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Good Samaritan Regional Medical Center

THE SHIFT IN LIPID MANAGEMENT GUIDELINES
Objectives

- Review the previous lipid management guidelines (ATP III)
- Discuss what prompted the change in guidelines
- Review the new lipid management guidelines (ACC/AHA)
- Discuss clinical implications of the new guidelines
- Review case exams applying the new guidelines.
- Discuss weaknesses/controversy surrounding the new guidelines
- Discuss future areas of continued research/improvement
Where we were


The ATP III Process:

1. Obtain lipid level
2. Identify patients with CHD or CHD risk equivalent
3. Determine presence of major CHD risks factors
4. If 2+ risk factors in pts with out CHD or CHD risk equivalent, assess 10-yr CHD risk
5. Determine risk category
   a) Establish LDL goal of therapy
   b) Need for therapeutic lifestyle changes
   c) Determine level for drug consideration
6. Initiate therapeutic lifestyle changes if LDL above goal
7. Consider adding drug therapy if LDL exceeds specified level (after 3 months of TLC, except for CHD or risk equivalent group)

Where we were

- ATP III guidelines
  - Establishing CVD risk
  - Establishing LDL goals depending on risk category
  - When to initiate TLC and medications

**CHD risk equivalents**
- PAD
- AAA
- CAS (sx or >50% )
- DM
- 2+ risk factors and 10 yr risk >20%

The major independent risk factors identified in risk factor counting include:

- Cigarette smoking
- Hypertension (BP ≥140/90 mmHg or on antihypertensive medication)
- Low HDL cholesterol (<40 mg/dL)
- Family history of premature CHD (CHD in male first-degree relative <55 years; CHD in female first-degree relative <65 years)
- Age (men ≥45 years; women ≥55 years)

If a person has a high HDL cholesterol (≥60 mg/dL), one risk factor is subtracted from the count. If the person has type 2 diabetes, this person is classified as having a CHD risk equivalent (see Section II.12.b).
Where we were

- In this model, patients with multiple (2+) risk factors are further risk stratified by using the Framingham risk scoring model to determine 10-year risk of hard HCD (myocardial infarction + CHD death), which can affect LDL goal.

- Framingham risk calculator

Table III.1–3. Categories of 10-Year Risk for Persons with Multiple (2+) Risk Factors

<table>
<thead>
<tr>
<th>Risk Categories</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;20% (CHD risk equivalents)</td>
</tr>
<tr>
<td>10–20%</td>
</tr>
<tr>
<td>&lt;10%</td>
</tr>
</tbody>
</table>
Table III.1-5. Estimate of 10-Year Risk for Men (Framingham Point Scores)

<table>
<thead>
<tr>
<th>Age</th>
<th>Points</th>
<th>Total Cholesterol</th>
<th>Points at Ages 20–39</th>
<th>Points at Ages 40–49</th>
<th>Points at Ages 50–59</th>
<th>Points at Ages 60–69</th>
<th>Points at Ages 70–79</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–34</td>
<td>-9</td>
<td>&lt;160</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>35–39</td>
<td>-4</td>
<td>160–199</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>40–44</td>
<td>0</td>
<td>200–239</td>
<td>7</td>
<td>5</td>
<td>3</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>45–49</td>
<td>3</td>
<td>240–279</td>
<td>9</td>
<td>6</td>
<td>4</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>50–54</td>
<td>6</td>
<td>≥280</td>
<td>11</td>
<td>8</td>
<td>5</td>
<td>3</td>
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<tr>
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<tr>
<td>70–74</td>
<td>12</td>
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<td></td>
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<tr>
<td>75–79</td>
<td>13</td>
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<table>
<thead>
<tr>
<th>Points at Ages 20–39</th>
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<th>Points at Ages 70–79</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonsmoker</td>
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<td>0</td>
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<td>0</td>
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<tr>
<td>Smoker</td>
<td>8</td>
<td>5</td>
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</table>

