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- A Review of USPSTF Recommendations for Use of Novel Markers in Risk Stratification
- Risk Stratification of Dyslipidemia in the Pediatric Population

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Part of the great appeal of lipidology is the rapidly changing science and the translation of that science into clinical practice. One recent example is proprotein convertase subtilisin/kexin type 9 (PCSK9), a convertase that coordinates LDL catabolism by chaperoning the LDL-receptor into the hepatocytes for degradation. PCSK9 (originally neural apoptosis-regulated convertase 1, or NARC-1) was first linked to LDL catabolism in 2003 and, in only seven years, human trials have been initiated to evaluate the potential benefits of utilizing anti-PCSK9 antibodies to reduce LDL-C levels. After a few major disappointments, the pipeline for new lipid-altering therapies and anti-atherosclerotic agents has grown significantly during the past few years. In addition, because of the international epidemic of obesity and associated dyslipidemia, the NLA is uniquely positioned as the best professional organization to address unmet educational needs, as has been recognized by the global medical community. For these reasons, excitement for the field of lipidology and the role of the NLA has grown dramatically during the past few years.

The NLA is gearing up for a new wave of educational programs to continue its leadership role in bringing the latest scientific advances to clinicians in an evolving area of medicine. On the international front, the NLA offered Masters in Lipidology™ programs in October in India and Australia. Additional international educational programs are being developed and will be initiated in 2011. To keep up with the expanding new science in lipidology, we are planning a new Masters course focusing on HDL prior to the national NLA meeting in New York City in May 2011. This course will focus on those certified in lipidology and will be one of the first efforts to meet anticipated criteria for maintenance of certification requirements.

Novel therapies for familial hypercholesterolemia (FH) may be approved by the Food and Drug Administration (FDA) in the next year, and the Foundation of the NLA is funding a public awareness program to highlight the need for better screening and referral of FH patients to specialists who can provide the best care for these difficult-to-treat patients. Our primary care education programs regarding cardiometabolic risk and outreach to other organizations, such as the Preventive Cardiovascular Nurses Association (PCNA), the American Society of Hypertension (ASH) and the Obesity Society, continue to progress.

As your president, I look forward to hearing your feedback. The field of lipidology has never been more exciting and the NLA, as a relatively new organization, has made tremendous strides in developing the professional clinical lipidologist. As the field continues to become more complicated, the medical community will look to us to translate these scientific advances into practice. Let me know how you feel we can best meet the great challenges ahead. Stay tuned, because 2011 will be a year of great opportunity.
From the SWLA President:  
Chapter to Embark on Two Key Initiatives

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Discuss this article at www.lipid.org  
Go to “Topics/Lipid Spin” and look for “Chapter to Embark on Two Key Initiatives.”

It is a privilege and a pleasure for the Southwest Lipid Association (SWLA) to author this issue of the Lipid Spin. Our chapter encompasses the states of Arizona, Colorado, Montana, Louisiana, New Mexico, Oklahoma, Texas and Wyoming, and we have had the fortune of welcoming more than 60 new members this past year.

In this issue, I would like for colleagues to take note of the case study regarding LDL and Lipoprotein(a)-apheresis. Our membership is keenly aware that there are many options for treating patients with familial hypercholesterolemia, and the procedure outlined in these pages by Drs. Deepti Bulchandani, James Falko and Patrick Moriarty constitutes a viable option for many.

Reflecting on the year-to-date, our members have taken initiative in educational events of regional interest, including, among others:

- Co-hosting the Winter Clinical Lipid Update in San Francisco this past February with the Pacific Lipid Association;
- Launching the inaugural “How to Avoid a Heart Attack” Symposium, which took place in Denver in June and was established by longtime SWLA member Dr. Tom Haffey; and
- Participating with the Lifestyle Working Group at NHLBI, which oversees the evidenced-based impact of lifestyle on CVD risk and is chaired by SWLA member Dr. Robert Eckel.

Looking ahead, SWLA is poised to lead two main initiatives for the coming year: 1) Developing educational programs for providers and the general population throughout the region; and 2) Expanding the breadth of the chapter, focusing on pediatrics and mid-level providers.

National Health and Nutrition Examination Survey (NHANES) data has shown that awareness of dyslipidemia is high but treatment, even in high-risk groups, rarely exceeds 50 percent of the at-risk population, with less than 50 percent of those at target. Realizing that most providers know the lipid targets, the SWLA Chapter’s goal is to expand the understanding of reasons why individuals do not get to goal and to teach strategies that facilitate attaining appropriate targets.

An important component of attaining and maintaining an individual at goal is the combination of compliance and adherence; thus, we are developing population-based programs to educate patients about the need for long-term treatment to help prevent stroke, heart attack and death.

Success in our first goal will require that we address the second goal, which is to work closely with our colleagues in pediatrics to expand screening and treatment of lipid disorders as the epidemic of obesity in children and adolescents grows.

To succeed we will need the assistance of the many nurse practitioners (NP’s) and physician assistants (PA’s) who express interest in clinical lipidology. We are working hard to increase membership and involvement from individuals throughout our region’s pediatric community.

An excellent time to invite new pediatric colleagues to join us will be in March 11–13, 2011, when SWLA co-hosts the Spring Clinical Lipid Update in Austin, Texas. ■
Our approach to the patient with a lipid disorder is based on a time-tested model utilized pervasively in the practice of internal medicine. The patient is evaluated, diagnosed and then treated. An individualized treatment strategy is then created after considering the diagnosis and context in which that diagnosis presents. For some reason, however, this approach appears to be uncommon. The evaluation of the patient with a lipid disorder all too often is made in a manner that would be considered substandard were it applied to any other area of internal medicine.

Imagine the following scenario: A patient presents to a clinic complaining of sweats and chills. Based solely on this reported history, the treating practitioner assumes these must be symptoms of fever, prescribes aspirin, and sends the patient on his way. While this approach seems far-fetched, it is played out over and over again in the management of lipid disorders.

Routinely, when we perform an initial evaluation of the dyslipidemic patient, we ask the simple question, “What is your diagnosis?” Rarely does the patient know the answer. This interrogatory might seem to be placing an undue burden on the patient; after all, how many patients know whether the cause of their hypothyroidism is autoimmune thyroiditis, or whether their anemia is the result of a hemoglobinopathy? If it is considered unreasonable that a patient should know his or her diagnosis, then how about referring practitioners? In a referral-based setting, shouldn’t there at least be a diagnosis on the chart? Or even presumptive reasoning from the referring practitioner? Sadly, when it comes to lipid disorders, this too is rarely the case. The most common referral we see is “elevated cholesterol.”

So you may query, “Is elevated cholesterol a diagnosis?” We contend it is not. Just as “fever” and “anemia” are not legitimate diagnoses—they are consequences of disease processes—hyperlipidemia is also the result of a disease process that causes the lipid abnormality. Our teaching, therefore, focuses on a diagnosis-based lipid evaluation in the context of a solid cardiovascular risk assessment to yield a proper plan for care.

Liberopoulos, et al. recently reported an unusual case of a patient with new-onset hyperlipidemia. The ultimate diagnosis was multiple myeloma-induced amyloidosis of the kidney causing nephrotic syndrome with lipid abnormalities. While multiple myeloma is clearly not a common cause of dyslipidemia, the case serves to demonstrate the importance of making a diagnosis in the evaluation of the lipid patient. We have come to know that patients with elevated LDL cholesterol (LDL-C) are not always at increased risk for cardiovascular disease, and those with low LDL-C may indeed be at high risk for cardiovascular disease. Even in the presence of low LDL-C, elevated...
Apolipoprotein B (Apo B) containing lipoproteins impact cardiovascular risk. Thus, lipoproteins have moved to the forefront of lipidologists’ evaluation and treatment paradigms. Similarly, high HDL cholesterol (HDL-C) levels have been shown to have anti-atherogenic effects in some and pro-atherogenic effects in others. We now understand that the effects of HDL extend way beyond HDL-C levels. Finally, the role of elevated triglycerides continues to evolve. For a very long time, patients with severely elevated triglyceride syndromes were assumed to be at low risk for cardiovascular disease. We now know that, in some cases, these patients can develop fatty liver, insulin resistance, dyslipoproteinemia and cardiovascular disease above and beyond their risk for pancreatitis. Additionally, patients with moderately elevated triglycerides and low HDL-C exhibit increased cardiovascular risk independent of their low or normal LDL-C levels, often because of elevated levels of Apo B containing lipoproteins.

Every evaluation of a lipid clinic patient should include a diagnostic approach that falls in line with the accepted evaluation and treatment of all other disease states treated by medical practitioners. How could we prescribe appropriate antibiotics if we do not know the cause of an infection? Indeed, the management of an infection requires substantial modification under a number of special circumstances: an immunocompromised state, renal or hepatic disease, or a recent hospitalization. Other important questions to answer include: Is the fever from cancer, exposure or autoimmune disease? Treating the underlying cause is tantamount to understanding the prognosis and implementing a sensible therapeutic plan.

In our clinic we first describe the dyslipidemia. This is a phenotypic description, utilizing the Fredrickson criteria. Once the dyslipidemia has been described—and this includes lipids and lipoproteins—we proceed with a multi-axis diagnostic approach to explain the underlying cause of the abnormality. We consider genetics, then lifestyle, followed by secondary disease states, iatrogenic causes (medications or other treatments), followed by causes such as the surreptitious use of alcohol, supplements, etc.

This approach serves many purposes. First, it returns us to the fundamentals of internal medicine, refocusing the evaluation on a diagnosis and underlying cause. Second, it serves to identify other potentially life-threatening diseases that may need treatment, such as diabetes, renal, hepatic or even neoplasm. Finally, it reminds us that we cannot treat lipids in a vacuum. Co-morbid conditions such as diabetes, cardiovascular disease and hypertension may require the use of different medications because of a patient’s particular lipid diagnosis. Most important, however, is the information that this diagnostic pathway gives us about risk. We treat lipids for two primary reasons: to reduce the risk of pancreatitis and to reduce the risk of cardiovascular events. To accomplish the latter, we must first accurately assess a person’s cardiovascular risk. The diagnosis itself often imparts risk independent of the lipid or lipoprotein values. Treating someone without first obtaining this information would be like driving a vehicle while wearing a blindfold.

Once a diagnosis has been established, risk can then be assessed by incorporating this information into other currently available “calculators” such as the Adult Treatment Panel III (ATP3), Framingham, Reynolds, or lifetime risk scores. Understanding risk and diagnosis also helps us determine our lipid and lipoprotein goals. Only with this information in hand can we intelligently move forward with treatment interventions. This, in many cases, will be treating an underlying condition, changing medications that may be causing dyslipidemia or focusing on lifestyle changes. Seeing a single case of a young man with low HDL-C from androgenic steroid abuse is enough to remind us that simple changes and interventions can often yield dramatic long-term health benefits.

A proper diagnostic approach to dyslipidemia is a simple application of fundamental medical evaluation and treatment processes that enable us to determine the cause, risks and best intervention strategies to improve the health and well-being of our patients. It is time to go “back to the future” and approach dyslipidemia as we do every other disorder. What would Dr. House, chief of “diagnostic medicine” do? He would start with a differential diagnosis. And so should we.

References listed on Page 40.

“A physician is obligated to consider more than a diseased organ, more even than the whole man—he must view the man in his world.”

—Harvey Cushing
Lovaza® Is Not the Only Fish Oil Containing Concentrated and Purified EPA and DHA

Note from the Editors—Dr. Seth Baum submitted the following letter regarding the article, “PLA Chapter Update: Prescription Fish Oil and Blue Cross of Idaho” from the Summer 2010 issue of the Lipid Spin (Page 32, Volume 8).

In regard to the Summer 2010 Lipid Spin article “Prescription Fish Oil and Blue Cross of Idaho,” the case was made that Lovaza® is inherently different from all other non-prescription brand fish oils. This requires clarification. The authors state, “dietary supplement fish oil contains a high percentage of non-omega-3 material such as saturated fat… environmental contaminants including pesticides and heavy metals” and “Lovaza® is the only omega-3 product properly purified, tested and indicated for any lipid disorder.” They also state, “Manufacturers of dietary supplements are regulated under the CGMPs used for food products, which only regulate the preparation, packaging and holding of dietary supplements under safe conditions. Thus… there is no guarantee that what’s on the label is in the bottle.”

However, the authors later acknowledge that as of 2010, “The FDA announced a final ruling establishing dietary supplement CGMP requirements, which will require manufacturers to evaluate the identity, purity, quality, and strength of their products.” In other words, the FDA now demands that what is written on a supplement’s label must be in the bottle.

