2015

Comparing the 2013 ACC/AHA & 2014 NLA Dyslipidemia Guidelines and Their Impact on Clinical Decision Making

Alexander Forbes
Midwestern University

Kevin Grimes
Midwestern University

Jocelyn York
Midwestern University

Laura Tsu
Chapman University, ltsu@chapman.edu

Recommended Citation

Forbes A, Grimes K, York J, Tsu LV. Comparing the 2013 ACC/AHA & 2014 NLA Dyslipidemia Guidelines and their Impact on Clinical Decision Making. *Arizona Journal of Pharmacy* 2015;24-30.

Comparing the 2013 ACC/AHA & 2014 NLA Dyslipidemia Guidelines and Their Impact on Clinical Decision Making

CONTINUING EDUCATION

Comparing the 2013 ACC/AHA & 2014 NLA Dyslipidemia Guidelines and their Impact on Clinical Decision Making

by Alexander Forbes, Pharm.D. Candidate, Midwestern University College of Pharmacy-Glendale Class of 2015, Kevin Grimes, Pharm.D.Candidate Midwestern University College of Pharmacy-Glendale Class of 2015, Jocelyn York, Pharm.D. Candidate Midwestern University College of Pharmacy-Glendale Class of 2015, and Laura Tsu, Pharm.D., BCPS, Assistant Professor, Pharmacy Practice, Midwestern University College of Pharmacy-Glendale

Goal:

This home-study CPE activity has been developed to educate pharmacists on the similarities and differences between the 2014 NLA Recommendations for Dyslipidemia Management and the 2013 ACC/AHA Guidelines for Treatment of Blood Cholesterol.

At the conclusion of this CPE activity, successful participants should be able to:

Objectives for Pharmacists:

1. Identify the major differences in treatment recommendations for dyslipidemia between the 2013 ACC/AHA Guidelines and the new 2014 NLA Recommendations for dyslipidemia.
2. List the classifications of lipoprotein lipid levels in adults.
3. Accurately identify targets for intervention in the treatment of dyslipidemia.
4. Assess a patient's ASCVD risk and the treatment goals based on risk category.
5. Discuss lifestyle and drug therapies recommended to reduce morbidity and mortality in patients with dyslipidemia.
6. Apply NLA guidelines to formulate and evaluate initial or existing therapy to specific patient cases.

Objectives for Technicians:

1. Identify the major differences in treatment recommendations for dyslipidemia between the 2013 ACC/AHA Guidelines and the new 2014 NLA Recommendations for Dyslipidemia.
2. List the classifications of lipoprotein lipid levels in adults.
3. Learn how the pharmacist can use NCA guidelines and the ASCVD risk to assess and evaluate patients.

Introduction

Dyslipidemia, or high cholesterol, is a major risk factor for the development of heart disease, the leading cause of death in the United States (US).[1] The Centers for Disease Control and Prevention estimates that 71 million Americans, roughly one-third of the entire population, have high low-density lipoprotein (LDL) cholesterol.[2] This staggering number emphasizes the need for proper management of high cholesterol in the US and around the world. Sadly, it's estimated that only one-third of the 71 million Americans with high LDL are well-controlled. This presents a significant public health challenge for the medical community. Over the past decade and a half, dyslipidemia management has been the focus of numerous organizations, all aiming to decrease the morbidity and mortality associated with poor lipid control. And progress has been made: the relative rate of death related to heart disease has decreased by approximately 31% from 2000-2010.[3] However, there is much more that still needs to be accomplished in the fight against dyslipidemia.

Many organizations and agencies have compiled recommendations for the management of dyslipidemia. Though commonalities exist, there are stark differences between these varied guidelines. This continuing education article strives to compare and contrast previous recommendations with the recent National Lipid Association (NLA) recommendations, as to provide a clear and comprehensive understanding of the varied approach to management of dyslipidemia.

