Objectives

- Identify emerging trends in drug therapy and their place in patient care practices.
- Compare and contrast the recommendations for cholesterol management from the National Cholesterol Education Panel (ATP III), American College of Cardiology/American Heart Association, and National Lipid Association.
- Explain the relationship between LDL cholesterol and cardiovascular risk.
- Describe clinical situations where statins should be used to lower cardiovascular risk.
- Discuss the role of nonstatins (niacin, fibrates, etc) in the management of dyslipidemia.

Questions We’ll Answer Today

- What are key recommendations from the ACC/AHA cholesterol guidelines?
- How do the proposed NLA recommendations differ from ACC/AHA guidelines?
- What patients may benefit from statin therapy?
- Which cardiovascular risk calculator should be used?
- When should nonstatins be prescribed?

2013 ACC/AHA Cholesterol Guidelines

- First major revision since 2002 National Cholesterol Education Program Adult Treatment Panel III (ATP III)
- Overview of guideline process:
  - Studies included
  - Rating of evidence
  - Conflict of interest disclosure
- Published with 3 other ACC/AHA guidelines:
  - Assessment of CV Risk
  - Lifestyle management
  - Obesity

Disclosures

Family

- Reid Blackwelder, MD, FAAP
  - Dr. Blackwelder reports that he has received honoraria from the American Academy of Family Physicians (AAFP).
- Peter J. Czark, MD, MS
  - Nothing to disclose
- Donald W. Kirk, MD
  - Nothing to disclose

Terry A. Jacobson, MD, FAHA, FACR, FNL

- Dr. Jacobson reports that he has provided consulting services to Amarin, AstraZeneca, Merck & Co., and Regeneron/Sanofi.
- Neil Z. Stone, MD, MACR, FAHA, FACPC
  - Nothing to disclose

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The editors of this activity and its publisher, Therapeutic Research Center, have no relevant financial interests related to the content of this CME/CE activity.

Nesta O’Mara, PharmD, BCPS

- Dr. O’Mara reports that her spouse is employed by Celgene.

2014 Cholesterol Controversy

The Current Cholesterol Controversy
PL VOICES: The Current Cholesterol Controversy

2013 ACC/AHA Cholesterol Guidelines Primary Recommendations

- Encourage adherence to a healthy lifestyle
- Consider statins for patients shown to benefit
- Ensure statin safety by using them in suitable patients and monitoring appropriately
- Discuss statin risk/benefit BEFORE starting therapy especially for primary prevention
- Use the new Pooled Cohort Equations to estimate 10-yr CV risk
- Start with the appropriate intensity of statin therapy
- Be aware there isn't evidence to treat to specific LDL or non-HDL goals
- Monitor for adherence to lifestyle and statin therapy

Four Statin Benefit Groups

<table>
<thead>
<tr>
<th>Atherosclerotic cardiovascular disease</th>
<th>Secondary Prevention</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL ≥ 150 mg/dL</td>
<td>High-intensity*</td>
</tr>
<tr>
<td>Ages 40 to 75 with diabetes LDL 70-189 mg/dL</td>
<td>Moderate-intensity</td>
</tr>
<tr>
<td>Ages 40 to 75 10-year CV risk ≥ 7.5%</td>
<td>Moderate- to High-intensity</td>
</tr>
</tbody>
</table>

- * Adjust statin intensity if side effects are a concern (e.g., previous statin intolerance, drug interactions)

Pooled Cohort Equations Cardiovascular Risk Estimator

- Determines:
  - 10-year risk of MI or stroke
  - Lifetime risk
- Includes African Americans and women
- Replaces Framingham risk assessment
- Threshold of 7.5%
- Download an App or find it at: http://my.americanheart.org/cvriskcalculator

Initiating and Monitoring Statins

- Start at the appropriate intensity dose
- Usually not necessary to titrate
  - No evidence that this prevents side effects
  - Evidence that this hinders achieving target doses
- Exceptions:
  - Older than 75, history of statin intolerance, using meds that interact with statins
  - Abnormal liver function
- Monitoring
  - Check lipids 4-12 weeks after starting and then every 3 to 12 months

Statin

<table>
<thead>
<tr>
<th></th>
<th>Moderate-intensity</th>
<th>High-intensity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lower LDL by 30% to 49%</td>
<td>Lower LDL by ≥ 50%</td>
</tr>
<tr>
<td>Atorvastatin (Lipitor)</td>
<td>10 to 20 mg</td>
<td>40 to 80 mg</td>
</tr>
<tr>
<td>Rosuvastatin (Crestor)</td>
<td>5 to 10 mg</td>
<td>20 to 40 mg</td>
</tr>
<tr>
<td>Simvastatin (Zocor)</td>
<td>20 to 40 mg</td>
<td>--</td>
</tr>
<tr>
<td>Pravastatin (Pravachol)</td>
<td>40 to 80 mg</td>
<td>--</td>
</tr>
<tr>
<td>Lovastatin (Mevacor)</td>
<td>40 mg</td>
<td>--</td>
</tr>
<tr>
<td>Fluvastatin (Lescol)</td>
<td>80 mg</td>
<td>--</td>
</tr>
<tr>
<td>Pitavastatin (Livalo)</td>
<td>2 to 4 mg</td>
<td>--</td>
</tr>
</tbody>
</table>

Generics available for atorvastatin, simvastatin, pravastatin, lovastatin, and fluvastatin.
The Role of Nonstatins