<table>
<thead>
<tr>
<th>HDL</th>
<th>Points</th>
<th>Systolic BP</th>
<th>If Untreated</th>
<th>If Treated</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥60</td>
<td>-1</td>
<td>&lt;120</td>
<td>0</td>
<td>0</td>
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<tr>
<td>50–59</td>
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<td>1</td>
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<tr>
<td>40–49</td>
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<td>130–139</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>&lt;40</td>
<td>2</td>
<td>140–159</td>
<td>1</td>
<td>2</td>
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<td></td>
<td>≥160</td>
<td>2</td>
<td>3</td>
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<table>
<thead>
<tr>
<th>Point Total</th>
<th>10-Year Risk</th>
<th>Point Total</th>
<th>10-Year Risk</th>
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<tr>
<th>smoker</th>
<th>Points at Ages 20–39</th>
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<td>130–139</td>
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<td>≥160</td>
<td>4</td>
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<th>10-Year Risk</th>
</tr>
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<td>&lt;1%</td>
<td>20</td>
<td>11%</td>
</tr>
<tr>
<td>9</td>
<td>1%</td>
<td>21</td>
<td>14%</td>
</tr>
<tr>
<td>10</td>
<td>1%</td>
<td>22</td>
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<td>1%</td>
<td>23</td>
<td>22%</td>
</tr>
<tr>
<td>12</td>
<td>1%</td>
<td>24</td>
<td>27%</td>
</tr>
<tr>
<td>13</td>
<td>2%</td>
<td>≥25</td>
<td>≥30%</td>
</tr>
<tr>
<td>14</td>
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</tr>
<tr>
<td>15</td>
<td>3%</td>
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<tr>
<td>16</td>
<td>4%</td>
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<td></td>
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<tr>
<td>17</td>
<td>5%</td>
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</tr>
<tr>
<td>18</td>
<td>6%</td>
<td></td>
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</tr>
<tr>
<td>19</td>
<td>8%</td>
<td></td>
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</tr>
</tbody>
</table>
Where we were

LDL GOALS!!

Table IV.1–1. LDL Cholesterol Goals for Three Risk Levels

<table>
<thead>
<tr>
<th>Risk Level</th>
<th>LDL-C Goal</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHD and CHD Risk Equivalent</td>
<td>&lt;100 mg/dL</td>
</tr>
<tr>
<td>Multiple (2+) Risk Factors</td>
<td>&lt;130 mg/dL*</td>
</tr>
<tr>
<td>0–1 Risk Factor</td>
<td>&lt;160 mg/dL</td>
</tr>
</tbody>
</table>

* LDL-C goal for multiple-risk-factor persons with 10-year risk >20 percent = <100 mg/dL.
Where we were

### Table IV.2-1. Therapeutic Approaches to LDL Cholesterol Lowering In Persons with CHD or CHD Risk Equivalents

<table>
<thead>
<tr>
<th>Subcategory of LDL Cholesterol Level</th>
<th>LDL Cholesterol Goal</th>
<th>Level at Which to Initiate Therapeutic Lifestyle Changes (TLC)</th>
<th>Level at Which to Initiate LDL-Lowering Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥130 mg/dL</td>
<td>&lt;100 mg/dL</td>
<td>≥100 mg/dL</td>
<td>Start drug therapy simultaneously with dietary therapy</td>
</tr>
<tr>
<td>100–129 mg/dL</td>
<td>&lt;100 mg/dL</td>
<td>≥100 mg/dL</td>
<td>Consider drug options*</td>
</tr>
<tr>
<td>&lt;100 mg/dL</td>
<td>&lt;100 mg/dL</td>
<td>TLC &amp; emphasize weight control and physical activity</td>
<td>LDL-lowering drugs not required</td>
</tr>
</tbody>
</table>

* Some authorities recommend use of LDL-lowering drugs in this category if an LDL cholesterol <100 mg/dL cannot be achieved by TLC. Others prefer use of drugs that primarily modify other lipoprotein fractions, e.g., nicotinic acid and fibrate. Clinical judgment also may call for withholding drug therapy in this subcategory.

### Table IV.2-2. Management of LDL Cholesterol In Persons with Multiple (≥2) Risk Factors

<table>
<thead>
<tr>
<th>10-Year Risk</th>
<th>LDL Goal</th>
<th>LDL Level at Which to Initiate Therapeutic Lifestyle Changes (TLC)</th>
<th>LDL Level at Which to Consider Drug Therapy (After TLC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;20%</td>
<td>&lt;100 mg/dL</td>
<td>≥100 mg/dL</td>
<td>See CHD and CHD risk equivalent</td>
</tr>
<tr>
<td>10–20%</td>
<td>&lt;130 mg/dL</td>
<td>≥130 mg/dL</td>
<td>≥130 mg/dL</td>
</tr>
<tr>
<td>&lt;10%</td>
<td>&lt;130 mg/dL</td>
<td>≥130 mg/dL</td>
<td>≥160 mg/dL</td>
</tr>
</tbody>
</table>