While it is true that Lovaza® is the only omega-3 fish oil product with an indication to treat a disorder, specifically triglycerides over 500 mg/dL, the converse of this is also true—Lovaza® is not indicated for primary or secondary prevention, or for the management of triglycerides that are less than 500 mg/dL. Any prescribing by physicians that strays from this single FDA indication constitutes off-label use. Unfortunately, the vast majority of Lovaza® scripts are written off-label, unnecessarily costing our already overburdened healthcare system hundreds of millions of dollars.

We all prescribe drugs off-label, but only when there is no reasonable substitute. When it comes to fish oils, there are first-rate alternatives. From a triglyceride-lowering standpoint, DHA and EPA have the same impact; there is an approximately 8 percent reduction in TGs for every 1,000 mg combined EPA+DHA consumed. From an anti-inflammatory standpoint, the same holds true: Whether DHA and EPA exist in Lovaza®, a supplement, or in fish, they are the same. As far as the American Heart Association (AHA) and the European Society of Cardiology (ESC) are concerned, it doesn’t matter which fish oil pill you choose; just be sure to get enough EPA and DHA.

But can we be sure that a given alternate fish oil supplement has been adequately purified? To be assured of a particular fish oil’s contents and quality (under USP guidelines) one can simply refer to the independent organization that is recognized as the watchdog of the supplement world, ConsumerLab.com. On their website, you will find a number of oils that can be safely used for your patients’ “off label” needs. And, is it true that “From six to sixteen capsules per day would be required as an equivalent dose [to four Lovaza® pills]?” No, it is not. In fact, one fish oil supplement contains 160 mg more EPA and DHA per pill than Lovaza®.

In sum, to treat patients with TGs over 500, Lovaza® is a great choice. I suggest that in other circumstances, using the best supplement brand fish oil is safe, meets AHA and ESC guidelines, and results in far less cost.

—Seth J. Baum, MD, FACC, FACPM, FAHA, FNLA
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Disclosure statement: Dr. Baum founded VitalRemedyMD, a company that manufactures fish oil supplements.
Clinical Feature: The Upcoming ATP IV Guidelines

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Discuss this article at www.lipid.org
Go to “Topics/Lipid Spin” and look for “The Upcoming ATP IV Guidelines.”

The highly anticipated fourth version of the National Cholesterol Education Program (NCEP) expert panel on high cholesterol—Adult Treatment Panel (ATP) IV—will be available in early 2011, 10 years after ATP III1 was first published and seven years after the ATP III revised update.2 A wealth of intervening evidence from lipid-lowering trials and large cohorts have accumulated over this period and lead to natural assumptions about the most significant changes to be emphasized in ATP IV. Likely major differences from ATP III will broadly include modifying risk estimation of coronary heart disease (CHD) risk and more aggressive treatment of those at elevated CHD risk.

Assessing CVD Risk
The NCEP-ATP III initial report published in 20011 emphasizes using traditional risk factors such as age > 45 for men and > 55 for women, male sex, hypertension, smoking, low HDL cholesterol (HDL-C), and family history of premature CHD to characterize an individual’s CHD risk. If more than one risk factor is present, the guideline recommends calculating the Framingham Risk Score (FRS)2 for estimating the short-term (10-year) risk of developing a CHD event and treating subjects based on their risk category (low: 0-9 percent, intermediate: 10-20 percent, and high: > 20 percent). For high risk subjects or patients with existing CHD or a CHD equivalent, the LDL cholesterol (LDL-C) goal is < 100 mg/dL with an optional goal for < 70 mg/dL based on the ATP III update published in 2004.3 Patients with diabetes or peripheral vascular disease are considered CHD risk equivalents and treated to the same goals. The LDL-C goal for intermediate risk individuals, which constitute a sizeable portion of middle-aged Americans, is < 130 mg/dL.

Despite these advances using the ATP III risk assessment algorithm, significant numbers of individuals who develop CHD events are categorized as low or intermediate risk by the FRS and do not receive recommendations for therapeutic lifestyle changes (TLC) or initiation of lipid-lowering therapies.4 This paradox is most accentuated in the young and in women who are invariably classified as low risk by the FRS.5, 6 Since ATP III, the Reynolds Risk Score (RRS) has been developed to improve risk estimation beyond the FRS and may be recommended as an optional alternative risk assessment tool in ATP IV.7
The RRS was initially developed for use in women and derived from almost 25,000 mostly white female health professionals age > 45 (median age 52) participating in the Women’s Health Study (WHS). A simplified model of seven risk factors, including age, systolic blood pressure, total cholesterol, HDL-C, smoking, high-sensitivity C-reactive protein (hs-CRP), and parental history of premature myocardial infarction (MI) showed improved risk estimation beyond the FRS in those with a FRS between 5-19 percent. A similar RRS has been developed for men.8 The RRS differs from the FRS by incorporating hs-CRP and parental history of premature MI, and is available as a simple web-based calculator at www.reynoldsriskscore.org. Limitations of the RRS include lack of external validation and use of a non-population based cohort for derivation of risk estimates. Also, the RRS has minimal impact on women categorized as low-risk by the FRS (< 5 percent), which make up the majority of women in the U.S. population.9 The most recent guideline updates from the Canadian Cardiovascular Society also incorporate the alternative use of RRS for CHD risk estimation.10

Although ATP III provided brief mention of atherosclerosis imaging techniques to refine CHD risk assessment, including coronary calcium (CAC) and carotid artery intima media thickness (CIMT) testing, evidence for their improved clinical utility beyond the FRS was limited at the time of that report. Recent data have emerged demonstrating incremental benefit of CAC and CIMT,11, 12 including enhanced risk reclassification beyond the FRS. These studies will need further corroboration13 but will likely result in stronger endorsement in ATP IV for the optional use of these imaging modalities in intermediate risk individuals for refining CHD risk.

Perhaps the simplest way to capture those at increased risk is to expand the intermediate risk range from FRS of 10-20 percent to 6-20 percent. Part of the justification for restricting the intermediate risk group to the 10-20 percent range in ATP III was enhanced cost-effectiveness of statins at this level of risk. However, the widespread availability of generic statins favors expanding their indication using this metric. In addition, several studies show that individuals with a FRS of 6-9 percent have similar surrogate markers of CVD risk as do those with 10-20 percent risk and that additional testing to refine risk has similar clinical utility across 6-20 percent risk.6, 7, 14, 15 The recently published JUPITER study assessing the impact of rosuvastatin 20 mg in healthy men and women with normal lipid levels and hs-CRP ≥ 2 mg/L demonstrated that the benefits of CHD risk reduction with high-potency statin therapy was extended to those with a FRS below 10 percent as well as those with no ATP III risk factors,16 supporting the concept that many of these “low risk” individuals may benefit from CHD risk reduction therapies by expanding the intermediate risk range from 10-20 percent to 6-20 percent. Whether or not an elevated hs-CRP is required to extend the use of statin therapy to seemingly “lower” risk subjects is not answered in the JUPITER study due to the lack of an arm with normal hs-CRP levels. Given the other unresolved controversies surrounding this trial, it seems unlikely that ATP IV will provide strong endorsement of hs-CRP testing in low risk individuals.13

A notable controversy that must be addressed in ATP IV is the focus on short term vs. lifetime risk of CHD. One-half of all men and one-third of women at age 40 will develop CHD during their lifetimes, and as many as half of all individuals under age 50 have low short-term but high lifetime risk of CVD, with a greater burden of subclinical atherosclerosis and higher atherosclerosis progression rates than those at low short term and low lifetime risk.17 Algorithms have been published suggesting approaches to calculation and communication of lifetime risk,18, 19 but none have been validated. Until further data are available, the panel may advocate for heightened awareness of the lifetime risk concept, with more aggressive lifestyle promotion, and possibly a lower threshold
for preventive therapies for those at high lifetime CHD risk. The lifetime risk concept may be particularly useful in women, who have high lifetime risk but are often under-treated based on low short-term risk as calculated by the FRS.20

**Treatment Targets**

The ATP III update in 2004 was partially prompted by the publication of several trials supporting the concept of “lower is better” with further CHD risk reduction by more aggressive LDL-C reduction that went beyond 100 mg/dL in high risk individuals and 130 mg/dL in intermediate risk subjects. That document recommended the “optional” goal LDL-C of < 70 mg/dL and <100 mg/dL for those at high and intermediate risk, respectively. Since then several randomized controlled trials of patients status-post acute coronary syndrome as well as those with stable CHD show consistent reductions in CHD events when using a high-potency statin and achieving an LDL-C of ~60-80 mg/dL compared with using moderate-potency statins and achieving an LDL-C of ~100 mg/dL (Figure 1).21 Further evidence of a continuous effect of lipid-lowering on CHD risk comes from angiographic imaging studies that show actual coronary atheroma regression once LDL-C levels are lowered beyond 80 mg/dL with high-potency statins (Figure 2).22 This continuous effect of CHD risk reduction with LDL-C lowering occurs even in intermediate risk subjects with average baseline LDL-C levels, with significant CHD risk reductions of 21 percent in the ASCOT study23 and 44 percent in the JUPITER study (Figure 3).16 No concerning safety signals have emerged with intensive LDL-C lowering. Thus, it is likely that ATP-IV will remove the “optional” wording and strongly recommend targets of LDL-C < 70 mg/dL for high risk individuals and LDL-C < 100 mg/dL for all intermediate risk subjects based on the accumulated evidence.

Alternative treatment targets other than LDL-C such as non-HDL-C cholesterol and apolipoprotein B (ApoB) have been studied and incorporated in recent updated guidelines by the respective Canadian10 and European societies44 as well as by the 2008 Consensus Report by the American Diabetes Association and the American College of Cardiology Foundation.25 Non-HDL-C was identified as an alternative treatment target in ATP III once LDL-C goals were achieved or if fasting triglycerides were above 200 mg/dL. Accumulating evidence has shown superiority of ApoB levels as a lipid measure in assessing both risk and response to therapy;26 however, clinical testing for ApoB has not become widespread in the U.S. In contrast, non-HDL-C is easily calculated from a standard lipid panel and does not require fasting status. With the increasing prevalence of obesity, metabolic syndrome, and diabetes, the prevalence of elevated triglycerides has also increased, decreasing the accuracy of LDL-C calculation by the Friedewald formula. We anticipate that ATP IV will strengthen its recommendation and advocate for the use of non-HDL-C as an equivalent treatment target along with LDL-C, with goals 30 mg/dL higher than LDL-C targets, to facilitate measurement in the clinic and rapid determination of need for lipid-lowering and response to therapy. In ATP III, the last step (Step 9) in the risk assessment and treatment algorithm included low HDL-C both as a risk factor for ischemic heart disease and as an atherogenic marker.

**Figure 2. Atherosclerosis regression with intensive lipid lowering: ASTEROID.**

**Figure 3. Intensive LDL lowering reduces CHD events in primary prevention.**
factor and potential treatment target once LDL-C and non-HDL-C goals were reached. It also focused on non-HDL-C as a therapeutic target in the setting of elevated triglycerides, rather than triglyceride levels per se. While the evidence is robust for the associations between HDL-C and triglycerides and CHD risk, evidence that directly targeting these lipid fractions will result in CHD risk reduction independent of LDL-C lowering is lacking.27 We suspect that ATP IV may follow their Canadian and European counterparts and de-emphasize HDL-C (and triglycerides) as treatment targets but rather as indicators of metabolic syndrome and other risk factors that can be directly modified.

Treatment Therapies
The ATP III guidelines listed several different drug classes affecting lipid metabolism and did not hierarchically promote any particular class of drugs to achieve LDL-C and non-HDL-C targets. While it is clear that multiple drugs can effectively lower LDL-C and/or non-HDL-C, including statins, fibrates, niacin, omega-3 fatty acids, and cholesterol-absorption inhibitors, statins have the most robust randomized clinical trial evidence for their efficacy in reducing CHD events.28 At the same time, recent impactful randomized trials involving statin therapy did not specifically test various LDL-C goals, but rather various statin potency strategies. The agent used in randomized controlled trials of intensive lipid-lowering in high-risk patients was uniformly atorvastatin 80 mg versus less potent statins and doses. In addition, statin trials involving low to intermediate risk subjects such as ASCOT23 and JUPITER16 demonstrated improved outcomes with the strategy of statin use (10 mg of atorvastatin and 20 mg of rosuvastatin, respectively) versus placebo without titration to any pre-specified LDL-C targets.

