Overview of Clinical Guidelines in Lipid Management
Primary Objective

• Compare and contrast current guidelines on the management and treatment of patients with dyslipidemia to prevent ASCVD
National Cholesterol Education Program
Adult Treatment Panels (ATP)

ATP I

- LDL-C primary target:
  - High risk >160 mg/dL or ≥130 mg/dL with 2 or more risk factors (RFs)—<130 mg/dL considered desirable
- HDL-C considered a major RF but not considered for screening purposes – concerns re: measurement accuracy and science base
- Population guide also published

ATP II

- 1993: Emphasized risk status as a guide to treatment intensity.
- Recommended HDL-C screening
- Set <100 mg/dL for LDL-C goal in those with CVD
- Emphasized physical activity and weight reduction to enhance diet therapy
### NCEP ATP III (2002): Expanded Risk Groups

<table>
<thead>
<tr>
<th>Exceptionally High Risk (CHD Risk Equivalent)</th>
<th>Major Risk Factors</th>
<th>“Negative” Risk Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHD</td>
<td>Cigarette smoking</td>
<td>HDL &gt; 60 mg/dL</td>
</tr>
<tr>
<td>Other vascular disease</td>
<td>Hypertension</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>Low HDL-C (&lt;40 mg/dL)</td>
<td></td>
</tr>
<tr>
<td>&gt;20% Framingham Risk Score</td>
<td>Family history</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(Male &lt;55 yr, Female &lt;65 yr)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Age</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(Male &gt;45 yr, Female &gt;55 yr)</td>
<td></td>
</tr>
</tbody>
</table>

 ATP III (continued)

- Identified LDL-C <100 mg/dL optimal
- Raised definition of low HDL-C from < 35 to < 40 mg/dL
- Acknowledged triglycerides as an independent risk factor for CHD – set <150 mg/dL as normal – if triglycerides >500 mg/dL, triglyceride lowering should be first target to prevent pancreatitis
- Special focus on the metabolic syndrome
- Focus on treatment beyond LDL-C: triglycerides and HDL-C, with an introduction of non-HDL-C as a secondary target

ATPIII: Increased Emphasis on Non-HDL Cholesterol when Triglycerides ≥200 mg/dL

Non-HDL-C = Total cholesterol – HDL-C
## ATPIII – Treat to Goal Based on Risk

<table>
<thead>
<tr>
<th>Patient Classification</th>
<th>LDL-C Goal (mg/dl)</th>
<th>non-HDL-C Goal* (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Low risk</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(0-1 risk factors)</td>
<td>&lt;160</td>
<td>&lt;190</td>
</tr>
<tr>
<td><strong>Moderate Risk</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(At least 2 risk factors and 10 yr FRS &lt;20%)</td>
<td>&lt;130</td>
<td>&lt;160</td>
</tr>
<tr>
<td><strong>High Risk</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(CHD or CHD Risk Equivalent)</td>
<td>&lt;100</td>
<td>&lt;130</td>
</tr>
</tbody>
</table>


* If triglycerides > 200 mg/dl
Updates to ATPIII: More Intensive LDL-C Goals for Higher Risk Patients

Recommended LDL-C treatment goals

- If it is not possible to attain LDL-C <70 mg/dL because of a high baseline LDL-C, it generally is possible to achieve LDL-C reductions of >50% with more intensive LDL-C lowering therapy, including drug combinations.

*And other forms of atherosclerotic disease.²

†Factors that place a patient at very high risk: established cardiovascular disease (CVD) plus:
- multiple major risk factors (especially diabetes); severe and poorly controlled risk factors (e.g., cigarette smoking); metabolic syndrome (triglycerides [TG] ≥200 mg/dL + non–HDL-C ≥130 mg/dL with HDL-C <40 mg/dL); and acute coronary syndromes.¹

American Diabetes Association/American College of Cardiology Consensus Statement 2008

Treatment Goals in Patients with Cardiometabolic Risk and Lipoprotein Abnormalities

