NEW GUIDELINES FOR TREATMENT OF CHOLESTEROL: IMPLICATIONS FOR THE PREVENTION OF HEART DISEASE AND STROKE

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I have no relevant conflicts of interest

SLIDES ARE POSTED
UCSF OSHER MINI MEDICAL SCHOOL FOR THE PUBLIC--WEB SITE
http://ucsfcmecom/minimedicalschool/courses/cancer-and-heart-disease/

EXPLAINING THE DECREASE IN DEATHS FROM CVD
1980 to 2000: death rate fell by approximately 50% in both men and women
2000 to 2010: Death still falling: down 31%
• About 1/2 from acute treatments, 1/2 from risk factor modification
• Reductions in cholesterol: 1/4

Go, Circulation, 2014
Placebo-Controlled Statin Trials

Reductions in Major Coronary Events Relative to Placebo

A RISK-BASED APPROACH

The benefit from any given intervention is a function of:
1) The relative risk reduction conferred by the intervention, and
2) The native risk of the patient

Prevention Of CVD in Women

- Overwhelming majority of recommendations are the same for women and for men
- But...there are gender differences in the magnitude of the absolute potential benefits

Some Definitions and Abbreviations

- LDL: Low density lipoprotein ("L" for lousy)
- HDL: High density lipoprotein (the "good cholesterol")
- Total cholesterol: the sum of LDL + HDL + triglycerides/5
- hs-CRP: highly sensitive-C-reactive protein (a measure of inflammation)

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Mosca, Circulation 2011
Some Definitions and Abbreviations

- ASCVD: atherosclerotic cardiovascular disease (coronary heart disease (CHD) and stroke)
- USPSTF: US Preventive Services Task Force
- ACC: American College of Cardiology
- AHA: American Heart Association

2013 ACC/AHA Guidelines

Importance of Lifestyle Recommendations

- Heart healthy diet
- Regular aerobic exercise
- Desirable body weight
- Avoidance of tobacco

2013 ACC/AHA Guidelines

What is New?

- 4 groups of patients who benefit from statins
- Identifies high and moderate intensity statins
- No LDL treatment targets
- Non-statin therapies no not provide acceptable risk reduction
- Estimate 10-year ASCVD risk with new equation

Heart Protection Study: Vascular Events by Baseline LDL-C

<table>
<thead>
<tr>
<th>Baseline Feature</th>
<th>Statin (10,269)</th>
<th>Placebo (10,267)</th>
<th>Risk Ratio and 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL (mg/dL)</td>
<td></td>
<td></td>
<td>Statin better</td>
</tr>
<tr>
<td>&lt;100</td>
<td>285</td>
<td>360</td>
<td>Statin worse</td>
</tr>
<tr>
<td>≥100 &lt;130</td>
<td>670</td>
<td>881</td>
<td></td>
</tr>
<tr>
<td>≥130</td>
<td>1087</td>
<td>1365</td>
<td></td>
</tr>
<tr>
<td>ALL PATIENTS</td>
<td>2042 (19.9%)</td>
<td>2606 (25.4%)</td>
<td></td>
</tr>
</tbody>
</table>

24% reduction
(p<0.00001)
### 2013 ACC/AHA Guidelines

#### Four Groups of Patients Who Benefit From Statins

- Individuals with clinical ASCVD
- Individuals with primary elevations of LDL \( \geq 190 \)
- Individuals age 40-75 with diabetes and LDL \( \geq 70 \)
- Individuals without ASCVD or diabetes, age 40-75, with LDL \( \geq 70 \), and 10 year risk 7.5% or higher

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### 2013 ACC/AHA Guidelines

#### What Statin for Each Group?

- **Individuals with clinical ASCVD:**
  - Treat with: high intensity statin, or moderate intensity statin if > age 75
- **Individuals with primary elevations of LDL \( \geq 190 \):**
  - Treat with: high intensity statin
- **Individuals age 40-75 with diabetes and LDL \( \geq 70 \):**
  - Treat with: moderate intensity statin, or high intensity statin if risk over 7.5%
- **Individuals without ASCVD or diabetes, age 40-75, with LDL \( \geq 70 \), and 10 year risk 7.5% or higher:**
  - Treat with: moderate-to-high intensity statin

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### High Intensity vs. Moderate Intensity Statin

- **High Intensity:** lowers LDL by >50%
  - Atorvastatin 40 - 80
  - Rosuvastatin 20 - 40

- **Moderate Intensity:** lowers LDL by 30-50%
  - Atorvastatin 10 - 20
  - Rosuvastatin 5 – 10
  - Simvastatin 20 - 40
  - Pravastatin 40 – 80
  - Lovastatin 40
How Best To Calculate 10 Year Risk?

