Lipid Guidelines 2018: Updates from ACC/AHA Guidelines 2013

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Objectives and Disclosures

• Disclosures: NIH GRADE Study; Pharmaceutical Trials, none active now

• Objectives
  – Know the four categories of high CVD risk from the ACC/AHA 2013 Lipid Guidelines (ATP IV)
  – Know what the major philosophical change between ATP III and ATP IV
  – Know what the ACC Expert Consensus Decision Pathway is and what changes in the ACC/AHA guidelines are suggested
<table>
<thead>
<tr>
<th>Risk Categories</th>
<th>NCEP ATP III</th>
<th>AHA/ACC – ATP IV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3 main risk categories: CHD / CHD risk equivalent (DM, Clinical CHD, symptomatic CAD, PAD) 2+ risk factors &amp; 10-yr risk ≤ 20% 0-1 risk factors &amp; 10-yr risk &lt;10%</td>
<td>4 statin benefit groups: Clinical ASCVD Primary LDL-C elevations ≥190 mg/dl DM without clinical ASCVD No DM/CVD with 10-yr ASCVD risk ≥7.5%</td>
</tr>
<tr>
<td>Rx targets</td>
<td>LDL-C primary target &lt;100mg/dl &lt;130mg/dl (&lt;100 if risk 10-20%) &lt;160mg/dl (in the order of categories mentioned above)</td>
<td>Intensity of statin therapy High intensity statin therapy (LDL-C reduction ≥50%) recommended for most patients in 4 statin benefit groups</td>
</tr>
<tr>
<td>Rx recommendations</td>
<td>Statin (or bile acid sequestrants or nicotinic acid) to achieve LDL-C goal</td>
<td>Maximally tolerated statin first-line to reduce risk of ASCVD events</td>
</tr>
</tbody>
</table>
ATP IV: a little more abstract

**ATP III**
- RISK FACTOR COUNTING
- TREAT TO LDL GOAL
- ADDRESS NON-HDL TARGET

**ATP IV**
- THERE IS NO TARGET
- THE **INTENSITY** OF STATIN THERAPY IS THE FOCUS OF TREATMENT
ATP-IV (ACC-AHA 2013 Guidelines)

• How many of you have adopted the ATP IV guidelines in your lipid practice by reducing the LDL-C by >50% for those at high risk of CVD?

• How many of you believe that if the LDL-C too low it will place patients at risk for adverse effects?

• How many of you treat patient with Familial Hyperlipidemia?
A Comparative Analysis of Current Lipid Treatment Guidelines

**Fixed-dose strategies**

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<thead>
<tr>
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<tbody>
<tr>
<td>Risk score</td>
<td>PCE to determine 10-yr risk of non-fatal and fatal hard ASCVD events (CHD and CVA)</td>
<td>QRISK2 to determine 10-yr risk of non-fatal and fatal CVD events (CHD, CVA, PAD)</td>
<td>FRS or PCE to determine 10-yr risk of non-fatal and fatal CVD events</td>
</tr>
</tbody>
</table>

**Target-level strategies**

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</thead>
<tbody>
<tr>
<td>Risk score</td>
<td>SCORE chart to estimate 10-yr risk of fatal CVD</td>
<td>Modified FRS to estimate 10-yr risk of non-fatal and fatal CVD</td>
<td>Lifetime FRS to estimate lifetime risk of non-fatal and fatal CVD</td>
<td>PCE or FRS or lifetime FRS</td>
<td>FRS to determine 10-yr risk of non-fatal and fatal CVD</td>
</tr>
</tbody>
</table>
RISK ESTIMATORS

• Risk estimators are derived from large studies in the United States or Europe. All include age, sex, total cholesterol, HDL-C, and systolic blood pressure as predictors.

• However, ethnicity, treatment for hypertension, diabetes, and smoking status are only included in some; thus, patient risk may vary with different estimators.
Outcomes are different between risk estimators

• Outcome for the FRS is the most inclusive, predicting 10-year risk of coronary heart disease, cerebrovascular events, peripheral artery disease, or heart failure.