Background

Cholesterol, triglycerides and lipoproteins comprise the major lipids in the human body and when transported in the blood stream, are known as lipoproteins. There are three major serum lipoproteins: LDL, high-density lipoprotein (HDL) and very low-density lipoprotein (VLDL) which are carried in the blood as triglycerides (TG). Dyslipidemia is defined as a disorder of these key lipoproteins. This disease state may commonly be characterized by an elevation in total cholesterol, an elevation in LDL, an elevation in TG, or a decrease in HDL concentrations in the blood. Progression of dyslipidemia is facilitated through a number of mechanisms. As LDL levels increase in the blood, the particles become lodged in the artery wall, causing atherosclerotic lesions. Once in the artery wall, LDL becomes oxidized, triggering an immune response via macrophages. Macrophages, in an attempt to engulf and clear the LDL particles,

unintentionally cause an acceleration of LDL oxidation. Further involvement of the immune system leads to an inflammatory response and formation of atherosclerotic plaques. Eventually, after years of repetitive vessel damage, formed plaques and cholesterol deposits begin to occlude blood vessels leading to atherosclerotic cardiovascular disease (ASCVD). ASCVD encompasses all cardiovascular disease that is attributable to atherosclerotic plaque formation including, but not limited to, myocardial infarction, angina, and peripheral artery disease. It is this ASCVD that is of most concern when discussing management of dyslipidemia and prevention of cardiovascular events.[4]

Timeline of Dyslipidemia Management

The past decade and a half has seen the update and release of three distinct dyslipidemia guidelines. The first, produced by the National Cholesterol Education Program (NCEP), were known as the Adult Treatment Panel (ATP) guidelines. ATP I was released in 1988 followed by ATP II in 1993. The most recent and applicable update to these recommendations was released in 2002 and was known as ATP III. The ATP III recommendations focused on intensive LDL lowering strategies mediated by goal-directed therapy as well as primary prevention in patients with multiple risk factors.[4] For many years, the ATP III guidelines were the standard of care in clinical practice until the 2013 release of the American College of Cardiology/American Heart Association (ACC/AHA) dyslipidemia recommendations. The ACC/AHA 2013 guidelines demonstrated a shift in approach to lipid management. While primary prevention remained a focus, goal-directed therapy did not. Instead, intensive statin therapy became the center of the ACC/AHA recommendations, with little regard to other aspects of clinical management. Because the ACC/AHA guidelines are still relatively new, their implementation and understanding in clinical practice is still developing.

2013 ACC/AHA Guidelines Overview

The ACC/AHA expert panel took a different approach in regards to lipid management when compared to the ATP III guidelines. They determined that, based on available evidence, there was no significant morbidity or mortality benefit of titrating pharmacotherapy to target a specific LDL goal.[5] In addition, the percentage of ASCVD risk reduction that one goal level offered in comparison to another, for example lowering LDL-C to optimal (<100 mg/dL) versus lowering it to near optimal (100-129 mg/dL), was

Table 1 - Statin Benefit Groups*

Individuals with clinical ASCVD
Individuals with primary elevation of LDL-C ≥190 mg/dL
Individuals age 40-75 with Diabetes Mellitus with LDL-C 70-189 mg/dL
Individuals without diabetes or clinical ASCVD who are 40-75 years of age with LDL-c 70-189 mg/dL and who have an estimated 10-year ASCVD risk 7.5% or higher
*Adapted from reference 7

Table 2 - High- Moderate- and Low- Intensity Statin Therapy&*

High-Intensity Statin Therapy	Moderate-Intensity Statin Therapy	Low-Intensity Statin Therapy
Daily dose lowers LDL-C on average, by ≥ 50%	*Daily dose lowers LDL-C on average, by 30-50%*	*Daily dose lowers LDL-C on average, by ≤ 30%*
Atorvastatin 40-80 mg	Atorvastatin 10-20 mg	Simvastatin 10 mg^
Rosuvastatin 20-40 mg	Rosuvastatin 5-10 mg	Pravastatin 10–20 mg
	Simvastatin 20-40 mg	Lovastatin 20 mg
	Pravastatin 40-80 mg	Fluvastatin 20–40 mg^
	Lovastatin 40 mg	Pitavastatin 1 mg^
	Fluvastatin 40 mg bid	
	Fluvastatin XL 80 mg^	
	Pitavastatin 2-4 mg^	

***Individual response may vary between each patient in clinical practice**
^FDA approved but have not been evaluated by RCT's
*Adapted from reference 7