<table>
<thead>
<tr>
<th></th>
<th>LDL-C (mg/dL)</th>
<th>Non-HDL-C (mg/dL)</th>
<th>Apo B (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Highest-risk patient</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>– Known CVD</td>
<td>&lt;70</td>
<td>&lt;100</td>
<td>&lt;80</td>
</tr>
<tr>
<td>– Diabetes plus ≥1 additional major CVD risk factor*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High-risk patients</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>– No diabetes or known CVD but ≥2 major CVD risk factors*</td>
<td>&lt;100</td>
<td>&lt;130</td>
<td>&lt;90</td>
</tr>
<tr>
<td>– Diabetes but no other major CVD risk factors*</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Major risk factors beyond dyslipidemia include smoking, hypertension, and family history or premature CHD.

What Happened to ATP IV?

- ATP IV originally planned for release in 2011
  - Part of comprehensive NHLBI Cardiovascular Prevention Guidelines
  - NEW EVIDENCE - BASED APPROACH
  - Postponed many times
  - Mid 2013 NHLBI announces that they will not be publishing guidelines but instead will compile available data and provide to ‘partner organizations’ to come up with guidelines
  - Consensus statement published by ACC/AHA November 2013
2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines Endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation, American Pharmacists Association, American Society for Preventive Cardiology, Association of Black Cardiologists, Preventive Cardiovascular Nurses Association, and WomenHeart: The National Coalition for Women with Heart Disease

Recommendation 1: Continue to Focus on TLC
Lifestyle as the Foundation for ASCVD Risk Reduction Efforts

• It must be emphasized that lifestyle modification (i.e., adhering to a heart healthy diet, regular exercise habits, avoidance of tobacco products, and maintenance of a healthy weight) remains a critical component of health promotion and ASCVD risk reduction, both prior to and in concert with the use of cholesterol lowering drug therapies.
• Healthy diet or lifestyle modifications were recommended as background therapy for the RCTs of cholesterol-lowering drug therapy.
• See the 2013 Lifestyle Management Work Group Guideline for lifestyle recommendations for healthy adults.

Recommendation 2: Use Statins in these 4 Groups Regardless of Lipid Levels

1) Established Atherosclerotic Cardiovascular Disease (ASCVD)
2) Baseline LDL-C at least 190 mg/dl
3) Diabetes w/o ASCVD and age 40-75
4) At least 7.5% estimated 10-year ASCVD risk and age 40-75
   • Should start a ‘conversation’ about statin initiation

Recommendation 3: Use Only Evidence-Based Statin Doses

- Moderate Intensity Statin (lowers LDL-C by 30-50%)
  - Age over 75 with ASCVD
  - Diabetes and 10 year ASCVD risk <7.5%
  - Primary prevention with 10 year ASCVD risk at least 7.5% (moderate or high intensity)
  - Not a candidate for high intensity statin

- High Intensity Statin (lowers LDL-C by approximately 50%)
  - Age <75 years and ASCVD
  - Baseline LDL-C > 190 mg/dl
  - Diabetes and 10 year ASCVD risk >7.5%
  - Primary prevention with 10 year ASCVD risk at least 7.5% (moderate or high intensity)

# Definition of High, Moderate and Low Intensity Statin Agents and Doses

<table>
<thead>
<tr>
<th>High Potency Statin</th>
<th>Moderate Potency Statin</th>
<th>Low Intensity Statin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily dose lowers LDL-C by at least 50%</td>
<td>Daily dose lowers LDL-C by 30-50%</td>
<td>Daily dose lowers LDL-C 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 2x daily 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>

Recommendation 4: Non-statin Medications Not Generally Recommended

• “Because few trials have been performed with non-statin cholesterol-lowering drugs in the statin era, and those that have were unable to demonstrate significant additional ASCVD event reductions in the RCT populations studied, there was less evidence to support the use of non-statin drugs for ASCVD prevention”

– May be a role in truly statin intolerant or those who achieve a less than adequate therapeutic response.