In addition to providing concomitant more stringent LDL-C targets, it is probable that ATP IV will advocate for up-front treatment with a high-potency statin (atorvastatin 80 mg or equivalent) in all patients at high risk (FRS > 20 percent or CHD risk equivalent) as well as “consideration” for up-front treatment using at least moderate-potency statins in all intermediate risk individuals (FRS 6-20 percent) regardless of baseline LDL-C. The Canadian and European updated guidelines10, 24 do not recommend fibrates (except for fasting triglyceride > 500 mg/dL) or niacin, given the lack of compelling evidence, and we anticipate that ATP IV will highlight this lack of evidence for adjunctive therapies29 and give clinical equipoise to bile-acid sequestrants, fibrates, and niacin as well as omega-3 fatty acids and cholesterol-absorption inhibitors as options in those who have not met their LDL-C or non-HDL-C goals on maximum potency statin, or who continue to have significant metabolic abnormalities and increased risk.

Conclusion
The last several years since the 2004 update to ATP III have seen exciting advances in the application of lipid lowering therapies and efforts to reduce CHD risk. We have highlighted several anticipated modifications in ATP IV due in 2011 related to: 1) improved CHD risk estimation by expanding the intermediate risk group from FRS 10-20 percent to 6-20 percent, consideration of alternative risk assessment algorithms such as the Reynolds Risk Score, especially in women, and use of additional biomarkers such as hs-CRP and atherosclerotic imaging such as CAC and CIMT in intermediate risk subjects to further refine risk; 2) emphasizing lower LDL-C targets in all individuals with any increased CHD risk and consideration of non-HDL-C as an alternative primary target; 3) de-emphasizing triglyceride and HDL-C as targets of therapy; and 4) emphasizing high-potency statin therapy for individuals at high risk and up-front statin use in all those at intermediate risk to maximize CHD risk reduction and attainment of LDL-C and non-HDL-C goals.

References listed on Page 40.

Disclosure Statement:
Dr. Khera has received honoraria related to consulting from Daiichi Sankyo. Dr. Rohatgi has no relevant disclosures.

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<tr>
<th>FRS ≤ 5 percent Low risk</th>
<th>• Recommend periodic CHD risk assessment every 3-5 years</th>
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<tr>
<td>FRS 6-20 percent Intermediate risk</td>
<td>• Consider using the Reynolds Risk Score or atherosclerotic imaging (CAC or CIMT) to further refine CHD risk</td>
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<td></td>
<td>• Recommend up front TLC and statin therapy to achieve LDL-C &lt; 100mg/dL and non-HDL-C &lt; 130 mg/dL with a goal of 40-50 percent lipid lowering</td>
</tr>
<tr>
<td>FRS &gt; 20 percent High risk (or CHD equivalent)</td>
<td>• Recommend up front TLC and high-potency statin therapy to achieve LDL-C &lt; 70mg/dL and non-HDL-C &lt; 100 mg/dL with a goal of 40-50 percent lipid lowering</td>
</tr>
<tr>
<td></td>
<td>• Use triglyceride and HDL-C levels as indicators of modifiable risk factors but not as treatment targets</td>
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<td></td>
<td>• Emphasize global CVD risk reduction with statin therapy given the widespread availability of generic statins and robust randomized clinical trial evidence</td>
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FRS = Framingham Risk Score  TLC = Therapeutic lifestyle change  CIMT = Carotid intima media thickness  CHD = Coronary heart disease  CAC = Coronary Calcium

Table 1. Anticipated key modifications in ATP IV.
Cardiovascular disease (CVD) is the leading cause of morbidity and mortality in the United States. Evidence now indicates that the atherosclerotic disease process begins in childhood, is progressive throughout life, and the rate of progression is greatly increased by lipid abnormalities and their severity. Children and adolescents with high cholesterol levels are more likely than the general population to have high levels when they become adults. The growing epidemic of overweight/obesity in children and adolescents has been shown to be associated with an increase in other CVD risk factors, suggesting a need for screening and early intervention to prevent an epidemic of CVD in the young adult population.

Autopsy studies performed in young subjects such as Pathobiological Determinants of Atherosclerosis in Youth (PDAY) found that cardiovascular risk factors such as elevated cholesterol and blood pressure were associated with the extent of fatty streaks and fibrous plaques in the aorta and coronary arteries. The Bogalusa Heart Study found that the prevalence and extent of atherosclerotic lesions increased with age and correlated with elevations in total cholesterol, LDL cholesterol, triglycerides, blood pressure and body mass index, as well as lower concentration of HDL during childhood and an exponential rise in the extent of atherosclerotic lesions was seen with increasing number of risk factors. Ultrasound has been used to non-invasively assess the thickness of the intimal media thickness (IMT) within the carotid arteries as an indicator of the
atherosclerotic process. The Muscatine Study showed that increased carotid IMT on carotid ultrasonography in adults aged 33 to 42 years was associated with increased total cholesterol and high blood pressure in childhood. The Cardiovascular Risk in Young Finns Study showed a positive correlation of CVD risk factors in adolescence with carotid IMT in adulthood. While these studies demonstrate the need for early intervention to prevent the progression of atherosclerosis, the question of whether to recommend universal screening in the pediatric population remains open.

Unlike the adult population, there are no universally accepted clinical screening tools or risk scores to estimate CV risk in children and adolescents.

One possible framework that could be applied to the pediatric population is the metabolic syndrome, which is a clustering of risk factors for CVD that are associated with multiple metabolic abnormalities, including, obesity, insulin resistance, fatty liver, elevated uric acid, and diabetes. Asymptomatic coronary and aortic atherosclerosis in young persons in the Bogalusa Heart Study were directly related to the number of cardiovascular risk factors clustered under the metabolic syndrome. Although there is no consensus as to criteria for metabolic syndrome in children and adolescents, age appropriate percentiles are an option for identifying metabolic abnormalities, thus facilitating the identification of those who will be at increased risk for CVD as adults. Screening for dyslipidemia may be a reasonable addition to regular health maintenance visits in at-risk children and adolescents.

Existing guidelines for screening and management of lipoprotein abnormalities are based on the National Heart, Lung and Blood Institute’s National Cholesterol Education Program (NCEP) on blood cholesterol levels in children and adolescents. It was published in 1992 and subsequently adopted by the American Academy of Pediatrics (AAP), with a clinical update in 2008. Screening by means of a fasting lipid profile is recommended in children and adolescents with a positive family history of premature CVD (parent or grandparent; < 55 years of age for men and < 65 years of age for women) or a parent with a history of high cholesterol level (> 240 mg/dL). It is also recommended that pediatric patients for whom family history is not known or those with other CVD risk factors, such as overweight (BMI > 85th percentile, < 95th percentile), obesity (BMI > 95th percentile), hypertension (blood pressure > 95th percentile), cigarette smoking, or diabetes mellitus, be screened with a fasting lipid profile. For these children, the first screening should take place after two years of age. Screening after 10 years of age should account for the normal decline in LDL-C seen with puberty. Screening before two years of age is not recommended. If values are within the reference range on initial screening, the patient should be retested in three to five years. Children with Type 2 diabetes should be screened at diagnosis after achieving glycemic control, regardless of age and screening should be repeated every two years if the initial screen is normal. Once dyslipidemia is identified, therapeutic lifestyle changes are strongly emphasized as pharmacologic therapy may not be required at these early stages if a healthy lifestyle can be implemented and maintained.

Based on recognition that elevated LDL cholesterol levels had a strong correlation with the development of coronary disease

<table>
<thead>
<tr>
<th>Adiposity: Abdominal Circumference or BMI</th>
<th>Fasting Plasma Glucose or OGTT glucose</th>
<th>Systolic Blood Pressure or Diastolic Blood Pressure</th>
<th>HDL Cholesterol (mg/dL)</th>
<th>Triglycerides (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AC ≥ 90th percentile</td>
<td>Fasting plasma glucose ≥ 110</td>
<td>≥ 90th percentile</td>
<td>≤ 40</td>
<td>≥ 110</td>
</tr>
<tr>
<td>AC ≥ 75th percentile</td>
<td>Fasting plasma glucose ≥ 110</td>
<td>&gt; 90th percentile</td>
<td>&lt; 50</td>
<td>≥ 110</td>
</tr>
<tr>
<td>BMI z score ≥ 2.0</td>
<td>2 hour OGTT Glucose 140-200</td>
<td>&gt; 95th percentile</td>
<td>&lt; 5th percentile</td>
<td>&gt; 95th percentile</td>
</tr>
</tbody>
</table>

Table 1. Proposals for the Metabolic Syndrome criteria in children and adolescents.
in adults, the NCEP guidelines published in 1992\textsuperscript{11} recommended two strategies to lower elevated cholesterol levels in children and adolescents: a population-based approach and a targeted approach. This general strategy has been maintained and food and salt.\textsuperscript{14,15} The intake of trans fatty acids (major source being partially hydrogenated fats used in fried foods) is to be restricted to < 1 percent of total calories per the new guidelines\textsuperscript{14,15} as trans fatty acids have been shown to increase fat < 7 percent of total calories) initially upon confirmation of hyperlipidemia instead of previous recommendations which suggested a progression from AHA Step 1 to Step 2 Diet.\textsuperscript{11,17} Resins (bile acid sequestrants) continue to be

<table>
<thead>
<tr>
<th>Age Group (years)</th>
<th>Obesity (Waist Circumference)</th>
<th>Triglycerides</th>
<th>HDL-C</th>
<th>Blood Pressure</th>
<th>Glucose (mmol/L) or Known T2DM</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 to &lt; 10</td>
<td>≥ 90\textsuperscript{th} percentile</td>
<td>Metabolic syndrome cannot be diagnosed, but further measurements should be made if there is a family history of metabolic syndrome, T2DM, dyslipidemia, cardiovascular disease, hypertension, and/or obesity.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10 to &lt; 16</td>
<td>≥ 90\textsuperscript{th} percentile or adult cutoff if lower</td>
<td>≥ 1.7 mmol/L (≥ 150 mg/dL)</td>
<td>&lt; 1.03 mmol/L (&lt; 40 mg/dL)</td>
<td>Systolic ≥ 130 mm Hg or diastolic ≥ 85 mm Hg</td>
<td>≥ 5.6 mmol/L (100 mg/dL) (or known T2DM)</td>
</tr>
<tr>
<td>16+</td>
<td>Use existing IDF criteria for adults</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

HDL-C: High Density Lipoprotein Cholesterol; T2DM: Type 2 Diabetes; OGTT: oral glucose tolerance test

Table 2: The IDF definition of the at-risk and the metabolic syndrome in children and adolescents. \textsuperscript{23}

LDL concentration.\textsuperscript{16} The individual or targeted approach focuses on children and adolescents at high risk such as those with family history of CVD or dyslipidemia or personal history of dyslipidemia or CVD risk factors. This would involve a higher level of dietary intervention (dietary cholesterol < 200 mg/dL and < 7 percent of total calories from saturated fat) and drug therapy for lowering LDL cholesterol is recommended in children > 10 years of age whose LDL cholesterol remains elevated after an adequate 6-12 month trial of dietary therapy.

Implementation of such a dietary intervention would require dietary counseling and changes in the home environment and motivation from all family members to make healthy food choices. The ADA consensus statement on the management of dyslipidemia in children and adolescents with diabetes\textsuperscript{12} recommends the AHA Step 2 Diet (dietary cholesterol < 200 mg/dL and saturated recommended as first choice treatments for this age group—however, compliance is very poor. Statins are now an option for individuals eight years and older as there is now clinical trial data demonstrating their short-term efficacy and safety in adolescents.\textsuperscript{18,19} The initial goal of statin therapy is to lower the LDL-C to < 160 mg/dL, while the lower target of 130 or even 110 may be considered when there is a strong family history of CVD, especially with other risk factors including obesity, diabetes mellitus, metabolic syndrome, and other higher-risk situations.

References listed on Page 40.

Disclosure Statement: Drs. Karanchi, Daniels and Wyne have no relevant disclosures.
After history, physical exam, basic lab and application of the Framingham Risk Score, long-term preventive concerns and immediate cardiovascular care concerns prompt me to ask additional questions, both initially and, often, in follow-up. Are there additional risk factors for development or progression of atherosclerosis? Is there increased probability of atherosclerotic events? Is there ischemia? If there is no evidence of ischemia, is there actual evidence of atherosclerosis? The answers to these questions may lead to risk reclassification, most usefully and most often in intermediate-risk patients but sometimes even in the low- or high-risk patients; those answers, therefore, may alter my approach to the patient’s management.

The relevant history affecting Adult Treatment Panel III (ATP III) defined risk status should include myocardial infarction (MI), stroke, transient ischemic attack (TIA) and heart failure, especially if these can be documented. Angina, claudication, or focal neurologic symptoms, and family history of atherosclerotic disease or major risk factors all, to varying degrees, influence the assessment of risk for my patient.