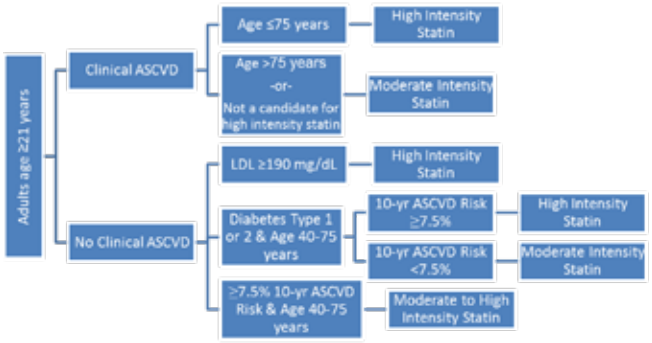

Figure 1 – Adapated from reference 7

never quantified in studies. Therefore, the idea that the lowest level is best was not supported in the ACC/AHA guidelines. They did, however, conclude that evidence did support a significant morbidity and mortality benefit with moderate to high intensity statin use. Based on this data, the panel concluded that the sole focus of treatment should be on intensive statin therapy. Upon review of current clinical trial and epidemiologic data, the ACC/AHA expert panel stated that there were four specific "statin benefit" groups (Table 1). Additionally, the panel advocated the use of the Pooled-Cohort ASCVD Risk Calculator to further identify high risk patients.6 There are a number of online versions of this Pooled-Cohort calculator available to aid pharmacists in risk stratifying patients. The ACC/AHA then classified the intensity of certain statins for use in the previously discussed statin benefit groups (Table 2). The intensity of a statin was defined by the percent reduction in LDL-C, as deduced from systematic reviews of RCT's. Finally, based upon an individual's ASCVD risk and statin benefit group, their

need for a moderate or high intensity statin could be determined. The ACC/AHA created a final algorithm to guide statin therapy (Figure 1).

2014 NLA Recommendations Overview

The National Lipid Association (NLA) is an accredited, multidisciplinary organization consisting of physicians, pharmacists, and other healthcare professionals and researchers whose focus is on enhancing lipid management in clinical practice. The NLA Expert Panel's Recommendations for Patient-Centered Management of Dyslipidemia utilized current randomized controlled data along with epidemiological and genetic studies to determine beneficial interventions on clinical ASCVD events.[7] The panel focused on a patient-centered approach to lipid management and emphasized the importance of clinical judgment based on individual factors. The NLA made six major evidence-based conclusions which guided the formation of the recommendations:

1. An elevated level of cholesterol carried by circulating apolipoprotein (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.

In light of the recent compelling evidence found in randomized-controlled trials (RCTs), epidemiological and genetic studies, the NLA recommendations shift away from the previous focus on LDL cholesterol as the sole contributor to ASCVD risk. The expert panel concluded that non-HDL-C, in conjunction with LDL-C, are the primary targets of therapy, with non-HDL-C being a preferred primary target over LDL-C. This is because non-HDL-C is thought to be a better predictor of ASCVD morbidity and mortality as it includes the cholesterol carried by all lipid particles that are potentially atherogenic. Therefore, non-HDL presumably provides a more accurate picture of an individual patient's risk. The NLA suggests that a reduction in levels of atherogenic cholesterol will proportionally reduce the risk of ASCVD events in patients with dyslipidemia.

The NLA provides an optional secondary target for treatment in certain patients. ApoB is a lipoprotein that is found on the surface of LDL-C particles. Each LDL-C particle contains one molecule of apoB; therefore, the concentration of apoB in the bloodstream is directly proportional to the number of circulating atherogenic particles. Unfortunately, apoB has not been consistently shown to be a superior measurement in comparison to non-HDL-C and levels of apoB can be altered by current statin use. These limiting factors relegate the use of apoB to an optional target for treatment. It is important to note that the pharmacological effect that statins have on cholesterol levels is that it most often lowers cholesterol concentrations to a greater extent than it does apoB levels. The apoB remaining after treatment goals for non-HDL-C and LDL-C (see Table 3) are reached is recognized as a contributor to any remaining ASCVD risk. Therefore, apoB levels may then be targeted to further reduce this risk after individuals reach their goal levels for non-HDL-C and LDL-C.

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.