Recommendation 5: No LDL or non-HDL Goals

A New Perspective on LDL–C and/or Non-HDL–C Treatment Goals

• The Expert Panel was unable to find RCT evidence to support continued use of specific LDL–C and/or non-HDL–C treatment targets.

• The appropriate intensity of statin therapy should be used to reduce ASCVD risk in those most likely to benefit.

Committee’s Rationale for Doing Away with Treatment Goals

• The difficulty of giving up the treat-to-goal paradigm was deliberated extensively over a 3-year period.
• However, the RCT evidence clearly shows that ASCVD events are reduced by using the maximum tolerated statin intensity in those groups shown to benefit.
• After a comprehensive review, no RCTs were identified that titrated drug therapy to specific LDL–C or non-HDL–C goals to improve ASCVD outcomes.

Recommendation 6: Use New ‘Global Risk’ Assessment for Primary Prevention

- Use Pooled Cohort Equations to estimate 10-year ASCVD risk in both white and black men and women.

- By more accurately identifying higher risk individuals for statin therapy, the guideline focuses statin therapy on those most likely to benefit.

- It also indicates, based on RCT data, groups that may not benefit.

- Before initiating statin therapy, this guideline recommends a discussion by clinician and patients.

[http://my.americanheart.org/cvriskcalculator](http://my.americanheart.org/cvriskcalculator)

Committee’s Rationale for Using 7.5% Global Risk Cut-off (As Opposed to Lipid Levels)

• Use of the RCT inclusion criteria (from RCTs that found a reduction in ASCVD events to guide initiation of statin therapy) would result in:
  – Treatment of 16% of individuals with <2.5% estimated 10-year ASCVD risk
  – Treatment 45% of those with 2.5% to <5% estimated 10-year ASCVD risk (many would say inappropriately)
  – No treatment of 38% of those with >7.5% 10-year ASCVD risk would not have been identified as candidates for statin therapy.

Controversy Concerning Pooled Cohort Risk Calculator

• Estimated that new risk assessment tool identifies 32.9% of primary prevention patients as potentially eligible for statin therapy
  – ATPIII paradigm would identify 31.9% as eligible for statin therapy
  – 75% overlap

• Does not include novel risk factors or biomarkers

• May overestimate risk
  – External validation not done prior to introduction
  – No evidence base for its use

Psaty BM & Weiss NS, JAMA 2014;311:461-462
Ioannides JPA, JAMA 2014;311:463-464
Recommendation 7: Consider ‘Emerging Risk Factors’ In Selected Patients

- Consider additional assessment of ASCVD risk in Group 4 with 5 - 7.4% 10 year risk

  LDL-C $\geq 160$ mg/dL
  Family history premature ASCVD
  CAC score $\geq 300$ Agatston units (or 75th percentile for age)
  hs-CRP $\geq 2$ mg/L
  Ankle-brachial index $< 0.9$
  High lifetime risk risk for age 20-59

### NLA Expert Panel:
Clinical Utility of Inflammatory Markers and Advanced Lipid Testing

<table>
<thead>
<tr>
<th>Risk Level</th>
<th>CRP</th>
<th>LpPLA2</th>
<th>ApoB</th>
<th>LDL-P</th>
<th>Lp(a)</th>
<th>HDL or LDL subfrac</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low Risk</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;5% 10 year</td>
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<tr>
<td>Intermediate</td>
<td></td>
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<td></td>
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<tr>
<td>5-20% 10 year</td>
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<td></td>
</tr>
<tr>
<td>High Risk</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>&gt;20 10 year</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family History</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recurrent Events</td>
<td></td>
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</tr>
</tbody>
</table>

- **Not Recommended**
- **Consider in Selected Patients**
- **Reasonable for Many Patients**
- **Recommended for Routine Assessment**

Recommendation 8: 
Put Statin Safety in Context

- Incidence of adverse events in RCTs per 100 statin treated individuals
  - 0.1-0.3 excess cases DM
  - 0.01 excess cases myopathy
  - 0.01 excess cases hemorrhagic stroke