• The ACC/AHA Pooled Cohort Risk Equations are restrictive, predicting 10-year risk for first hard ASCVD event, defined as coronary heart disease death, nonfatal myocardial infarction (MI), or stroke.

• The SCORE estimator is most specific, predicting 10-year risk of fatal atherosclerotic event, including MI, stroke, other occlusive arterial disease, or sudden cardiac death.
Thresholds for treatment

- Thresholds for which treatment is recommended range between 5% and 20% 10-year risk of ASCVD.
- The lowest threshold is from the ESC/EAS, which recommends statin treatment for patients with 5% to 10% 10-year ASCVD risk and LDL-C $\geq 100$ mg/dl.
- ESC/EAS recommends use of the SCORE risk estimator, which has the strictest outcome by predicting risk of only fatal events.
- The highest threshold for treatment is $\geq 20\%$ 10-year ASCVD risk using the FRS estimator, which predicts risk of the broadest outcomes.
Thresholds for treatment

• The ACC/AHA, USPSTF, and VA-DoD recommend treatment at thresholds of $\geq 7.5\%$, $\geq 10\%$, and $\geq 12\%$ 10-year risk of ASCVD respectively, using the ACC/AHA Pooled Cohort Risk Equations.

• All of the guidelines recommend treatment for patients with LDL-C $\geq 190$ mg/dl.

• Of adults age 40 to 65 years, a comparative analysis estimated the ACC/AHA and ESC/EAS guidelines respectively recommend statin treatment in 43.8% versus 39.1%.
Guidelines Evidence Base

**ACC/AHA**
- Randomized controlled trials (RCT) of statin therapy
- Meta-analyses of RCT

**NLA, ESC, CCS**
- RCT of statins and non-statin drug therapy
- Meta-analyses of RCT
- Observational epidemiologic studies
- Genetic studies
- Metabolic studies
- Mechanistic studies
## Central Focus of Guideline

<table>
<thead>
<tr>
<th>ACC/AHA</th>
<th>NLA, ESC, CCS</th>
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<tbody>
<tr>
<td>Identification of patient groups benefiting from statin therapy</td>
<td>Identification of an individual patient’s ASCVD risk based on clinical parameters and risk factors</td>
</tr>
<tr>
<td>Initiation and maintenance of high or moderate intensity statin therapy</td>
<td>Initiation of ASCVD risk-based lipid-lowering therapy</td>
</tr>
<tr>
<td>Abandonment of lipid goals</td>
<td>Maintenance of lipid goals to assess effective reduction of atherogenic lipoproteins and enhance adherence</td>
</tr>
<tr>
<td>Avoidance of non-statin therapy because of “unfavorable risk/benefit ratio.”</td>
<td>Use of high or moderate dose statins, ±non-statins, if necessary, to achieve goals</td>
</tr>
</tbody>
</table>
Controversies of 2013 ACC/AHA Removal of LDL Goals

• Concern over message to patients and providers
  – Are cholesterol levels no longer important
  – Role of LDL goals in patient motivation
  – Providers not follow up on patients lipid response
Controversies of 2013 ACC/AHA Removal of LDL Goals

• Do we need a target to support adherence/lifestyle changes

• Does a lack of RCT evidence mean lack of benefit
  – Decades of clinical experience with treating to target

• Effect on current performance measures
  – Will quality assurance measures follow these guidelines
the 4 statin benefit groups

1) Secondary Prevention in those with clinical ASCVD
2) Primary Prevention in those with LDL ≥ 190
3) Primary Prevention in those with DM, age 40-75, with LDL 70-189
4) Primary Prevention in those without DM, age 40-75, with LDL 70-189, & a 10 year ASCVD risk ≥ 7.5% (using a new Risk Calculator)
Individuals Not in a Statin Benefit Group

- In those for whom a risk decision is uncertain, these factors may inform clinical decision making:
  - Family history of premature ASCVD
  - Elevated lifetime risk of ASCVD
  - LDL-C ≥160 mg/dL
  - hs-CRP ≥2.0 mg/L
  - CAC score ≥300 Agaston units
  - ABI <0.9
- Statin use still requires discussion between clinician and patient
3 critical questions

• Critical Question 1:
  – What is the evidence for LDL and non-HDL goals for secondary prevention of ASCVD?

