Summary – Implementing new Dyslipidemia Guidelines

- ASCVD (Atherosclerotic Cardiovascular Disease) has large impact on health.
- Statins and aspirin are underutilized cost saving approaches that reduce impact.
- Implementation of new guidelines can facilitate cost effective interventions to reduce ASCVD risk.

Impact on Americans

- Modeled statin and aspirin risk reduction, primary prevention

<table>
<thead>
<tr>
<th>Drug</th>
<th>Reduction</th>
<th>Cost Avoided</th>
</tr>
</thead>
<tbody>
<tr>
<td>aspirin 81 mg</td>
<td>17%</td>
<td>$7,700</td>
</tr>
<tr>
<td>atorvastatin 40 mg</td>
<td>42%</td>
<td>$6,453</td>
</tr>
<tr>
<td>both</td>
<td>54%</td>
<td>$9,288</td>
</tr>
</tbody>
</table>

- Treatment is cost saving to health system

  | Discounted Medical Costs | $1,638   |
  |                          | $6,453   |
  |                          | $9,288   |

- Published modeling of statin benefit

<table>
<thead>
<tr>
<th>Year</th>
<th>Statins Used</th>
<th>Benefit-to-cost ratio</th>
<th>Cost Avoided</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012</td>
<td>34.8 million</td>
<td>4:1</td>
<td>$2.5 billion</td>
</tr>
</tbody>
</table>
  | 20 million US adults were statin candidates, missing statins by ATP 3. Statin use would have prevented
  | 23,000 deaths, 34,540 AMI hospitalizations ($2.5 billion costs avoided)
  | 12,800 stroke hospitalizations ($260 million costs avoided)
  | Cost saving to the system in multiple publications. |

**Statins benefit across range of baseline lipids**

<table>
<thead>
<tr>
<th>Baseline LDL mg/dL</th>
<th>Events (% per annum)</th>
<th>RR (CI) per 1 mmol/L reduction in LDL-C</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 76</td>
<td>0.4%</td>
<td>0.76 (0.61-0.97)</td>
</tr>
<tr>
<td>77-116</td>
<td>1.9%</td>
<td>1.10 (0.91-1.31)</td>
</tr>
<tr>
<td>117-136</td>
<td>3.0%</td>
<td>1.17 (0.95-1.45)</td>
</tr>
<tr>
<td>&gt; 135</td>
<td>4.1%</td>
<td>1.20 (0.98-1.44)</td>
</tr>
</tbody>
</table>

LDL 130 to 90 same benefit as LDL 80 to 40

*Lancet* Nov 9, 2010

**Statins benefit across “disease” state**

<table>
<thead>
<tr>
<th>Previous vascular disease</th>
<th>Events (% per annum)</th>
<th>Primary prevention</th>
<th>RR (CI) per 1 mmol/L reduction in LDL-C</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHD</td>
<td>3%</td>
<td>0.79 (0.69-0.91)</td>
<td></td>
</tr>
<tr>
<td>Non-CHD CHD</td>
<td>5%</td>
<td>0.76 (0.67-0.88)</td>
<td></td>
</tr>
<tr>
<td>Primary prevention</td>
<td>1%</td>
<td>0.75 (0.69-0.82)</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>2%</td>
<td>0.78 (0.70-0.88)</td>
<td></td>
</tr>
<tr>
<td>Type 1 diabetes</td>
<td>3%</td>
<td>0.76 (0.68-0.85)</td>
<td></td>
</tr>
<tr>
<td>Type 2 diabetes</td>
<td>4%</td>
<td>0.78 (0.70-0.88)</td>
<td></td>
</tr>
<tr>
<td>No diabetes</td>
<td>5%</td>
<td>0.75 (0.69-0.82)</td>
<td></td>
</tr>
</tbody>
</table>

*Lancet* Nov 9, 2010

**4 Major Statin Benefit Groups**

1. Clinical ASCVD, start atorvastatin 40-80 mg
2. LDL >= 190, start atorvastatin 40-80 mg
3. DM age 40-75
   - A-Risk >= 7.5%, start atorvastatin 40 mg
   - A-Risk < 7.5%, start atorvastatin 20 mg (s40)
4. By A-Risk. May code “dyslipidemia”
   - >= 15%, start atorvastatin 40 mg
   - 7.5-14.9%, discuss atorva 40 mg
   - 5.0 to 7.4%, consider atorva 20 mg (s40)
   - May consider “additional factors”

**Statin caveats**

- Consider lower doses, clinical judgment and/or shared decision making in patients with any of the following: baseline LDL < 70, age >= 76 years, liver disease, muscle disorders, Asian race, history of statin intolerance, or use of interacting drugs.
- No recommendation regarding statins in patients with NYHA class II-IV Heart Failure or patients on maintenance hemodialysis.

**Clinical ASCVD. 1st benefit group:**
- History of MI, angina, revascularization, stroke, TIA, peripheral arterial disease, repaired AAA.
- vs “Subclinical”
  - Elevated CAC score, ABI < 0.9, aortic atherosclerosis, aortic ectasia, unrepaired AAA.
  - Appropriate to run A-Risk and take into consideration.