- Monitoring of Statin Safety and Efficacy
  - Measure lipid panel and LFTs at baseline
  - Check CK in patients who have or develop muscle disease or symptoms
  - Follow-up LFTs only if symptoms
  - Check repeat lipids in 4-12 weeks to assess response

Population Health Aspects of 2013 ACC/AHA Guidelines

- Will lead to more patients treated with statins
- Will likely decrease absolute risk of ASCVD across population (treating more true positives)
- Will increase number of patients taking statins who would never have had a ASCVD event (treating more false positives)
- Will increase number of patients who will not be treated due to guidelines but will develop ASCVD (treating fewer false negatives)

Probably a net benefit – but what does this mean for individualized medicine?

What does this mean for pay-for-performance and the concept of ‘control’ rates
ACC/AHA Guidelines Not the Only Word

• American Diabetes Association (ADA) Guidelines
• European Society of Cardiology/European Atherosclerosis Society (ESC/EAS) Guidelines
• American Association of Clinical Endocrinologists (AACE) Guidelines
• International Atherosclerosis Society (IAS) Guidelines
• National Lipid Association (NLA) Recommendations
American Diabetes Association (ADA): Lipid Goals and Treatment

<table>
<thead>
<tr>
<th>Age</th>
<th>Risk factors</th>
<th>Recommended statin dose*</th>
<th>Monitoring with lipid panel</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;40 years</td>
<td>None</td>
<td>None</td>
<td>Annually or as needed to monitor for adherence</td>
</tr>
<tr>
<td></td>
<td>CVD risk factor(s)**</td>
<td>Moderate or high</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Overt CVD***</td>
<td>High</td>
<td></td>
</tr>
<tr>
<td>40–75 yrs</td>
<td>None</td>
<td>Moderate</td>
<td>As needed to monitor adherence</td>
</tr>
<tr>
<td></td>
<td>CVD risk factors</td>
<td>High</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Overt CVD</td>
<td>High</td>
<td></td>
</tr>
<tr>
<td>&gt;75 years</td>
<td>None</td>
<td>Moderate</td>
<td>As needed to monitor adherence</td>
</tr>
<tr>
<td></td>
<td>CVD risk factors</td>
<td>Moderate or high</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Overt CVD</td>
<td>High</td>
<td></td>
</tr>
</tbody>
</table>

*In addition to lifestyle therapy.
**CVD risk factors include LDL cholesterol ≥100 mg/dL (2.6 mmol/L), high blood pressure, smoking, and overweight and obesity.
***Overt CVD includes those with previous cardiovascular events or acute coronary syndromes.

In clinical practice, providers may need to adjust the intensity of statin therapy based on individual patient response to medication (e.g.: side effects, tolerability, LDL-C)

Diabetes Care 2015;38, S1-98)

<table>
<thead>
<tr>
<th></th>
<th>Desirable Levels Moderate Risk</th>
<th>Desirable Levels High Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>(HTN, Fam Hx, low HDL-C, smoking, or established CVD)</td>
</tr>
<tr>
<td>LDL-C (mg/dl)</td>
<td>&lt;100</td>
<td>&lt;70</td>
</tr>
<tr>
<td>Non-HDL-C (mg/dl)</td>
<td>&lt;130</td>
<td>&lt;100</td>
</tr>
<tr>
<td>Triglycerides (mg/dl)</td>
<td>&lt;150</td>
<td>&lt;150</td>
</tr>
<tr>
<td>Total C/HDL-C</td>
<td>&lt;3.5</td>
<td>&lt;3.0</td>
</tr>
<tr>
<td>Apo B (mg/dl)</td>
<td>&lt;90</td>
<td>&lt;80</td>
</tr>
<tr>
<td>LDL-P (mmol/L)</td>
<td>&lt;1200</td>
<td>&lt;1000</td>
</tr>
</tbody>
</table>

## ESC/EAS Guidelines: Risk Assessment

### LDL- C Baseline

<table>
<thead>
<tr>
<th>Total CV Risk (%) (SCORE)</th>
<th>&lt;70</th>
<th>70-100</th>
<th>100-155</th>
<th>155-190</th>
<th>&gt;190</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-5</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5-10</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>&gt; 10</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

- **No lipid intervention**
- **Lifestyle intervention**
- **Lifestyle intervention, Consider drug if not controlled**
- **Lifestyle intervention, Consider drug***
- **Lifestyle Intervention and Immediate drug intervention**


*In patients with MI, statin therapy should be considered irrespective of LDL-C
ESC/EAS: Treatment Targets

Which Target?