The second major conclusion from the NLA asserts that the amount that cholesterol is reduced in the blood proportionally reduces ASCVD risk. A meta-analysis evaluating the relationship between non-HDL-C lowering and coronary heart disease risk reduction compiled data from 14moderate to high intensity statin dose placebo and active control trials. Researchers found that a 1% reduction in non-HDL-C resulted in a 4.5-year coronary heart disease (CHD) relative risk reduction of 1%.[8] It would stand to reason that a greater reduction in atherogenic cholesterol would result in an overall decreased risk of cardiovascular events. This reduction is mediated by cholesterol-targeting medications, namely statins, diet and exercise.

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

The NLA based the recommendation for increased intensity of statin therapy in proportion to an individual's risk on current evidence and clinical consensus. The conclusion is thus: as an individual's ASCVD risk increases, the need for greater reduction in atherogenic cholesterol is also required to

prevent a cardiovascular event. This intensive decrease is mediated by the use of appropriate statin therapy (Table 2). It stands to reason that if a greater reduction of cholesterol is necessary, then a higher intensity statin should be more efficacious than a lower intensity statin. The Cholesterol Treatment Trialists' Collaboration undertook meta-analyses of individual trial data examining the efficacy and safety of lower versus higher intensity statin doses. Researchers found that higher intensity regimens resulted in significantly fewer major vascular events [15% RR (95% CI 11—18); p<0.0001], revascularization [19% RR (95% CI 15—24); p<0.0001] and ischemic stroke [16% RR (95% CI 5—26); p=0.005].[9] Therefore, the NLA's third major conclusion is supported.

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.

The basis of this major conclusion was founded on the fact that there can be significant differences between a patient's short-term risk and their lifetime risk. The NLA recommends avoiding a "one-size-fits-all" approach and instead advocates for a comprehensive work-up of each patient and an individual treatment plan tailored to their specific short-term and lifetime ASCVD risk.

5. For patients in whom lipid-lowering drug therapy is indicated, statin treatment is the primary modality for reducing ASCVD risk.

Statin therapy has proven to be the golden standard in dyslipidemia management. This stems from the fact that statins provide the greatest percentage LDL-C lowering and therefore, the greatest reduction in cardiovascular risk. High intensity statins lower LDL-C by an average of 50% from baseline whereas moderate intensity statins provide a 30-50% reduction in LDL-C (Table 2). Alternative lipid-lowering therapies do not provide as substantial a mortality benefit as statins and therefore are reserved as last-line therapy if a patient is unable or unwilling to continue statin therapy.

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

ASCVD is multifactorial and involves more than dyslipidemia management. Comorbid disease states can further contribute to ASCVD risk, such as diabetes, hypertension and coronary artery disease. Additionally, poor diet and cigarette smoking compound CHD risk. Smoking alone is attributed to 30% of all CHD deaths in the United States, though this number is likely higher.[10] Addressing these additional risk factors in conjunction with proper dyslipidemia management can further decrease an individual's ASCVD risk.

How the Guidelines Differ – Risk Assessment

When comparing the ACC/AHA guidelines with the NLA recommendations, there are significant differences that arise when assessing an individual's cardiovascular risk. While both guidelines similarly define clinical evidence of ASCVD, the approach to further risk stratification differs. The ACC/AHA utilizes the Pooled-Cohort calculator to determine an individual's 10-year risk of developing ASCVD. The combination of clinical ASCVD, age, and the 10-year risk score all contribute to the ultimate decision of whether a patient receives a moderate or high intensity statin. The NLA on the other hand, only recommends using the Pooled-Cohort calculator as a supplement when determining an individual's treatment strategy. Where the ACC/AHA only recommends the use of their own calculator for further risk assessment, the NLA gives the option of either the ATP III Framingham risk calculator, the Framingham long-term (30-year), or the ACC/AHA Pooled Cohort Equations calculator. The NLA acknowledges that scoring calculators provide only an estimate of risk for these patients, and should be used as a means of more accurately reclassifying moderate risk individuals as high risk for optimal treatment outcomes.[7] The NLA recommends consideration of other factors that may influence risk categorization to the high risk category for more appropriate treatment goals. The presence of metabolic syndrome and other clinical risk indicators that warrant the use of the Pooled-Cohort calculator are outlined in Table 8. The ACC/AHA on the other hand incorporates the risk calculator into assessing risk for determining appropriate statin intensity for two of the four statin benefit groups: patients with diabe-

tes type 1 or 2 age 40-75 years, and patients without diabetes age 40 to 75 years with a 10-year assessment score of ≥ 7.5%.[7]