### Table IV.2-3. Management of LDL Cholesterol In Persons with Zero to One (0–1) Risk Factor

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>LDL Goal</th>
<th>LDL Level at Which to Initiate TLC</th>
<th>LDL Level at Which to Consider Drug Therapy (After TLC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–1 Risk Factor*</td>
<td>&lt;160 mg/dL</td>
<td>≥160 mg/dL</td>
<td>≥190 mg/dL†</td>
</tr>
</tbody>
</table>

* Most persons with 0–1 risk factor have a 10-year risk for CHD <10 percent.
† Drug therapy optional for LDL-C 160–189 mg/dL (after dietary therapy).
Where we were

Table VI.1-1. Suggestions for Combined Use of TLC and Drug Therapy

- Intensive LDL lowering with TLC, including therapeutic dietary options (plant stanols/sterols and/or increased viscous fiber)
  - May obviate need for drug therapy
  - Can augment LDL-lowering drug therapy
  - May allow for lower doses of drugs
- Weight control plus increased physical activity
  - Reduces risk beyond LDL-cholesterol lowering
  - Constitutes primary management of the metabolic syndrome
  - Raises HDL-cholesterol levels
  - Enhances reduction of non-HDL cholesterol
- Initiating TLC before drug consideration
  - For most persons, a trial of dietary therapy of about 3 months is advised before initiating drug therapy
  - Unsuccessful trials of dietary therapy without drugs should not be prolonged indefinitely if goals of therapy are not approached in a reasonable period; drug therapy should not be withheld if it is needed to reach targets in persons with a short-term and/or long-term CHD risk that is high.
- Initiating drug therapy simultaneously with TLC
  - For severe hypercholesterolemia in which dietary therapy alone cannot achieve LDL targets
  - For those with CHD or CHD risk equivalents in whom dietary therapy alone will not achieve LDL targets

Average Percent Reduction in LDL Cholesterol With Usual Starting Dose and Maximal Statin Dose*

<table>
<thead>
<tr>
<th>Medication</th>
<th>Starting Dose</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lovastatin</td>
<td>20, 80 mg</td>
<td>24%</td>
</tr>
<tr>
<td>Pravastatin</td>
<td>20, 80 mg</td>
<td>24%</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>20, 80 mg</td>
<td>35%</td>
</tr>
<tr>
<td>Fluvastatin</td>
<td>20, 80 mg</td>
<td>18%</td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>10, 80 mg</td>
<td>37%</td>
</tr>
</tbody>
</table>

* Maximum dose currently approved by the FDA.
† Administered in divided doses.

Figure VI.1-1. Progression of Drug Therapy

- Initiate LDL-lowering drug therapy
  - 6 wks
- IF LDL goal not achieved, intensify LDL-lowering therapy
  - 6 wks
- IF LDL goal not achieved, intensify drug therapy or refer to a lipid specialist
  - Q-4-6 mos
- Monitor response and adherence to therapy

- Start statin or bile acid sequestrant or nicotinic acid
- Consider higher dose of statin or add bile acid sequestrant or nicotinic acid
- IF LDL goal achieved, treat other lipid risk factors
Where we are now

Why the change:
- Strategies for using drug therapy to reduce ASCVD events have been advocated, including treat-to-cholesterol target, lower cholesterol is better, and risk-based treatment approaches.
- Only 1 approach has been evaluated in multiple RCTs – the use of fixed doses of cholesterol-lowering drugs to reduce ASCVD risk.

The goal: provide a comprehensive guideline for the evidence-based treatment of blood cholesterol to reduce ASCVD risk. These recommendations are designed to inform clinical judgment, not to replace it.
Where we are now

- What’s new in the guidelines?
  - These are BIG changes!
  - While still promoting therapeutic lifestyle change as foundation of treatment, this is much less emphasized than in ATP III
  - Focus on ASCVD risk reduction: 4 statin benefit groups
  - No more use of LDL treatment targets
  - Global risk assessment for primary prevention using new Pooled Cohort Equations (no longer using Framinghams) to more accurately identify higher risk individuals that would benefit most from statin therapy.
  - Appropriate intensity of statin therapy depending on risk is the new goal of treatment
    † Moderate-intensity statin: decrease LDL by 30-50%
    † High-intensity statin: decrease LDL by >50%
Where we are now