**2nd benefit group: LDL > 190**

- Evaluate secondary causes: Check TSH, UA, biliary obstruction (Liver Panel ALT, Alk Phos, Bilil), meds/supplements, anorexia, pregnancy. Repeat Lipid Panel with workup.
- Lifestyle: low in saturated and trans fats. If TG also elevated more likely to respond to diet.
- No risk calculation recommended for persistent LDL>190.
- "Achieve at least a 50% reduction in LDL." A40-80.
- Screen family members.
LDL >= 190 and childbearing potential

- Statin recommended in those over age 10.
- Transition to high intensity statin as reach adulthood.
- Discuss with girls / women the importance of contraception while on statin (preg category X)
- When childbearing timing is right, patient may go off statin during conception, pregnancy, and breast feeding.
- Many can achieve 10+ years of statin protected decreased atherosclerotic burden prior to coming off statins for child bearing.

Feedback letter

Dear Mr.

Your cholesterol is much improved! Congratulations! Continue your cholesterol medicine to help keep your arteries open.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>CHOL &gt;200</td>
<td></td>
<td>338 (H)</td>
<td>179</td>
</tr>
<tr>
<td>TRIG &lt;150</td>
<td></td>
<td>268 (H)</td>
<td>184 (A)</td>
</tr>
<tr>
<td>HDL &gt;=40</td>
<td></td>
<td>49</td>
<td>48</td>
</tr>
<tr>
<td>LDL C (LDL-C) &lt;100</td>
<td></td>
<td>235 (H)</td>
<td>94</td>
</tr>
<tr>
<td>CHOL/HDL &lt;5.0</td>
<td></td>
<td>8.9 (H)</td>
<td>3.7</td>
</tr>
<tr>
<td>ALT 17 - 63 units/L</td>
<td></td>
<td>64 (H)</td>
<td>40</td>
</tr>
</tbody>
</table>

Be well,
Ron Scott, MD
800-954-8000

ACC / AHA 10 yr ASCVD Risk (A-Risk)

- “Pooled Cohort Equations”
  - Atherosclerosis Risk in Communities (ARIC)
  - Cardiovascular Health Study (CHS)
  - Coronary Artery Risk Development in Young Adults (CARDIA)
  - Framingham Original and Offspring
- Hard ASCVD, 10 years
  - CHD death, non-fatal MI, fatal/nonfatal stroke
- Tested using traditional RFs + newer markers. Internal and external validation.

A-Risk features

- Women and AA have disproportionately more stroke, resulting in higher average A-Risk than FRS.
- New race variable – Black / African Americans are higher risk given other variables.
- For other races use non-black option. (Hispanic, Asian Americans, etc)
- Inclusion of diabetes variable.
- Aug 2014 study showed A-Risk correlated well with disease on CT angio.
- 3/29/14 REGARDS validation . . .
Calibration – REGARDS Commercial

Calibration – REGARDS Medicare

**2013 ACC/AHA cholesterol guideline better than NCEP ATP 3**

LDL-C cut-points are the main problem

- Subclinical atherosclerosis - CT angiography
- 2013 Cholesterol GI assigned to statin:
  - Fewer patients with no plaque: 36% vs 43%
  - More patients with heavy plaque: 52% vs 53%
  - More patients with >50% stenoses: 76% vs 43% in trials
  - 90% vs 60% other coronaries
- No correlation LDL-C levels with plaque
- Removing LDL-C cut-points improves accuracy NCEP ATP 3

2013 guideline supplement p 62

**Average A-risk in Trials**

<table>
<thead>
<tr>
<th>Randomized Clinical Trial</th>
<th>RRR for ASCVD</th>
<th>Estimated A-risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>MEGA lower intensity statin</td>
<td>24%</td>
<td>5.1%</td>
</tr>
<tr>
<td>AFCAPS lower intensity statin</td>
<td>26%</td>
<td>6.9%</td>
</tr>
<tr>
<td>JUPITER high intensity statin</td>
<td>44%</td>
<td>7.6%</td>
</tr>
</tbody>
</table>

**Benefits (NNT) outweighs risks (NNH) by safe margin**

Atorva 40 mg is more cost Saving to KP than lower intensity statins

<table>
<thead>
<tr>
<th>High intensity statin (RRR 45%)</th>
<th>Low and moderate intensity statin (NNT 15% &amp; 25%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>atorvastatin 40-80 mg</td>
<td>atorvastatin 10-20 mg</td>
</tr>
</tbody>
</table>

**Estimated Costs**

- $1,638
- $6,453
- $9,288
4th benefit group: statin recs by A-Risk levels
- >= 15%, start atorvastatin 40 mg
  - At this level, additional KP system, team tactics may be deployed. Higher priority group to treat.
- 7.5-14.9%, discuss atorvastatin 40 mg
  - Statin risk reduction discussion, with "incorporation of patient preferences".
- 5.0 to 7.4%, consider atorva 20 mg (s40)
  - Given smaller margin of benefit, more incorporation of patient preferences and "additional factors".