For patients that fall under the high or very-high risk categories, the NLA states that quantitative risk scoring is not necessary when certain disease states are also present. These conditions include diabetes mellitus type 1 or 2, chronic kidney disease stage 3B or greater, LDL-C ≥190mg/dL (severe hypercholesterolemia) and the presence of ASCVD. The NLA argues that quantitative risk scoring in these patients often results in underestimation of the patients true risk for an ASCVD event, and should therefore be avoided to allow for a more accurate determination of patient treatment options.[7] Individuals in the moderate risk category with two major risk factors for ASCVD (Table 5) are often risk assessed for purpose of evaluating pharmacotherapy when these uncertainties still exist despite their risk category. The greatest benefit of quantitative risk scoring in moderate risk patients is in determining if justification exists for initiating pharmacotherapy when it may have otherwise been held. So in general, the NLA give clinicians the option of performing quantitative risk scoring for patients without high risk conditions who nonetheless may be at an increased risk of an ASCVD event, or for those who have higher risk factors warranting further consideration. As emphasized previously, this approach differs from the ACC/AHA Guidelines that utilize quantitative risk scoring as an essential part of the ASCVD classification system.

How the Guidelines Differ – Treatment Goals

While the ACC/AHA guidelines make no direct assessment to which lipid measurement correlates greatest with ASCVD risk, the NLA expert panel recognizes non-HDL as a superior treatment target compared to the traditionally measured LDL-C. The expert panel discusses that non-HDL accounts for more types of cholesterol that contribute to ASCVD, and that non-HDL-C better predicts morbidity and mortality over LDL-C.[7,11] Target treatment goal recommendations may be the most significant difference between the ACC/AHA guidelines and the NLA recommendations. The ACC/AHA guidelines decision to not target treatment goals was based upon their review of 23 RCTs for primary and secondary prevention (6 for primary and 19 for secondary with 2 studies encompassing both populations-ASPEN and AURORA) and was two of their three critical questions that they addressed while formulating their guidelines. The authors did not find enough data in these studies to support the use of specific treatment goals.[7] On the contrary, even though the NLA expert panel recognizes in their review of available RCTs that treating patients to specific atherogenic cholesterol goals have not been tested as primary efficacy, they view treatment goals as a necessary measure in the management of dyslipidemia. The NLA states that implementing treatment goals enhances patient-clinician communication and assures that appropriate risk reduction is occurring. The specific goals for each risk group in the NLA guidelines are outlined in Table 9.Finally, when comparing the ACC/AHA and NLA treatment goals, it is important to analyze follow-up recommendations. The ACC/AHA suggest an initial baseline fasting lipid panel at time of pharmacotherapy initiation and follow up at 4 to 12 weeks to access for adherence to pharmacotherapy and lifestyle modifications. Once a patient has been stabilized on pharmacotherapy, the ACC/AHA suggests follow-up every 3-12 months thereafter.5 The NLA guidelines recommend similar time frames for follow up with multiple visits over 6 months in which target goal levels should be obtained, and once goal has been reached follow up should occur every 4 to 12 months.[7]

Pharmacotherapy Management

The pharmacist's role in dyslipidemia management is applicable across multiple patient care settings. Whether in an inpatient or outpatient setting, a pharmacist's understanding of basic monitoring, adverse events, and laboratory values are crucial in providing the best care to individual patients. In addition to a fasting lipid panel periodically as recommended above, liver function tests (LFTs) should be evaluated at baseline, and creatine kinase (CK) should be evaluated in select patients. However, routine monitoring of these lab values is not currently recommended and should only be repeated upon a patient's symptomatic presentation or based upon clinical judgment.[12]

Pharmacists should monitor for side effects of statin therapy, the most common of which are muscle pain and weakness, and gastrointestinal upset and headache. More severe adverse effects include myopathies and rhabdomyolsis, though the incidence is rare. Pharmacists should evaluate patients

muscle pain and recommend laboratory testing of LFTs or CK if indicated. In those patients who present with muscle pain, symptoms may improve upon switching to a different statin. Other strategies suggested by the NLA include a modified dosing regimen, such as every other day, or lowering the total daily dose. For those patients who absolutely cannot tolerate a statin, other classes of medications may be considered, either alone or in addition to the statin (Table 6). Of note, the NLA does not support the use of combination drug therapy prior to reaching the maximum tolerated statin dose, as evidence justifying this is lacking.

