A Case Study in Dyslipidemia Management - Incorporating NLA Recommendations into Practice
Hosted by the Southeast Chapter of the National Lipid Association

Moderator:
Ralph La Forge, MSc, CLS, FNLA

Speaker:
Harold E. Bays, MD, FNLA
Polling Question 1

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True
False

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In observational studies both Non-HDL-C and LDL-C predict ASCVD risk, and when these are discordant, risk is more closely aligned with non-HDL-C.

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The high risk threshold is defined as ≥10% using Adult Treatment Panel III Framingham Risk Score for hard CHD (MI or CHD death) and ≥7.5% using the 2013 Pooled Cohort Equations for hard ASCVD (MI, stroke or death from CHD or stroke) or ≥45% using the Framingham long-term (to age 80) CVD (MI, CHD death or stroke) risk calculation.

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Case study: 61-year-old man

- Prior myocardial infarction at age 59
- Stopped smoking at age 59
- Dyslipidemia treated with atorvastatin 40 mg per day
- BP acceptable on anti-hypertensive medication
- Diabetes mellitus treated with metformin and sulfonylurea
- One aspirin per day
- History of 2 units per day alcohol intake

TG = 350 mg/dl  
LDL-C = 75 mg/dl  
TC = 180 mg/dl  
HDL-cholesterol = 30 mg/dl  
Ncn-HDL-C = 150 mg/dl  
BMI = 30 kg/m²  
Fasting glucose = 140 mg/dl  
HbA1c = 6.8%
NLAs Strategic Plan

• In the past few years, the NLA has moved forward with a strategic plan for a comprehensive set of lipid recommendations, with an expectation for yearly updates as the scientific and clinical evidence evolve.

• Although the release of the recommendations contained herein was accelerated as a result of the release of the American College of Cardiology/American Heart Association guidelines, the formulation of these recommendations is consistent with the NLA’s prior strategic plan.
Original Contribution

National Lipid Association Annual Summary of Clinical Lipidology 2015

Harold E. Bays, MD, FTOS, FACC, FACE, FNLA *, Peter H. Jones, MD, FACP, FNLA, W. Virgil Brown, MD, FNLA, Terry A. Jacobson, MD, FACP, FNLA
Abstract: The National Lipid Association (NLA) Annual Summary of Clinical Lipidology 2015 is a summary of principles important to the patient-centered evaluation, management, and care of patients with dyslipidemia. This summary is intended to be a “living document,” with future annual updates based emerging science, clinical considerations, and new NLA Position and Consensus Statements. The goal is to provide clinicians an ongoing resource that translates the latest advances in medical science toward the evaluation and treatment of patients with dyslipidemia. The NLA Annual Summary of Clinical Lipidology was first proposed in 2012, and this 2015 version is the first published issue. It was founded on evidence-based medicine and is generally consistent with established national and international lipid guidelines. Where definitive evidence was lacking, the best available evidence was applied. This summary should not be interpreted as rules or directives with regard to the most appropriate care of an individual patient because no set of recommendations or guidelines can have 100% applicability to an individual patient. Thus, evaluation and treatment decisions should be based on individual circumstances. As such, this document should be used in conjunction with, and not a replacement for, the preferences of patients with dyslipidemia and the judgment of their treating clinician.

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NLA Recommendations for Patient-Centered Management of Dyslipidemia

Part 1 -- Final
Part 2

• Part 2 of the NLA Recommendations for Patient-Centered Management of Dyslipidemia is in development and will cover the following topics:
  – Lifestyle therapies
  – Groups with special considerations
    • Children, adolescents, pregnant women, and older patients
    • Gender and ethnic differences
    • Patients with congestive heart failure (CHF)
    • Patients with human immunodeficiency virus (HIV)
    • Patients with selected chronic inflammatory states and immune disorders
    • Patients with residual risk despite statin therapy
  – Strategies to assist with patient adherence
  – Team-based collaborative care
NLA Expert Panel Members

Terry A. Jacobson, MD (Co-Chair)  
Matthew K. Ito, PharmD (Co-Chair)  
Kevin C. Maki, PhD  
Carl E. Orringer, MD  
Harold E. Bays, MD  
Peter H. Jones, MD  

James M. McKenney, PharmD  
Scott M. Grundy, MD, PhD  
Edward A. Gill, MD  
Robert A. Wild, MD, PhD  
Don P. Wilson, MD  
W. Virgil Brown, MD
Conceptual Framework for Formulation of NLA Expert Panel Recommendations

• Various guidelines and recommendations have been issued in the last few years that contain material differences.