• Critical Question 2:
  – What is the evidence for LDL and non-HDL goals for primary prevention of ASCVD?

• Critical Question 3:
  – For primary and secondary prevention of ASCVD, what is the impact on lipid levels, effectiveness, and safety of specific cholesterol modifying drugs?
clinical vignette # 1

A 63 yo WM smoker with HTN comes to see you for a post hospital f/u visit 1 week after suffering a STEMI. He was discharged on atorvastatin 80 mg, antiplatelet, BB, and ACEI. He recalls that his last PCP had prescribed simvastatin 80 mg years ago and he stopped it secondary to leg cramps. He recalls he was on amlodipine for his HTN at that time as well. He is worried he will have leg cramps and wants to stop the atorvastatin or at least decrease the dosage. What do you tell him?
clinical vignette # 1

A: Let him decrease to atorvastatin 20 mg since patients seem to better tolerate this dosage

B: Tell him to have a consultation with his chiropractor and get his advice on lipid management

C: Check his CK, lipid profile, and liver enzymes now (& at every subsequent visit), then decide

D: Explain to him the proven benefit of aggressive secondary prevention with high dose statin therapy
CQ 1: Is there evidence to treat to specific LDL or non-HDL targets in secondary prevention?

- There was NO DATA identified to treat to a specific LDL goal in those with clinical ASCVD*
  - 19 RCTs used **FIXED DOSE** statin therapy
    - *The 4S trial did titrate to a specific target of an LDL <100 mg/dl in 37% of the patients.
    - **ALLIANCE** trial (Am J Med 2005;118:Suppl 12A:16-21) treated to an LDL<80mg/dl vs maximum Atorvastatin dose of 80 mg/d.
      » (-)17% lower event rate vs usual care

- In patients with clinical ASCVD, even if moderate or low intensity statin therapy results in an LDL < 100, the evidence suggests that **higher intensity** statin therapy provides a greater risk reduction in ASCVD events

- There was NO DATA to support treating to specific non-HDL targets either
moderate vs high

MODERATE INTENSITY STATIN THERAPY

MODERATE intensity lowers LDL by 30-49%

- Atorvastatin 10 or 20 mg
- Rosuvastatin 5 or 10 mg
- Simvastatin 20 or 40 mg
- Pravastatin 40 or 80 mg
- Lovastatin 40 mg
- Fluvastatin 40 mg BID

HIGH INTENSITY STATIN THERAPY

HIGH intensity lowers LDL by ≥ 50%

- Atorvastatin 40* or 80 mg
- Rosuvastatin 20 or 40 mg

*IDEAL down-titrated to 40 mg when 80 was not tolerated
clinical vignette # 2

A 60 BF presents to you for follow up. At her last visit you mentioned that you wanted to talk to her about statin therapy to decrease her risk of stroke & MI. She is very concerned because she has been seeing the ads on TV asking patients to call 1-800-SUE-DOCS if you developed diabetes while taking statin therapy.

The patient does not smoke, she is treated with 2 anti-hypertensives (treated BP 142/88), her BMI is 31. Her mother was diabetic and had CVA at age 62. The patient’s lipid profile shows TC 200, LDL 125, HDL 55, TG 130. Fasting glucose is 109, A1c is 5.9%. Using the risk calculator, her 10 year estimated risk of ASCVD is 8.7%. So what do you advise?
clinical vignette # 2

A: She should focus only on LSM because LSM reduces ASCVD more than any statin could dream of, and you don’t want to get sued

B: Go ahead and put her on Bydureon to help cancel out the risk of diabetes development then add pravastatin 10 mg daily

C: Measure carotid intima media thickness & obtain a BOSTON advanced lipid profile, then decide

D: Have a Risk discussion and recommend that she start a moderate or high intensity statin
CQ 2: Is there evidence to treat to specific LDL and non-HDL targets in primary prevention?