- LDL-C recommended primary target
- Non-HDL-C optional secondary target in combined dyslipidemia, diabetes, metabolic syndrome or CKD
- ApoB optional secondary target
- HDL not recommended as a target

LDL Goal

- Very High Risk: <70 mg/dl
- High Risk: <100 mg/dl
- Moderate Risk: <115 mg/dl

ESC/EAS: Drug Therapy

- Prescribe statin as first line drug
- In setting of statin intolerance or inability to reach LDL-C target with highest recommended or tolerated dose consider:
  - bile acid sequestrant,
  - nicotinic acid, or
  - cholesterol absorption inhibitor
- In particular high risk patients, consider lowering triglycerides with add on therapy
  - Fibrates (Recommended)
  - Nicotinic Acid
  - Omega 3’s

IAS: Atherogenic Cholesterol

• LDL-C = traditional primary target
  – Optimal <100 mg/dl
• Non-HDL-C = Preferred as target of therapy
  – Optimal <130 mg/dl
• Optimal levels are NOT goals of therapy
• Goals determined by clinical judgment and may be country specific

International Atherosclerosis Society, 2013 (www.athero.org)
IAS: Focus on Long Term (Not 10 Year) Risk of ASCVD (Up to Age 80)

<table>
<thead>
<tr>
<th>Risk Level</th>
<th>Lifetime Risk (Up to Age 80)</th>
<th>Therapy</th>
<th>Therapeutic Intensity</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>At least 45%</td>
<td>Max Lifestyle Mod + Drugs ‘Indicated’</td>
<td>High</td>
</tr>
<tr>
<td>Moderately High</td>
<td>30-44%</td>
<td>Max Lifestyle Mod + Drugs ‘Consideration’</td>
<td>Moderately High</td>
</tr>
<tr>
<td>Moderate</td>
<td>15-29%</td>
<td>Max Lifestyle Mod + Drugs ‘Optional’</td>
<td>Moderate</td>
</tr>
<tr>
<td>Low</td>
<td>&lt;15%</td>
<td>Public Health Guidelines</td>
<td></td>
</tr>
</tbody>
</table>

No specific targets, but when drug therapies employed, optimal levels usually represent a reasonable goal of therapy. General recommendations may need to be revised on a country-specific basis.

International Atherosclerosis Society, 2013 (www.athero.org)
IAS: Drug Therapy: Primary Prevention

• Statins are first line therapy
• In those who are statin intolerant, several optional are available:
  – switching to different statin,
  – reducing dose; every other day dosing
  – use of alternative drugs (ezetimibe, bile acid resin, nicotinic acid)
  – maximizing lifestyle interventions

International Atherosclerosis Society, 2013 (www.athero.org)
IAS: Drug Therapy: Secondary Prevention

• Statin first line therapy
  – Use maximum tolerated doses

• Usually treat to optimal LDL-C (<70 mg/dl) and non-HDL-C (<100 mg/dl)

• May require combination therapy
  – Bile Acid Sequestrant or ezetimibe for LDL-C reduction
  – Nicotinic acid or fibrate for high triglycerides

International Atherosclerosis Society, 2013 (www.athero.org)
## Comparison of Recent Major Guidelines Up to 2013