**Is There Evidence of Atherosclerosis?**
If the asymptomatic patient has none of the standard risk factors, no history of atherosclerotic events, and no family history of atherosclerotic events, I generally do not look further for evidence of atherosclerosis. I make a distinction, however, between no risk and low risk and, in a low-risk patient, generally will look further, non-invasively, for evidence of atherosclerosis that may reclassify the risk status. I also use these studies for risk recategorization in an intermediate-risk patient. In high-risk patients, I use these studies for possible reclassification and to get a better idea of the extensiveness of their atherosclerotic involvement; in very-high-risk patients, these studies help me appreciate the extensiveness of the atherosclerotic disease at this and future times.

If justified by relevant history or physical findings, carotid duplex ultrasound (CDU) is useful, not just to evaluate degree of stenosis but to look for evidence of atherosclerotic plaque, calcified or not, major or minor, and to measure carotid intima media thickness (CIMT). If CDU is not justified by codeable diagnoses, screening CIMT can be done very inexpensively. If done carefully, CIMT can show significant thickening for age and gender, and I at least increase my estimate of long-term atherosclerotic risk. Significant thickening alone or a mild amount of plaque is unlikely to increase my treatment aggressiveness in an older patient, but it does increase the aggressiveness of my preventive treatment in younger patients. I do not use this information, however, to lower the pre-test estimate of risk.

Ankle-brachial index (ABI) can be done at no or minimal additional cost in the course of the physical exam. If abnormal, I take this as an indication of atherosclerotic vascular disease, and this increases my estimate of risk. If the ABI is significantly abnormal, and/or the patient has significant relevant symptoms, I proceed with ultrasound segmental pressures to help evaluate the
I use the coronary artery calcification score (CACS) as another assessment of atherosclerosis. We do not yet have a quantitative way of adding this information to the risk calculation, but a score of more than 400 makes me reclassify an estimate from low or intermediate to high risk of atherosclerotic events and progression. A score of 100 to 400 would raise my risk estimate from low to intermediate. A score of anything between 1 and 100 raises at least my estimate of long-term risk; the younger the patient, the more weight I give that information.

The indications for computed tomography angiography (CTA) may be somewhat arguable but, if it is done, any degree of observed non-obstructive or minimally obstructive atherosclerotic plaque causes me to increase the risk estimate in ways similar to the CACS.

Is There Evidence of Ischemia?

Stress testing in its various forms—stress electrocardiogram, stress radio-nucleotide perfusion imaging, stress echocardiogram—is useful in looking for ischemia and, if done as exercise stress, in looking at overall functional capacity. Although an abnormal stress test implies the presence of ischemia and underlying atherosclerosis, I make clear to the patient that a normal stress response does not mean the absence of atherosclerosis. If a stress test is abnormal, even if arteriograms are indicated, I use the studies discussed above to evaluate the extensiveness of the atherosclerotic process in the coronary arteries and in the cerebrovascular and peripheral vascular systems.

Biomarkers of ischemia—troponin levels, for example—as such clearly are useful in evaluating for acute ischemia, but I do not order them in a stable outpatient. In the clinic setting, I may order a creatine kinase (CK) level to help evaluate skeletal muscle abnormality. If I order it as an indicator of myocardial ischemia, I should be asking for stat results for an acute care decision.

Biomarkers for Added Evaluation of Atherosclerotic Risk

I use additional biomarkers for possible risk status reclassification or to help explain why a patient has more disease than I would expect based on identified risk factors—if I think the information is likely to alter my treatment or long-term atherosclerosis surveillance of the patient. As with the imaging studies, I do not pursue added biomarker data in an asymptomatic patient with no standard risk factors. I also try to make a distinction between risk factors that have a proved or highly likely causative role versus those that are non-causative markers of risk.

I use high-sensitivity C-reactive protein (hs-CRP) as a marker of risk for atherosclerotic events, with remaining uncertainty about its role as a marker versus a cause of that risk. Because inflammation or infection generally can affect the CRP level, and because the direct causative role is not clearly proved, I do not include it as a target of treatment in a person with low risk and no evidence of atherosclerosis. I do use its elevation as a reason to further lower the LDL cholesterol in patients in intermediate- and high-risk categories after repeating the measure at least once more, preferably twice. This is important because of the multiple factors than can alter the level.

Lipoprotein-associated phospholipase A2 (Lp-PLA2) appears to play a direct role in plaque inflammation, and I include this in the assessment of patients in intermediate- and high-risk categories to help further guide the intensity of LDL reduction and sometimes in deciding at what interval to repeat an atherosclerosis study such as CDU.

In all patients except those with low risk and no evidence of arteriosclerotic cardiovascular disease (ASCVD), I order Lp(a) testing to add to the risk assessment and to help guide my decision about using niacin and how far to uptitrate that medicine. In a small number of patients with evidence of disease progression in spite of aggressive medical treatment, a high Lp(a) level may be a reason for me to consider treating with LDL apheresis, a very effective way of lowering Lp(a).

Apolipoprotein B (Apo B) and LDL particle number appear to have greater predictive value than LDL-C, and I use one or the other in initial assessment of intermediate- and high-risk patients and, subsequently, to help decide whether to push beyond what I think is optimal LDL treatment once that is achieved. This latter reason generally is what prompts me to look at more detailed lipid particle analysis.

As more biomarkers of atherosclerotic risk become available, the question I will keep in mind is whether it will alter my treatment or surveillance of the patient.

Lastly, three thoughts: Sometimes the practicality of third-party insurance coverage makes me compromise what I consider to be the ideal approach to a patient. I sometimes use a piece of imaging datum or biomarker datum to help persuade a patient to be as aggressive in managing his disease as I think he should be. It is important to make sure the patient understands the limitations of negative/normal findings when some level of risk already has been established. ■

Disclosure Statement: Dr. Rubenstein has no relevant disclosures.
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When staff at the Methodist Hospital Medical Weight Management Center encountered a patient who desperately needed to shed weight for a heart transplant, they knew much was at stake. The patient had abused his body for decades, and their program presented his only option on a route to an untimely death.

Their mission? Help the 60-year-old man safely lose 60 lbs. over the course of three-to-six months without regaining more than 10 lbs.

“Initially, this patient was not a candidate for bariatric surgery, because he was just too ill,” said Peter H. Jones, MD, who directs the center in Houston.

As the center’s sole physician, Dr. Jones collaborates with dietitians, certified diabetes educators and licensed professional counselors to run a very low calorie diet program that is primarily driven by weekly group support meetings and individual meetings that involve counseling and nutritional guidance.

After participating in the center’s program for six months, the patient was amazed when he reached the goal weight needed to qualify for a heart transplant. Even more jaw-dropping was the news that, as a result of his success, he no longer needed one because his cardiac function improved so much from the weight loss.

“We’ve also had two referrals for patients to lose weight in order to get them eligible to receive lung transplants,” Dr. Jones said. “Both were successful in losing weight and had lung transplants, and their lives were completely turned around. These individuals would have died otherwise.”

Cases such as these motivate the center’s staff to help patients take charge of their health and their overall lives—a cause Dr. Jones feels works best with a multidisciplinary approach.

One of the center’s strongest partnerships is with the hospital’s bariatric surgery program, which sends referrals for patients, such as those over age 65, who are not optimal surgical candidates. The bariatric surgery program also coordinates with the center’s dietitians and counselors for pre-bariatric assessments and post-surgery support groups.

“The comparative weight loss for patients who use our program and for those who undergo bariatric surgery is about the same, with a loss of about 3 to 5 pounds per week,” Dr. Jones said. “Some patients don’t like surgery and will seek a medical treatment approach, while others are failures of a variety of diet programs and would otherwise opt to go to surgery.”

In addition to partnering with the hospital’s bariatric surgery department, the center offers programs tailored for diabetics and women—particularly women with a history of gestational diabetes—who need to manage their weight during pregnancy.

In the program, patients start on either the low-calorie diet of 1,000 calories daily...
if their body mass index (BMI) is no more than 32, or the very low-calorie diet of 800 calories (high protein, low carbohydrate) daily if their BMI is higher. Most take from 20 to 24 weeks to achieve their target weight but continue to participate in follow-up sessions up to a year after reaching their goal.

Patient follow-up is essential for enforcing structure and accountability, Dr. Jones said, noting that medical weight management programs sometimes fail by not providing patients with an organized, responsible environment that encourages them to be honest about their lifestyle changes.

“The challenging part in using this multidisciplinary approach is getting patients to change their attitudes about health,” he said. “Group meetings are used to coach them for a new lifestyle—not only for their relationships with food but also for their association with physical activity.”

Conquering a patient’s psychological health is the most important tool for success in weight control, he said, adding that food can be considered a socially acceptable addiction.

“The key message that we want our patients to understand is that the emotional relationship with food is enormous,” Dr. Jones said. “It starts with many of us when we are young, and we continue to use food as our emotional psychiatrist as we grow older whenever we feel lonely, tired, bored and stressed.”

Patients are pleased to observe that, while it may take several months to drop extra weight, the health benefits of their participation are immediate: enhanced insulin sensitivity and improved lipid profiles are observed within weeks of starting the program.

About 75 percent of patients are self-referred after speaking with someone else who had success with the program, said Devin Volding, a licensed clinical social worker and behavioral sciences doctoral candidate at the University of Texas School of Public Health-Houston.

“If someone in your office loses 50 pounds, others notice and ask that person about it,” he said.

Of the approximately 25 percent of patients who are referred by physicians, a subset of them are recommended by musculoskeletal practitioners who require pre-surgical weight loss before conducting knee or hip replacement surgery.

Some patients do so well that they can stave off the cost and recovery period associated with having a knee replacement for some time, Volding said, noting that the program also forces patients to take their work-life balance into account.

“From a behavioral standpoint, there are some folks out there who are just trying to make ends meet and they don’t realize that the piece they are missing is often having little time or focus on themselves,” he said. Approximately 1,500 people participate annually in the center’s programs at one of the four Houston sites where it is offered by The Methodist Hospital.

In one success story, a patient lost about 300 pounds over the course of 18 months. While not all weight loss is that dramatic, any amount leads to measurable success for the program’s patients.

“Success is really a change in a person’s attitude towards self-care,” Dr. Jones said. “Even if a person were just to lose 10 percent of their weight and drop from 200 pounds to 180 pounds, that improves one’s attitude and helps the patient feel enabled to make meaningful changes.”
With an ever-increasing number of biomarkers, genetic markers and imaging markers being discovered and reported—all as having significant association with cardiovascular disease—the clinician is often faced with the basic questions of whether and perhaps how best to use a given marker in clinical practice. The marker may have value in monitoring therapy, such as LDL-C, or for improved risk prediction. There are several statistical metrics required for a marker to be considered for use in risk prediction. In this article, we discuss them and provide examples.

Criteria for Risk Prediction
The American Heart Association recently published a scientific statement detailing the criteria that a marker needs to satisfy to be considered for use in risk prediction. The first requirement is association of the marker with the outcome of interest. Statistical tests such as odds ratio, hazards ratio or risk ratio can accomplish these associations. The marker must then be able to add to traditional risk prediction schemes such as Framingham Risk scores or the Atherosclerosis Risk in Communities (ARIC) Coronary Risk Score (ACRS). This holds both for “discriminating” those who go on to have events from those who do not and for identifying models whose predicted risk “calibrate(s)” better with the observed risk.

The most commonly used statistic to evaluate “discrimination” is the C-index or the C-statistic. This is (AUC) the area under the receiver operator characteristics curve (ROC). The ROC plots sensitivity (true positive) against 1-specificity (true negatives). Values can range from 0.5 (i.e., chance) to 1.0 (perfect discrimination). To evaluate a test performance often on the same graph the specificity is plotted against 1-sensitivity. Note these are also the positive and negative likelihood ratios. The C-statistic is relatively insensitive to change and may not change significantly even though some markers are clearly associated with risk.

Another statistic is called the integrated discrimination improvement (IDI) test. It takes into account both the sensitivity and specificity of those classified as higher and lower risk by the “novel” marker and, in turn, describes the net effect of discrimination of the marker.

Calibration compares the observed and expected risk. The “goodness” of the model fit is tested using tests in the Chi-square family. You may read about the
Hosmer-Lemeshow or the Groonsby-Borgan goodness-of-fit tests.

The number of people who will be impacted by addition of the “novel” marker is also an important consideration. This can be estimated using reclassification tables. These describe the number of people who change risk categories (i.e., move up or down in risk categories). Be aware however that the mere description of the number of people reclassified does not address whether the reclassification was appropriate. In other words, if a marker results in reclassifying 10 percent of the population to a higher risk group, how does one know if this was correct or not? The “net reclassification index” (NRI) is a test statistic that can help with this question by estimating the overall impact of reclassification by evaluating the overall effect of correct and incorrect reclassification. For example, if a person who has an event in follow-up is reclassified to a higher-risk group, the reclassification is appropriate, as opposed to a person who is reclassified to a lower-risk group. The NRI, therefore, looks at the net effect of reclassification among those who experience events (case) and those who do not experience events (control).

