careful consideration of an extensive body of higher quality evidence derived from randomized controlled trials (RCTs), and systematic reviews and meta-analyses of RCTs.

Comment: it is problematic that the vast majority of evidence considered in ALL other lipid guidelines was excluded from this guideline!
Point 2

Through a rigorous process, four groups of individuals were identified for whom an extensive body of RCT evidence demonstrated a reduction in atherosclerotic cardiovascular disease (ASCVD) events (including coronary heart disease [CHD], cardiovascular deaths, and fatal and nonfatal strokes) with a good margin of safety from statin therapy:
Four Statin Benefit Groups:

- Individuals with clinical ASCVD (acute coronary syndromes, or a history of MI, stable or unstable angina, coronary or other arterial revascularization, stroke, TIA, or peripheral arterial disease presumed to be of atherosclerotic origin) without New York Heart Association (NYHA) class II-IV heart failure or receiving hemodialysis.

- Individuals with primary elevations of low-density lipoprotein cholesterol (LDL-C) ≥190 mg/dl.

- Individuals 40-75 years of age with diabetes, and LDL-C 70-189 mg/dl without clinical ASCVD.

- Individuals without clinical ASCVD or diabetes, who are 40-75 years of age with LDL-C 70-189 mg/dl, and have an estimated 10-year ASCVD risk of 7.5% or higher.
Point 2 (cont.)

Four Statin Benefit Groups:

• Individuals with clinical ASCVD (acute coronary syndromes, or a history of MI, stable or unstable angina, coronary or other arterial revascularization, stroke, TIA, or peripheral arterial disease presumed to be of atherosclerotic origin) without New York Heart Association (NYHA) class II-IV heart failure or receiving hemodialysis.

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• Individuals without clinical ASCVD or diabetes, who are 40-75 years of age with LDL-C 70-189 mg/dl, and have an estimated 10-year ASCVD risk of 7.5% or higher.

Comment: These 4 categories are well-founded and practical, and this is the major strength of this guideline.
Point 3

Individuals in the fourth group can be identified by using the new Pooled Cohort Equations for ASCVD risk prediction, developed by the Risk Assessment Work Group.
Point 3

Individuals in the fourth group can be identified by using the new **Pooled Cohort Equations for ASCVD risk prediction**, developed by the Risk Assessment Work Group.

Comment: This risk calculator is a good step forward from the Framingham Risk Equation, especially by offering lifetime risk and comparisons to optimal risk.
Lifestyle modification (i.e., adhering to a heart healthy diet, regular exercise habits, avoidance of tobacco products, and maintenance of a healthy weight) remains a critical component of health promotion and ASCVD risk reduction, both prior to and in concert with the use of cholesterol-lowering drug therapies.
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Comment: Separate lifestyle guidelines are potentially helpful but also somewhat cumbersome. It is good to be reminded and encouraged in this regard.
Point 5

There is no evidence to support continued use of specific LDL-C and/or non–high-density lipoprotein cholesterol (non–HDL-C) treatment targets. The appropriate intensity of statin therapy should be used to reduce risk in those most likely to benefit. Nonstatin therapies, whether alone or in addition to statins, do not provide acceptable ASCVD risk reduction benefits compared to their potential for adverse effects in the routine prevention of ASCVD.
Point 5

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Comment: This is by far the most controversial aspect of these guidelines and it poses two large problems:
1. “No evidence” actually just means that only a few, excluded, trials have tested this question directly. By ignoring the enormous evidence that “lower is better”, this aspect of the guidelines is very likely to do much more harm than good!
2. Most nonstatins have few risks and there is substantial evidence for benefit (albeit not proof). Their virtual elimination is not helpful.
This guideline recommends use of the new Pooled Cohort Equations to estimate 10-year ASCVD risk in both white and black men and women. By more accurately identifying higher risk individuals for statin therapy, the guideline focuses statin therapy on those most likely to benefit. It also indicates, based on RCT data, those high-risk groups that may not benefit.
Point 6

This guideline recommends use of the new Pooled Cohort Equations to estimate 10-year ASCVD risk in both white and black men and women. By more accurately identifying higher risk individuals for statin therapy, the guideline focuses statin therapy on those most likely to benefit. It also indicates, based on RCT data, those high-risk groups that may not benefit.