- New perspective on LDL, and leaving the treat-to-goal paradigm behind
  - No RCTs were identified that titrating drug therapy to specific LDL-c goals to improve ASCVD outcomes.
  - Problems with the treat to target approach:
    † Current clinical trial data do not indicate what the target should be
    † Do not note the magnitude of additional ASCVD risk reduction that would be achieved with one target lower than another
    † Does not take into account potential adverse effects from multidrug therapy that might be needed to achieve a specific goal.
  - May result in under treatment with evidence based statins or overtreatment with non-statin medications that have not been shown to reduce ASCVD risk (despite potential decrease in LDL or inc in HDL)
Where we are now

Examples:

1. **Secondary prevention:** evidence supports high dose statin, not tx to LDL goal. Thus, patient with LDL 78 on Atorvastatin 80mg is receiving EB tx. No evidence to suggest benefit from adding non-statins (niacin, fenofibrate) to reach goal.

2. **Primary prevention:** DM2 patients, benefit of LDL lowering are substantial. LDL often lower in DM patients. Thus goal directed tx supports use of lower statin doses than evidence shows is beneficial (potential undertreatment).
Where we are now

4 groups identified where benefit of statin therapy clearly outweighs the risk

1. Clinically evident atherosclerotic cardiovascular disease (secondary prevention)
2. Patient with LDL > 190 (primary prevention)
3. Patients with DM 1 or DM 2 and LDL > 70
4. Patients without DM, aged 40-75y/o, with LDL > 70, with 10-yr risk > 7.5% according to new pooled cohort equation.
Where we are now

Pooled Cohort Risk Assessment Equations:
- New method of risk assessment in primary prevention
- Estimates 10-yr risk of ASCVD event including CHD and stroke. Framingham estimated risk for hard CHD event (non-fatal MI or CHD death).

- Pooled cohort variables
  - Gender
  - Age
  - Race
  - Total Cholesterol
  - SBP
  - Receiving tx for HTN?
  - DM?
  - Smoker?

Framingham variables:
- Age
- Total cholesterol
- HDL cholesterol
- Smoker?
- SBP (treated and untreated)
Figure 2. Major recommendations for statin therapy for ASCVD prevention

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.

Adults age ≥21 y and a candidate for statin therapy

Clinical ASCVD

Yes

Age ≤75 y
High-intensity statin
(Moderate-intensity statin if not candidate for high-intensity statin)

Yes

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

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%

Yes

Diabetes Type 1 or 2 Age 40-75 y

Yes

Moderate-intensity statin

No

Yes

Estimated 10-y ASCVD risk ≥7.5%* High-intensity statin

No

≥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
**Figure 1. 2013 American College of Cardiology–American Heart Association Guidelines for Use of Statin Therapy in Patients at Increased Cardiovascular Risk.**

Persons with clinical atherosclerotic cardiovascular disease (CVD) include those with an acute coronary syndrome and those with a history of myocardial infarction, stable or unstable angina, coronary or other arterial revascularization, or stroke, transient ischemic attack, or peripheral arterial disease that is presumed to be of atherosclerotic origin. High-intensity statin therapy is recommended for most patients meeting these criteria. Patients predisposed to adverse statin effects (including those with impaired renal or hepatic function, other serious coexisting conditions, a history of statin intolerance, concomitant use of drugs affecting statin metabolism, an age of >75 years, or unexplained elevations in alanine aminotransferase levels >3 times the upper limit of the normal range) should use moderate-intensity statin therapy when high-intensity statin therapy would otherwise be recommended. The 10-year risk of atherosclerotic CVD is calculated with the use of the new risk calculator available at http://my.americanheart.org/cvriskcalculator or at http://www.cardiosource.org/science-and-quality/practice-guidelines-and-quality-standards/2013-prevention-guideline-tools.aspx. LDL denotes low-density lipoprotein, and NYHA New York Heart Association.
Table 1. High-Intensity and Moderate-Intensity Statin Therapy, According to 2013 American College of Cardiology–American Heart Association (ACC-AHA) Cholesterol Guidelines.