• An NLA Expert Panel was formed to prepare a set of consensus recommendations intended to inform, not replace, clinical judgment regarding dyslipidemia management.

• The NLA Expert Panel recommendations for Patient-Centered Management of Dyslipidemia were prepared after a comment period to allow input and advice to be obtained from other experts and organizations.

  • A patient-centered approach dictates that clinical judgment take into account the circumstances, objectives, and preferences of each individual patient.
Conceptual Framework (continued)

• The panel considered evidence from randomized controlled trials (RCTs), including primary, subgroup and pooled analyses where available, as well as evidence from epidemiological, metabolic, mechanistic and genetic studies.

• The panel acknowledges that the primary results from RCTs represent the strongest evidence from which to draw conclusions about benefits and risks of treatment strategies. However, the available RCT evidence has limitations, is often incomplete, or is of uncertain relevance to patients with characteristics that may differ in important ways from those who participated in the RCTs.
Guiding Principles/Conclusions

1. An elevated level of cholesterol carried by circulating Apo B-containing lipoproteins (non-HDL-C and LDL-C, termed atherogenic cholesterol) is a root cause 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.
Guiding Principles/Conclusions

3. The intensity of risk-reduction therapy should generally be adjusted to the patient’s absolute risk for an ASCVD event.

4. Atherosclerosis is a process that often begins early in life and progresses for decades before resulting in a clinical ASCVD event. Therefore, 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-lowering drug therapy is indicated, statin treatment is the primary modality for reducing ASCVD risk.

6. Non-lipid ASCVD risk factors should also be managed appropriately, particularly high blood pressure, cigarette smoking, and diabetes mellitus.
Importance of Lifestyle Therapies

• The NLA Expert Panel’s consensus view is that lifestyle therapies are an important element of risk-reduction therapies, whether or not drug therapy is used.
• The application of pharmacotherapy to dyslipidemia management has been enormously successful, and may be needed in those with sufficient risk.
• Large-scale RCTs, involving, in aggregate, hundreds of thousands of participants, have shown that drug therapies (particularly statins) that lower atherogenic cholesterol levels are effective for reducing ASCVD morbidity and mortality.
• However, results from observational studies strongly suggest that lifestyle habits have an important impact on atherogenic cholesterol levels, as well as other related disturbances (i.e., obesity, hypertension, and insulin resistance).
Usefulness of Treatment Goals

• The NLA Expert Panel’s consensus view is that treatment goals are useful as means to ensure that the aggressiveness of therapy to lower atherogenic cholesterol is matched to absolute risk for an event, and to facilitate effective communication between patients and clinicians while maximizing long-term adherence to the treatment plan.

• The strategy of treating patients to a specific level of LDL-C or non-HDL-C has not been tested in any of the large trials assessing ASCVD morbidity or mortality.
  – However, results from RCTs that have employed various methods for lowering atherogenic cholesterol (pharmacotherapy, diet, ileal bypass surgery) have indicated that lower on-treatment levels have been consistently associated with lower absolute risk for an ASCVD event, and generally align with results from observational studies suggesting a log-linear relationship between levels of atherogenic cholesterol and absolute ASCVD event risk.
Targets of Therapy – Atherogenic Cholesterol

- Atherogenic cholesterol (non-HDL-C and LDL-C) levels are the primary targets of therapy. Non-HDL-C is listed first because the panel consensus was that it is a better primary target than LDL-C.
  - Non-HDL-C is more predictive of ASCVD risk than LDL-C in observational studies, and with regard to changes or on-treatment levels in clinical trials.
  - When non-HDL-C and LDL-C are discordant, risk is more closely aligned with non-HDL-C.
  - Non-HDL-C testing is universally available, requires no additional cost, and may be obtained in the non-fasting state.
Targets of Therapy – Apo B

• Apolipoprotein B (Apo B) is considered an optional, secondary target for therapy. Apo B concentration is:
  – Strongly associated with ASCVD event risk;
  – More predictive of ASCVD risk than LDL-C, but not consistently superior to non-HDL-C;
  – A potential contributor to lipoprotein-related residual risk, as it may remain elevated in some individuals who have attained their non-HDL-C and/or LDL-C goals;
  – May be accurately assessed in the non-fasting state.