Comment: As for Point 3, this risk calculator is a good step forward from the Framingham Risk Equation, especially by offering lifetime risk and comparisons to optimal risk.
Point 7

No recommendations are made to inform treatment decisions in selected individuals who are not included in the four statin benefit groups. In these individuals whose 10-year risk is <7.5% or when the decision is unclear, other factors including family history of premature ASCVD, LDL-C >160 mg/dl, high-sensitivity C-reactive protein ≥2 mg/dl, coronary calcium score ≥300 Agatston units or ≥75th percentile for age, sex, ethnicity, and ankle-brachial index <0.9, or elevated lifetime risk of ASCVD may be used to enhance the treatment decision making.
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No recommendations are made to inform treatment decisions in selected individuals who are not included in the four statin benefit groups. In these individuals whose 10-year risk is <7.5% or when the decision is unclear, other factors including family history of premature ASCVD, LDL-C >160 mg/dl, high-sensitivity C-reactive protein ≥2 mg/dl, coronary calcium score ≥300 Agatston units or ≥75th percentile for age, sex, ethnicity, and ankle-brachial index <0.9, or elevated lifetime risk of ASCVD may be used to enhance the treatment decision making.

Comment: Further consideration and testing is reasonable for patients outside the 4 statin groups. Coronary calcium scoring is particularly useful, as is LDL-C >160 mg/dL.
Point 8

High-intensity statin therapy is defined as a daily dose that lowers LDL-C by ≥50% and moderate-intensity by 30% to <50%. All patients with ASCVD who are age ≤75 years, as well as patients >75 years, should receive high-intensity statin therapy; or if not a candidate for high-intensity, should receive moderate-intensity statin therapy.
Point 8

High-intensity statin therapy is defined as a daily dose that lowers LDL-C by ≥50% and moderate-intensity by 30% to <50%. All patients with ASCVD who are age ≤75 years, as well as patients >75 years, should receive high-intensity statin therapy; or if not a candidate for high-intensity, should receive moderate-intensity statin therapy.

Comment: A major aspect of these guidelines is a well founded push towards higher-intensity statins. The near-total exclusion of low-intensity statins, however, is unfortunate.
Point 9

Those with an LDL-C $\geq 190$ mg/dl should receive high-intensity or moderate-intensity statin therapy, if not a candidate for high-intensity statin therapy. Addition of other cholesterol-lowering agents can be considered to further lower LDL-C. Diabetics with a 10-year ASCVD $\geq 7.5\%$ should receive high-intensity statins and <7.5% moderate-intensity statin therapy. Persons 40-75 years with a $\geq 7.5\%$ 10-year ASCVD risk should receive moderate- to high-intensity statin therapy.
Point 9

Those with an LDL-C $\geq 190$ mg/dl should receive high-intensity or moderate-intensity statin therapy, if not a candidate for high-intensity statin therapy. Addition of other cholesterol-lowering agents can be considered to further lower LDL-C. Diabetics with a 10-year ASCVD $\geq 7.5\%$ should receive high-intensity statins and $<7.5\%$ moderate-intensity statin therapy. Persons 40-75 years with a $\geq 7.5\%$ 10-year ASCVD risk should receive moderate- to high-intensity statin therapy.