Additionally, pharmacists should evaluate the potential for drug-drug interactions. Simvastatin, atorvastatin and lovastatin are substrates for CYP3A4 and are therefore, the three statins most likely to interact with other medications. CYP3A4 inhibitors are of most concern, as they can increase serum concentrations of these statins and put patients at an increased risk of toxicity. However, atorvastatin is less reliant on 3A4 for metabolism and is involved in fewer clinically significant interactions when compared to simvastatin and lovastatin. Gemfibrozil inhibits glucuronidation, an important elimination pathway for all statins and should therefore be avoided with all statin therapy. Fenofibrate is an appropriate alternative to gemfibrozil and appears to be safe and effective when used with statins.[13] Finally, patients should be counseled on avoidance of grapefruit juice while taking simvastatin and lovastatin due to inhibition of 3A4. Consumption is not contraindicated in atorvastatin use but intake should be limited to less than 1 liter per day. Table 7 lists other potential drug-drug interactions with select statin therapies.

Finally, patients with severe hypercholesterolemia (LDL-C ≥190 mg/dL) can present significant treatment challenges. Even with combination therapy, goal levels of atherogenic cholesterol may not be achievable in this despite utilizing the most aggressive treatment options tolerable. In an effort to reduce morbidity and mortality in patients with severe hypercholesterolemia, the NLA recommends a reduction in atherogenic cholesterol by at least 50% instead of the standard goals outlined in Table 3. Although new medication classes are being studied that may eventually make the standard goals in this year's recommendations achievable in patients with excessively elevated cholesterol levels, this alternative treatment approach remains the most practical option until new agents are proven safe and efficacious.

Therapeutic Lifestyle Changes

The ACC/AHA and the NLA recognize the importance of lifestyle modifications as a key component of dyslipidemia management. The expert panel recommends a 3-month trial of lifestyle therapy for patients who fall into the low to moderate risk categories prior to drug therapy. For high and very high risk patients, however, drug therapy may be initiated at the same time as lifestyle therapy.

Lifestyle changes should be a focus at every visit, with an emphasis on diet, exercise and smoking cessation. Patients with dyslipidemia should be educated on how to maintain a balanced diet, low in saturated fats and sodium and high in fiber. The DASH diet and the AHA's dietary recommendations are all highly recommended diet plans and can aid in both cholesterol and blood pressure reduction.[14,15] While pharmacists can provide basic nutritional education and support, referral to a registered dietician is recommended. Additionally, moderate to high intensity exercise ideally targeting 150 minutes per week (30 minutes per day for 5 days) is highly encouraged. For those patients who are overweight or obese, a weight loss of 5% to 10% of body weight over 6 months is recommended. Smoking cessation should be encouraged at each follow-up and referral to patient resources, should be provided as needed.

Conclusion

Clinical practices in the medical community are constantly adapting as new data becomes available. This is illustrated by the rapidly changing lipid recommendations over the past decade and a half. A thorough review of the 2013 ACC/AHA guidelines in comparison to the newly released 2014 NLA recommendations reveals both commonalities as well as differences. The release of the NLA recommendations saw the resurrection of lipid goals while retaining the focus on intensive statin therapy. As a pharmacist, it is fundamental to have an understanding these current practice guidelines and familiarize oneself with the preceding relevant recommendations.

Pharmacists play a significant role in the management of patients with dyslipidemia. They are some of the most accessible members of the health

care team and are convenient resources for patients. They have the potential to make substantial interventions in patient care, involving encouragement of therapeutic lifestyle changes, adverse drug event monitoring, and medication adherence. Given that pharmacists work closely alongside medical practitioners, it is essential to remain up to date on the current evidence based guidelines, as to provide accurate and timely pharmacotherapy recommendations.