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Treat Based On</th>
<th>Treat to Specific Target</th>
<th>First Line Therapy</th>
<th>Alternative or Add-On Therapies</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACC/AHA (2013)</td>
<td>Risk Group</td>
<td>No</td>
<td>Statin</td>
<td>None</td>
</tr>
<tr>
<td>ADA (2013)</td>
<td>Risk Group</td>
<td>Yes (LDL-C)</td>
<td>Statin</td>
<td>Generally Not Recommended</td>
</tr>
<tr>
<td>ESC/EAS (2011)</td>
<td>Risk Group and LDL-C</td>
<td>Yes (LDL-C +/- nonHDLC or ApoB)</td>
<td>Statin</td>
<td>BAS, CAI, nicotinic acid, fibrate, omega 3</td>
</tr>
<tr>
<td>IAS (2013)</td>
<td>Risk Group</td>
<td>No</td>
<td>Statin</td>
<td>BAS, CAI, nicotinic acid, fibrate</td>
</tr>
</tbody>
</table>

BAS = Bile Acid Sequestrant  
CAI = Cholesterol Absorption Inhibitor
NLA Recommendations for Patient Centered Management of Dyslipidemia

- Part 1 Executive Summary published in 2014
- Part 1 Full Summary in 2015
- Meant to enhance, not supplant, ACC/AHA and other guidelines

Journal of Clinical Lipidology 2014; 8: 473–488
Journal of Clinical Lipidology 2015; 9; 129 -169
NLA Recommendations
Guiding Principles

1. An elevated level of atherogenic cholesterol – cholesterol carried by apo B-containing lipoprotein particles (non-HDL-C and LDL-C) – is causally related to the development of atherosclerosis
   – the key underlying process contributing to most clinical ASCVD events.

2. Reducing elevated levels of atherogenic cholesterol will lower ASCVD risk in proportion to the extent that atherogenic cholesterol is reduced.
   – This benefit is presumed to result from atherogenic cholesterol lowering through multiple modalities, including lifestyle and drug therapies.

NLA Recommendations
Guiding Principles (continued)

3. Lifestyle intervention is central to efforts at ASCVD prevention
4. The intensity of risk reduction therapy should be adjusted to the patient’s absolute risk for an ASCVD event.
   – Atherosclerosis is a process that often begins early in life and progresses for decades before resulting in a clinical ASCVD event.
   – Both intermediate-term and long term/lifetime risk should be considered when assessing the potential benefits and hazards of risk reduction therapies.
5. For patients in whom lipid drug therapy is indicated, statin treatment is the primary modality for reducing ASCVD risk.
6. Other ASCVD risk factors should be managed appropriately

NLA Recommendations
Stepwise Approach in ASCVD Risk Assessment

1. Identify Very High Risk
   - ASCVD
   - Diabetes with at least 2 major risk factors or end organ damage

2. Identify High Risk
   - Diabetes with 0-1 major risk factors and no end organ damage
   - Chronic Kidney Disease (CKD) stage 3 or 4
   - LDL at least 190 mg/dl

3. Count Major Risk Factors
   - 0-1 = Low Risk (unless other conditions – see next slide)
   - 2 = Use risk scoring
     • <10% = Moderate Risk
     • At least 10% = High Risk
   - 3 or more = High Risk

**NLA Recommendations**

**Other Risk Indicators-Consider for ‘Refinement’ of Risk**

1. A severe disturbance in a major ASCVD risk factor
   - Such as multi-pack per day smoking, strong family history, severe hypertension or very low HDL-C
2. Indicators of subclinical atherosclerosis
   - Particularly coronary artery calcium ≥300 Agatston units or ≥75th percentile for age, sex and ethnicity
3. Long-term ASCVD risk ≥40%
   - Lloyd-Jones 2006 Framingham risk calculator (or others)
4. High-sensitivity C-reactive protein ≥2.0 mg/L
5. Advanced Lipid Parameters
   - Apolipoprotein B ≥120 mg/dL
   - LDL particle concentration ≥1600 nmol/L
   - Lipoprotein (a) ≥50 mg/dL (protein) using an isoform insensitive assay
6. Urine albumin / creatinine ratio ≥30 mg/g