• There was NO DATA to treat to specific LDL targets*

• There was NO DATA to treat to specific non-HDL targets
  – RCTs used FIXED DOSE statin therapy

AFCAPS/TEXCAPS*
MEGA
*(AFCAPS-TEXCAPS titrated for an LDL goal <110 mg/dl and the MEGA trial titrated Pravastatin for a TC <200 mg/dl)
the risk calculator
the risk calculator

• Use it to calculate a 10 year risk of first ASCVD event in those without ASCVD, ages 40-75, with an LDL 70-189. Can be used in those WITH DM or those WITHOUT DM

• If the 10 year risk is > 7.5%, the benefit of statin therapy clearly outweighs the risk

• Those with a 10 year risk of 5 – 7.5% showed a similar RR however the potential for AE > RR
the risk calculator

• Based on pooled cohort equations for RCTs
  – ARIC, CHS, CARDIA, Framingham & Offspring Cohorts
• Variables that met inclusion criteria:
  – Age, TC, HDL, systolic BP, DM smoking status
• Applicable to non-Hispanic whites and AA
• Admittedly OVER-estimates for Hispanic & Asian American populations
• Admittedly UNDER-estimates for American Indian populations
the risk discussion

• Shared decision making
• A time to revisit LSM and address other RF
• Discuss potential for ASCVD risk reduction
• Discuss adverse effects
  – New onset DM (dose dependent)
    • 1 per 1000 in moderate intensity (prevention of 5.4 ASCVD events)
    • 3 per 1000 in high intensity (5.9 ASCVD events)
  – Myopathy (1 in 10000) & Hemorrhagic CVA (1 in 10000)
• Discuss drug – drug interactions
• Discuss patient preferences
if you like ordering more tests..

• In primary prevention, if the risk-based decision is unclear, consider:
  – Family hx of premature CVD
  – Hs CRP
  – CAC
  – ABIs

• 69 WF with (+) family history of CVD in MGM, MGF and paternal uncle
69WF with Statin Intolerance

Cholesterol

mg/dL

HDL Cholesterol

mg/dL

LDL Cholesterol

mg/dL
NMHI Coronary Calcium Score (Brief):
Calcium Score

Calcium Scoring Procedure
High resolution, non-contrast, limited CT images of the heart, coronary arteries, and proximal great vessels performed. Coronary artery calcium scanning and three-dimensional scoring was done according to a standardized protocol.

Indications:
Family history of heart disease Hypercholesterolemia Hypertension

Results:

<table>
<thead>
<tr>
<th>Anatomy</th>
<th>Calcium Score (Agatston)</th>
<th>Volume (mm3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left Main:</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Right Coronary Artery:</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Left Anterior Descending:</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Circumflex:</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total:</td>
<td>0</td>
<td>0</td>
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</table>

Calcium Score of: 0

Translation of Calcium Score
Risk of coronary events associated with increasing coronary artery calcium score after adjustment for standard risk factors.

Recommendations

Calcium Score = 1-50: Consider aspirin therapy and aggressive lifestyle modifications.
Calcium Score = 51-100: Consider aspirin and statin therapy. Aggressive lifestyle modifications.
Calcium Score = 101-300: Aspirin and statin therapy. Consider cardiology consult.
Calcium Score = >300: Aspirin and statin therapy. Stress testing. Cardiology consult.

Your total calcium score of 0 is between the 0th and 25th percentile for women between the ages of 65 and 69. This means that 0 percent of people this age and gender had less calcium than was detected in this study.
A 58 yo WM with hx of 3 v CABG about 2 years ago comes in to see you for follow up. He is not smoking. He is taking his meds as prescribed. He exercises regularly. BP is well controlled and BMI is 24. On rosuvastatin 40 mg his LDL is 116, HDL is 32, TG 145.