The formula is [Probability (up|case) – Probability (down|case)] – [Probability (up|control) - Probability (down|control)]

Pr = probability, up = reclassified to higher risk, down = reclassified to lower risk.

You may also see clinical NRI used. This is the NRI when only the intermediate risk groups (i.e., the risk group where the new marker is likely to have the most effect) is considered.

So it is complicated when trying to decide if adding a test is useful in risk prediction. Statistical testing in risk prediction needs to consider several important things. An example important to clinical practice follows.

Example of Assessing a Marker for Use in Risk Prediction

We reported whether the addition of carotid intima media thickness (CIMT) and/or the presence/absence of carotid plaque improved risk prediction beyond traditional risk factors (TRFs) in the ARIC study.3 Traditional risk factors included age, systolic blood pressure, antihypertensive medication use, total cholesterol, high-density lipoprotein cholesterol (HDL-C), gender, diabetes, and smoking status.

Addition of CIMT+carotid plaque to the ARIC coronary risk score (ACRS) which included the risk factors noted above increased the AUC from 0.742 (ACRS only) to 0.755 (ACRS + CIMT + plaque information) (95 percent Confidence Interval for the difference in adjusted AUC was 0.008 to 0.017) while the IDI was significantly improved as well. So we found out that adding CIMT+plaque to traditional risk factors improved discrimination (i.e., better differentiated those who had CHD events from those who did not).

Adding CIMT+plaque reclassified 12.4 percent of the 13,145 people to a lower risk category and reclassified 10.8 percent to the higher risk group. When we applied a “Goodness-of-Fit” test, although model fit improved with the addition of CIMT+plaque, none of the models had a good fit suggesting that although adding CIMT+plaque to traditional risk factors improved model calibration, it was still not adequate (i.e., there is more room for improvement).

We found that adding CIMT+plaque had an NRI of 9.9 percent (clinical NRI 21.7 percent) suggesting that among those reclassified by adding CIMT and plaque, the net effect of reclassification was good resulting in more appropriate classification of risk. As a comparison the NRI for C-reactive protein in men has been reported to be 5.3 percent (Clinical NRI 14.2 percent)4 and for coronary calcium score 25 percent (Clinical NRI 55 percent).5

In summary, when CIMT and carotid plaque were added to the Traditional Risk Factors in the ARIC study for prediction of CHD events there was improved discrimination, and better calibration. This suggested to us that CIMT+plaque improves CHD risk prediction beyond traditional Risk Factor assessment alone as used in ARIC. We repeated the same analysis adding CIMT and plaque to the FRS and again found that there was significant improvement in CHD risk prediction. Be alert, however, that improvement in risk prediction using data from a completed study does not answer the important question: if a strategy incorporates a new marker in risk prediction, will it improve patient outcomes? That needs to be put to the test. It also does not answer or address whether this approach is cost-effective (here we define cost-effective as a comparison of incremental cost of testing and treatment versus incremental benefit).

References listed on Page 41.

Disclosure Statement:
Drs. Nambi and Virani have no relevant disclosures.
In 2009, the United States Preventive Services Task Force (USPSTF) published a report on the value of using nine non-traditional risk factors—high-sensitivity C-reactive protein (hs-CRP), ankle-brachial index (ABI), leukocyte count, fasting blood glucose, periodontal disease, carotid intima media thickness (CIMT), coronary artery calcification (CAC) score on electron-beam computed tomography (EBCT), homocysteine, and lipoprotein(a)—in assessing cardiovascular disease (CVD) risk. This recommendation applied to the 10–20 percent (intermediate) 10-year Framingham Risk Score (FRS-IR) category, which includes about 31 percent and 7 percent of asymptomatic U.S. men and women, respectively, all between the ages of 40 to 79 years and without diabetes mellitus (DM). Examples of people who fall into the intermediate-risk category include a 60-year-old male smoker with untreated hypertension and a 60-year-old female with untreated hypertension and hyperlipidemia. The USPSTF employed systematic reviews using a hierarchial approach to reassign people assessed as FRS-IR to either a high-risk or low-risk stratum and, thereby, improve outcomes. They concluded that there was insufficient evidence to assess the balance of benefits and harms of these non-traditional risk factors to screen asymptomatic men and women with no history of CHD. Herein, we discuss very briefly some aspects of this report.

**hs-CRP**

Summary evidence—10 good-quality studies, 13 fair-quality studies and two meta-analyses—suggested that an elevated hs-CRP predicted a higher CHD risk independent of FRS. After adjustment for multiple covariates, the summary relative risk estimate for incident CHD was 1.58 (CI, 1.37 to 1.83) for an hs-CRP level greater than 3.0 mg/L, compared with less than 1.0 mg/L. Thus, C-reactive protein is perhaps the only risk marker for which magnitude of benefit could be estimated by modeling based on information about predictive value and prevalence among people at intermediate risk. Buckley and colleagues reviewed the evidence and estimated the additive benefit of hs-CRP to traditional Framingham risk factors. The model predicts that 11 percent of men in the intermediate group would be reclassified as high risk; if those reclassified men are provided intensive risk-reduction therapy, it could avert 47.8 CHD events over 10 years per 1,000 among men ages 40 to 79 years.
More recently, the JUPITER trial\(^3\) results have been published, wherein 17,802 apparently healthy people with low-density lipoprotein cholesterol (LDL-C) levels less than 130 mg/dL and hs-CRP ≥ 2.0 mg/L were randomized to rosuvastatin, 20 mg daily or placebo. At 1.9 years, rosuvastatin produced significant reduction in most CVD outcomes. However, the statin group had a higher rate of self-reported diabetes and one-third of the cohort had the metabolic syndrome, suggesting that a sizable number would have had the disease substrate for CVD, despite the apparent normality of the cohort. Although the relative risk reduction was significant, absolute risk reduction was less than modest—event rate reduced from 1.8 percent in the placebo group to 0.9 percent in the rosuvastatin group; a number needed to treat of 111 over 1.9 years. One can argue that the external validity of the study is largely limited to those similar to the ones recruited in the JUPITER study.

Last but not least, as an analyte, hs-CRP shows great variability and levels depend on the quality of the assay used. Levels are to be increased in a variety of situations such as inflammatory states and surgery.

**Carotid IMT**

Summary evidence—one fair- and two good-quality longitudinal studies—suggests that CIMT predicts CHD independent of FRS in asymptomatic people (1,300 to 16,000 men and women who showed a relative risk of 1.19 to 3.80).\(^4\)\(^-\)\(^6\) Adding CIMT scores to a risk prediction equation based on traditional risk factors modestly improved the prediction of subsequent CHD among healthy adults, particularly for men.\(^7\) Recently, 10-year results of the Carotid Atherosclerosis Progression Study (CAPS)\(^8\) (N=4904; no prior CVD) revealed that CIMT was significantly and independently predictive for CVD events. Compared with a model using the FRS, one with CIMT reclassified 8.1 percent of subjects. In 30 percent, this reclassification was correct as confirmed with the actual outcome over 10 years. However, net reclassification improvement (-1.41 percent) and the integrated discrimination improvement (0.04 percent) were both not statistically significant. More subjects were shifted to lower than to higher risk categories by the inclusion of CIMT. Overall, the question remains as to whether reliable CIMT assessments can be done routinely outside of research settings; for now, it can be said that it may not be useful as a risk stratification tool for members of the general population.

**Coronary Artery Calcium**

Poor- to fair-quality evidence indicates that higher CAC scores on EBCT predict CHD events independent of Framingham risk factors on the basis of a systematic review of eight cohort studies. Three good-quality population cohort studies and five fair-quality studies\(^9\)\(^-\)\(^14\) reported that the highest CAC score groups had significantly greater relative risk estimates than the lowest score groups.

Chironi, et al.\(^15\) measured CAC with electron-beam-computed tomography in 500 asymptomatic, untreated hypercholesterolemic men and re-calibrated the 10-year Framingham CHD risk by adding CAC score information (post-CAC test risk) via an algorithm integrating relative risk and expected distribution of CAC in the population tested. Proportions of low (<10 percent), intermediate (10–20 percent) and high (> 20 percent) risk categories, and of eligibility for lipid-lowering treatment, were compared between Framingham risk and post-CAC test risk. The addition of CAC to risk prediction resulted in downgrading rather than upgrading risk and did not change treatment eligibility, except in intermediate-risk subjects less frequently eligible for treatment.

Another study\(^16\) not reviewed in the USPSTF report looked at the prevalence of subclinical atherosclerosis as defined as CAC score ≥ 0, CIMT ≥ 75th percentile, or plaque ≥ 1.5 mm, in the groups with low, intermediate and high FRS among 136 asymptomatic subjects. The CIMT and CAC values were used to determine “vascular age” and “coronary calcium” age, respectively, with established nomograms. In the 103 low-risk (FRS < 10 percent) subjects, 41 percent, 50 percent, 59 percent, and 66 percent had CAC scores ≥ 0, CIMT ≥ 75th percentile, plaque ≥1.5 mm, and CIMT ≥ 75th percentile or plaque ≥1.5 mm, respectively. In the 33 subjects with intermediate (n = 14) or high (n= 19) FRS, 70 percent, 81 percent, 87 percent, and 87 percent had CAC scores > 0, CIMT ≥ 75th percentile, plaque ≥1.5 mm, and CIMT ≥ 75th percentile or plaque ≥1.5 mm, respectively. Of subjects with coronary calcium scores of zero, 52 percent had carotid plaque. Adjusted for FRS, body mass index (BMI) was an independent predictor of abnormal CIMT in the low-FRS group, but not of abnormal CAC. Mean vascular CIMT age was significantly higher than coronary calcium age (61.6 ± 11.4 vs. 58.3 ± 11.1 years, P = .001), and both were significantly higher than chronologic age (56.9 ± 10.1 years) (P < .0001 and P < .04, respectively).

Several caveats apply. First, nearly the entire published clinical outcome data from CAC are based on results obtained from EBCT. However, EBCT systems are now being widely replaced with multidetector CT (MDCT) systems. EBCT, which was produced by one manufacturer, provided much more standardization than exists for the various generations of MDCT systems from different manufacturers. Standardization guidelines have been proposed for MDCT\(^17\) but are rarely used. Studies with earlier MDCT technology (4-16 slices) have demonstrated that
Lipoprotein(a) Level
Fair-quality evidence indicates that the lipoprotein(a) level predicts CHD events after adjustment for some Framingham risk factors, but no studies calculated a Framingham risk score, assessed predictive value beyond Framingham risk scoring, or assessed whether lipoprotein(a) contributes to reclassification from intermediate to another risk category. In a systematic review and meta-analysis of four good- and 11 fair-quality studies, 12 of the 15 found a positive association. A meta-analysis of the 15 fair- and good-quality studies that excluded baseline CHD and CVD showed an increased relative risk of 1.59 (CI, 1.29 to 1.97) when comparing lipoprotein(a) levels of 300 mg/L or greater with levels less than 300 mg/L. The pooled estimate was similar among men and women, and the association between lipoprotein(a) levels and CHD was greater in studies with follow-up times of more than 10 years. No studies attempted to evaluate the prevalence and applicability of lipoprotein(a) level in intermediate-risk participants.

Also, with respect to vascular disease, the predictive efficacy of lipoprotein (a) tends to vary as a function of ethnicity. Predictability is higher in South Asians and low in African-Americans with intermediate performance in Caucasians.

Impaired Fasting Glucose
Fair-quality evidence indicates that impaired fasting serum glucose (defined as levels of 5.55 to 6.94 mmol/L [100 to 125 mg/dL]) is a weak predictor of CHD, independent of Framingham risk factors, in people without diabetes. Two good- and five fair-quality studies had conflicting results. One good-quality study showed a weak association between the fasting glucose level and CHD after four years of follow-up [hazard ratio, 1.09 (95 percent CI, 1.02 to 1.16) per 0.72-mmol/L (13 mg/dL) increase in fasting glucose level], after adjusting for the FRS without diabetes, and the other good-quality study found no association after eight years of follow-up [adjusted hazard ratio, 1.05 (CI, 0.94 to 1.17)]. The remaining fair-quality cohort studies compared patients with an elevated fasting glucose level to those with a normal fasting glucose level and found no significant increased risk for CHD.

Homocysteine Level
Fair-quality evidence indicates that elevated homocysteine levels predict CHD events after adjustment for some Framingham risk factors; however, no studies calculated a Framingham risk score, assessed predictive value beyond Framingham risk scoring, or assessed whether homocysteine levels contribute to reclassification from intermediate to another risk category. Results from 21 studies in 20 cohorts were conflicting; 16 found a positive association and five found no association or a negative association. When all good- or fair-quality studies of participants without previous coronary disease were pooled, each 5-µmol/L increase in homocysteine level was associated with an 18 percent increase in the risk for coronary events (1.21 [CI, 1.10 to 1.32]). However, none of the studies addressed the prevalence and applicability of homocysteine levels in intermediate-risk participants.