“Additional factors”
Providers may incorporate into statin and aspirin risk reduction discussion.
- Subclinical ASCVD:
  - Unrepaired AAA, Aortic Athero, Aortic Ectasia
  - CAC ≥ 300 or ≥ 75th % for age, ABI < 0.9
- Other “additional factors”
  - Elevated Lifetime Risk of ASCVD
  - Family history of premature ASCVD
  - Primary LDL ≥ 160, hsCRP ≥ 2 mg/L
- Aspirin candidates, if close to threshold prioritize statin start, then recalculate risk.
- Smokers willing quit smoking first, then recalculate risk.

Aspirin 81 mg daily for primary prevention (+/- DM)
- In men age 45-69 years, women age 55-69 years, A-Risk >= 15%, start aspirin.
- In men age 45-59 years, women age 55-59 years, A-Risk 5-14.9%, discuss aspirin.
- In men and women age 60-69 years, A-Risk 10-14.9%, discuss aspirin.
- In men and women age 70-79 years, A-Risk >= 15%, discuss aspirin.

Note: History of GI bleed or daily NSAID use is associated with increased risk of GI bleed with aspirin.

Use of aspirin
Are adults at risk for cardiovascular disease currently taking aspirin?

% on aspirin 7/29/14

Z = -1.7

2013  37.57%
2014  38.04%

Do you take aspirin daily or every other day?

primary prev
men 45-79
women 55-79
CV risk by survey
Proactive Care tab, CMSS

Artery Graphic Tool

Promote Adherence

Atorvastatin + aspirin start smartphrase

--- Your 10 year risk of heart attack or stroke is elevated. Luckily, there are 2 medicines when taken together can reduce your risk about 50%. I recommend taking atorvastatin (Lipitor) and aspirin 81 mg (baby or low dose) daily to reduce your risk.

- Can use dot phrase to pull into emails and letters to members when communicating results.
- Pivot emphasis from LDL to A-Risk if that is how they qualify for statin.
Jim Jones

A-Risk 20.3%

- Age 63, African American male
- TC 220, HDL 35, SBP 142, Taking Prinzide
- No diabetes, does not smoke.

- Start atorva 40 mg and aspirin 81 mg

Loretta Jones

A-Risk 12.5%

- Age 63, African American female
- TC 220, HDL 35, SBP 138, taking Prinzide
- No diabetes, does not smoke.

- Discuss atorva 40, repeat A-Risk.
- If A-Risk still > 10% discuss aspirin.

John Smith

A-Risk 6.1%

- Age 53, white male
- TC 235, HDL 42, LDL 172, SBP 119, no meds
- No diabetes, does not smoke.

- “Consider” atorva 20 mg, repeat A-Risk.
- If A-Risk still > 5% discuss aspirin.

Statin benefit outweighs new DM risk

- JUPITER rosuvastatin 20 mg daily:
  - In those without RF for DM: 86 CV events prevented, and 0 cases of increased DM.
  - In those with RF for DM: 134 CV events prevented (MI stroke, death) and 54 new cases of DM. (28% increase)
  - 40 day acceleration of progression to DM.
- Compare to 55% reduced MI, 44% reduced combined endpoint, 20% lower mortality.


Additional details

- For statin intolerance,
  - Consider holding statin for 2 weeks.
  - Consider check and treat high TSH (hypothyroid) and low vitamin D.
  - Can try atorvastatin 10 mg, 3 times a week. Patients that do not tolerate starting doses can often tolerate low, infrequent doses and/or a different statin (rosuvastatin 5 mg once a week)
  - If a statin does not work out mark specific statins on allergy section of chart with side effect.
  - For complete statin intolerance or inadequate response to statins consider colestipol or ezetimibe ½ tab.
**Statins and Cognitive Function. Reassuring Evidence**

- Systematic review.
  - No increased incidence of Alzheimer disease, dementia or cognitive performance, executive function, memory, or processing speed.
  - FDA postmarketing surveillance statins similar to losartan, clopidogrel
- Taiwan study Aug 2013
  - More statin exposure and higher intensity statins correlate with less new onset dementia.

*Ann Intern Med Nov 2013  Wu, Lin, ESCC; August 31, 2013*

**Lab Monitoring**

- Baseline: Lipid Panel, ALT, TSH, A1C
- “Lipid Panel 4-12 weeks after initiation of statin therapy.” - ACC/AHA
  - May use to promote statin adherence
- After that as clinically indicated. Lipid Panel, TSH, A1C, ALT when desired, convenient.
  - Consider when lab trip is triggered by another condition (K, Cr for Prinzide monitoring)
- Plan to change systemic support (POE, etc) to facilitate Lipid Panel minimum every 5 years.

**Summary – Implementing new Dyslipidemia Guidelines**

- ASCVD (Atherosclerotic Cardiovascular Disease) has large impact on health.
- Statins and aspirin are underutilized cost saving approaches that reduce impact.
- Implementation of new guidelines can facilitate cost effective interventions to reduce ASCVD risk.

**Questions?**