• Optional Apo B goals for primary and secondary/very high risk prevention are <90 and <80 mg/dL, respectively
  – Measurement is typically not necessary until goal levels of atherogenic cholesterol have been achieved.
Targets of Therapy – Apo B (continued)

• Clinicians may consider measuring LDL particle concentration as an alternative to Apo B.

  • Additional information about LDL particle concentration and Apo B may be found at www.lipid.org/practicetools/guidelines/consensus_recommendations: Clinical Utility of Inflammatory Markers and Advanced Lipoprotein Testing: Advice form an Expert Panel of Lipid Specialists

• The NLA Expert Panel acknowledges that measurement of LDL particle concentration can be useful clinically, particularly once non-HDL-C and LDL-C goals have been attained.
# Classifications of Cholesterol and Triglyceride Levels in mg/dL

<table>
<thead>
<tr>
<th></th>
<th>Non-HDL-C</th>
<th>HDL-C</th>
<th>LDL-C</th>
<th>Triglycerides</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;130</td>
<td>Desirable</td>
<td>&lt;100</td>
<td>&lt;150</td>
</tr>
<tr>
<td>&lt;130</td>
<td>Desirable</td>
<td></td>
<td>&lt;150</td>
<td>Normal</td>
</tr>
<tr>
<td>130-159</td>
<td>Above desirable</td>
<td></td>
<td>100-129</td>
<td>150-199</td>
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<tr>
<td>160-189</td>
<td>Borderline high</td>
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<td>130-159</td>
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<td>190-219</td>
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<td>160-189</td>
<td>200-499</td>
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<tr>
<td>≥220</td>
<td>Very high</td>
<td></td>
<td>≥220</td>
<td>≥500</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Very high</td>
</tr>
</tbody>
</table>
## Treatment Goals for Non-HDL-C, LDL-C, and Apo B in mg/dL

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>Treatment Goal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Non-HDL-C</td>
</tr>
<tr>
<td>Low</td>
<td>&lt;130</td>
</tr>
<tr>
<td>Moderate</td>
<td>&lt;130</td>
</tr>
<tr>
<td>High</td>
<td>&lt;130</td>
</tr>
<tr>
<td>Very High</td>
<td>&lt;100</td>
</tr>
</tbody>
</table>
Targets of Therapy – Triglycerides

- An elevated triglyceride level is not a target of therapy *per se*, except when very high (severe; $\geq 500$ mg/dL).
- When triglycerides are between 200-499 mg/dL, the targets of therapy are non-HDL-C and LDL-C.
- When the triglyceride concentration is very high ($\geq 500$ mg/dL, and especially if $\geq 1000$ mg/dL), reducing the concentration to $<500$ mg/dL to prevent pancreatitis becomes the primary goal of therapy.
HDL-C

• The level of HDL-C is an important risk indicator and used in risk factor counting and quantitative risk assessment. Low HDL-C is also a component of the metabolic syndrome.

• HDL-C is not recommended as a target of therapy *per se*, but the level is often raised as a consequence of efforts to reduce atherogenic cholesterol through lifestyle and drug therapies.
Metabolic Syndrome

• Metabolic syndrome is recognized as a multiplex risk factor for both ASCVD and type 2 diabetes mellitus.

• Increased adiposity and insulin resistance appear to be central pathophysiologic features of this cluster of interrelated metabolic and hemodynamic disturbances.