Old issues
- Hard vs. hard + soft CHD end points (angina)
- CHD or CVD
- Include diabetes or not
- Include peripheral vascular disease or not
- Race/ethnicity (usually not)
- Include family history and hs-CRP (Reynolds)
- Ranges vs. exact numbers
- Paper vs. computer vs. phone

How Best To Calculate 10 Year Risk?

Insufficient shared decision making

Pooled Cohort Risk Assessment Equations
- Age
- Gender
- Race (White/African American)
- Total cholesterol (170 mg/dl)
- HDL cholesterol (50 mg/dl)
- Systolic BP (110 mmHg)
- Yes/no meds for BP
- Yes/no DM
- Yes/no cigs
- Outcome: 10-year risk of total CVD (fatal and non-fatal MI and stroke)
How Best To Calculate 10 Year Risk?  
Baron Approach Winter 2015

- Use both Framingham CHD calculator and new ACC/AHA CV risk calculator
- Include both in shared decision-making discussion

How Best To Calculate 10 Year Risk?  
Mayo Clinic Statin Choice Decision Aid:

- http://statindecisionaid.mayoclinic.org/index.php/statin/index?PHPSESSID=0khk8nm14h9vubjm3423e6h6b2
63 year old woman with prior MI

<table>
<thead>
<tr>
<th>LDL</th>
<th>115</th>
</tr>
</thead>
<tbody>
<tr>
<td>HDL</td>
<td>45</td>
</tr>
<tr>
<td>TG</td>
<td>160</td>
</tr>
</tbody>
</table>

The best next step in lipid management is:

1. Atorvastatin 40 mg
2. Rosuvastatin 10 mg
3. Pravastatin 40 mg
4. Simvastatin 40 mg
5. Lovastatin 40 mg
6. Whatever works to get her LDL below 70 mg/dl

2013 ACC/AHA Guidelines
What Statin for Each Group?

- Individuals with clinical ASCVD:
  - Treat with: high intensity statin, or moderate intensity statin if > age 75

The best next step in lipid management is:

1. Atorvastatin 40 mg
2. Rosuvastatin 10 mg
3. Pravastatin 40 mg
4. Simvastatin 40 mg
5. Lovastatin 40 mg
6. Whatever works to get her LDL below 70 mg/dl
63 year old woman, with prior MI. Takes atorvastatin 80 mg.

**LDL** 95  
**HDL** 40  
**TG** 200

The best next step in lipid management is:

1. Continue current therapy  
2. Switch to rosuvastatin 40 mg  
3. Add fenofibrate  
4. Add fish oil  
5. Add niacin  
6. Add ezetimibe

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**Summary Lipid-Lowering Drugs**

- Statins are treatment of choice based on RCT to decrease risk
- No evidence to support adding niacin or fibrates to statins
- If completely statin-intolerant, niacin may reduce CVD risk (weak evidence)
- Fibrates appear to lower MI risk, but no other CVD endpoints
- Ezetimibe: little clinical impact

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**Summary Lipid-Lowering Drugs**

- Ezetimibe: new study (IMPROVE-IT) presented as abstract November 2014
- 18,000 ACS patients (40% from North America)
- RCT: Simvastatin vs simvastatin + ezetimibe. Took 7 years. Death, MI, Stroke
- Simvastatin: 34.7% vs Simva/ezetimibe 32.7% (270 fewer events over 7 years)
2013 ACC/AHA Guidelines
What Statin for Each Group?

- Individuals with clinical ASCVD:
  - Treat with: high intensity statin, or moderate intensity statin if > age 75

The best next step in lipid management is:

1. Continue current therapy
2. Switch to rosvastatin 40 mg (Also potentially correct, but medication still on patent)
3. Add fenofibrate
4. Add fish oil
5. Add niacin
6. Add ezetimibe

63 year old woman, no traditional risk factors

LDL 155
HDL 55
TG 160
SBP 120
No BP meds
No DM
Non smoker

The best next step in lipid management is to calculate 10 year risk and:

1. Continue current therapy (no meds)
2. Begin atorvastatin 40
3. Begin atorvastatin 10
4. Begin simvastatin 20
5. Begin sustained release niacin
6. Begin red yeast rice
2013 ACC/AHA Guidelines
What Statin for Each Group?