Should you add more medications to his regimen of asa, BB, statin, long acting nitrate, and diuretic/ACE in order to get his lipid profile in better standing?
clinical vignette # 3

A: Add VASCEPA – (Eicosapentenoic Acid,EPA)
B: Add ezetimibe because he remembers being on it once but stopped it due to $$$
C: Add NIACIN to get his HDL out of the red zone and back into the black zone
D: Let him ride
CQ 3: For primary and secondary prevention, what is the impact on lipids levels, effectiveness, and safety of specific cholesterol modifying drugs?

• NO DATA to support routine use of non-statin drugs combined with statin therapy to further reduce ASCVD events
  – Review included statins, fibrates, niacin, bile acid sequestrants, ezetimibe, O-3 fatty acids
  – AIM-HIGH: adding NIACIN to achieve non-HDL targets did NOT reduce ASCVD risk
    • Niacin raised HDL by 25%, decreased TG by 30%, but no improvement in CV outcomes.
    • IMPROVE-IT: Ezetimibe did lower events ~6% below statin alone

• NO DATA for ASCVD outcomes in statin intolerant patients
ATP IV strengths to consider

• Encourages a “risk discussion” with patients in regards to primary prevention
• Strictly evidence based
• The bulk of the content is undisputed
• 10 year risk of ASCVD includes CHD & stroke
  – ATPIII 10-year risk only in CHD (MI and CHD death)
• More relevant for women and AA populations
ATP IV weaknesses to consider

• Strictly evidence based
  – Limited or NO DATA for > 75 and < 40
• The risk calculator is controversial and may significantly overestimate risk
• Forgotten populations: diabetics < 40 y/o and chronic kidney disease and any measure of social deprivation.
• Younger patients often have a high lifetime risk and a low short term (10 year) risk
On-Treatment LDL-C and CHD Events

% with CHD Events, Projected to 5 Years

Primary Prevention

\[ y = 0.046x - 1.53 \]

\[ R^2 = 0.95 \]

Mean or Median LDL-C, mg/dL

Data abstracted from original publications
Relationship Between LDL-C Levels and CHD Events in Secondary Prevention

Coronary Heart Disease Risk According to LDL-C Level

CHD=Coronary heart disease, LDL-C=Low-density lipoprotein cholesterol

# How low is too low?

<table>
<thead>
<tr>
<th>Clinical Trial (publication year)</th>
<th>Number of Patients Achieving Very Low LDL-C</th>
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<tbody>
<tr>
<td></td>
<td>&lt; 50 mg/dL</td>
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<tr>
<td>OSLER® (2015)</td>
<td></td>
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<tr>
<td>ODYSSEY LONG-TERM7 (2015)</td>
<td></td>
</tr>
<tr>
<td>IMPROVE-IT® (2015)</td>
<td></td>
</tr>
<tr>
<td>JUPITER® (2008)</td>
<td>4,154</td>
</tr>
<tr>
<td>PROVE-IT® (2004)</td>
<td></td>
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<tr>
<td>TNT10 (2005)</td>
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</table>

Table 1. Clinical trials reporting the number of subjects achieving very low LDL-C
2016 ACC Expert Consensus Decision Pathway on the Role of Non-Statin Therapies for LDL-Cholesterol Lowering in the Management of Atherosclerotic Cardiovascular Disease Risk

A Report of the American College of Cardiology Task Force on Clinical Expert Consensus Documents

Endorsed by the National Lipid Association

Writing Committee

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Pamela B. Morris, MD, FACC, Vice Chair
Christie M. Ballantyne, MD, FACC
Kim K. Birtcher, PharmD, AACC
David D. Daly, Jr., MD
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Margo B. Minissian, PhD, ACNP, AACC
Carl E. Orringer, MD, FACC, FNLA*
Sidney C. Smith, Jr., MD, FACC

*National Lipid Association Representative.
2016 Expert Consensus Decision Pathway: Rationale