Comment: It is good to consider nonstatins as indicated here, although the lack of broader consideration for these medications is a weakness of this guideline.
Point 10

The following are no longer considered appropriate strategies: treat to target, lower is best. The new GL recommends: treat to level of ASCVD risk, based upon estimated 10-year or lifetime risk of ASCVD. The guidelines provided no recommendations for initiating or discontinuing statins in NYHA class II-IV ischemic systolic heart failure patients or those on maintenance hemodialysis.
Point 10
The following are no longer considered appropriate strategies: treat to target, lower is best. The new GL recommends: treat to level of ASCVD risk, based upon estimated 10-year or lifetime risk of ASCVD. The guidelines provided no recommendations for initiating or discontinuing statins in NYHA class II-IV ischemic systolic heart failure patients or those on maintenance hemodialysis.

Comment: As for Point 5, this is the biggest single problem with this guideline. Getting rid of “treat to target” and “lower is best” is (a) unwarranted by any reasonable reading of the data, (b) undoes decades of teaching in lipids, and (c) is likely to result in an increase in ASCVD risk!
Perspective

In primary prevention, the cholesterol guidelines recommend not only the risk calculation, but also the physician–patient review of the risk and the decision to take a statin. It is important to realize that the ASCVD risk calculator is heavily influenced by age. A 65-year-old man and a 71-year-old woman with optimal risk factors have a >7.5% 10-year risk. This is where physician judgment, statin safety issues, and a consideration of patient preferences can inform this decision. Prescription of a statin is not automatic, but part of a comprehensive approach to risk reduction that begins with the use of the ASCVD risk calculator and with the assumption that the physician is addressing each of the modifiable risk factors.
An International Atherosclerosis Society Position Paper:
Global Recommendations for the Management of Dyslipidemia

2014 IAS Lipid Guidelines: Brief Summary

### Optimal/Goal

<table>
<thead>
<tr>
<th>Patient Type</th>
<th>LDL-C</th>
<th>Non-HDL-C</th>
<th>1(^o) Treatment</th>
<th>2(^o) Rx</th>
<th>Consider Combo Rx w/</th>
</tr>
</thead>
<tbody>
<tr>
<td>1(^o) prevention</td>
<td>&lt;100</td>
<td>&lt;130</td>
<td>Lifestyle</td>
<td>Statin</td>
<td>CAI/BAS</td>
</tr>
<tr>
<td>2(^o) prevention</td>
<td>&lt;70</td>
<td>&lt;100</td>
<td>Lifestyle</td>
<td>Statin</td>
<td>CAI/BAS</td>
</tr>
<tr>
<td>HTG</td>
<td>?</td>
<td>?</td>
<td>Lifestyle</td>
<td>Statin</td>
<td>Niacin/Fibrate</td>
</tr>
</tbody>
</table>

Innovations include:
1. Multiple lines of evidence
2. Equal emphasis on LDL-C and non-HDL-C
3. Major emphasis on lifetime risk
4. Region-specific risk estimation
5. 1\(^o\) emphasis on lifestyle intervention over drug therapy

Trial Design/Interpretation Issues in 2013 ACC/AHA Cholesterol Guidelines

• NHLBI decision (~ 5 y ago) was to:
  – Focus only on highest quality data (multi RCTs, RCT-meta-analyses)
  – Exclude ~all other evidence, on which all other guidelines (ATP I-III, IAS, ESC, Canadian) are/have been based (+ single RCTs, biological & observational data, expert opinion)

• Δ evidence rules → Δ guidelines (no real change in data)

• No RCTs re: LDL-C goals → no goals

Not from RCTs proving goals are no good!

Stone, NJ. Circulation 2013 epub 12 November
My Proposed Rx Approach (AACG/IAS Hybrid)

• Use 4 pt categories for stain Rx
  – ASCVD
  – DM2 (+ older DM1)
  – Severe hypercholesterolemia
  – 10 y risk >7.5% (vs higher vs lifelong?)

• Use simplified Non-HDL-C & LDL-C goals

• Non-HDL-C ≥ LDL-C

• Consider non-statin adjuncts for
  – Residual dyslipidemia
  – Residual CVD risk

• Allow low-intensity statins