*Journal of Clinical Lipidology (2014) 8, 473–488*
NLA Recommendations

Targets of Therapy

• Non-HDL-C and LDL-C are the primary targets of therapy
  – Non-HDL-C given primacy

• Triglycerides = primary target of therapy if >500 mg/dl and especially if >1000 mg/dl

• ApoB = secondary, optional target of therapy
  – Goals < 90 mg/dl for primary and <80 mg/dl for secondary prevention

# NLA Recommendations

Initiate Therapy Based on Risk and Lipid Levels and Treat to Specific Goal

<table>
<thead>
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<th>Criteria</th>
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<td>&lt;130 (&lt;100)</td>
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• At least 3 RF  
• DM with 0-1 other RFs and no end organ damage  
• CKD stage 3 or 4  
• LDL-C >190 mg/dl | >130 (>100)# | <130 (<100) |
| Very High | • Established ASCVD  
• DM with at least 2 other RFs or end organ damage | >100 (>70)# | <100 (<70) |

*Consider other risk markers  
# Consider moderate or high intensity statin in patient with ASCVD or DM regardless of baseline lipid levels

NLA Recommendations

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*Consider other risk markers  
# Consider moderate or high intensity statin in patient with ASCVD or DM regardless of baseline lipid levels
NLA Recommendations
Drug Therapy Considerations

• Moderate or high intensity statin is first line
  – Start with appropriate dose and evaluate response and tolerance

• Alternate lipid drugs may be considered
  – As add-on therapy if unable to reach goal on highest tolerated dose of statin; ezetimibe preferred
  – Statin intolerance or contraindication; ezetimibe, bile acid resins
  – When triglycerides remain >500 mg/dl; fibrates and/or omega 3

• Therapy may be continued in patient with achieved LDL-C < 40 mg/dl in absence of symptoms
Groups with Special Considerations: Patients with Residual Risk Despite Statin and Lifestyle Therapy

- Until the CV outcomes trials are completed with PCSK9 inhibitors, these drugs should be considered primarily in: 1) patients with ASCVD who have LDL-C $\geq 100$ mg/dL (non-HDL-C $\geq 130$ mg/dL) while on maximally-tolerated statin (±ezetimibe) therapy; and 2) heterozygous FH patients without ASCVD who have LDL-C $\geq 130$ mg/dL (non-HDL-C $\geq 160$ mg/dL) while on maximally-tolerated statin (±ezetimibe) therapy.

- In addition, PCSK9 inhibitor use may be considered for selected high risk patients with ASCVD (e.g., recurrent ASCVD events) who have atherogenic cholesterol levels below the specified values, but above their treatment goals (i.e., LDL-C $\geq 70$ mg/dL [non-HDL-C $\geq 100$ mg/dL]). Such use would be based on clinical judgment, weighing the potential benefits relative to the ASCVD event risk and the risks and costs of therapy.
NLA Part 2 Recommendations: Children and Adolescents

- Universal lipid screening of all children, regardless of general health or the presence or absence of ASCVD risk factors, is recommended between 9-11 years of age, with repeat lipid screening at 20 years of age, or earlier if dyslipidemia is present.

- If a child or adolescent patient is screened and has a fasting or non-fasting non-HDL-C level $\geq 145$ mg/dL, then additional follow-up is recommended. Two fasting lipid profiles should be obtained and the results averaged for evaluation of the most appropriate course of action.

• Lipid Screening
  – Birth-2 yrs: No lipid screening
  – Age 2-8: No routine lipid screening*
  – Age 9-11: Universal screening with non-fasting lipid panel
  – Age 12-16: No routine lipid screening*
  – Age 17-21 Universal screening with non-fasting lipid panel

*Consider screening with fasting lipid panel in select patients with high risk characteristics
Summary

• Lipid Guidelines continue to evolve
  – Constant struggle between simplicity and comprehensiveness
• Although the goal is to have completely evidenced based guidelines, our evidence base is incomplete
  – Expert opinion will continue to play a role
• Guidelines are just that – continue to individualize therapy
• Involve patient in decision making to enhance adherence/compliance