• The presence of the metabolic syndrome indicates high potential to benefit from lifestyle therapies, particularly weight loss if overweight/obese and increased physical activity.
  – Successful lifestyle intervention will reduce adiposity and insulin resistance, improving multiple physiological disturbances that may contribute to risk, including the metabolic syndrome components, as well as indicators of inflammation and thrombogenicity.
Major Risk Factors for ASCVD

1. Age
   Male ≥45 years
   Female ≥55 years

2. Family history of early CHD
   <55 years of age in a male first-degree relative, or
   <65 years of age in a female first-degree relative

3. Current cigarette smoking

4. High blood pressure (≥140/≥90 mm Hg, or on blood pressure medication)

5. Low HDL-C
   Male <40 mg/dL
   Female <50 mg/dL
High or Very High Risk Patient Groups

• Quantitative risk scoring is not necessary for initial risk assessment in patients with the following conditions*:
  – Diabetes mellitus, type 1 or 2
  – Chronic kidney disease, Stage ≥3B
  – LDL-C ≥190 mg/dL - severe hypercholesterolemia phenotype, which includes FH
  – ASCVD

*Patients in these categories are all at **high or very risk** for an ASCVD event and should be treated accordingly.
Criteria for Classification of ASCVD

• Myocardial infarction or other acute coronary syndrome
• Coronary or other revascularization procedure
• Transient ischemic attack
• Ischemic stroke
• Atherosclerotic peripheral arterial disease
  – Includes ankle/brachial index <0.90
• Other documented atherosclerotic diseases such as:
  – Coronary atherosclerosis
  – Renal atherosclerosis
  – Aortic aneurysm secondary to atherosclerosis
  – Carotid plaque, ≥50% stenosis
## Criteria for ASCVD Risk Categories

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>Criteria</th>
</tr>
</thead>
</table>
| Low               | ▪ 0-1 major ASCVD risk factors  
                      ▪ Consider other risk indicators, if known                                                                                         |
| Moderate          | ▪ 2 major ASCVD risk factors  
                      ▪ Consider quantitative risk scoring  
                      ▪ Consider other risk indicators                                                                                                 |
| High              | ▪ ≥3 major ASCVD risk factors  
                      ▪ Diabetes mellitus (type 1 or 2)  
                      ▪ 0-1 other major ASCVD risk factors, and  
                      ▪ No evidence of end organ damage  
                      ▪ Chronic kidney disease Stage 3B or 4  
                      ▪ LDL-C ≥190 mg/dL (severe hypercholesterolemia)  
                      ▪ Quantitative risk score reaching the high risk threshold                                                                       |
| Very High         | ▪ ASCVD  
                      ▪ Diabetes mellitus (type 1 or 2)  
                      ▪ ≥2 other major ASCVD risk factors or  
                      ▪ Evidence of end organ damage                                                                                                   |
### Criteria for ASCVD Risk Assessment, Treatment Goals, Levels at Which to Consider Drug Therapy

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>Criteria</th>
<th>Treatment Goal</th>
<th>Consider Drug Therapy</th>
</tr>
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<tbody>
<tr>
<td></td>
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<100 | ≥130  
≥100 |
| Very High     | ▪ ASCVD*  
▪ Diabetes mellitus* (Type 1 or 2)  
▪ ≥2 other major ASCVD risk factors or  
▪ Evidence of end organ damage | <100  
<70 | ≥100  
≥70 |

*For patients with ASCVD or diabetes mellitus, consideration should be given to use of moderate or high intensity statin therapy, irrespective of baseline atherogenic cholesterol levels.*
Risk Indicators (Other Than Major ASCVD Risk Factors) That Might Be Considered For Risk Refinement

1. A severe disturbance in a major ASCVD risk factor, such as multi-pack per day smoking, or strong family history of premature CHD
2. Indicators of subclinical disease, including coronary artery calcium
   - ≥300 Agatston units is considered high risk
3. LDL-C ≥160 and/or non-HDL-C ≥190 mg/dL
4. High-sensitivity C-reactive protein ≥2.0 mg/L
5. Lipoprotein (a) ≥50 mg/dL (protein) using an isoform insensitive assay
6. Urine albumin / creatinine ratio ≥30 mg/g
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Question and Answer Session
Please submit questions for the speaker in the Q & A form on the right hand column of your screen.

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Thank you for attending this Lipid Insights program.

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