Ankle-Brachial Index (ABI)
A recent well-conducted meta-analysis of 16 population-based cohort studies concluded that lower ABI is associated with an increased risk for CVD events and mortality, independent of FRS. However, because of particular aspects of the meta-analysis, this evidence cannot provide an unbiased determination of how many asymptomatic men without known vascular disease would be reclassified from the intermediate classification obtained by using Framingham factors alone to a higher cardiac-risk stratum. This analysis did provide an unbiased estimate that approximately 10 percent of women would be reclassified from intermediate to high CHD risk.

Leukocyte Count
Three good- and three fair-quality cohort studies and one meta-analysis examined the value of leukocyte count in predicting CHD risk, independent of Framingham
risk factors, in participants without known coronary disease. The results of these studies are conflicting: Four of the studies found an independent predictive value for leukocyte count, whereas the others did not. The USPSTF concluded that there is at least fair evidence of no association between leukocyte count and the risk for coronary events.

**Periodontal Disease**

Fair-quality evidence indicates that periodontal disease can predict CHD risk independent of Framingham risk factors. A meta-analysis performed by Humphrey and colleagues examined the results from three good- and four fair-quality cohort studies in North America and Finland, which included from 175 to more than 100,000 men and women and had follow-up that ranged from five to 21 years; pooled data from six of these studies showed a hazard ratio of 1.24 (CI, 1.01 to 1.51) for any CHD or CVD event. Of note, these studies did not consistently define periodontal disease or CHD outcomes.

Periodontal bone loss was an important risk factor for subsequent CHD, with two studies showing statistically significant relative risks that ranged from 1.36 to 1.90. A meta-analysis of four cohort studies showed that tooth loss, a component of periodontal disease, predicts CVD events independent of Framingham risk factors. Investigators observed an increased risk for CHD or CVD events among those with 0 to 10 teeth at baseline, compared with those who had from 25 to 32 teeth (combined risk estimate, 1.41 [CI, 1.22 to 1.63]).

No information was available about prevalence or applicability in populations at intermediate risk for CHD events.

**What Others Say**

The American Heart Association encourages Framingham risk assessment in asymptomatic people, advises against CAC assessment by EBCT in asymptomatic people at low and high risk (those at ≤ 10 percent – > 20 percent 10-year risk, respectively), and states that “it may be reasonable to consider use of CAC measurement in intermediate-risk patients based on available evidence that demonstrates incremental risk prediction against the use of hs-CRP as a risk marker in the general population and against the use of other inflammatory markers.”

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The ATP III states that homocysteine level, hs-CRP level, CIMT, and CAC score on EBCT may be useful in certain circumstances, but it does not recommend incorporating any emerging risk factors into risk assessment for all people receiving primary prevention risk assessment.

**Research Needs and Gaps—as Identified by USPSTF**

For hs-CRP, ABI, and EBCT, high priority should be given to determining the benefits and harms of aggressive treatment for people reclassified from intermediate to high risk on the basis of additional information obtained from these tests.
For hs-CRP and ABI, the priority is to assess the health effect of reclassifying those at high and intermediate risk for CHD events by RFS into lower-risk categories on the basis of this assessment. Similar studies for EBCT would be useful.

The predictive value and prevalence of periodontal disease, increased CIMT and elevated lipoprotein(a) should be examined in conjunction with traditional Framingham risk factors for predicting CHD events and death.

Conclusions
Many novel CV risk factors have been proposed over the past decade, but for a risk factor to be considered clinically useful, it must be readily measurable, there must be considerable evidence linking the risk factor to CVD, and modifying treatment must be available. It also must add to the information obtained from existing risk factors. Additionally, it becomes necessary to determine whether the value is a risk mediator or a risk marker. In other words, the question is whether a phenomenon causes CVD or whether the phenomenon is noted because CVD is present—sometimes referred to as an epiphenomenon. To be considered a risk mediator, the factor must not only show a strong correlation with an increased likelihood of CVD but must also directly contribute to the development of disease. A risk marker is likely elevated because of the existence of a disease state but does not contribute to disease progression. Many times the challenge is in designing outcome trials that will help answer this question precisely. For example, statin therapy results in pleitropic actions, and results seen in trials such as the JUPITER trial cannot conclusively be attributed to improvement in serum levels of hs-CRP, despite the overwhelming evidence from observational and longitudinal studies that have clearly established a link between elevated hs-CRP and CVD outcomes. There is a growing need for designing elegant randomized controlled clinical trials in those with the Framingham intermediate-risk status, stratified according to the presence or absence of a non-traditional risk factor and subject to a treatment intervention. It may not always be possible to have a placebo arm in all such studies or have a hard clinical endpoint such as all cause mortality or CVD outcomes. Some of these studies may well have surrogate endpoints because of a variety of factors, cost of conducting a large trial over a long period of time being the most significant one.

References listed on Page 41.

Disclosure Statement:
Drs. McNeal and Raghavan have no relevant disclosures.
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Case Study: Management of Angina in a Patient with Increased Lipoprotein(a) Levels—Use of LDL-apheresis

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Discuss this article at www.lipid.org
Go to “Topics/Lipid Spin” and look for “Management of Angina in a Patient with Increased Lipoprotein(a) Levels.”

A 48-year-old female patient with a history of coronary artery disease (CAD), peripheral arterial disease (PAD), cerebral vascular disease (CVD) and chronic angina for the past two years, despite intense anti-anginal medication (nitroglycerin transdermal 0.6-0.8 mg/h patch, and sublingual 0.6 mg/PRN calcium channel blockers, beta blockers) was referred to the University of Kansas Atherosclerosis and LDL-Apheresis Center for further evaluation and treatment. Her risk factors included family history of atherosclerosis, hypertension and dyslipidemia; multiple family members have increased Lp(a) levels.

Her extensive cardiovascular history included interventional procedures such as femoral popliteal stent placement (2007 and 2008), carotid endarterectomy (2005), coronary artery bypass grafting (2005) and percutaneous coronary intervention (2006 and 2008). Prior to presentation to our clinic, the patient’s lipid-lowering medications included simvastatin/ezetimibe (40/10 mg/day) and, more recently, rosuvastatin in 20-40 mg/day, fenofibrate (145 mg/day) and Omega-3 fatty acid (1-3 grams/day).

The patient’s chief complaint on presentation to the clinic consisted of chronic uncontrolled angina and persistent claudication. The physical examination was grossly unremarkable except for bilateral carotid bruits. Her blood pressure was 112/60; her body mass index (BMI) was 26.6 kg/m². Initial laboratory data showed total cholesterol of 141 mg/dL; triglycerides, 215 mg/dL; HDL-C, 20 mg/dL; LDL-C, 78 mg/dL; hsCRP, 2.19 mg/L; Lp(a), 88 mg/dL (normal< 30);...
fibrinogen, 404 mg/dL (normal 200-400); and normal thyroid function. The patient was tried on niacin (Niaspan) on multiple occasions but failed because of intense flushing, even with food and aspirin. Upon returning to the clinic (2-month period) with no change in her complaints of angina and blood work, LDL-apheresis was approved and initiated. Following the first treatment (Liposorber Kaneka [Osaka, Japan]), the patient’s LDL-C and Lp(a) each were lowered by more than 80 percent (Table 1). Her anginal pain had improved and resulted in the discontinuation of nitroglycerin therapy. The patient also stated significant improvement of her PAD symptoms. To determine if hemodynamics, in particular blood rheology (its slow characteristics), had an influence on the patient’s symptomatic improvement, we measured blood viscosity before and after the first treatment (Table 2). Because of the patient’s mild anemia (hemoglobin 11.5 mg/dL), the pre- and post-apheresis blood viscosity levels were very low, thus it was unlikely to have had a major influence on her anginal symptoms. Now, more than three years after initiating treatments biweekly and, more recently, every three or four weeks, the patient has not experienced another cardiovascular event, anginal pain or any need for nitroglycerin therapy. In addition, she no longer has any claudication and has a marked improvement in her sense of well being.

**Discussion**

Lp(a) is a macromolecular complex assembled from Apolipoprotein a (Apo a) and LDL. Several studies have suggested an association of elevated Lp(a) with recurrent atherothrombotic complications. Elevated Lp(a) may be an independent predictor of worsening cardiovascular disease in patients who have control of other risk factors. Plasma levels of Lp(a) may be reduced with medications such as nicotinic acid and estrogens. LDL-apheresis is a therapy for patients with familial hypercholesterolemia and is an alternate method for reducing Lp(a) in patients intolerant of or resistant to aggressive medical therapy. Treatments have been associated with improvement in angina-like symptoms, and the reduction of Lp(a) during apheresis may be the underlying mechanism contributing to improvement in clinical symptoms such as angina. This case demonstrates the acute clinical benefits of LDL-apheresis for a patient with CAD, CVD, PAD, chronic angina and abnormally high Lp(a) levels but normal LDL-C.

An examination of a five-year registry of 628 patients who underwent combined LDL-apheresis with a wide array of lipid-lowering medications—mostly statins—demonstrated remarkable improvement of anginal symptoms in 87 percent of the patients. One of the postulated mechanisms underlying this phenomenon is improvement in endothelial function resulting from apheresis treatment. Based on National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) guidelines, Lp(a) is currently classified as an “emerging risk factor” for CHD. It has been shown by subtle changes on cardiac magnetic resonance imaging (MRI) that a single apheresis session improves cardiac microvascular function in patients with elevated Lp(a) and may be the mechanism contributing to the improvement of angina in our patient.

At present there are no specific guidelines to measure Lp(a) in patients with controlled LDL levels, but many lipid specialists will set an LDL goal of 15–30 mg less than the typical LDL goal if Lp(a) levels are increased (>30 mg/dL or >75 nmol/L). Despite its known benefits, apheresis is performed in only a minority of qualified patients. In addition to reducing plasma cholesterol, apheresis can alter other markers of vascular disease, including inflammation, rheology, thrombosis and fibrinolysis. This form of therapy should be considered in these types of patients. Our patient was granted approval by her insurance carrier because of her severe symptoms and repeated admissions to her local hospital in Colorado. Finally, future studies should investigate the value of measuring Lp(a) in patients with uncontrolled anginal symptoms and normal lipid levels.

**References listed on Page 41.**

**Disclosure Statement:** Drs. Bulchandani, Falko and Moriarty have no relevant disclosures.
Cardiovascular disease (CVD) is prevalent and costly, and it remains the most common cause of death in the United States.\(^1\) Considering CVD’s tremendous impact, healthcare providers must assist patients in reducing overall risk. The collective expertise of team-based patient care can provide care to more patients and improve overall healthcare quality.\(^2,3\) The National Cholesterol Education Program Adult Treatment Panel III recognizes that there is a treatment gap and many patients do not receive adequate lipid management. It advocates using the collaborative care of pharmacists as an intervention to improve adherence with its recommendations.\(^4\)

This article reviews outcomes from recent publications of practice models that use pharmacists as team members to manage lipids and impact CVD.