<table>
<thead>
<tr>
<th>High-intensity statin therapy</th>
<th>Moderate-intensity statin therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily dose lowers LDL cholesterol level by approximately ≥50% on average</td>
<td>Daily dose lowers LDL cholesterol level by approximately 30% to &lt;50% on average</td>
</tr>
<tr>
<td>Recommended: atorvastatin, 40 to 80 mg; rosvastatin, 20 to 40 mg</td>
<td>Recommended: atorvastatin, 10 to 20 mg; rosvastatin, 5 to 10 mg; simvastatin, 20 to 40 mg; pravastatin, 40 to 80 mg; lovastatin, 40 mg; extended-release fluvastatin, 80 mg; fluvastatin, 40 mg twice a day; pitavastatin, 2 to 4 mg</td>
</tr>
</tbody>
</table>

Table 5. High- Moderate- and Low-Intensity Statin Therapy (Used in the RCTs reviewed by the Expert Panel)*

<table>
<thead>
<tr>
<th>High-Intensity Statin Therapy</th>
<th>Moderate-Intensity Statin Therapy</th>
<th>Low-Intensity Statin Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily dose lowers LDL–C on average, by approximately ≥50%</td>
<td>Daily dose lowers LDL–C on average, by approximately 30% to &lt;50%</td>
<td>Daily dose lowers LDL–C on average, by &lt;30%</td>
</tr>
<tr>
<td>Atorvastatin (40†)–80 mg Rosuvastatin 20 (40) mg</td>
<td>Atorvastatin 10 (20) mg Rosuvastatin (5) 10 mg Simvastatin 20–40 mg‡ Pravastatin 40 (80) mg Lovastatin 40 mg Fluvastatin XL 80 mg Fluvastatin 40 mg bid Pitavastatin 2–4 mg</td>
<td>Simvastatin 10 mg Pravastatin 10–20 mg Lovastatin 20 mg Fluvastatin 20–40 mg Pitavastatin 1 mg</td>
</tr>
</tbody>
</table>

* Data from various trials included in the RCTs (42, 43, 44, 58, 60–62) included in 2013 ACC-AHA cholesterol guidelines.
Case Examples

Example 1:
- **White man with high cholesterol**
  - 57 yr of age
  - Total cholesterol, 255 mg/dl
  - HDL cholesterol, 45 mg/dl
  - Systolic blood pressure, 110 mm Hg
  - Not taking antihypertensive medication
  - Not diabetic
  - Nonsmoker
  - Calculated 10-yr risk of CHD or stroke, 7.2%

Should statin therapy be recommended? If so, what dose intensity?
Case Examples

Example 2:

- *White male smoker with high cholesterol*
  - 42 yr of age
  - Total cholesterol, 250 mg/dl
  - HDL cholesterol, 40 mg/dl
  - Systolic blood pressure, 130 mm Hg
  - Not taking antihypertensive medication
  - Not diabetic
  - Smoker
  - Calculated 10-yr risk of CHD or stroke, 9.0%

Should statin therapy be recommended? If so, what dose intensity?
Case Examples

Example 3:

- Elderly black man
  - 79 yr of age
  - Total cholesterol, 150 mg/dl
  - HDL cholesterol, 40 mg/dl
  - Systolic blood pressure, 120 mm Hg
  - Not taking antihypertensive medication
  - Not diabetic
  - Non-smoker
  - Calculated 10-yr risk of CHD or stroke, 13.7%

- Should statin therapy be recommended? If so, what dose intensity?
Case Examples

Example 4

- White woman with diabetes
  - 48 yr of age
  - Total cholesterol, 180 mg/dl
  - HDL cholesterol, 55 mg/dl
  - Systolic blood pressure, 130 mm Hg
  - Not taking antihypertensive medication
  - Diabetic
  - Nonsmoker
  - Calculated 10-yr risk of CHD or stroke, 1.8%

- Should statin therapy be recommended? If so, what dose intensity?
Where we are now

**Safety recommendations:**

- **Class Ia**
  - Must select appropriate statin dose based on patient characteristics, level of ASCVD risk and potential for adverse effects.
  - Use moderate intensity statins in patients (even in high intensity therapy recommended) when characteristics predisposing to statin associated adverse effects are present
    - Multiple or serious comorbidities, including impaired renal or hepatic function.
    - History of previous statin intolerance or muscle disorders.
    - Unexplained ALT elevations >3 times ULN.
    - Patient characteristics or concomitant use of drugs affecting statin metabolism.
    - >75 years of age.

- **Liver function:**
  - Class Ia: baseline LFTs should be obtained prior to initiation of statin therapy
  - Class IIa: it is reasonable to check LFTs during therapy if symptoms suggesting hepatotoxicity arise.