- Provide more specific guidance on the adequacy of statin therapy and whether or when to use non-statin therapies if response to statins is deemed inadequate or less than anticipated
- Extend beyond 2013 evidence base to incorporate recent trial data and address current gaps in care for LDL-C lowering to reduce ASCVD risk
- Consider use of drugs FDA-approved after publication of 2013 guideline (alirocumab, evolocumab)
2016 Expert Consensus Decision Pathway: Questions Addressed

1. In what **patient populations** should non-statin therapies be considered?

2. In what **situations** should non-statin therapies be considered?
   - When is the **amount of LDL-C lowering** less than anticipated, less than desired, or inadequate, and which treatment options should be considered in patients who are truly statin intolerant?

3. If non-statin therapies are to be added, **which agents** or therapies should be considered and in **what order**?
2017 Focused Update of the 2016 ACC Expert Consensus Decision Pathway on the Role of Non-Statin Therapies for LDL-Cholesterol Lowering in the Management of Atherosclerotic Cardiovascular Disease Risk

A Report of the American College of Cardiology Task Force on Expert Consensus Decision Pathways

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http://dx.doi.org/10.1016/j.jacc.2017.07.745
### Figures 2A and 2B

<table>
<thead>
<tr>
<th>Adults ≥21 Years of Age With Clinical ASCVD, on Statin for Secondary Prevention, Baseline LDL-C 70-189 mg/dL</th>
<th>2016 ECDP</th>
<th>2017 ECDP Focused Update</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Thresholds for consideration of net ASCVD risk reduction benefit in patients with clinical ASCVD without comorbidities were ≥50% reduction in LDL-C and may consider LDL-C &lt;100 mg/dL. Thresholds for patients with clinical ASCVD with comorbidities were ≥50% reduction in LDL-C and may consider LDL-C &lt;70 mg/dL.</td>
<td><strong>Thresholds for consideration of net ASCVD risk-reduction benefit are LDL-C reduction ≥50% and may consider LDL-C &lt;70 mg/dL or non-HDL-C &lt;100 mg/dL for all patients with clinical ASCVD and baseline LDL-C 70-189 mg/dL.</strong></td>
</tr>
</tbody>
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**Comment/Rationale:** The writing committee considered the results of the cardiovascular outcomes trials, IMPROVE-IT (Improved Reduction of Outcomes: Vytorin Efficacy International Trial) and FOURIER, demonstrating the safety and efficacy of the addition of ezetimibe or evolocumab to maximally tolerated statin therapy in patients with clinical ASCVD and on-statin-treatment LDL-C levels of approximately 70 mg/dL in IMPROVE-IT and 92 mg/dL in FOURIER (2,6). Based on consideration of all available evidence, the consensus of the writing committee members is that lower LDL-C levels are safe and optimal in patients with clinical ASCVD due to the increased risk of recurrent events.

Thresholds in patients with clinical ASCVD with and without comorbidities are LDL-C <70 mg/dL or non-HDL-C <100 mg/dL.

Considerations that may favor the initial choice of ezetimibe include: patients who require <25% additional lowering of LDL-C, patients with recent ACS <3 months, cost considerations with recent availability of generic ezetimibe and future cost savings, ease of use as oral agent with low pill burden, patient preferences, heart failure, hypertension, age >75 years, diabetes, stroke, CABG, PAD, eGFR <60 ml/min/1.73 m², and smoking.

If patients with clinical ASCVD and comorbidities require >25% additional lowering of LDL-C, a PCSK9 inhibitor may be preferred as the initial non-statin agent. The clinician-patient discussion should consider the extent of available scientific evidence for net ASCVD risk reduction benefit, cost, administration by subcutaneous injection, every 14-day or monthly dosing schedule, and storage requirements (refrigeration).
2017 Focused Update

The 2017 Focused Update also includes the following factors that may be considered for the identification of higher-risk patients with clinical ASCVD: age ≥65 years, prior MI or non-hemorrhagic stroke, current daily cigarette smoking, symptomatic PAD with prior MI or stroke, history of non-MI related coronary revascularization, residual coronary artery disease with ≥40% stenosis in ≥2 large vessels, HDL-C <40 mg/dL for men and <50 mg/dL for women, hs-CRP >2 mg/L, or metabolic syndrome (7).
WHAT IS NEW ON THIS TOPIC: HYPERLIPIDEMIA

A Cochrane review found that for every 1,000 persons treated with a statin for five years, 18 avoid myocardial infarction, angina, or stroke (number needed to treat = 56). This review focused on studies that included fewer than 10% of participants with known cardiovascular disease.