Table 3 – NLA Classifications of Cholesterol and Triglyceride levels in mg/dL

Non-HDL-C	
<130	Desirable
130-159	Above desirable
160-189	Borderline high
190-219	High
≥220	Very high
LDL-C	
<100	Desirable
100-129	Above desirable
130-159	Borderline high
160-189	High
≥190	Very high
HDL-C	
<40 (men)	Low
<50 (women)	Low
Triglycerides	
<150	Normal
150-199	Borderline high
200-499	High
≥500	Very high

Adapted from reference 8

Table 4 – NLA Risk Assessment

Major Risk Factors for ASCVD	Evidence of Clinical ASCVD Criteria	High or Very High Risk Patient Groups
• Age - Male ≥45 years - Female ≥55 years • Family history of early CHD - Male <55 years of age first degree relative - Female <65 years of age first-degree relative • Current cigarette use • High blood pressure (≥140/≥90 mmHg) or on blood pressure medication • Low HDL-C - Male <40 mg/dL - Female <50 mg/dL	• MI or ACS • Coronary or other revascularization procedure • Ischemic stroke or TIA • 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	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 or severe hypercholesterolemia phenotype • ASCVD

Adapted from reference 8

Table 6 - Lipoprotein Metabolism of Other Agents

Drug class	Lipoproteins	Effects
Bile Acid Sequestrants	LDL-C Non-HDL-C HDL-C TG	↓15-30% ↓4-16% ↑3-5% ↓0-10%
Nicotinic Acids	LDL-C Non-HDL-C HDL-C TG	↓5-25% ↓8-23% ↑15-35% ↓20-50%
Fibric Acids	LDL-C Non-HDL-C HDL-C TG	↓5-20% ↓5-19% ↑10-20% ↓20-50%
Cholesterol Absorption Inhibitor	LDL-C Non-HDL-C HDL-C TG	↓13-20% ↓14-19% ↑3-5% ↓5-11%
Long-Chain Omega-3 Fatty Acids	LDL-C Non-HDL-C HDL-C TG	↓6%-↑25% ↓5-14% ↑5%-↓7% ↓19-44%

Adapted from reference 8

Table 5 - Comparison of ACC/AHA and NLA Treatment Goals

	2013 ACC/AHA Guidelines	2014 NLA Recommendations
1	No recommendation for non-HDL-C vs. LDL-C	Recommends monitoring of non-HDL-C over LDL-C
2	• Excludes target lipid goals • 4 statin benefit groups 1. Clinical ASCVD 2. LDL-C ≥190 mg/dL 3. 40-75 years old with DM (I or II) 4. Absence of ASCVD or DM, 40-75 years old with LDL-C 70-189mg/dL and an estimated 10-year ASCVD risk ≥ 7.5%	• Utilizes treatment lipid goals and pharmacotherapy therapy intervention levels • Risk Category Target Goal (Non-HDL-C, LDL-C) 1. Low (<130, <100) 2. Moderate (<130, <100) 3. High (<130, <100) 4. Very High (<100, <70)
3	Follow up visit in 4 to 12 weeks to assess adherence, then every 3 to 12 months	Goal levels should be reached by approximately 6 months, then follow-up every 3-12 months

Adapted from reference 8

Table 7 - Statin Metabolism

Statin	Metabolic Pathway	Potential Interactions
Lovastatin Simvastatin Atorvastatin	3A4	Ketoconazole, itraconazole, cyclosporine, erythromycin, clarithromycin, ritonavir Gemfibrozil
Rosuvastatin	Minimal 2C9	Cyclosporine, gemfibrozil
Fluvastatin	2C9, 3A4, 2D6	Warfarin, gemfibrozil
Pitavastatin	Minimal 2C9	Gemfibrozil
Pravastatin	None significant	Gemfibrozil

Adapted from reference 17

Table 9 - NLA Criteria for ASCVD Risk Assessment, Treatment Goals for Atherogenic Cholesterol, and Levels at Which to Consider Drug Therapy

Risk category	Criteria	Treatment goal Non-HDL-C mg/dL LDL-C mg/dL Apo B mg/dL*	Consider drug therapy Non-HDL-C mg/dL LDL-C mg/dL Apo B mg/dL*
Low	• Major ASCVD risk factors • Consider other risk factors, if known	<130 <100 <90*	≥190 ≥160
Moderate	• 2 major ASCVD risk factors • Consider quantitative risk scoring • Consider other risk indicators	<130 <100 <90*	≥160 ≥130
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	<130 <100 <90*	≥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 <80*	≥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.