- **The deal with DM**
  - Class Ia: patients receiving statin therapy should be evaluated for new onset DM
Where we are now

Myalgias and CK:
- Class IIa: reasonable to measure baseline CK if at risk for adverse muscle events, and it is reasonable to check a CK if muscle symptoms
- Class III: CK should not be routinely measured
- Class IIa: Reasonable to use the provided management algorithm in patients with muscle symptoms while on statins
8. It is reasonable to evaluate and treat muscle symptoms, including pain, tenderness, stiffness, cramping, weakness, or fatigue, in statin-treated patients according to the following management algorithm:

- To avoid unnecessary discontinuation of statins, obtain a history of prior or current muscle symptoms to establish a baseline before initiating statin therapy.
- If unexplained severe muscle symptoms or fatigue develop during statin therapy, promptly discontinue the statin and address the possibility of rhabdomyolysis by evaluating CK, creatinine, and a urinalysis for myoglobinuria.
- If mild to moderate muscle symptoms develop during statin therapy:
  - Discontinue the statin until the symptoms can be evaluated.
  - Evaluate the patient for other conditions that might increase the risk for muscle symptoms (e.g., hypothyroidism, reduced renal or hepatic function, rheumatologic disorders such as polymyalgia rheumatica, steroid myopathy, vitamin D deficiency, or primary muscle diseases.)
  - If muscle symptoms resolve, and if no contraindication exists, give the patient the original or a lower dose of the same statin to establish a causal relationship between the muscle symptoms and statin therapy.
  - If a causal relationship exists, discontinue the original statin. Once muscle symptoms resolve, use a low dose of a different statin.
  - Once a low dose of a statin is tolerated, gradually increase the dose as tolerated.
  - If, after 2 months without statin treatment, muscle symptoms or elevated CK levels do not resolve completely, consider other causes of muscle symptoms listed above.
  - If persistent muscle symptoms are determined to arise from a condition unrelated to statin therapy, or if the predisposing condition has been treated, resume statin therapy at the original dose.
Monitoring recommendations

- Initial fasting lipid panel
- Fasting lipid panel at 4 to 12 weeks after starting statin to determine patient’s adherence
- Then, every 3 to 12 months to reinforce adherence
Figure 5. Statin Therapy: Monitoring therapeutic response and adherence

Assess medication and lifestyle adherence
Fasting lipid panel

Anticipated therapeutic response?

Indicators of anticipated therapeutic response and adherence to selected statin intensity:
- High-intensity statin therapy† reduces LDL-C approx. ≥50% from the untreated baseline.
- Moderate-intensity statin therapy reduces LDL-C approx. 30% to <50% from the untreated baseline.

Yes

Reinforce continued adherence
Follow-up 3-12 mo

Intolerance to recommended dose of statin therapy

No

Less-than-anticipated therapeutic response

Reinforce medication adherence
Reinforce adherence to intensive lifestyle changes
Exclude secondary causes of hypercholesterolemia (Table 6)

Follow-up 4-12 wk

Management of statin intolerance
(Table 8, Rec 8)

Anticipated therapeutic response?

Yes

Reinforce improved adherence
Increase statin intensity‡
OR
Consider addition of nonstatin drug therapy

Follow-up 4-12 wk & thereafter as indicated

No

Follow-up 4-12 wk
Implications in clinical practice:

- Overall, these guidelines will move treatment towards statins for a broader range of patients than ATP III.
- Deemphasize the use of non-statin agents
- It seems that there would be an elimination of routine assessments of LDL cholesterol in patients receiving statins as target levels are no longer emphasized, but this is not true.
- Use of new risk calculator (in primary prevention), which is certain to target larger numbers of patients for statin therapy.
Where we are now

- Weaknesses/Limitations/Controversy:
  - Identified patients for whom available data do not support statin therapy and no recommendations are made:
    1. Age >75y/o without clinical ASCVD
    2. Dialysis patients
    3. NYHA II, III, or IV heart failure
  - LDL goals give patients something to work towards
  - Many have expressed concern about the new Pooled Cohort risk calculator.
    † It has not been prospectively tested for its accuracy in predicting cardiovascular risk
    † There is concern that the new calculator overestimates observed risk
Where we are going

Future research needed:

- Outcomes of RCTs to eval statins in primary prevention in adults >75y/o
- Outcomes of RCTs evaluating alternative treatment strategies for ASCVD risk reduction. Includes titration to specific LDL goals vs fixed dose statin.
- RCTs to determine whether submaximal statin doses + nonstatin tx reduce ASCVD risk in statin intolerant patients
- Further evaluation of statin induced DM
- More data regarding patients with CHF or ESRD on HD
Resources