Pharmacist-provided patient care has a positive impact on clinical and humanistic outcomes.\(^5\) Chisholm-Burns, et al., used meta-analyses to evaluate 298 randomized controlled trials to determine the effects of pharmacists-provided patient care. Most of the trials were done in outpatient settings. When compared with other care models, which were predominately usual care, the pharmacist-provided care was associated with better management of LDL-C (mean difference -6.3 ± 0.12, \(p=0.01\); 95% CI = -6.5 to -6.0); blood pressure (mean difference for systolic blood pressure -7.8 mm ± 1.5 Hg, \(p<0.001\), CI = -9.7 to -5.8; mean difference for diastolic blood pressure -2.9 ± 0.7 mm Hg, \(p=0.001\), CI = -3.8 to -2.0); and A1C (mean difference -1.8% ± 0.5, \(p=0.005\), CI = -2.7 to -0.9). Pharmacist-provided care was associated with higher scores for medication adherence (standardized mean difference, 0.6 \(p=0.001\)), patient knowledge (standardized mean difference, 1.1, \(p=0.001\)) and the quality of life/general health dimension (standardized mean difference, 0.1, \(p=0.003\)).\(^5\)

Several recent studies highlight the benefit of pharmacist-provided care to LDL-C reduction and LDL-C goal attainment.\(^6\) Fabbio, et al., documented LDL-C reduction in a pharmacist-managed telephone lipid clinic in a Veterans Affairs medical center. Patients were referred by primary care providers. The mean LDL-C reduction was 44.3 ± 45.2 from baseline (\(p<0.001\)).\(^6\) Gerrald, et al., showed that a pharmacist-managed lipid clinic in a
hospital-based outpatient setting improved attainment of the LDL-C goal. The patients were referred by cardiologists, the cardiovascular rehabilitation program, and the anticoagulation clinic. The patients had face-to-face appointments with the pharmacist. The mean LDL-C was reduced from 103.1 ± 45.1 mg/dL at baseline to 81.5 ± 28.1 mg/dL (p<0.0001), and 82.9 percent of patients reached their LDL-C goal, compared to 55.3 percent at baseline (p<0.0001). Miller, et al., demonstrated that a pharmacist-managed statin interchange program, which switched atorvastatin to a new formulary regimen of simvastatin, rosuvastatin or ezetimibe-simvastatin was associated with increased lipid control compared with usual care. The pharmacists provided care in the family medicine clinic, and usual care was provided in internal medicine, cardiology and endocrinology clinics in a university-based healthcare system. Usual care was associated with decreased lipid control, and the mean LDL-C increased from 78.3 to 85.2 mg/dL in the usual care group (p=0.01) after statin interchanges. More patients attained their LDL-C goal (<100 mg/dL) in the pharmacist-managed conversion program (97 percent) than in the usual care group (75 percent) after the statin conversion. Birtcher, et al., determined that patients enrolled for three or more years in a multidisciplinary secondary prevention lipid clinic in a cardiology practice with a pharmacist on the team had lower LDL-C levels and were more likely to achieve their LDL-C goal (<100 mg/dL) and an optional goal (<70 mg/dL) than patients who received usual care from a cardiologist.

Kaiser Permanente has incorporated pharmacists in team-based care for many years. The pharmacy service was developed in 1998 and follows more than 11,000 patients. It provides comprehensive long-term management of patients with coronary artery disease. The service has at least 19 clinical pharmacists. The pharmacists ensure that all patients with coronary artery disease receive evidence-based medication. This includes lipid-lowering therapy, beta blockers, angiotensin-converting enzyme inhibitors post myocardial infarction. They also monitor and control other diseases that increase cardiovascular risk—dyslipidemia, hypertension, diabetes mellitus, tobacco abuse. They provide patient education, recommend non-prescription therapy, and serve as a resource to the other healthcare providers. Merenich, et al., included four cohorts: those enrolled early in any portion of the program (< 90 days after their event) and followed continuously, those with delayed enrollment in any portion of the program (≥ 90 days after their event) and followed continuously, those enrolled in any portion of the program with inconsistent follow-up, and those with no exposure to the program. The patients were considered to be “continuously enrolled” if they received care from both the nurse- and pharmacist-managed portions and the transition period between the portions was ≤ 30 days. There were 4,896 patients included in the analysis. Patients in the early and delayed cohorts were followed for an average of 3.5 and 3.7 years, respectively. Compared with patients not exposed to any portion of the program, patients enrolled in the program had lower rates of all-cause or coronary heart disease-related mortality (p <0.0001). Patients enrolled < 90 days after their coronary event had lower combined nonfatal coronary events and all-cause mortality compared with the other groups (p <0.001).

Team-based patient care that includes a pharmacist improves lipid management and positively impacts cardiovascular disease outcomes in a variety of healthcare settings. Considering the impact and magnitude of cardiovascular disease and its treatment gaps, it is important to use the expertise of all healthcare providers to maximize patient outcomes.

References listed on Page 41.

Disclosure Statement: Ms. Ross and Dr. Birtcher have no relevant disclosures.
Several of our board members have been extremely active this year. Dr. Robert Eckel, past president of the American Heart Association and a national and international authority in our field, has been busy chairing the Lifestyle Working Group at the National Heart, Lung and Blood Institute (NHLBI) that oversees the evidenced-based impact of lifestyle on cardiovascular disease (CVD) risk. Dr. Eckel is also a member of the Adult Treatment Panel IV. It is currently anticipated that updates on guidelines for cholesterol, blood pressure, and overweight/obesity will be drafted by mid-2011. Dr. Tom Haffey, a recent SWLA board member and governor of the Colorado Chapter of the American College of Cardiology (ACC), established his annual symposium, “How to Avoid a Heart Attack”, this past June in Denver. More than 150 people attended the event, for which the Foundation of the NLA provided grant funding.

NLA notables presenting included President Dr. Michael Davidson and former Southeast Lipid Association (SELA) President Carol Mason, MSN. The Association of Black Cardiologists was represented by its vice president, NLA member Dr. Karol Watson, who was able to provide her insight from the female perspective. Dr. Eckel entertained attendees with his excellent review of the current state of clinical lipidology. He was joined on the program by two former AHA state presidents, Drs. Barry Molk and Richard Flanigan. The program content and logistics were directed by Marilyn Haffey, MSN, Lt. Col., Ret., and Adele Serio, RN. An additional opportunity for an update on such topics as aspirin resistance, Plavix resistance and emerging genetic markers was included in the evening program. Plans are underway to repeat the symposium in May 2011, with the emphasis shifting to “How to Avoid a Stroke—Putting it All Together.” I am sure Dr. Haffey is most grateful for the Foundation of the NLA’s support.

Regional Access to Apheresis and FH
Finally, I would like colleagues to be aware of this issue’s case study focusing on LDL and lipoprotein(a)-apheresis. In our region, there are multiple sites that utilize this procedure, including Dallas, Denver, Houston, Oklahoma City and San Antonio. One in 500 suffers from familial hypercholesterolemia (FH), and estimates indicate that more than 600,000 FH patients live in the U.S. About 6,000 of these patients would qualify for this procedure. Reimbursement is relatively easy to obtain for patients for whom diet and maximum drug therapy has either been ineffective or not tolerated. Patients qualify with an LDL-C ≥ 200 mg/dL.
with coronary artery disease, or CAD) or LDL-C ≥ 300 mg/dL. The procedure takes from two to four hours and results in a reduction of LDL-C and lipoprotein(a) of 70 percent to 85 percent. Volume exchange is approximately 1.5 liters. Side effects are minimal with an incidence of less than one percent of hypotension, flushing and nausea. Even in selected patients—such as the one discussed in this issue of Lipid Spin, with only an increase in lipoprotein(a) and active vascular disease—reimbursement sometimes can be obtained. The International Classification of Diseases 9 (ICD-9) code for typical FH is 272.0, and Medicare and more than 50 insurance companies approve the procedure. Patients, however, need to be committed to the treatment, which is done every two or three weeks. Dr. Eckel and I have been treating several patients at the University of Colorado over the course of two years without any new cardiac events. This is similar to what has been reported in the literature. The improvement is related to marked LDL and lipoprotein (a) reduction, with its downstream effect of suppression of the coagulation system, suppression of inflammatory factors and adhesion molecule expression, stabilization of atheromatous plaque, suppression of platelet aggregation, improvement of blood rheology, and improvement of blood flow.

In summary, our SWLA chapter is quite active, its membership growing, and we continue to collaborate with many organizations to realize our educational endeavors. We hope you will take part in our next enterprise this coming March in Austin, Texas, for the Spring Clinical Lipid Update, which we will co-host with the Pacific Lipid Association.

Youth Investigator Award

Lead presenters with accepted abstracts who are Young Investigators (in-training students, residents and fellows or members in practice for < 5 years) will receive free registration to the 2011 NLA Scientific Sessions. Submissions will also be eligible for the NLA Young Investigator Award and may be selected for oral presentation during the sessions.

For abstract categories and submission guidelines, visit www.lipid.org/posters.
**News and Notes**

**NLA’s International Efforts**
Hundreds of medical professionals in India and Australia participated in the NLA’s first international educational programs in October.

More than 200 cardiologists in Bangalore and Mumbai, India, attended our “Best of the NLA” educational symposia, which showcased our most in-demand presentations and featured faculty including Drs. Michael Davidson, Carl Orringer, Mary McGowan and Terry Jacobson.

An *International Masters in Lipidology™ course* debuted in Sydney, Australia, in late October. NLA faculty included Drs. Peter Toth and William Cromwell presenting alongside other international thought leaders such as Prof. John Chapman, President of the European Atherosclerosis Society, and Drs. Peter Clifton and David Sullivan, who serve as the current and past presidents for the Australian Atherosclerosis Society.

The educational initiatives in India and Australia mark an exciting time in which the NLA is harnessing global relationships and reaching out to other countries to promote the advancement of research and professional development for those who work with lipids and related disorders.

The NLA also is pleased to announce our endorsement of a new international liaison, the Polish Lipid Association. The new organization is spearheaded by Dr. Maciej Banach from the Medical University of Lodz, Poland.

**Lipid University™ Graduates**
In August, the NLA and the Accreditation Council for Clinical Lipidology (ACCL) taught Lipid University™—a comprehensive, in-depth educational program on lipid science for medical sales professionals—at six U.S. sites. More than 400 Abbott Laboratories employees attended the training sessions. This group joined those from Merck & Co., who completed the two-day program in 2009. In early November, representatives from Kowa Pharmaceuticals America will participate in Lipid University™ courses.

Each candidate is eligible to take the Basic Competency certification exam offered by the ACCL. Earning this credential demonstrates a commitment to training and application of knowledge by the industry representatives.

**HDL Summit 2010 Highlights Available**
TheHeart.org and MedscapeCME.com now feature an audio roundtable and web monograph from the 3rd Annual NLA Summit on HDL Therapeutics, which was held at Annual Scientific Sessions in May 2010. To access these two highlights, please visit [http://www.theheart.org/article/1110391.do](http://www.theheart.org/article/1110391.do). Also, the written proceedings from the HDL Summit were published in the October/November issue of the *Journal of Clinical Lipidology*.

**NLA Staff Corner**

Amy Waller was promoted to Senior Communications Manager. She previously worked for Jacobs Engineering and the American Association of Clinical Endocrinologists (AACE). Amy graduated from Jacksonville University with a major in communications.

Brian Hart, Esq., joins the NLA as a Policy Analyst. He attended the Florida Coastal School of Law and is admitted to the Florida Bar. Brian will be responsible for ensuring compliance with organizational policy, while reviewing and examining existing programs and policies. Brian graduated from Indiana University with a major in political science.

Tad Kellermann joins the NLA as a Web Developer. He previously worked for the Florida Times-Union’s award-winning web division and has worked on numerous data delivery projects. He has worked in web-related technology for more than 10 years.

Meredith Meide joins the NLA as an Event Coordinator. She previously worked for The River Club and at the Ponte Vedra Inn and Club. Meredith graduated from Florida State University with a major in hospitality management and business administration.

Deborah Walker joins the NLA as an Administrative Coordinator. She will be responsible for the coordination of Executive, Board and related meetings throughout the year. Deborah graduated from the University of North Florida with a major in communications.
Call for Abstract Submissions
If you’re planning to submit a poster for the 2011 NLA Annual Scientific Sessions, make a note that we will need your abstract soon. The deadline for abstract submissions is March 4, 2011 by 5 p.m. EST. Accepted abstracts will be published in the May/June 2011 issue of the Journal of Clinical Lipidology.

Presenters who are Young Investigators (with accepted abstracts) will receive a $300 travel voucher and free registration to our Annual Scientific Sessions. These presenters also will be eligible for the NLA Young Investigator Award. For more details on topics and to submit your abstract online, please visit www.lipid.org/posters.

Nation’s Capital Hosts Summer CLU
The nation’s capital welcomed more than 250 attendees for the Summer Clinical Lipid Update, jointly sponsored in August by the NELA and SELA chapters. Sessions complemented the meeting’s overall theme, “The Intermediate Risk Patient,” and included programs on treating dyslipidemia, an epidemiology perspective on the JUPITER Trial, sharpening risk prediction using biomarkers, and lipid management in special risk populations.

In addition to the educational offerings, attendees trekked by the White House during a Practical Pedometer Walk that was led by Mr. Ralph La Forge to benefit the Foundation of the NLA. On Saturday evening, guests attended a benefit for the Foundation at the Mansion on O street, an eclectic hotel and museum that has more than 32 secret doors. After dinner and drinks, guests danced to Beatles hits performed by British Mania.