- Individuals without ASCVD or diabetes, 40-75, with LDL ≥ 70, and 10 year risk 7.5% or higher:
  - Treat with: moderate-to-high intensity statin

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63 yo woman, no risks

LDL 155, HDL 55, TG 160
SBP 120, No BP meds
Non smoker, No DM

10 yr CHD risk (old calculator): 2%
10 yr CV risk (new calculator): 4.5%

Therefore no medication recommended

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63 year old man, no traditional risk factors

LDL 155
HDL 55
TG 160
SBP 120
No BP meds
No DM
Non smoker

The best next step in lipid management is to calculate 10 year risk and:

1. Continue current therapy (no meds)
2. Begin atorvastatin 40
3. Begin atorvastatin 10
4. Begin simvastatin 20
5. Begin sustained release niacin
6. Begin red yeast rice
2013 ACC/AHA Guidelines
What Statin for Each Group?

- Individuals without ASCVD or diabetes, 40-75, with LDL ≥ 70, and 10 year risk 7.5% or higher:
  - Treat with: moderate-to-high intensity statin

63 yo man, no risks

LDL 155, HDL 55, TG 160
SBP 120, No BP meds
Nonsmoker, No DM

10 yr CHD risk (old calculator): 10%
10 yr CV risk (new calculator): 10.8%
“Toss-up.” Shared decision making. If start statin (per new guidelines), can start with moderate intensity statin

The best next step in lipid management is to calculate 10 year risk and:

1. Continue current therapy (no meds)- old (but toss-up)
2. Begin atorvastatin 40-new (but still close call)
3. Begin atorvastatin 10-new (but still close call)
4. Begin simvastatin 20-new (but still close call)
5. Begin sustained release niacin
6. Begin red yeast rice

Key is shared decision-making
Other Factors That Could Affect Treatment Decisions

- LDL $\geq 160$ mg/dl or evidence of genetic disorder
- Family history of premature ASCVD (<55 in first degree male relative, <65 in first degree woman)
- hs-CRP $\geq 2$ mg/dl
- Coronary calcium score $\geq 300$ (or $\geq 75\%$ for age, sex, ethnicity)
- Ankle brachial index <0.9
- Elevated lifetime risk of ASCVD

Stone, Circulation 2013

The Good and The Controversial of the New Cholesterol Guidelines

- Focus on healthy lifestyle is good
- Focus to use statins (and not other agents) is good
- Focus to treat patients at high risk is good
- Focus to treat all patients with LDL $<190$ mg/dl and treat patients with DM/existing CV disease is good
- Not having target LDL is controversial
- Adults with no DM or heart disease and 10-year calculated risk $>7.5\%$ (using new risk calculator) to be treated – controversial

NSAIDS and ASCVD

- Danish national study, 97,698 patients with prior heart attack. 44% received NSAIDS.
- NSAIDS associated with 42% increase in CV death (CI 1.36 – 1.49)
- Diclofenac 96% and rofecoxib 66% increase
- Ibuprofen 34% and naproxen 27% increase


Competing Risks

- Example: women with 10-year risk 10%
- Reduce risk by 30% with statins. Risk now 7%
- Add NSAID. Increase risk by 50%
- Total risk now back to 10%
Conclusions I

- Statins are effective and cost effective in selected groups of patients

- Screen most patients (shared decision-making) at age 21 (to identify those > LDL 190, other genetic lipid disorders)

Conclusions II

- Use statins in women with ASCVD, LDL ≥190 and diabetes

- For those without ASCVD and diabetes, calculate 10 year risk (how best uncertain), and treat those with risk greater than 7.5% (maybe 10%). Use shared decision making.

- Use appropriate intensity statin (high and moderate)

Conclusions III

- Monitor adherence, but do not treat to specific LDL goal

- Do not treat those over age 75 (unless ASCVD), on dialysis or moderate/severe CHF

- Do not treat with other lipid-modifying drugs in addition to statins (but may need if truly statin intolerant)

- Avoid other factors that raise risk as much as statins lower it (i.e. NSAIDS)