- Do NOT routinely use nonstatins:
  - Bile acid sequestrants, fibrates, niacin, fish oil, ezetimibe (Zetia)
- Adding nonstatin to statin:
  - Not shown yet to improve CV outcomes
  - Adding niacin or a fibrate to a statin doesn’t improve CV outcomes in patients with LDLs < 100 mg/dL
- Save nonstatins for:
  - Add-on for high-risk patients who don’t get anticipated benefit
  - Patients who can’t tolerate a statin
  - Triglycerides ≥ 500 mg/dL

Roles of nonstatin add-on therapies

- Need for statin dose titration
- Risk assessment tool

2014 NLA Cholesterol Recommendations

- Draft of consensus recommendations
  - Part 1 released May 2nd
  - Was open for public comment through May 31st
  - Will be published in Journal of Clinical Lipidology
  - Part 2 will follow with similar process
- Overview of consensus process:
  - Studies included
  - Strategic plan for recommendations
  - Conflict of interest disclosure

Comparing NLA to ATP III:

- Similarities & Differences
  - Draft of consensus recommendations
  - Similarities:
    - Encourages a healthy lifestyle
    - Counts risk factors to help determine CV risk category
    - Emphasizes LDL/non-HDL targets based on CV risk
    - Uses Framingham risk assessment
    - Uses statins as primary treatment
    - Uses nonstatins as add-on therapy if needed to reach treatment goals
  - Differences:
    - Non-HDL now considered a PRIMARY target of therapy
    - Apo B secondary target of therapy

Key Differences Between ACC/AHA and ATP III or NLA

- Role of lipid targets
- Risk assessment tool
- Need for statin dose titration
- Role of nonstatin add-on therapies
PL VOICES: The Current Cholesterol Controversy

Applying the Evidence in Your Practice

Meet Ginny

- 52-year-old obese, African American female
- Hypertension, poorly-controlled
- 152/88 mmHg
- Lisinopril/HCTZ 40/25 mg
- Amiodipine 10 mg
- No family history of CV disease

Baseline

<table>
<thead>
<tr>
<th>Factor</th>
<th>Value</th>
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<tbody>
<tr>
<td>Total cholesterol</td>
<td>205</td>
</tr>
<tr>
<td>HDL</td>
<td>28</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>290</td>
</tr>
<tr>
<td>Non-HDL</td>
<td>177</td>
</tr>
<tr>
<td>LDL</td>
<td>118</td>
</tr>
</tbody>
</table>

Current

<table>
<thead>
<tr>
<th>Factor</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol</td>
<td>152</td>
</tr>
<tr>
<td>HDL</td>
<td>51</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>155</td>
</tr>
<tr>
<td>Non-HDL</td>
<td>103</td>
</tr>
<tr>
<td>LDL</td>
<td>70</td>
</tr>
</tbody>
</table>

Ginny’s Risk...According to ACC/AHA Risk Estimator

- 10-year risk of MI or stroke > 7.5%
- Age 40-75 years
- Moderate- or high-intensity statin

Ginny’s Risk...According to Framingham

- 10-year risk > 7.5%
- Non-HDL > 177
- Consider drug therapy

Meet William

- 68 years old, non-smoker
- Acute coronary syndrome (ACS) 3 months ago
- Clopidogrel and low-dose aspirin
- Has hypertension and diabetes:
  - BP 135/82 mmHg on lisinopril and carvedilol
  - A1C 7.2% on metformin and glipizide
- Taking atorvastatin 10 mg daily, tolerating it well

Ginny’s Risk...According to Framingham

- 2 risk factors
- Hypertension, Low HDL
- 10-year risk: 5%
- Non-HDL > 177
- Consider drug therapy

Treating Ginny

- 6 months later, she has tried two moderate-intensity statins
  - Simvastatin 20 mg...
  - Stopped due to muscle pain
  - Now on pravastatin 40 mg...
- Taking atorvastatin 10 mg daily, tolerating it well
**PL VOICES: The Current Cholesterol Controversy**

### Meet Steve
- 66-year-old healthy, African American male
- Runs 5 miles a day, not overweight
- Normal blood pressure
- Nonsmoker
- No family history of CV disease
- What is Steve’s risk?

**Baseline**
- Total cholesterol: 222
- HDL: 68
- Triglycerides: 165
- Non-HDL: 154
- LDL: 121

### Steve’s Risk...According to ACC/AHA Risk Estimator
- Age 40-75 years
- 10-year risk of MI or stroke > 7.5%
- Consider statin
- Discuss with patient

### Meet Gary
- 38-year-old white male
- Healthy, moderately active, watches diet, not overweight
- Significant family history of premature CV disease
  - Mother had fatal MI at age 47
  - Maternal uncle with MI and CABG at age 35
- Normal blood pressure, no diabetes
- Never smoked
- What is Gary’s risk?

**Baseline**
- Total cholesterol: 230
- HDL: 50
- Triglycerides: 100
- Non-HDL: 200
- LDL: 180

### Gary’s Risk...According to ACC/AHA Risk Estimator
- Age 38: - Have to use age of 40 to estimate risk
  - Risk:
    - 10-year risk of MI or stroke 1.8%
    - Lifetime risk is 50%
  - Consider statin
  - Discuss with patient

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**Individualize treatment**
- Consider guidelines and recommendations
- Use evidence to make informed decisions
- Involve the patient