*Apo B is a secondary, optional target of treatment

Adapted from reference 8

Table 8 - Criteria for Clinical Identification of Metabolic Syndrome

Measure	Criteria
1. Elevated waist circumference	≥40 inches in men ≥35 inches in women
2. Elevated triglycerides*	≥150 mg/dL
3. Reduced HDL-C	<40 mg/dL in men <50 mg/dL in women
4. Elevated blood pressure*	Systolic ≥130 and/or diastolic ≥85 mm Hg
5. Elevated fasting glucose*	≥40 inches in men ≥35 inches in women

*Drug treatment with a triglyceride-lowering agent, drug treatment of elevated blood pressure, and drug treatment of elevated blood glucose are alternative indicators for metabolic syndrome

Adapted from reference 8

Dyslipidemia

References

1. Xu JQ, Kochanek KD, Murphy SL, Tejada-Vera B. Deaths: final data for 2007. Hyattsville, MD: US Department of Health and Human Services, CDC, National Center for Health Statistics; 2010. National Vital Statistics Report, vol. 58, no. 19.

2. CDC. Vital signs: prevalence, treatment, and control of high levels of low-density lipoprotein cholesterol. United States, 1999–2002 and 2005–2008. MMWR. 2011;60(4):109–14.

3. Go AS, Mozaffarian D, Roger VL et al. Heart disease and stroke statistics – 2014 update: a report from the American Heart Association. Circulation. 2014 Jan 21;129(3):e28-e292.

4. Third report of the expert panel on detection , evaluation, and treatment of high cholesterol in adults (the adult treatment panel III). Circulation. 2002.

5. Dipiro JT, Talbert RL, Yee Gc et al. Pharmacotherapy: a pathophysiologic approach, 9th edition. New York: McGraw-Hill Medical. 2008;1:11.

6. Stone NJ, Robinson JG, Lichtenstein AH et al. 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. Circulation. 2014;129(25 Suppl 2):S1-45.

7. Goff DC, Lloyd-Jones DM, Bennett D et al. 2013 ACC/AHA Guideline on the Assessment of Cardiovascular Risk: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. 2014; 129: S49-S73.

8. Jacobson TA, Ito MK, Maki KC et al. National Lipid Association recommendations for patient-centered management of dyslipidemia: Part 1 - executive summary. J Clin Lipidol. 2014;8(5):473-88.

9. Robinson JG, Wang S, Smith BJ et al. Meta-analysis of the relationship between non-high-density lipoprotein cholesterol reduction and coronary heart disease risk. J Am Coll Cardiol. 2009;53(4):316-22.

10. Baigent C, Blackwell L, Emberson J et al. Cholesterol treatment trialists' (CTT) collaboration: Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-anaylsis of data from 170,000 participants in 26 randomized trials. Lancet. 2010;376:1670-1681.

11. Ockene IS, Miller NH. American Heart Association task force on risk reduction: Cigarette smoking, cardiovascular disease and stroke. Circulation. 1997;96;3243-7.

12. Liu J, Sempos CT, Donahue RP et al. Non-high-density lipoprotein and very-low-density lipoprotein cholesterol and their risk predictive values in coronary heart disease. Am J Cardiol. 2006;98:1363-1368

13. McKenney JM, Davidson MH, Jacobson TA et al. Final conclusions and recommendations of the National Lipid Association Statin Safety Assessment Task Force. Am J Cardiol. 2006;97:89C-94C.

14. Davidson MH. Combination therapy for dyslipidemia: safety and regulatory considerations. Am J Cardiol. 2002;69:340-5.

15. US Department of Health and Human Services; National Institutes of Health; National Heart, Blood and Lung Institute. Your guide to lowering blood pressure with DASH. NIH Publication no. 06-4082, revised April 2006. Available at www.nhlbi.nih.gov/files/docs/public/heart/hbp_low.pdf. Accessed 10/23/14.

16. Lichtenstein AH, Appel LJ, Brands M et al. Diet and lifestyle recommendations 2006: A scientific statement from the American Heart Association Nutrition Committee. Circulation. 2006;114:82-96.

17. Wiggins BS, Saseen JJ. Pharmacist's guide to lipid management. Lanexa, Kasas:ACCP;2014:80-121.

ACPE UAN# 0100-0000-15-043-H04-P; 0100-0000-15-043-H04-T

To receive CPE credit you must complete the quiz and evaluations on page 40 & 42