A meta-analysis of 13 trials involving more than 90,000 patients found that statin use increases the overall absolute risk of developing diabetes mellitus by 0.39% (number needed to harm = 255) over four years.

In early 2016, the U.S. Food and Drug Administration withdrew approvals for extended-release niacin and delayed-release fenofibrate acid (fibrate) in combination with statins based on lack of cardiovascular benefit.

Hyperlipidemia: Drugs for Cardiovascular Risk Reduction in Adults
ALLEN R. LAST, MD, MPH, Medical College of Wisconsin Fox Valley Family Medicine Residency Program, Appleton, Wisconsin
JONATHAN D. FERENCE, PharmD, Wilkes University Nesbitt School of Pharmacy, Wilkes-Barre, Pennsylvania
ELIZABETH ROLLMANN MENZEL, MD, Medical College of Wisconsin Fox Valley Family Medicine Residency Program, Appleton, Wisconsin.
Am Fam Physician. 2017;95(2):78-87
Where do we go from here?

• Determine patient’s ASCVD risk. If the patient doesn’t have clinical ASCVD, use the ASCVD risk calculator and/or measure coronary artery calcium Score.

• Life Style modification

• Discuss benefits, risk, costs of lipid lowering tx to reduce patient’s risk. As the risk increases, the benefit of lipid lowering increases.
Where do we go from here?

• Thresholds for consideration of net ASCVD risk-reduction benefit are LDL-C ≥50% and may consider LDL-C ≤70 mg/dl or non-HDL-C ≤100 mg/dl for ALL patients with clinical ASCVD and baseline LDL-C 70-189 mg/dl.

• It is reasonable to consider adding either Ezetimibe or PCSK9 inhibitor based on the considerations of additional % LDL-C reduction desired, patient preferences, costs, route of administration.
Not Part of the Guidelines
How do we decide what the satisfactory LDL-C values are that balance benefit, safety, and cost?

Start with high potency-high dose statin for high-risk patients

Is there adequate LDL-C lowering?

Yes
Continue treatment

No
When LDL-C lowering is not achieved based on what the Clinician's assessment is, then treat to a threshold LDL-C level
LDL-C on Statin Tx and Risk of CVD

• One of the clearest and most elegant demonstrations of how important lower LDL-C is the meta-analysis of secondary prevention trials by Boekholdt et al.


Hunter-gather populations typically have low LDL-C (35-55 mg/dl); there is a log-linear relationship of CVD risk as a function of LDL-C and the Y-intercept (Hazard Ratio=1.0) occurs with an LDL-C of 40 mg.dl
More Tidbits

• Discordant LDL-C ... what is the significance and how can we determine if the LDL-C is discordant?
  – Non-HDL-C >130 mg/dl (Pischon T et.al. Circulation 2005;112:3375-3383)

• A meta-analysis of 8 secondary prevention trials using Statins, even when the LDL-C on Statins was <100 mg/dl, if the non-HDL-C was >130 mg/dl, those patients had a 41% excess risk for an acute CV event.
Do you use Fibrates in your practice?

• Subgroup analyses of patients in the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial suggested benefit with fenofibrate added to statins if the TG > 204 mg/dl and the HDL-C was < 34 mg/dl.

• There are 5 trials with a significant subgroup of patients (TG ≥ 204 mg/dl and HDL-C ≤ 34 mg/dl) that demonstrate significant reduction in vascular events when fibrates were used vs placebo.
Thank you!
Questions