Last Chance for Live Cardiometabolic Risk Management Courses
NLA is sponsoring two more live CME/CE courses this year:

November 16-17, 2010
“Best Practices in Cardiometabolic Risk Management”
Sponsored by the NLA and Primary Care Education
Hilton Anaheim
Anaheim, CA

December 3-5, 2010
“Best Practices in Cardiometabolic Risk Management”
Sponsored by the NLA and Primary Care Education
Charlotte Convention Center
Charlotte, NC

In a case-based interactive format, these courses supply guidance on ways to implement advanced risk assessment tools, advanced lipid testing, and treatment guidelines into everyday practice. Each course is offered as part of Primary Care Education’s Best Practices in Primary Care™ regional educational series. To sign up online, please visit http://www.primarycareed.com/conferences.html.
Foundation Update

The Foundation and Familial Hypercholesterolemia Featured in Jacksonville Magazine

Since the Foundation of the NLA decided to take on the cause of Familial Hypercholesterolemia (FH), the local media in Jacksonville, Florida—where the NLA is headquartered—has taken notice. A story about FH patient Katherine Wilemon, who was treated by NLA member Dr. John Guyton, is featured in the September issue of Jacksonville Magazine. To learn more about her story, please see the FH patient video and article posted on the Foundation’s website, www.lipidfoundation.org.

Who Are We?
The Foundation of the NLA is our organization’s charitable arm. The Foundation serves as an education and research, with an emphasis on serving professional, community and public health interests. Since its inception in December 2008, the primary focus of the Foundation has been to generate awareness of its grants program and identify public awareness opportunities that align with our mission to prevent cardiovascular events and death from dyslipidemia and related cardiovascular disorders.

Why Donate?
Replenishing the funds for the Foundation’s grants program is essential to the future viability and health of our organization—and contributions from members like you really add up. Did you know that if every NLA member donates $50, the Foundation will raise more than $125,000 to fund new programs? Thanks to our initial donors, the Foundation has supported more than 400 medical professionals and given more than $35,000 to aid local educational programs. With your help we can do even more.

What Have We Supported?

<table>
<thead>
<tr>
<th>Grant Program Name</th>
<th>Grant Applicant</th>
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<tbody>
<tr>
<td>16th Annual Clinical Management of Heart Disease—Cardiology Update 2009</td>
<td>Cardiovascular Institute of Philadelphia</td>
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<tr>
<td>2nd Annual Cardiovascular Disease Update: Strategies for Successful Care of the Cardiovascular Patient</td>
<td>UMC Native American Cardiology Program</td>
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<td>Cardiovascular Disease Protection Through Clinical Lipidology: A Primer with Contemporary Issues</td>
<td>Orange County Symposium</td>
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<td>Research Grant: On-line Learning Tool</td>
<td>College of Health and Human Development- Pennsylvania State University</td>
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<td>Fresno Diabetes Program</td>
<td>Sante Health Foundation</td>
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<td>Future Cardiovascular Risk Assessment and Treatment Now!</td>
<td>Northwest Physicians Network</td>
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<tr>
<td>Understanding and Regulating Sterol Homeostasis</td>
<td>St. Mary’s Medical Center</td>
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<tr>
<td>How to Avoid a Heart Attack</td>
<td>American College of Cardiology: Colorado Chapter</td>
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The NLA has many talented and accomplished professionals in our ranks. To honor their commitment to medicine, research and the highest levels of patient care, the NLA has established several ways to recognize them. The NLA is now accepting nominations for the following awards to be presented at the Annual Scientific Sessions in New York City.

- **Fellow of the NLA** – Fellowship in the National Lipid Association recognizes the excellence, innovation, and leadership of health professionals in the NLA with respect to clinical lipidology in private practice or academic settings. Fellowship is reserved for NLA members who have made significant regional and/or national contributions to the science and practice of clinical lipidology.

- **Distinguished Achievement Award** – The highest honor conferred by the NLA upon a member to recognize a major contribution to clinical lipidology (research, teaching, publishing, or service), whether as a single accomplishment or through lengthy career work.

To view the full qualifications or to submit a nomination visit www.lipid.org/awards. Nominations will be accepted until February 1, 2011.
March 11–13, 2011
Hyatt Regency Lost Pines • Austin, TX
Risk Stratification and Atherosclerosis Prevention in the Complex Patient: Improving Our Strategies

Program Highlights

- Challenging Case Studies
- Interactive Panel Discussions
- Evidence-based, Clinically-relevant Presentations
- Advanced Lipid Testing Dinner Symposium
- Practical Breakout Sessions and Workshops
- Exhibit Hall and Innovation Labs
- CME and CE Credits for Physicians, Nurses, Pharmacists and Registered Dietitians

Professional Development Courses

- Lipid Management Training Courses
- Masters in Lipidology™ Course
- Clinical Anthropometric Workshop for Cardiometabolic Risk Management Programs
- Tools for Evidenced Based Practice: Intensive Workshop

Register now at
www.lipid.org/springCLU

Program Chairs
Edward A. Gill, MD
John R. Nelson, MD
James M. Falko, MD
Kittie L. Wyne, MD, PhD

Jointly hosted by the Pacific and Southwest regional chapters
**Clinical Lipid Update – Spring 2011**  
**Jointly Hosted by the Pacific and the Southwest Regional Chapters**  
**March 11–13, 2011**  
**Austin, TX**

**Registration**

**Guest name(s), if attending meeting:**  

**Membership status:**
- [ ] I am currently a member.
- [ ] My application for membership has been submitted and confirmed.
- [ ] I will apply at www.lipid.org.
- [ ] Please send me membership information.

---

**Important Information**

*Master’s Course*
To purchase the NLA-SAP’s please go to: www.lipid.org/education/nlasap.

**Registration:** Registration and payment must be received no later than March 1, 2011. After this date a syllabus and name badge cannot be guaranteed—so register TODAY!

**Cancellation:** Telephone cancellations will not be accepted. A written notice of cancellation must be received no later than March 1, 2011. This includes Guest Fees.

**Special Needs:**

**ADA Compliance:**
Attendees who need additional reasonable accommodations or who have special needs should contact the NLA at 904-998-0854.

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### Circle Fee Based on Attendee Type

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<tr>
<th>Registrant Rate</th>
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<th>Trainee Rate</th>
<th>Industry Rate</th>
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<td>$695</td>
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- **Clinical Lipid Update**
  - Spring 2011
  - March 11–13, 2011
  - Includes course syllabus and one admission badge to Exhibit Hall for all food functions.

- **Join NLA and register for Clinical Lipid Update**
  - (If selecting this option, register online)
  - $495
  - N/A
  - $75
  - N/A

### Ancillary Courses

- **Masters in Lipidology™ Course**
  - March 10–11, 2011
  - $895
  - $695
  - $595
  - $1,200

- **Lipid Management Training Course**
  - March 10–11, 2011
  - $585
  - $395
  - $195
  - $900

**Registration Fee Total**

**Guest Fees**

- **Exhibit Hall Pass-Guest(s)**
  - $80
  - X____
  - $_____

**Guest Total**

**Combined Total Sections 2,3 & 4**

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**Payment Method**

- [ ] VISA
- [ ] MC
- [ ] AMEX
- [ ] Check

Make checks payable to the NLA.

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Honors and Recognition: Certified Achievers

The NLA congratulates the following individuals who passed the American Board of Clinical Lipidology (ABCL) or Accreditation Council for Clinical Lipidology (ACCL) exams in 2010, demonstrating competence in clinical lipidology and dedication to professional excellence.

2010 Diplomates
Sherley Abraham, MD; Astoria, NY
Gaurav Agarwal, MD; Valparaiso, IN
Hardeep Ahuja, MD; Menomonee Falls, WI
Ahmad Al-Sarraf, MD; Vancouver, Canada
Khalid Al-Waili, MD; Verdun, Canada
James Arter, MD; Gastonia, NC
Jerry Back, MD; Charleston, SC
Wald Barbouer, MD; Baltimore, MD
Demir Baykal, MD; Lawrenceville, GA
Ariel Brauchar, MD; Houston, TX
Eric Bush, MD; Great Barrington, MA
Joseph Conroy, DO; Darby, PA
Marco Corallo, DO; Beloit, OH
Wilfredo Corredera, MD; Lake Placid, FL
Ariel Brautbar, MD; Houston, TX
Eric Bush, MD; Great Barrington, MA
Joseph Conroy, DO; Darby, PA
Marco Corallo, DO; Beloit, OH
Wilfredo Corredera, MD; Lake Placid, FL
Naila Goldenberg, MD; Cincinnati, OH
Tariq Hameed, MD; Iowa City, IA
Henry Huang, MD; Los Angeles, CA
Lewis Johnson, MD; Jamesville, NY
Shahram Khorshidi, MD; San Marcos, CA
Jee Lee, MD; New York, NY
Joshua Liberman, MD; Milwaukee, WI
Prahjot Nijjar, MD; Philadelphia, PA
Karl Puetze, MD; Overland Park, KS
Binh An Phan, MD; Glenview, IL
Philip Rabito, MD; New York, NY
Sudha Ravilla, MD; Omaha, NE
James Reals, MD; Plano, TX
Chanda Sajja, MD; Leonardtown, MD
Justin Saunders, MD; Ann Arbor, MI
Dhun Sethna, MD; Pulaski, VA
Michael Shapiro, DO; Portland, OR
Santosh Sinha, MD; Pasadena, CA
Mark Speakman, MBChB; Montrose, CA
Jerzy Sterkowicz, MD; New Albany, OH
Robert Thompson, MD; Seattle, WA
Elizabeth Triana, MD; Fort Charlotte, FL
Ralph Vicari, MD; Melbourne, FL
Min-Shung Wu, MD; Vitalia, CA
Philippe Yostos, MBChB; Mississauga, Canada

2010 Clinical Lipid Specialists
Vincent Akridge, AHFS; Fort Myers, FL
Cynthia Bosch, ARNP, MS; Sarasota, FL
Michelle Bozovich, PharmD, CPP; Greensboro, NC
Deborah Croy, MSN, RN, ANP BC; Princeton, WV
Ashley Davila, MSN, RN, CNS; Austin, TX
Sondra DePalma, PA-C; Hershey, PA
Christina Fouse, MS, APN-CNP; Highland Park, IL
James Harris, MSN, Derry, NH

For a complete list of Diplomates and more information, visit www.lipidboard.org (ABCL) and www.lipidspecialist.org (ACCL)
2011 Meetings
March 10–12, 2011
PCNA 17th Annual Symposium
Orlando, FL

March 14–16, 2011
XVII International Symposium on Drugs Affecting Lipid Metabolism (DALM)
Doha, Qatar
Doha Ritz-Carlton

March 22–25, 2011
AHA EPI/NPAM
Atlanta, GA
Atlanta Marriott Marquis

April 3–5, 2011
ACC 2011
New Orleans, LA

May 21–24, 2011
ASH Annual Scientific Meeting
New York, NY

June 24–28, 2011
ADA Scientific Sessions
San Diego, CA

June 26–29, 2011
79th EAS Congress
Gothenburg, Sweden

July 14–17, 2011
SCCT 2011
Denver, CO
Hyatt Regency

August 27–31, 2011
ESC Congress 2011
Roissy, France

September 30–October 5, 2011
The Obesity Society’s Annual Scientific Meeting
Orlando, FL

2011 NLA Meetings
March 11–13, 2011
Clinical Lipid Update—Spring
Hosted by SWLA and PLA
Hyatt Lost Pines
Austin, TX

May 19–22, 2011
NLA Annual Scientific Sessions
Hosted by NELA
Sheraton Hotel and Towers
New York, NY

August 26–28, 2011
Clinical Lipid Update—Summer
Hosted by MWLA and SELA
Hilton Orlando Bonnet Creek
Orlando, FL

NLA Professional Development Courses
November 16–17, 2010
Best Practices in Cardiometabolic Risk Management CME/CE Course
Sponsored by the NLA and the Primary Care Network (PCN)
www.primarycareed.com
Anaheim, CA
Hilton Anaheim

December 3–4, 2010
Best Practices in Cardiometabolic Risk Management CME/CE Course
Sponsored by the NLA and the Primary Care Network (PCN)
www.primarycareed.com
Charlotte, NC
Charlotte Convention Center

March 10–11, 2011
Lipid Management Training Course
Masters in Lipidology™ Course
Austin, TX
Hyatt Lost Pines

May 18–19, 2011
Lipid Management Training Course
Masters in Lipidology™ Course
New York, NY
Sheraton Hotel and Towers

August 25–26, 2011
Lipid Management Training Course
Masters in Lipidology™ Course
Orlando, FL
Hilton Orlando Bonnet Creek
Editor's Corner


EBM Tools for Practice


Members have access to $900 in registration discounts. Renew your membership by January 1st.

SAVE the DATE for 2011

Mark your calendars to attend the NLA Scientific Meetings next year.

**SPRING 2011**

**CLINICAL LIPID UPDATE**

March 11–13

Austin, TX

Jointly hosted by the Pacific & Southwest regional chapters

**2011**

**SCIENTIFIC SESSIONS**

May 19–22

NYC

Hosted by the Northeast regional chapter

**SUMMER 2011**

**CLINICAL LIPID UPDATE**

August 26–28

Orlando, FL

Jointly hosted by the Midwest & Southeast regional chapters

Visit www.lipid.org